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Effects of aerobic exercise-based pulmonary rehabilitation on quality of life in pediatric asthma: A systematic review and meta-analysis

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ABSTRACT

Background: Pediatric asthma poses a significant global health burden, impacting the well-being and daily lives of affected children. Aerobic exercise-based pulmonary rehabilitation emerges as a promising intervention to address the multifaceted challenges faced by pediatric asthma patients.
Objectives: The purpose of this systematic review and meta-analysis was to comprehensively evaluate the effects of aerobic exercise-based pulmonary rehabilitation on pulmonary function and quality of life in pediatric asthma patients.
Methods: Randomized controlled trials (RCTs) involving pediatric participants (5–18 years) were included. Aerobic exercise program-based pulmonary rehabilitation interventions were assessed for their impact on actual and percentage predicted values of lung volumes and flow rates such as forced vital capacity (FVC), maximum mid-expiratory flow (FEF25–75), peak expiratory flow (PEF), forced expiratory volume in one second (FEV1), FEV1/FVC, and on quality of life (QoL) measures. A systematic search of databases, hand-searching, and consultation with experts identified relevant studies. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines guided study selection, data extraction, and quality assessment.
Results: The systematic review included 20 studies with diverse exercise interventions and outcomes. The meta-analysis using fixed-effects model showed that there was a significant improvement in FVC (% predicted) [SMD= 0.30, 95 %CI: 0.13, 0.48] and FEF25–75 (% predicted) [SMD= 0.31, 95 %CI: 0.03, 0.58] in the experimental group compared with the control group. Furthermore, using a random-effects model involving 12 studies, significant increases in the QoL [SMD= 0.70, 95 %CI: 0.14, 1.26] were found in the exercise group. Due to inter-study heterogeneity, additional analyses were conducted. Publication bias analysis indicated robustness, with no significant asymmetry in funnel plots.
Conclusion: Aerobic exercise-based pulmonary rehabilitation significantly enhances pulmonary function and quality of life in pediatric asthma patients. The findings, supported by improvements in FVC and FEF25–75, demonstrate the efficacy of these interventions. Quality of life measures also showed notable improvements. Despite inter-study heterogeneity, the results are robust, suggesting that aerobic exercise should be considered a valuable non-pharmacological strategy in managing pediatric asthma.

Introduction

Pediatric asthma is a prevalent chronic respiratory condition affecting a significant proportion of children globally.[1] The condition is characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, contributing to substantial morbidity in affected individuals.[2] Asthma poses a burden on the healthcare system and has a negative impact on the daily lives of children, often leading to limitations in physical activities, school absenteeism, and compromised overall well-being.[3]

While the management of pediatric asthma traditionally focuses on symptom control through medications, there is growing recognition of

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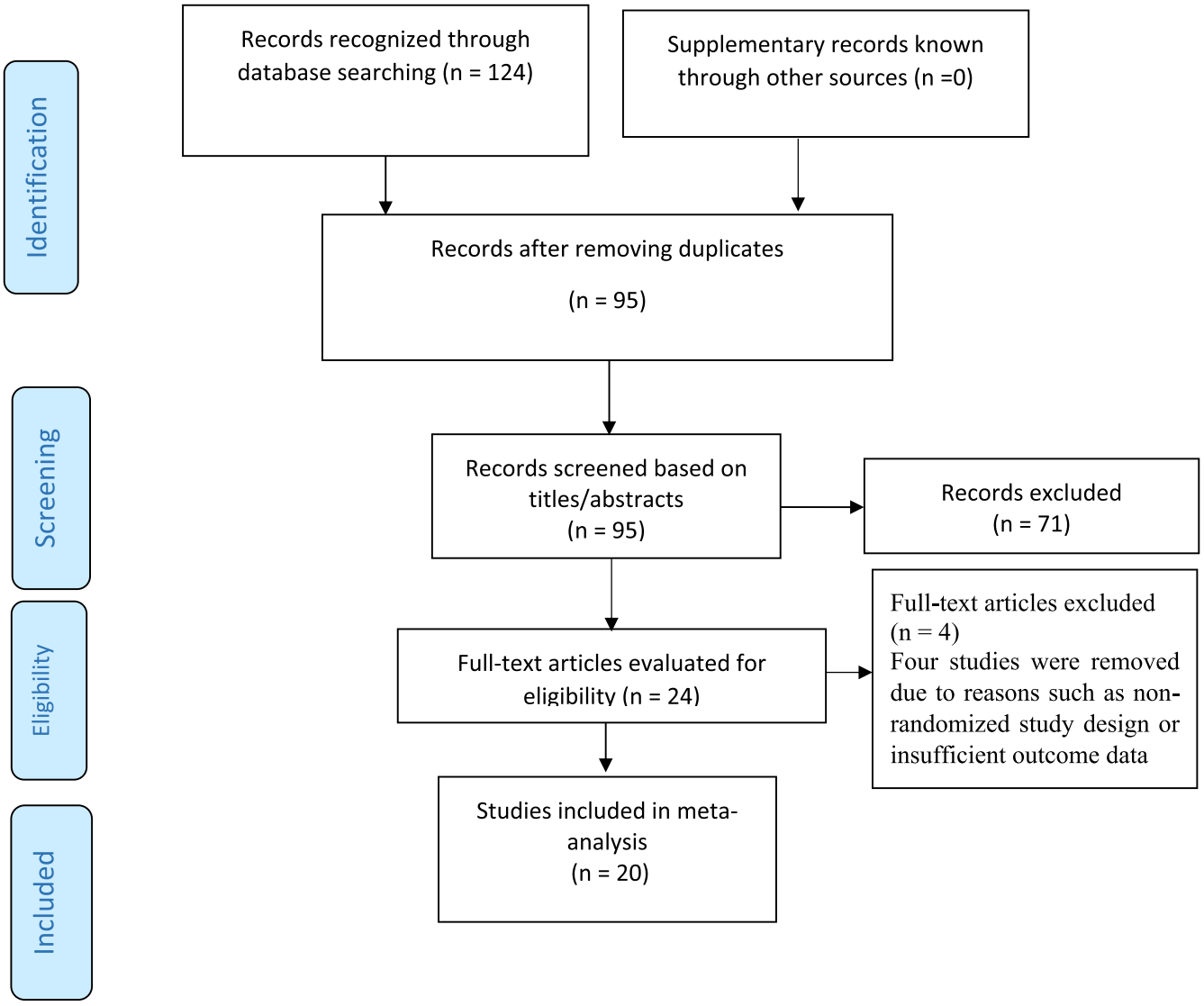

Fig. 1. PRISMA flow diagram for the investigated studies.

the need to address the broader impact of the condition on the quality of life in affected children.[4] Beyond merely controlling symptoms, interventions that enhance overall well-being and functionality are crucial. Among these interventions, aerobic exercise-based pulmonary rehabilitation emerges as a promising avenue for improving the lives of pediatric asthma patients.[5]

The existing literature on the effects of aerobic exercise-based pulmonary rehabilitation on pediatric asthma is relatively limited, creating a critical gap in our understanding of its potential benefits.[6] The purpose of this systematic review and meta-analysis is to comprehensively evaluate and synthesize the available evidence to assess the impact of aerobic exercise-based pulmonary rehabilitation on symptom improvement and quality of life in pediatric asthma patients.

Methods

Inclusion and exclusion criteria

Studies that included pediatric participants aged 5 to 18 years were considered. Only randomized controlled trials (RCTs) that implemented aerobic exercise-based pulmonary rehabilitation interventions were included. This encompasses structured exercise programs involving aerobic activities such as running, cycling, or swimming, specifically designed to improve pulmonary function in pediatric asthma patients. The primary outcome was improvement in lung volume tests, including forced vital capacity (FVC), maximum mid-expiratory flow (FEF25–75), peak expiratory flow (PEF), forced expiratory volume in one second (FEV1), FEV1/FVC, The secondary outcome was changes in quality of life, assessed through validated pediatric quality of life questionnaires.

Non-RCT study designs such as observational studies, case reports, and reviews. Interventions that did not include aerobic exercise-based pulmonary rehabilitation were excluded. Studies lacking relevant outcome measures or those not reporting quantitative data.

Search strategy

A systematic search was conducted in the following databases: PubMed, Embase, Cochrane Library, and PsycINFO. The search included articles published from inception to the present and the following keywords and their combinations used: “Pediatric asthma," "Aerobic exercise," "Pulmonary rehabilitation," "Quality of life," and "Randomized controlled trial." Additional methods involved hand-searching reference lists of relevant articles, contacting experts in the field for potential studies, and searching for ongoing or unpublished trials in clinical trial registries.

Table 1
Characteristics of included studies in the systematic review.

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
Yang et al.[7]	Chin/ 2023	[9.08±2.25, 9.45±2.56]/ [17.09±2.54, 16.00±1.91]	25/25	Endurance training (aerobic exercise) and respiratory muscle training (3–5 times/week, at least 30 min/ time)	Muscle strength training was carried out 2 times/day for 5 min/time. Children were required to quickly breathe the tricolor balls at the same time and then relax when all the tricolor balls reached the top. Then was recommenced alternate weeks of muscle endurance and muscle strength training. Muscle endurance training was carried out 2 times/day for 15 min/time. During endurance training, each child was required to blow and suck the ball for three seconds or more. For the exercise training, the child was able to select their aerobic exercise such as jogging, swimming, skipping or playing basketball with the following protocol: 3–5 times/week, at least 30 min/time, including 5–10 min in the warm-up stage, >20 min in the formal training stage, and 5–10 min in the relaxation stage.	12 weeks	The control group was given routine drug treatment and health education	FVC (%), FEV1 (%), FEV1/FVC (%), PEF (%), PedsQL	3
Elnaggar et al.[8]	Egypt/ 2021	[14.56 ± 1.36, 13.87 ± 1.13]/ [21.96 ± 1.82, 22.25 ± 1.95]	16/15	Inspiratory muscle training (20 min/time, 3 times/week) and respiratory training (30 min/time, 3 times/week)	the respiratory rehabilitation for a total of 30 min each session, three times/ week over 12 weeks including the following exercises: diaphragmatic breathing, pursed-lip breathing, breathing-hold and breathing control, manual expiratory passive therapy techniques, postural orientation techniques, relaxation techniques, and aerobic training on a treadmill or bicycle according to the preference of each child. The IMT was applied immediately after the respiratory rehabilitation session ended. We	12 weeks	The control group received placebo inspiratory muscle training with a fixed workload of 5 % of the pressure threshold.	FEV1 (%), FVC (%), FEV1/FVC (%)	4

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
					applied 40 %, and 50 % of maximal inspiratory pressure (IPmax). The IMT was performed in two phases as follow: phase I; children were trained to keep diaphragmatic breathing through the device for 15 breaths with 10-second rest intervals, and continue this paradigm for 15 min, Phase II; children were asked to breathe through the device continuously for additional 5 min to develop muscle endurance. The IMT group exercised for 20 min/session in total, three sessions per week over 12 weeks in succession.				
Wicher et al.[9]	USA/ 2010	[range of 7–18 years],[NR]	30/31	Endurance Training (3–5 times/week, at least 30 min/ time,2 times/ week, 60 min/ session)	The training participants in the study underwent a swimming program consisting of a total of 24 sessions, held twice a week, over a period of three months. They also took inhaled fluticasone (250 mcg, twice a day) daily and inhaled salbutamol when needed.	12 weeks	The control group was administered with inhaled fluticasone (250 mcg, twice daily) on a daily basis, and inhaled salbutamol was provided as needed.	FVC (L), FEV1 (L), FEV1/FVC (L), FVC (%), FEV1 (%), FEV1/ FVC (%), FEF25–75 (%)	2
Khodashenas et al.[10]	Iran/2019	[9.66 ± 3.7, 8.16 ± 2.3]/ [18.1 ± 3.2, 16.4 ± 1.6]	9/6	Endurance Training, Strength Training (3 times/week, 45 min/ session)	In the experimental group, every exercise session consisted of three parts: 5–10 min of warm-up exercises, 20-30 of the main exercises including aerobic and strength exercises, and 5–10 min of cool down exercises, each lasting 45 min and taking place three times a week. The program was followed consistently for a duration of 8 weeks.	8 weeks	Control groups received routine medications	FEV1 (%), FEV1(L), FVC (L), FEF25–75 (L/min), Quality of life in Iranian asthmatic children	2
Abdelbasset et al.[11]	Egypt/ 2018	[9.84±1.76, 10.04±1.52]/ [21.3 ± 3.02,22.13 ±4.1]	19/19	Endurance Training (3 times/week, 40 min/ session)	Each child in the aerobic exercise group engaged in a moderate-intensity aerobic exercise program for 10 weeks. The program consisted of exercise training at 50 %–70	10 weeks	The control group received only asthma medications without exercise intervention	FVC (%), FEV1(%), PAQLQ	2

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
					% of their maximum heart rate, with sessions occurring three times a week. Each exercise session lasted for 40 min and took place in the morning.				
Andrade et al.[12]	Brazil/ 2014	[11.7 ± 2.3, 11.4 ± 2.3]/ [20.9 ± 6.1, 18.7 ± 3.9]	10/17	Endurance Training (3 times/week, 40–50 min/ session)	The intervention consisted of supervised aerobic training performed three times a week for six weeks on an electric treadmill. The exercise consisted of a 5-min stretching period focused on the major muscle groups of the lower limbs, followed by 10-min of warm-up, 20-min of training in the first and second weeks and 30-min in the third to sixth weeks, followed by a 5-min cooling down period. If necessary, the participants were instructed to use b2 agonists prior to or during the exercise session.	6 weeks	Control group were directed to maintain their regular physical activity routines.	FVC (L), PEF (L/s), FEV1/FVC (L), PAQLQ	2
Counil et al.[13]	France /2003	[14 ± 0.6, 13.9 ± 0.8]/[48.9 ± 3.2, 46.8 ± 3.7]	7/7	Endurance Training (3 times/week, 45 min/ session)	The training group engaged in workouts at a level of intensity that matched their heart rate at the ventilatory threshold. They also incorporated 1-minute sprints at maximum aerobic power (MAP) every 4 min during their sessions. Each session lasted 45 min, with a frequency of 3 sessions per week.	6 weeks	Control group	FEV1 %, FEF25–75 %	2
Bingöl Karakoç et al.[14]	Turkey/ 2000	[10.8 ± 2.3, 10.2 ± 2.4]/ [NR]	16/12	Endurance Training, Respiratory Training (for 30 days)	Pulmonary rehabilitation program consisted of relaxation exercises, endurance exercises, breathing exercises and rhythmic mobilisation exercises. Patients and their parents had visited Physical Medicine and Rehabilitation Department at the first visit and they were thought to perform this program at home for 30 days.	4 weeks	Control group	FVC (%), FEV1 (%), PEF (%), FEF25–75 (%), Quality of life index	3
Basaran et al.[15]	Turkey/ 2006	[10.35 ± 2.2, 10.45 ± 2.1]/	30/28	Endurance Training (3	The exercise group underwent a	8 weeks	Control group was recommended to	FEV1 (%), FVC (%),	2

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
		[19.0 ± 3.8, 17.7 ± 3.2]		times/week, 60 min/ session, hospital)	submaximal aerobic training designed as a moderately intensive basketball training program including both lower and upper extremity activities. During the 8-week training program the sessions were performed 3 times a week for one hour in each session. A typical session in the gymnasium started with warm-up and callisthenics (15 min) followed by submaximal basketball training (30- 35 min), cool-down and flexibility exercises (10 min).		follow a respiratory exercise routine at home.	FEV1/FVC (%), PEF (%), PAQLQ	
Veldhoven et al.[16]	Netherlands /2001	[10.5 ± 1.2, 10.7 ± 1.2]/ [18.84 ± 1.09, 18.31 ± 1.28]	23/24	Endurance Training (3 times/week, twice a week for one hour, gymnasium, home)	The physical exercise programme was developed with the lessons in the gymnasium started with 10 min warming-up, followed by 20 min of fitness training (a) and 15–20 min of different physical activities (b). Before or after the exercise, explanation and information was given to the children about asthma and exercise to improve coping behaviour with asthma.	12 weeks	Conventional treatment or the control group did not receive any extra care (or treatment)	FEV1 (L), FEV1 (%), FVC (L), FEV1/FVC (L), PEF (L/ s)	2
Asher et al.	New Zealand /1990	[2.7 ± 1.7, 2.1 ± 2.9]/[17.80 ±1.05, 16.92+1.3]	19/19	Chest physical therapy (Each treatment period lasted about 1 hour)	Before every treatment patients received inhaled salbutamol (2.5 mg) via a nebulizer over 10 min, followed by a rest period of 20 min. This was followed by chest physical therapy lasting 20 to 30 min. Techniques were used to help achieve relaxation, clearance of secretions, thoracic mobility exercises, and postural correction exercises.	2 days	Control group with receiving inhaled salbutamol (2.5 mg)"	FVC (%), FEV1 (%), FEF25–75 (%)	1
Moreira et al.[17]	Portugal/ 2008	[12.9 ± 3.4, 12.5 ± 3.5]/ [20.25 ± 9.3, 20.25 ± 9]	17/17	Submaximal aerobic exercise (2 times/week, 50 min/ session, gymnasium)	The exercise group undertook submaximal aerobic exercise designed as a moderately intensive training programme including both lower and upper extremity activities. During the 12-week training	12 weeks	The control group subjects continued their usual daily routine.	FEV1 (%), FEF25–75 (%), Highest PEF (%), PAQLQ	3

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
					programme, the sessions were held twice a week, for 50 min per session. A typical session started with a warm-up period (10 min). This was followed by submaximal training (30–35 min), including aerobic exercises, strength training, and some balance and coordination exercises, and a cool-down period (7–10 min) with use of b2-agonists before the training or during the session				
Sanz-Santiago et al.[18]	Spain/ 2020	[12.1 ± 2.1, 11.1 ± 2.9]/ [0.95 ± 1.08, 0.42 ± 1.4]	25/28	Endurance Training, Resistance Training (3 times/week, 60 min/ session)	The exercise program was performed for 12 weeks, with a frequency of 3 days/ week. The type of exercise used was combined (resistance and aerobic) and the duration of each session was 60 min. The training started with a 10-min warm-up period (cycle ergometer), followed by the 20- to 40-min aerobic cycle ergometer training. Afterward, three circuits of the following 11 resistance exercises were performed: bench press, shoulder press, leg extension, leg press, leg curl, abdominal crunch, low back extension, arm curl, elbow extension, seated row, and lateral pulldown. For each exercise, the participants performed one set of 12 to 15 repetitions (total of approx. 20-s duration) with no rest period between exercises.	12 weeks	The control group followed routine clinical orientations	FEV1(L), FVC (L), FEV1/FVC, FEF25–75 (L/min), PAQLQ	2
Onur et al.[19]	Turkey/ 2011	[9.8 ± 1.8, 10.3 ± 2.0]/ [NR]	15/15	Endurance Training (2 times/week, 60 min/ session)	Training group received the pharmacological treatment and was assigned to exercise twice a week for an hour on a bicycle for eight weeks. During the eight week exercise programme, 15 min of warm-up exercise	8 weeks	Control group received only the pharmacological treatment (fluticazone 250 g/ day)	FVC (%) and FEV 1 (%)	2

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
					was followed by 45 min of cycling at the target heart rate.				
Yadav P et al.[20]	India/ 2021	[11.74 ± 1.56, 12.11 ± 1.74]/ [18.46 ± 2.68, 18.6 ± 3.13]	70/70	Endurance Training (45 min daily)	The participants engaged in yogic activities consistently for 45 min every day. At the beginning, they practiced under the guidance of a yoga expert for one week. Following that, they continued with one session under the expert's supervision and six days at home with their parents overseeing their practice, in addition to pharmacological treatment	12 weeks	Controls received only pharmacological treatment.	FVC (%), FEV1 (%), FEV1/FVC, PEF(%), PAQLQ	2
Wang J S et al.[21]	Taiwan/ 2009	[10 (95 %CI: 9–11), 10 (9–11)]/ [20.6 (18.4–22.5), 19.5 (17.8–21.6)]	15/15	Endurance Training, respiratory training (3 times/week 50minutes/ time)	The experimental group received 6-weeks swimming training under supervision (three sessions per week, each session being of 50 min duration) with regular treatment for asthma.	6 weeks	the control group received no specific intervention with regular treatment for asthma	FVC (%), FEV1 (%), FEV1/FVC (%), and FEF25–75 (%)	1
Weisgerber M C et al.[22]	USA/ 2003	[8.4 ± 1.5, 7.3 ± 0.6]/[20.11 ± 1.2, 16.98 ± 4.6]	5/3	Endurance Training (2 times/week 45 min/time)	Training group attended swimming classes twice a week for 45 min. During these sessions, participants focused on mastering vital safety skills, perfecting the front crawl technique, learning how to float and properly use a lifejacket, improving their endurance swimming abilities, mastering rotary breathing, practicing the elementary backstroke, honing their bobbing skills.	5–6 weeks	Control group	FEV1(L), FEV1 (%), FVC (%), FVC (L), PEF (%), PEF (L/s), FEF25–75 (%), FEF25–75 (L/min)	1
Bignall W J et al.[23]	USA, 2015	[15.53 ± 1.50, 15.29 ± 1.04], [NR]	14/16, School	Inspiratory Muscle Training (20minutes/ time)	intervention group received 20-min breathing retraining plus standard asthma education	4 weeks	Control group received 20 min of standard asthma education	FEV1 (L), Asthma QOL	2
Latorre-Román P Á et al.[24]	Spain/ 2014	[11.55 ± 1.01, 11.51 ± 1.42]/ [19.69 ± 3.20, 21.39 ± 4.78]	58/47, Indoor	Interval Training (3times/week 60minutes/ time)	The experimental group consisted of three 60-min weekly sessions of indoor physical exercise designed to enable alternating low intensity, such as walking, self-loading exercise, flexibility, coordination or relaxation, and high intensity, like	12 weeks	Control group	FEV1(L), PEF(L/s), PAQLQ	2

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Table 1 (*continued*)

Authors	Country/ Year	Age/BMI [intervention, control]	Participants (Intervention/ Control)	Intervention	Exercise protocol	Treatment Duration	Control Group	Outcome Measures	JADAD Score
					running, load exercises with a companion or team sports, for a period of 12 weeks.				
Zhang Y F et al.[25]	China/ 2019	[6.9 ± 2.3, 7.1 ± 2.7]/[NR]	36/36, Hospital	Endurance Training (3times/week 40minutes/ time)	Participants in the experimental group underwent a program that combined exercise training with the administration of montelukast. This program consisted of a 40-minute aerobic circuit training session. Each individual received their exercise training three times every week over a period of six weeks.	6 weeks	participants in the control group received montelukast alone	FEV1 (%), FEV1 /FVC (%, PADQLQ	3

Abbreviation: Forced vital capacity, FVC; forced expiratory volume in one second, FEV1; maximum mid expiratory flow, FEF25–75; peak expiratory flow, PEF; quality of life, QoL.

Study selection

The study selection process involved two independent reviewers screening titles and abstracts for initial eligibility. Full-text articles of potentially eligible studies were retrieved and assessed for inclusion based on the predefined criteria. Discrepancies are resolved through consensus, involving a third reviewer if necessary. A flowchart illustrating the study selection process is provided according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Data extraction

Data extraction was conducted independently by two reviewers using a standardized form. Extracted information included participant characteristics (age), intervention details (type, duration, frequency), and relevant outcome measures (quality of life scores, pulmonary function test results). Data was cross-verified, and discrepancies were resolved through discussion. Differences of opinion were addressed through a structured resolution process. Initially, the two primary reviewers discussed the discrepancies to understand each other's perspectives and attempted to reach a consensus. If they were unable to agree, a third reviewer, who was also knowledgeable about the subject matter, was consulted. The third reviewer evaluated the points of contention and provided an unbiased decision based on the evidence. This multi-step approach ensured that the data extraction process was thorough and accurate, minimizing potential biases and errors.

Quality assessment

The quality of included studies was assessed using the Jadad scale for RCTs, considering randomization, blinding, and withdrawals/dropouts. The Jadad scale, also known as the Jadad scoring system, is a tool used to assess the methodological quality of clinical trials, particularly randomized controlled trials (RCTs). It focuses on three main criteria: randomization (Was the study described as randomized?), blinding (Was there blinding of study subjects and investigators?), and withdrawals and dropouts (Were withdrawals and dropouts described?). Each item can be scored as follows: a score of 1 point is given for a positive response to the criteria, while a score of 0 is assigned for a negative response. Additionally, for the dropout criterion, if the study adequately accounts for withdrawals, it can receive an extra point, leading to a maximum possible score of 2 points for this criterion.

The total score of the Jadad scale ranges from 0 to 5, indicating the

Keypoints

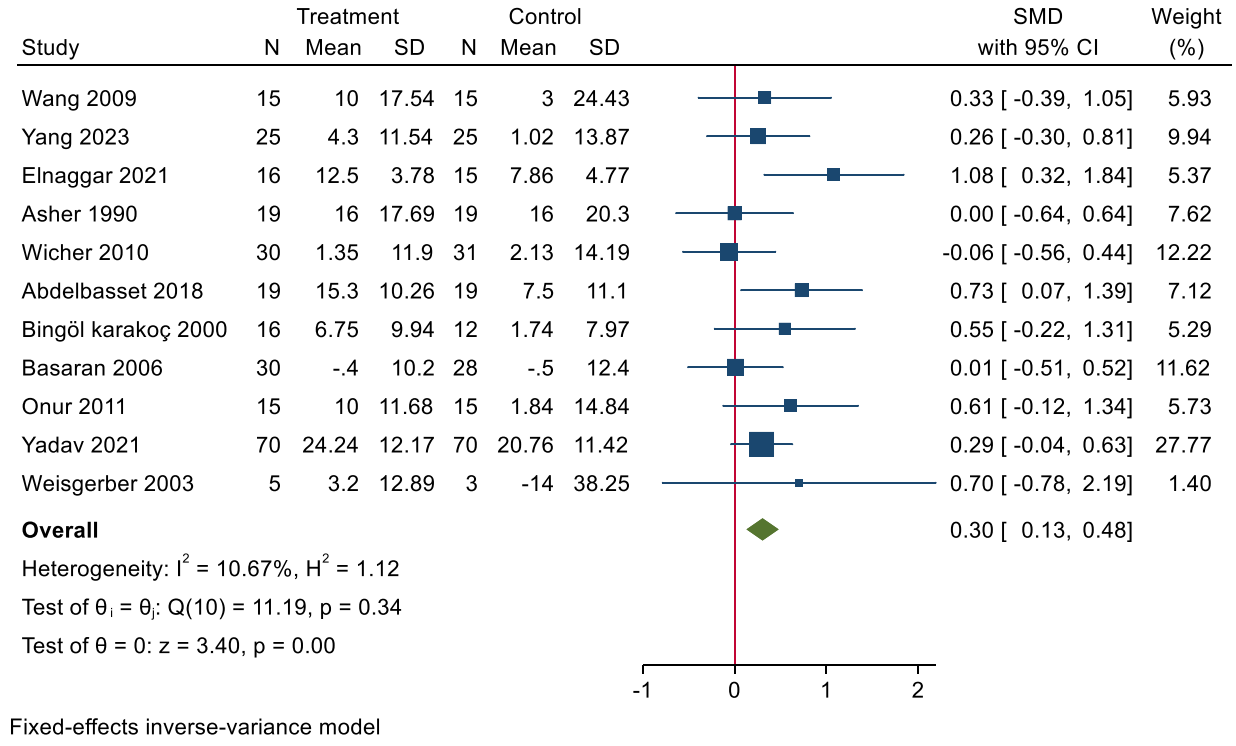
· **Significant Improvement in Lung Function and Quality of Life:** Aerobic exercise-based pulmonary rehabilitation significantly enhances forced vital capacity (FVC) and maximum mid expiratory flow (FEF25–75) in pediatric asthma patients, alongside notable improvements in quality of life scores.

· **Diverse and Robust Study Data:** The systematic review and meta-analysis included 20 randomized controlled trials with diverse exercise interventions, showing consistent positive effects despite some inter-study heterogeneity.

· **Physiological and Well-being Benefits:** The findings highlight both physiological benefits, such as enhanced lung capacity and airflow, and improved overall well-being, addressing the broader impacts of asthma on daily activities and quality of life.

· **Recommendation for Non-Pharmacological Strategy:** Aerobic exercise-based pulmonary rehabilitation is recommended as a valuable non-pharmacological strategy for managing pediatric asthma, with future research needed to confirm long-term benefits and optimize intervention protocols.

a)



b)

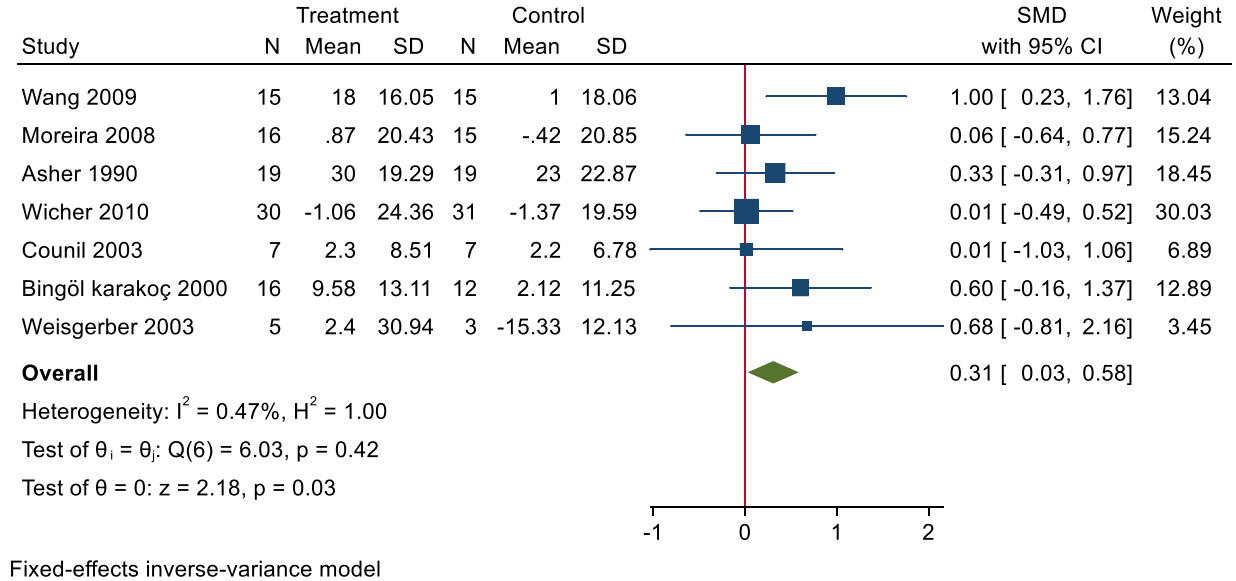
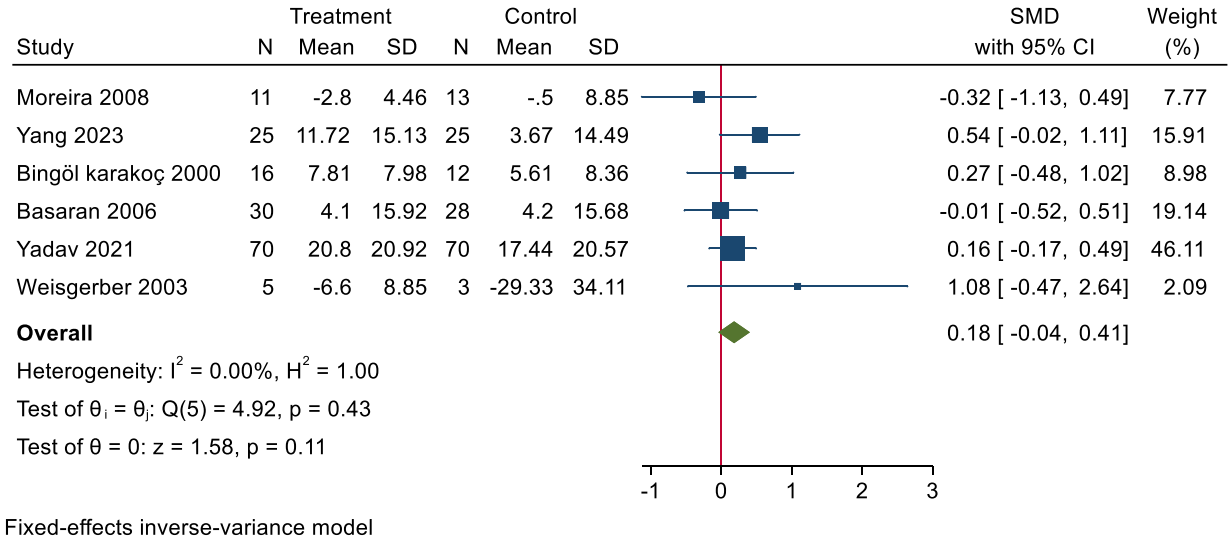


Fig. 2. A-K. The lung value tests and quality of life standardized mean differences estimates for a) FVC (% predicted), b) FEF25–75 (% predicted), c) PEF (% predicted), d) FEV1 (% predicted), e) FEV1/FVC (% predicted), f) PEF (L/s), g) FEF25–75 (L/min), h) FVC (L), i) FEV1 (L), j) FEV1/FVC, and k) QoL between intervention group (receiving exercise program supplementation) and control group.

c)



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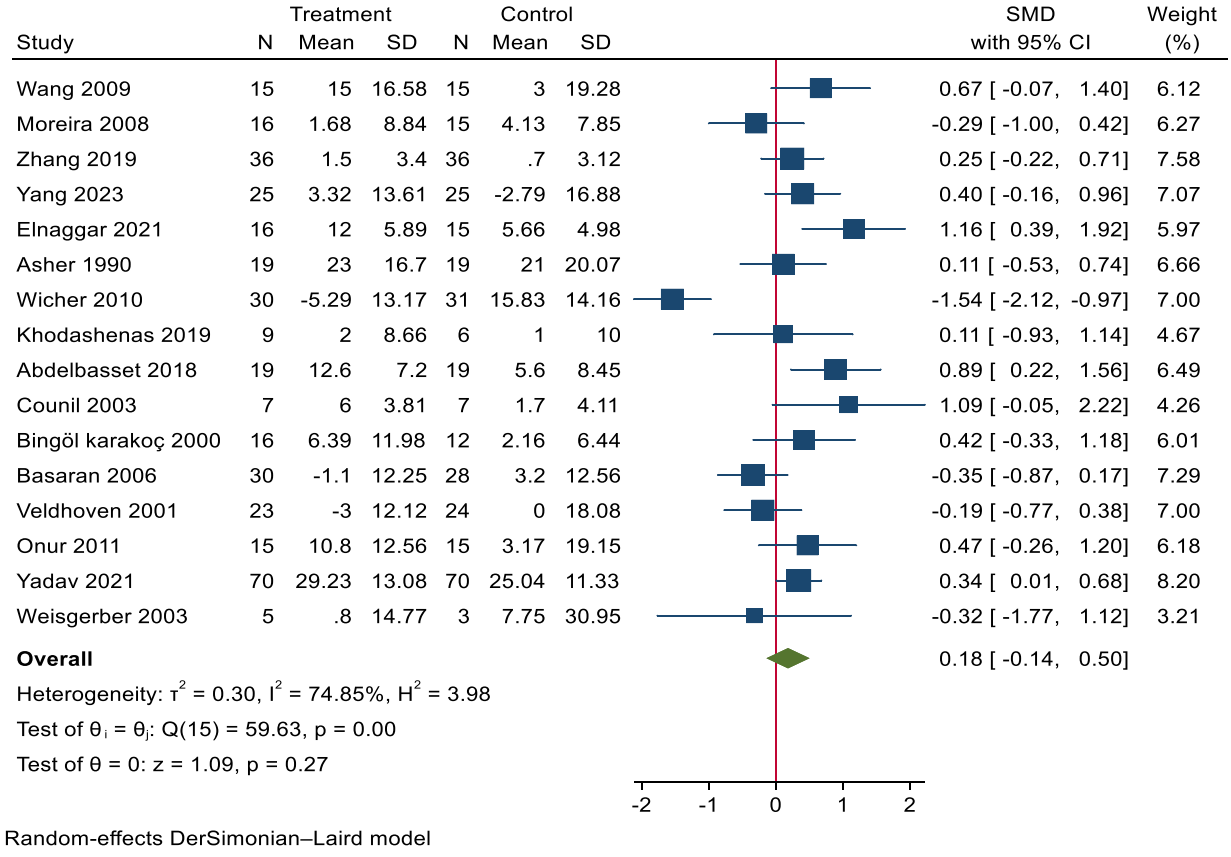
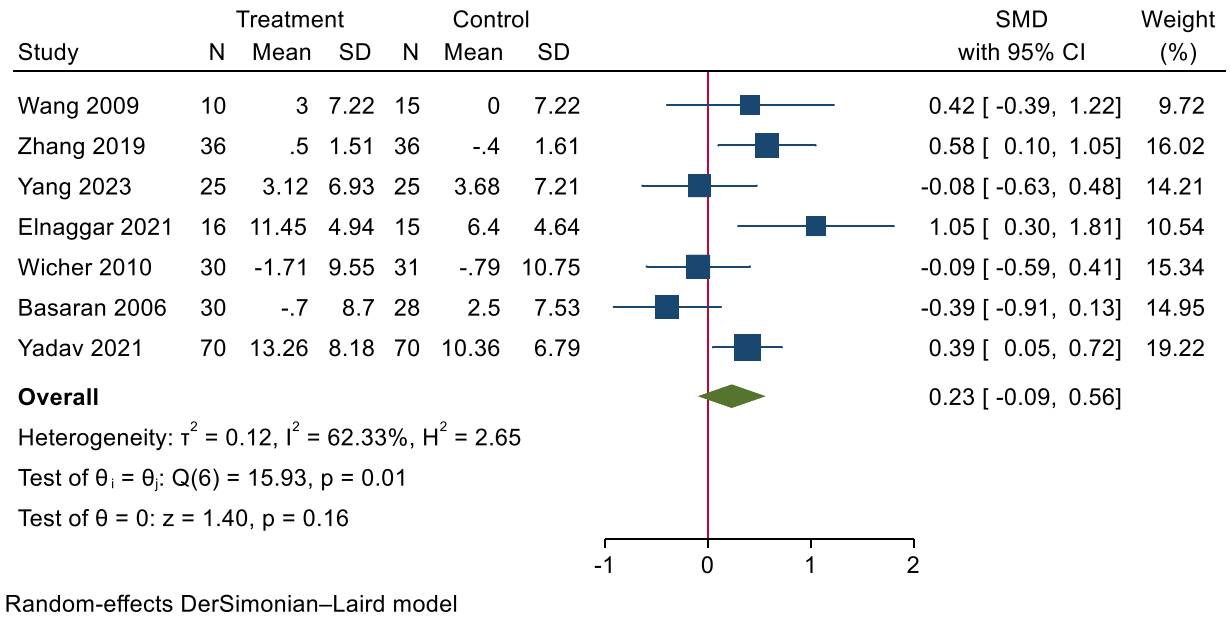


Fig. 2. (*continued*).

quality of the trial: 0–2 signifies low quality, 3–4 denotes moderate quality, and 5 reflects high quality. The Jadad scale is beneficial for researchers and clinicians as it allows for a quick assessment of the reliability of evidence from clinical trials, aiding in informed decision-making regarding treatment options. Because of its simplicity and effectiveness, it is widely used in systematic reviews and meta-analyses to evaluate the quality of included studies.

e)



f)

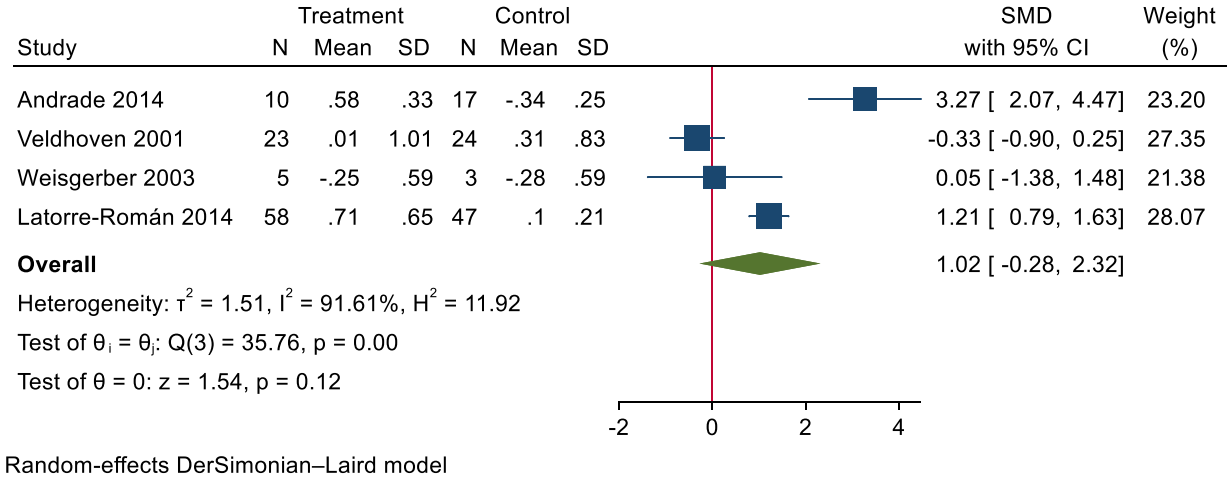


Fig. 2. (*continued*).

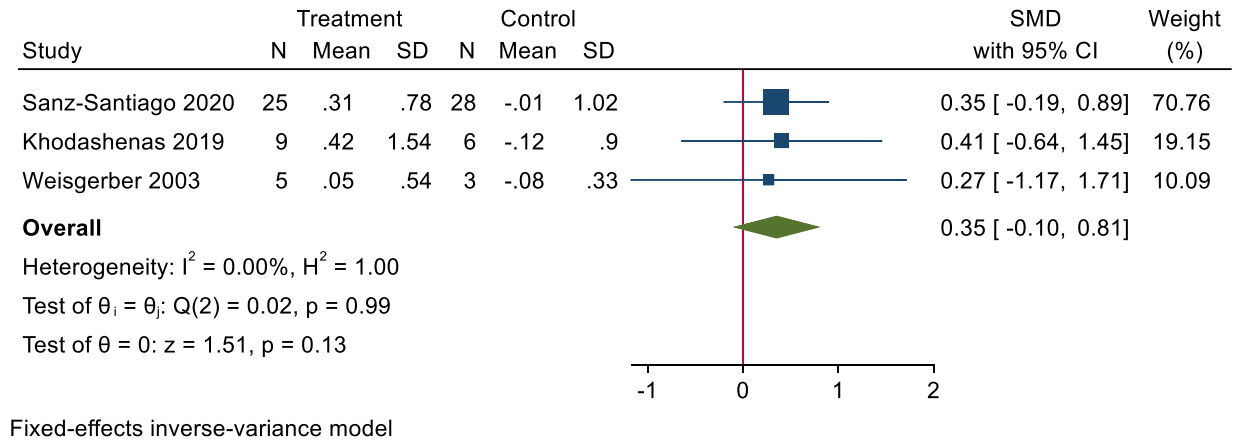
Statistical analysis

STATA version 14.0 (Stata Corp., College Station, TX) was used for the quantitative meta-analyses the value of Cochran's Q and I^2 tests were calculated to evaluate the heterogeneity degree. $I^2 > 50$ % with a P-value <0.1 shows existing heterogeneity among included trials. The standardized mean differences (SMDs) with 95 % Confidence intervals (CIs) were estimated as summary effect size. According to the existing heterogeneity across studies, we utilized a random-effects model when pooling standardized mean differences (SMDs) of the reported data. In cases where heterogeneity was not present, we applied a fixed-effects model. The effects of each trial on the overall pooled SMDs were examined using sensitivity analyses with the leave-one-out method. Subgroup analyses were conducted to estimate the effects of exercise intervention on our outcomes according to potential moderator variables. Egger's regression and funnel plot were applied to identify evidence of Potential publication biases statistically and visually among included studies in the current meta-analysis.

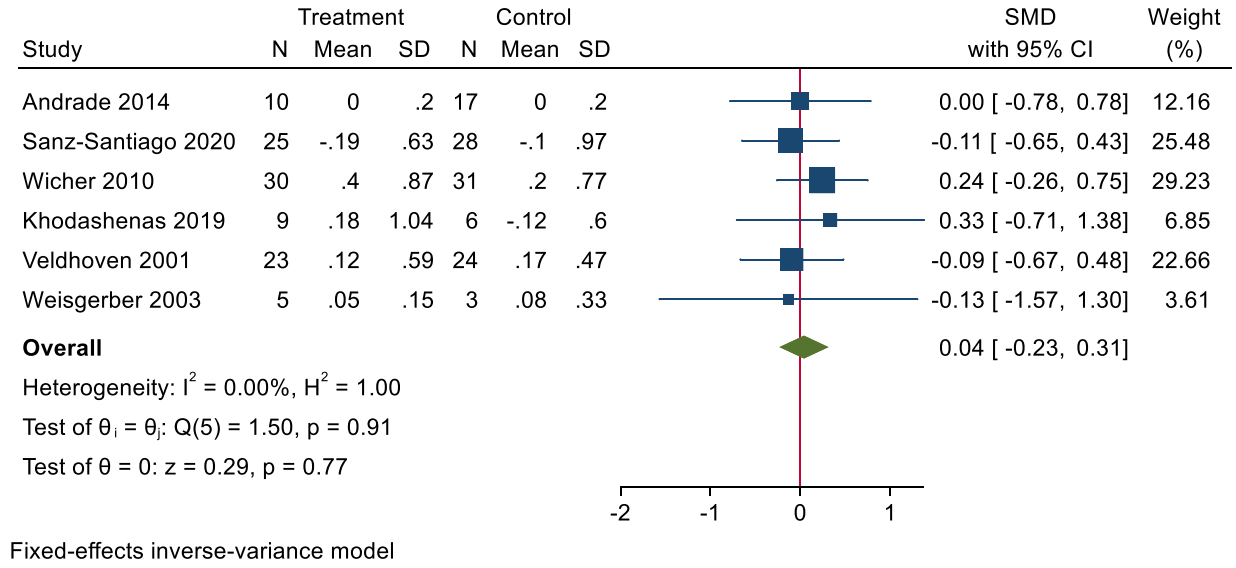
Results

In our comprehensive database search, we initially identified 124 records related to aerobic exercise-based pulmonary rehabilitation for children with asthma. Following a meticulous screening process, we removed 29 duplicate records, leaving us with 95 unique articles. Subsequently, the titles and abstracts of these articles were thoroughly

g)



h)



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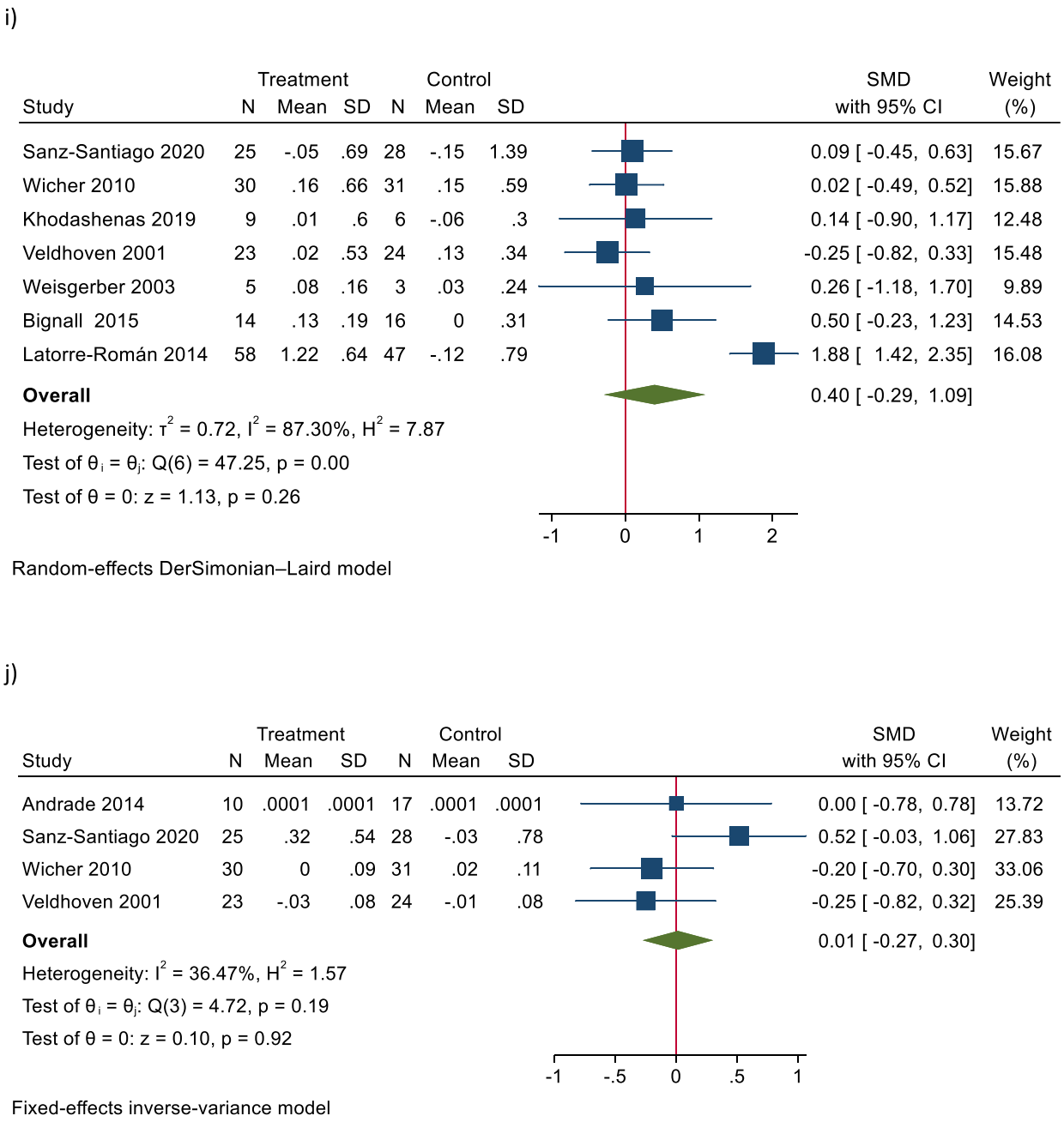
examined, resulting in the exclusion of 72 studies that did not meet our predefined inclusion criteria. After this initial screening, 23 articles were selected for full-text assessment. During the full-text screening phase, three studies were deemed ineligible due to reasons such as non-randomized study design or insufficient outcome data. Ultimately, we included 20 studies in our systematic review and meta-analysis, as illustrated in Fig. 1.

The systematic review included 20 studies that evaluated the effects of various exercise interventions on pulmonary function, asthma control, and quality of life in children with asthma. Table 1 provides an overview of the characteristics of these studies, including author names, publication year, country, participant details, intervention and control groups, treatment duration, outcome measures, and Jadad scores.

Meta-analysis findings on pulmonary lung functions tests

The effects of an exercise program on actual and percentage predicted values of lung volumes and flow rate tests, as well as quality of life in pediatric patients with asthma, are depicted in Fig. 2A-J. The meta-analysis conducted using a fixed-effects model indicated a significant improvement in FVC (% predicted) [SMD= 0.30, 95 % CI: 0.13, 0.48, $P < 0.01$; $I^2 = 10.67$ %; with 11 studies] and FEF25–75 (% predicted) [SMD= 0.31, 95 % CI: 0.03, 0.58, $P < 0.01$; $I^2 = 0.47$ %; with seven studies] in the experimental group compared to the control group.

Exercise training did not improve pulmonary function tests including PEF (% predicted) [incorporating 6 studies using a fixed-effects model, SMD= 0.18, 95 %CI: −0.04, 0.41, $P = 0.11$; $I^2 = 0.0$ %;], FEV1 (% predicted) [involving 16 studies using a random-effects model, SMD= 0.18, 95 %CI: −0.14, 0.50, $P = 0.27$; $I^2 = 0.30$ %], FEV1/FVC (% predicted) [utilizing 7 studies using a random-effects model, SMD= 0.23, 95 %CI: −0.09, 0.56, $P = 0.16$; $I^2 = 62.33$ %], PEF (L/s) [with 4 studies using a random-effects model, SMD= 1.02, 95 %CI: −0.28, 2.32, $P = 0.12$; $I^2 = 91.61$ %], FEF25–75 (L/min) [utilized 3 studies using a fixed-effects model, SMD= 0.35, 95 %CI: −0.10, 0.81, $P = 0.13$; $I^2 = 0.0$ %; with 3 studies], FVC (L) [incorporating 6 studies using a fixed-effects model, SMD= 0.04, 95 %CI: −0.23, 0.31, $P = 0.77$; $I^2 = 0.0$ %], FEV1



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(L) [involving 7 studies using a random-effects model, SMD= 0. 40, 95 % CI: −0.29, 1.09, $P = 0.26$; $I^2 = 87.30$ %], FEV1/FVC [incorporating 4 studies using a fixed-effects model, SMD= 0.01, 95 %CI: −0.27, 0.30, $P = 0.92$; $I^2 = 36.47$ %] when compared with the control groups.

Due to significant heterogeneity in FEV1 (% predicted), FEV1/FVC (% predicted), PEF (L/s), and FEV1 (L), we conducted additional analyses such as subgroup and sensitivity analyses. Subgroup analyses were based on the duration of the intervention (> eight weeks vs. ≤ 8 weeks) and the type of control group (control group vs. control group plus additional action). As shown in Table 2, exercise training had a significant impact on FEV1 (% predicted) when subgroup analysis was performed by type of control group (conventional treatment) [SMD= 0.30, 95 %CI: 0.01, 0.59, I^2= 35.25 %]. FEV1/FVC (% predicted) also showed changes in the conventional treatment subgroup [SMD= 0.39, 95 %CI: 0.08, 0.70, I^2=0.0 %].

The sensitivity analysis was conducted to determine the effects of each trial on the combined standard mean differences (SMDs). The findings remained consistent with the overall pooled SMD for FEV1 (L) (Fig. 3A). However, we observed significant changes in the pooled SMDs for FEV1 (%) after excluding the Wicher et al. study (SMD= 0.29, 95 % CI: 0.07, 0.51); for FEV1/FVC (%) after excluding the Basaran et al. study (SMD= 0.33, 95 %CI: 0.03, 0.63); and for PEF (L) after removing the Veldhoven et al. study (SMD= 1.52, 95 %CI: 0.03, 3.01) (Fig. 3B-D).

Meta-analysis findings on quality of life

There was a significant increase in the PAQLQ score in the exercise groups using a random-effects model (SMD= 0.70, 95 %CI: 0.14, 1.26, $P < 0.01$, with 12 studies) (Fig. 2K). Due to inter-study heterogeneity ($I^2 = 90.30$ %, $P < 0.01$), additional analyses were conducted. Subgroup analyses indicated that the pooled SMDs for quality of life scores in trials with a duration of more than eight weeks (SMD= 0.66, 95 %CI: 0.01,

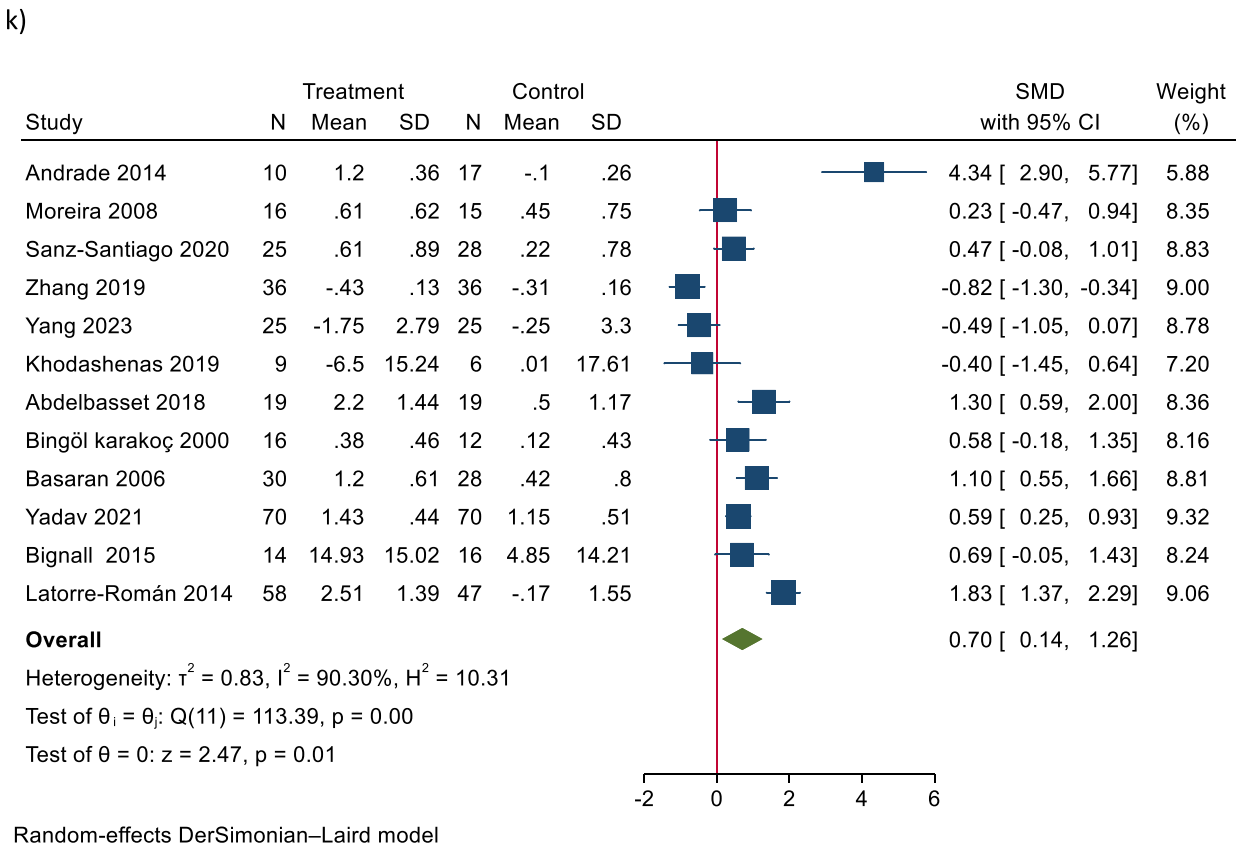

Fig. 2. (*continued*).

1.30) and trials with conventional control groups (SMD= 1.0, 95 %CI: 0.38, 1.62) remained statistically significant (Table 2). Sensitivity analysis showed no significant change between pre-and post-sensitivity SMDs for quality of life, except after removing the study by Andrade et al. (SMD= 0.47, 95 %CI: −0.03, 0.98) (Fig. 3E).

Publication bias

Evidence of publication bias was evaluated using Egger's regression test and asymmetry in the funnel plot. Egger's showed no statistically significant evidence of publication bias for meta-analyses assessing the effect of exercise program on FVC (% predicted) ($P = 0.17$), FEF25–75 (% predicted) ($P = 0.38$), PEF (% predicted) ($P = 0.60$), FEV1 (% predicted) ($P = 0.53$), FEV1/FVC (% predicted) ($P = 0.53$), PEF (L/s) ($P = 0.71$), FEF25–75 (L/min) ($P = 0.97$), FVC (L) ($P = 0.99$), FEV1 (L) ($P = 0.69$), FEV1/FVC ($P = 0.94$), and k) QoL ($P = 0.07$). The funnel plot of quality of life is shown in Suppl. Fig. 1A-K.

Discussion

The results demonstrate significant improvements in FVC (% predicted), FEF25–75 (% predicted), and quality of life measures in the exercise intervention group compared to control groups. These findings underscore the potential benefits of incorporating aerobic exercise into the management plan for children with asthma.

The observed improvements in FVC and FEF25–75 are noteworthy as they reflect enhancements in lung capacity and airflow, respectively. These changes suggest that regular aerobic exercise may lead to physiological adaptations that improve pulmonary function in pediatric asthma patients. The significant increase in quality of life scores further highlights the positive impact of exercise on the overall well-being of these children. Quality of life improvements are critical, as asthma often limits physical activities, leading to decreased participation in daily activities and social interactions.

Our findings align with previous studies that have reported the benefits of exercise in asthma management. However, the current meta-analysis adds to the existing literature by providing a comprehensive and quantitative synthesis of the effects of aerobic exercise on both pulmonary function and quality of life in pediatric asthma patients. This dual focus on physiological and quality-of-life outcomes offers a comprehensive perspective on the benefits of exercise-based interventions.

Despite the positive findings, there are several limitations in the data collection. The significant heterogeneity in some of the pulmonary function outcomes suggests variability in study designs, intervention protocols, and participant characteristics. To address this, we conducted subgroup and sensitivity analyses, which helped to identify potential sources of heterogeneity. For instance, subgroup analyses based on intervention duration and type of control group revealed that longer interventions and those with conventional control groups showed more pronounced benefits.

The sensitivity analyses also highlighted the effectof individual studies on the overall findings. For example, the exclusion of certain studies led to changes in the pooled SMDs for FEV1 (% predicted), FEV1/FVC (% predicted), and PEF (L).

Additionally, while the publication bias analysis indicated robustness in most outcomes, the potential for bias cannot be entirely ruled out. The funnel plot for quality of life, for instance, suggested some asymmetry, although Egger's test did not show statistically significant evidence of publication bias.

Another limitation is the variation in the measurement units of pulmonary function outcomes. Different units (e.g., liters versus percentage predicted) could influence the results. Future studies should standardize outcome measures to facilitate more accurate comparisons

Table 2
Subgroup analysis for effects of exercise program on lung value tests.

Subgroup variables		No. of studies	SMD (95 %CI)	I^2(%), P-value for heterogeneity
FEV1 (% predicted)	**Duration of study (weeks)**			
	≤ 8 weeks	9	0.22 (−0.4, 0.48)	17.22 %, $P = 0.29$
	> 8 weeks	7	0.10 (−0.52, 0.71)	87.89 %, <0.01
	Type of controls			
	Conventional Treatment	9	0.30 (0.01, 0.59)	35.25 %, $P = 0.14$
	Control group plus extra treatment	7	0.05 (−0.54, 0.65)	86.05 %, $P < 0.01$
FEV1/FVC (% predicted)	**Duration of study (weeks)**			
	≤ 8 weeks	3	0.19 (−0.47, 0.85)	74.0 %, $P = 0.02$
	> 8 weeks	4	0.27 (−0.15, 0.69)	62.91 %, $P = 0.04$
	Type of controls			
	Conventional Treatment	2	0.39 (0.08, 0.70)	0.0 %, $P = 0.95$
	Control group plus extra treatment	5	0.18 (−0.28, 0.64)	72.11 %, $P < 0.01$
PEF (L/s)	**Duration of study (weeks)**			
	≤ 8 weeks	2	1.68 (−1.47, 4.84)	91.25 %, $P < 0.01$
	> 8 weeks	2	0.46 (−1.05, 1.96)	94.41 %, $P < 0.01$
	Type of controls			
	Conventional Treatment	4	1.02 (−0.28, 2.32)	91.61 %, $P < 0.01$
	Control group plus extra treatment	–	–	–
FEV1 (L)	**Duration of study (weeks)**			
	≤ 8 weeks	3	0.36 (−0.19, 0.91)	0.0 %, $P = 0.85$
	> 8 weeks	4	0.44 (−0.57, 1.46)	93.55 %, $P < 0.01$
	Type of controls			
	Conventional Treatment	5	0.45 (−0.54, 1.44)	90.49 %, $P < 0.01$
	Control group plus extra treatment	2	0.18 (−0.27, 0.63)	12.09 %, $P = 0.28$
QOL	**Duration of study (weeks)**			
	≤ 8 weeks	6	0.81 (−0.25, 1.87)	92.02 %, $P < 0.01$
	> 8 weeks	6	0.66 (0.01, 1.30)	89.15 %, $P < 0.01$
	Type of controls			
	Conventional Treatment	8	1.0 (0.38, 1.62)	87.23 %, $P < 0.01$
	Control group plus extra treatment	4	0.11 (−0.84, 1.05)	90.82 %, <0.01

and meta-analyses.

The dual focus on physiological and quality-of-life outcomes invites further studies to explore not only how exercise affects lung function but also how it impacts overall well-being. Future research can expand on this by investigating different types of exercise and their specific effects on various outcomes. Additionally, the findings related to the effectiveness of longer interventions and varied control groups suggest that future studies should standardize these factors to better understand what works best in exercise interventions for asthma management. However, the variability across studies indicates a need for more homogenous research designs. Future studies should aim for standardized protocols in both interventions and participant selection to enhance the comparability of results. Furthermore, sensitivity analyses revealed that certain studies significantly influence overall outcomes, highlighting the need for comprehensive reporting and transparency regarding study design, participant characteristics, and context to ensure that results are robust and reliable. Lastly, the potential for publication bias underscores the importance of including unpublished data or studies with negative results in future meta-analyses to provide a more balanced understanding of exercise interventions.

Conclusion

In conclusion, aerobic exercise-based pulmonary rehabilitation significantly enhances pulmonary function and quality of life in pediatric asthma patients. These findings not only underline the effectiveness of structured aerobic exercise programs as a valuable non-pharmacological strategy in managing pediatric asthma but also offer crucial implications for future research.

To build upon the strengths of this meta-analysis, future research should focus on several critical areas. First, the dual emphasis on physiological and quality-of-life outcomes encourages the exploration of various exercise modalities and their specific impacts on different aspects of health in pediatric asthma patients. Investigating diverse forms of aerobic exercise—such as high-intensity interval training, continuous moderate exercise, or even incorporating play-based activities—could provide a broader understanding of what types of interventions work best.

Additionally, the analysis highlights the need for standardized research protocols. Variability across studies in intervention length, design, and participant characteristics indicates that establishing common protocols is essential for enhancing the comparability of results. Future studies should prioritize homogeneous designs to facilitate clearer insights into the effectiveness of aerobic exercise.

Moreover, addressing limitations related to publication bias is crucial. Researchers must ensure that both positive and negative findings are reported and included in meta-analyses. This transparency will contribute to a more balanced understanding of exercise interventions, allowing for better-informed clinical decisions.

Lastly, investigating the long-term effects of aerobic exercise interventions is vital. Understanding sustained benefits, potential adaptations, and any long-term changes in pulmonary function or quality of life will contribute significantly to establishing exercise as a cornerstone of asthma management in children.

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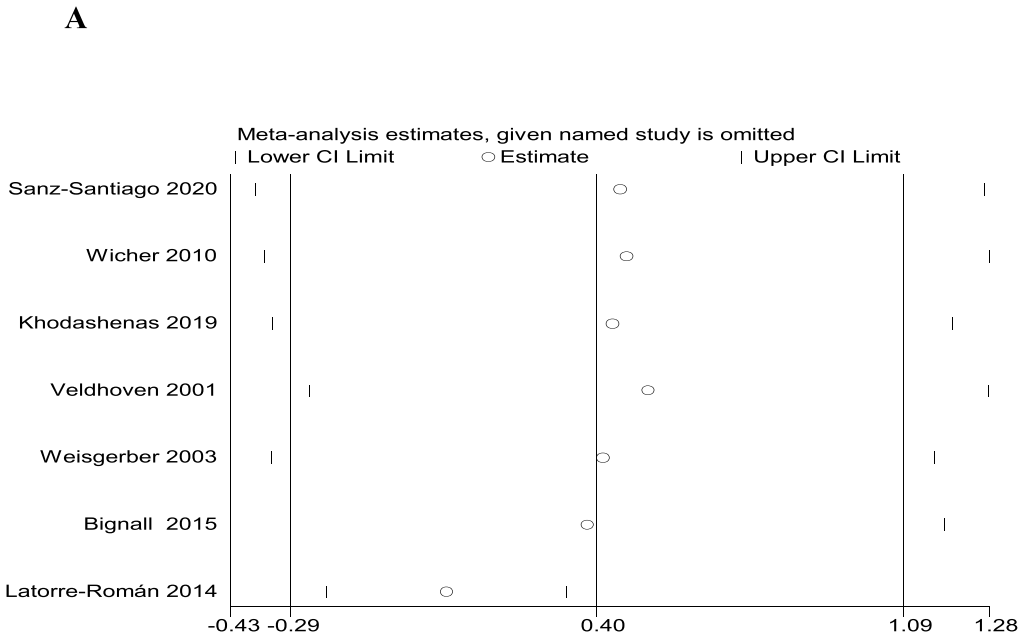

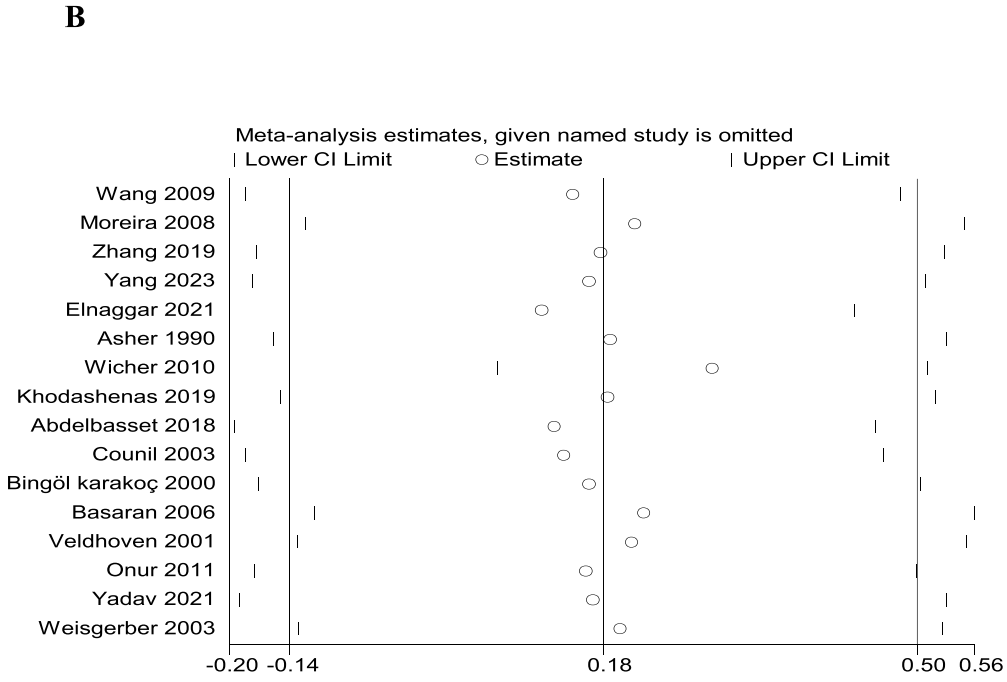

Fig. 3. A-B. Sensitivity analysis of lung value tests: A) FEV1(L), B) FEV1 (%), C) FEV1/FVC (%), D) PEF (L), E) QoL to assess the effects of every study on pooled standardized mean difference estimates.

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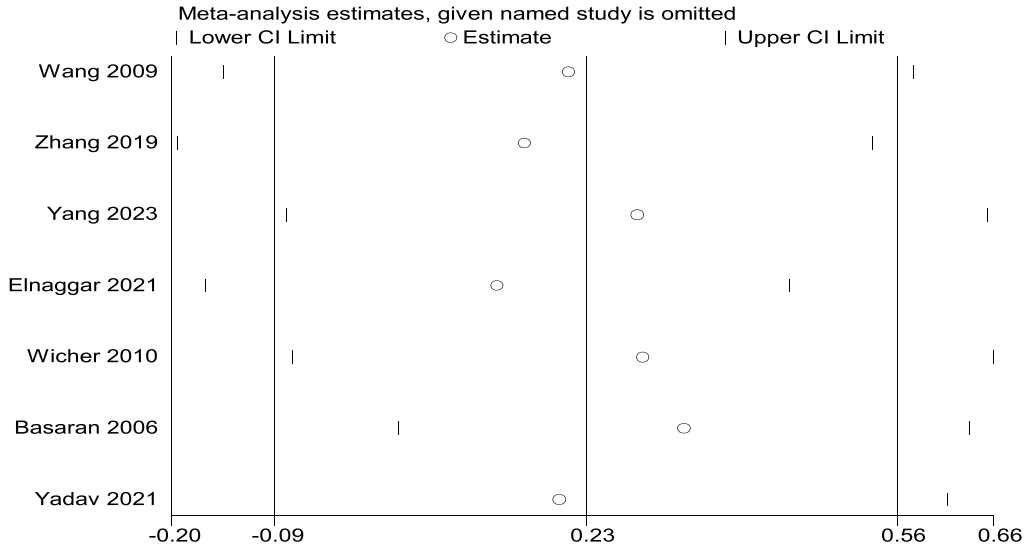

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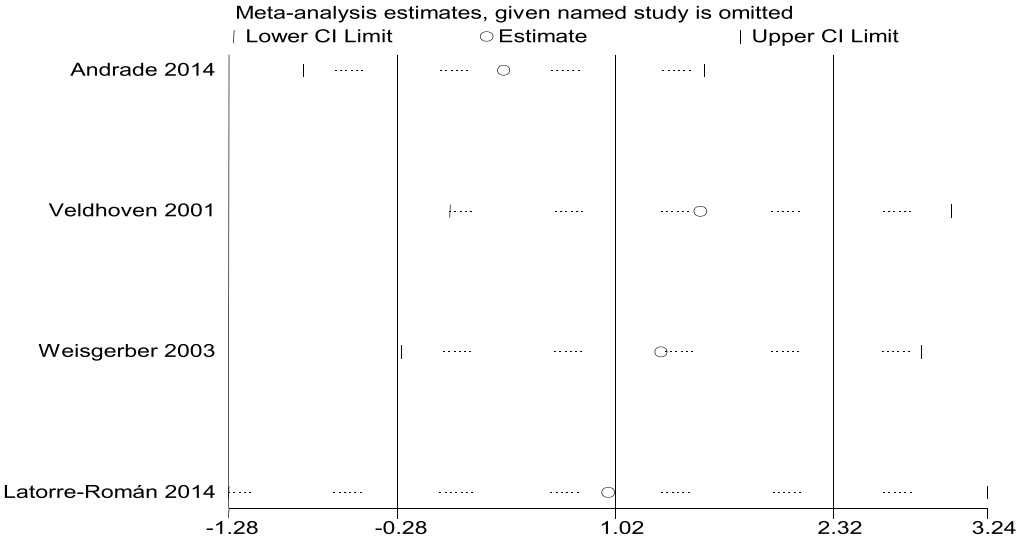

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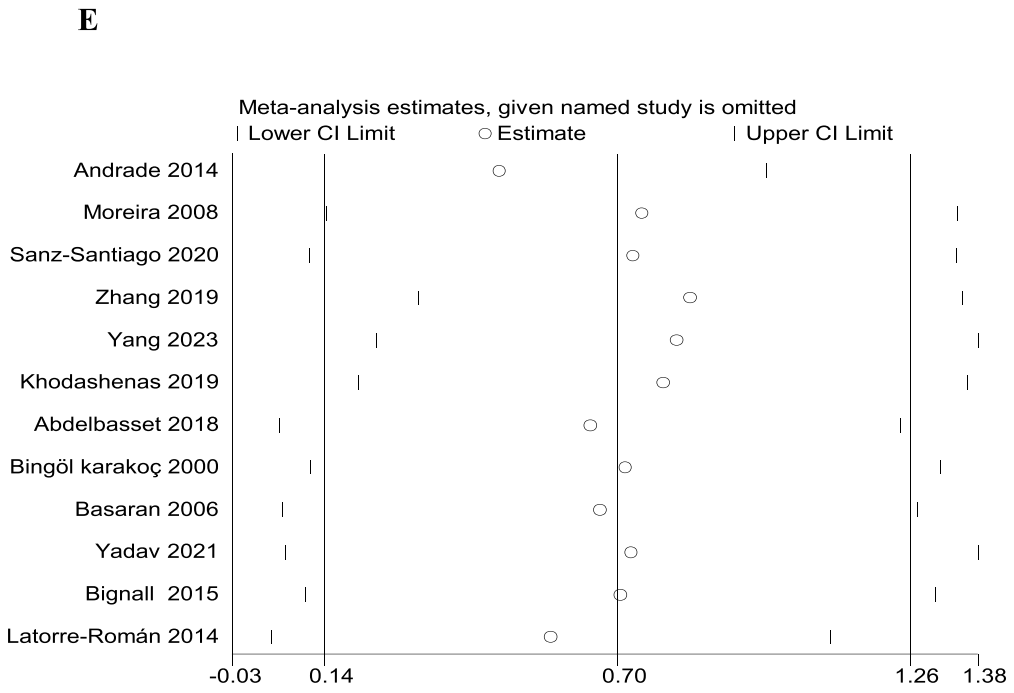

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Data availability

The data used to support the findings of this study are included within the article.

CRediT authorship contribution statement

Qunying Ma: Writing – original draft, Supervision, Software, Resources, Project administration, Investigation, Data curation, Conceptualization. **Min Lu:** Writing – original draft, Validation, Software, Project administration, Methodology, Data curation, Conceptualization. **Qiying Yang:** Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation. **Feng Gong:** Writing – original draft, Visualization, Validation, Project administration, Funding acquisition, Data curation, Conceptualization. **Li Zhou:** Writing – review & editing, Supervision, Software, Methodology, Investigation, Data curation, Conceptualization. **Dandan Xu:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no conflicts of interest related to this study. The research was conducted with the highest ethical standards and without any external influences that could have affected the outcomes or interpretation of the results.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hrtlng.2024.09.005.

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