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Normative Reference Values and Determinants of Pulmonary Function in Healthy Children and Adolescents: A Systematic Review and Meta-analysis

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Pulmonary Function test, Spirometry, Systematic Review, Children , Adolescents

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Abstract

Objective: Spirometry is one of the most vital assessment tools for evaluating pulmonary function in individuals. However, its reference values in various populations are different. This variation is most evident in children due to various variables like ethnicity, methodological variations, growth spurts, gaps in understanding and performing PFT, etc. Over or underestimation of normative values can misdiagnose a child for a pulmonary disorder. Hence, the present study aims to analyze different studies throughout the globe for reference values of PFT (FEV1, FVC, FEV1/FVC, PEFR) in healthy children as well as adolescents.
Materials and methods: Various studies reporting normative values of PFT in healthy school-going children between 1990 and 2024 were extracted from Google Scholar, PubMed and CINHAL according to inclusion criteria through the Rayyan platform. A total of 22 studies (16,754 cildren) were included using PRISMA guidelines. The required information was extracted by full-text review. Quality of studies was assessed using the QUADAS scale. A random-effects model and forest plots for pulmonary functions (FVC, FEV1, PEFR and FEF 25%-75%) were used to estimate heterogeneity and variations between studies in relation to gender.
Results: The pooled mean of FVC, FEV1, PEFR and FEF 25% - 75% was 2.53, 2.16, 4.77 and 2.92 liters for boys and 2.16, 1.92, 4.43 and 2.56 liters for girls, respectively. The heterogeneity was as high as 97.37 % for mean values of PEFR to minimum of 87.73 % for mean values of FVC. Multiple factors, including variable methodological differences, variations in sample size, differing age groups among children, and ethnic differences, in the included studies, lead to heterogeneity in all pulmonary function values.
Conclusions: Pulmonary function values are determinants of a healthy Pulmonary System. However, the heterogeneity and variations seen in mean values make the implementation of PFT difficult, especially for children, globally. Certain variables such as ethnicity, gender, and anthropometric measures, cannot be modified; however, methodology, procedure of testing, and sampling techniques must follow a generalized guideline throughout the globe. Furthermore, for clinical implications, predictive values to be considered should be ethnic-specific.

Introduction:

Spirometry plays a vital role in the clinical assessment and treatment of respiratory disorders. It has been used to monitor normal growth and diagnose respiratory problems at an earlier stage, not only for adults but also for the juvenile population. It is a rather easy, non-invasive, and practical approach for the evaluation of pulmonary abnormalities in children. Since the reference values are primarily used to interpret spirometric findings, their correctness has significant ramifications for individuals as well as medical practice.[1]

The use of precise reference values is crucial because comparison to inaccurate reference values

may result in a person being misdiagnosed as having normal or inadequate lung function, depriving them of required treatments or causing them to get unnecessary overtreatment.[2]

PFT reference values are dependent on many anthropometric variables like height, age, gender, and ethnicity. Other factors like testing methodology, understanding of the technique of performing forced expiratory maneuvers, etc, also play a crucial role in the findings of PFT values. Proper understanding and effective performance are key points before interpreting forced volume loops, especially in the pediatric population, as they have difficulty in understanding and cooperating during testing procedures. Hence, if a child-friendly environment is not adopted, results may not be accurate.

Across the globe, various studies are published with reference values of PFT for the pediatric and adolescent population. The PFT values vary in most of these studies. The cause for this difference can be discrepancies in independent variables (anthropometric measures), procedure and technique of testing or interpretation of data.

Need of the study:

There are notable variations in reported demographic characteristics in variables like age or gender distribution in samples, testing equipment, and methodologies across studies globally. [3] Moreover, even if there are numerous reference values available for PFT of normal children and adolescents, a lack of information about the sample populations and measurement methods, and/or improper statistical analysis may limit the extent to which these can be generalized to other populations.

Hence, the present study provides a systematic review and compiles existing literature on pulmonary function test parameters in healthy children to establish normative reference values and assess factors influencing pulmonary function across different age groups, sexes, and populations. Furthermore, a comprehensive analysis of studies across the globe highlights inconsistencies in methodologies while assessing PFTs in normal children globally is lacking. Finally, a meta-analysis is needed to identify the level of heterogeneity present for various PFTs (FVC, FEV1, PEFR, FEF 25% - 75%).

Aim and objectives of the study:

The primary aim of this review is to compile and analyze existing data to define normative values for pulmonary function parameters (e.g., FEV1, FVC, FEV1/FVC, PEFR) in healthy children and adolescents.

Additional goals include identifying and comparing the tools, testing procedures, and methodology utilized in various studies to conduct PFTs on children, as well as evaluating the studies' quality using the QUADAS questionnaire. The next step is to assess how confounding variables such as height, age, sex, and ethnicity affect the findings of pulmonary function tests in pediatric populations in good health. Lastly, to determine the variation in pulmonary function values (FVC, FEV1, PEFR, FEF25%–75% of FVC) between studies

Methods:

Search strategy:

This systematic review included articles that provided normative data (mean ± SD) of pulmonary functions assessed using spirometry or plethysmography in healthy children and adolescents. It was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement (Figure : 1). Finally, 22 articles fit the eligibility criteria and systematic review ws done for the same.

Eligibility criteria of papers:

The inclusion criteria of articles were 1) articles which portrayed normative values for PFT in healthy children (6 to 12 years) and/or adolescents (12 to 19 years), 2) studies which were published after 1990, 3) articles published in English, 4) Only original full text articles were included, 5) Articles which used

Spirometry for measurement of PFT. Studies were excluded if any article 1) enrolled adults or children less than 6 years of age; 2) with unclear description of the population; 3) used other equipment or method like plethysmography, pneumotechograph or blood gas analysis, 4) used any technique or method to incentivize, assists or motivate the participants; and/or 5) enrolled participants with any musculoskeletal, neurological, cardiovascular or respiratory disorders. [4]

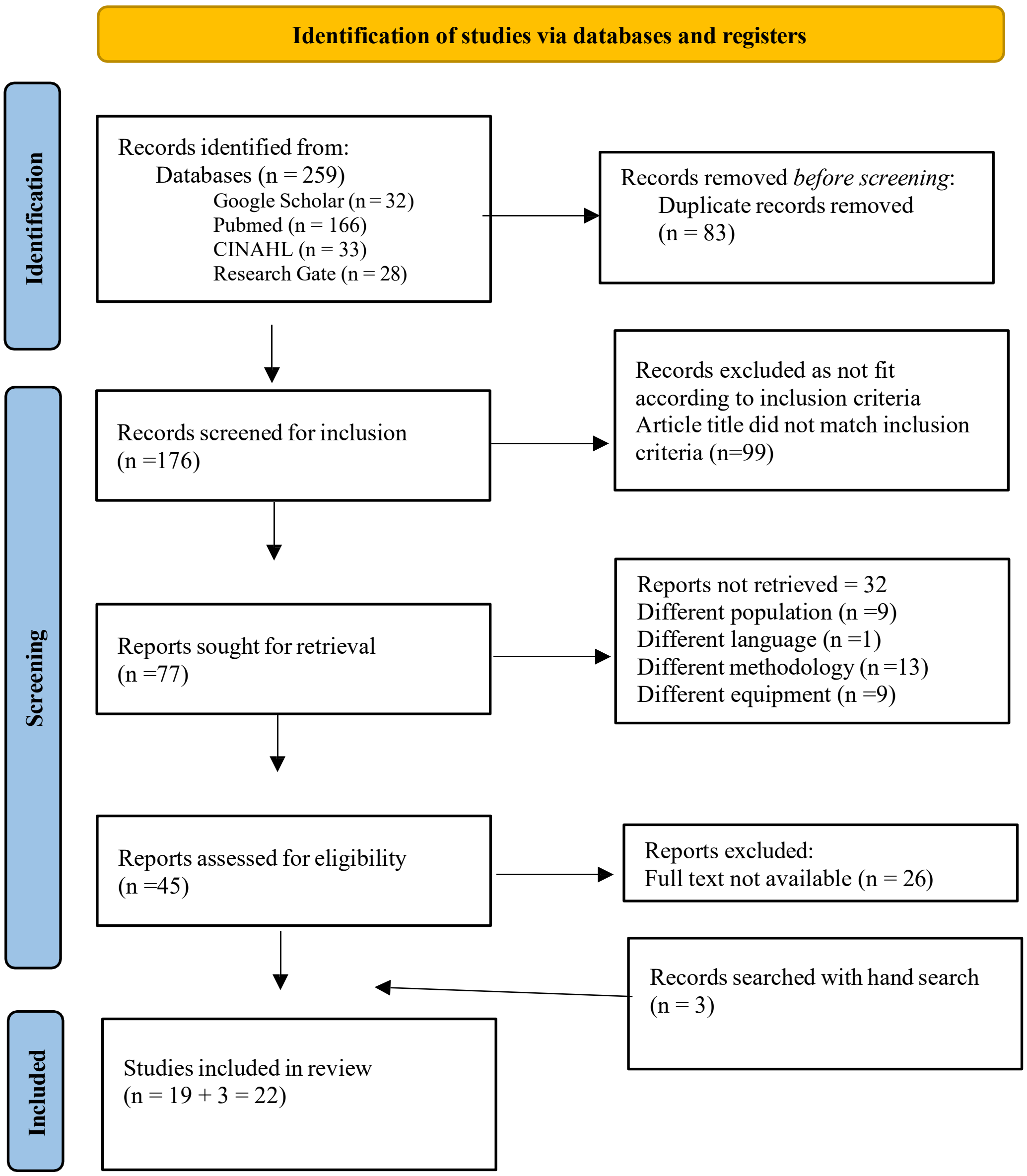


Figure - 1 PRISMA flow diagram

Stages of reference selection:

Different search engines for extraction of articles were "Google Scholar", "Pubmed" and "CINAHL".

Moreover, hand search also produced few articles (n=3) which fit inclusion criteria.

The search terms included various synonyms of PFT like "Pulmonary Function test", "lung function test", "spirometry" or "spirometric". These terms were combined with age-specific keywords like "children", "adolescents" or "pediatrics". Additionally, to include articles that specifically addressed reference values terms like "normative data" and "reference values" were utilized. Lastly, to ensure focus on type of study "cross-sectional" or "prediction equation" was included. Moreover, Boolean operations like "AND" and "OR" were used for combining above mentioned terms. The review period was considered from 1991 to 2024.

Study selection and data extraction:

The studies included were on spirometric reference values of normal children and adolescents. Titles and abstracts relevant to the study from the database search results were exported from search engines and saved in the Rayyan platform. Two reviewers (experience = 12 years, 10 years) independently checked each title and abstract. Whenever there was a disagreement between two reviewers on an article, a third reviewer (14 years of experience) resolved it.

If at least one reviewer considered an article eligible, the full text was sought. Two reviewers also evaluated the full-text articles and extracted information in a standard form.[4]The following information was extracted: 1) aspects of the study population, such as age, gender included, ethnicity, and mean height; 2) all PFT values were mentioned gender-wise in the form of Mean (Standard Deviation); 3) which assessment instrument was used for PFT. Those values that were not mentioned in a particular article were mentioned as "NR" (not reported).

Quality assessment or risk of bias assessment for selected papers:

QUADAS [5,6] Scale (Quality Assessment of Diagnostic Accuracy Studies) with 6 original questions and addition of four ad hoc questions, was adopted. Three biases: 1. Sample selection bias 2. methodological bias and 3. result bias were addressed by 10 questions.

A. SAMPLE SELECTION BIAS: (1) Was the spectrum of participants representative of the participants who will receive the test in practice? (2) Were selection criteria clearly described? (3) Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis, or, at least, confirmed verbally having no disease?

B. METHODOLOGICAL BIAS: (4) Was the execution of the index test described in sufficient detail to permit replication of the test? (5) Was the description of instruction and position/setup for the patient, type of equipment, and the outcomes at least reported? (6) Were withdrawals from the study explained? (7) Is it clearly specified where the sample was obtained? * (8) Is it clearly specified when the sample was obtained? *

C. RESULT BIAS: (9) Are statistical analyses full described? * (10) Are the limitations of the article specifically addressed? * (* **last four questions are ad hoc.**[5,6]) Scoring of quality questions was done by 0 if reasoning provided and by 1 if information was inappropriate, incomplete or missing. Final score (out of 10) represented risk of bias in the following categories: **0-2** = Low risk of bias, **3-5** = Moderate risk of bias, **6-8** = High risk of bias, **9-10** = Very high risk of bias. [5,6]. As shown in Table – 1.

Table – 1 Quality assessment and risk of Bias

Sr. No	Author	Year	1	2	3	4	5	6	7	8	9	10	Total	Risk of Bias
1	M H Shamssain et al	1991	0	1	1	1	0	1	0	1	0	1	6	High
2	R. V. Chougule et. al.	1994	0	0	0	0	0	0	1	1	1	1	4	Moderate
3	P P Sharma et. al.	1997	0	0	0	1	0	1	0	1	0	1	4	Moderate
4	V.K. Vijayan et. al.	2000	0	0	0	0	0	1	0	1	0	1	3	Moderate
5	Mary S M et. al.	2000	0	0	0	1	0	0	0	0	0	1	2	Low
6	M H Boskabady et. al.	2002	0	1	0	0	0	1	0	1	0	1	4	Moderate
7	M Golshan et. al.	2003	0	0	0	0	0	1	0	0	0	0	1	Low
8	Y. Trabelsi et. al.	2003	0	0	0	0	0	0	0	0	0	1	1	Low
9	David A Arnall et.al.	2009	0	0	0	0	0	0	0	1	0	0	1	Low
10	Sandeep Budhiraja et. al.	2010	0	0	0	0	1	1	1	1	1	0	5	Moderate
11	Tahera H Doctor et. al.	2010	0	0	0	1	0	0	0	0	0	1	2	Low
12	Meng-chiao Tsai et. al.	2010	0	0	0	0	0	0	0	0	0	1	1	Low
13	Kui feng et. al.	2011	0	0	1	1	0	0	0	0	0	1	3	Moderate
14	Mohamed Bougrida et. al.	2012	0	0	0	0	0	1	0	0	0	1	2	Low
15	Folly Messan	2013	0	0	0	0	0	1	0	0	0	1	2	Low
16	A. Alfrayh et. al.	2014	0	0	0	1	0	0	1	0	0	0	2	Low
17	Mei Jiang et. al.	2014	0	0	0	0	0	1	0	0	0	0	1	Low
18	Ewa Rebacz-Maron	2018	0	0	0	0	1	1	0	1	0	0	3	Moderate
19	Sara Sadik et.al.	2019	0	0	0	0	0	1	0	0	0	1	2	Low
20	R Aristizabal-Duque et.al	2019	0	0	0	0	0	0	0	0	0	0	0	Low
21	Jaksoel C. Silva et. al.	2019	0	0	0	0	0	1	0	1	0	0	2	Low
22	Peter Odion et. al.	2024	0	0	0	0	0	0	0	0	0	1	1	Low

The Quality assessment was done by two reviewers separately and checked for discrepancies in the score. In case of difference in score, the query in marking was resolved by the third reviewer. There is only one study that has a high risk of bias, seven studies have a moderate and fourteen studies have a low risk of bias. Only sixteen studies had –

1. mean values and SD of PFT values and
2. low or moderate risk of bias

were included in the meta-analysis to reduce any variability in the results of the meta-analysis.

Data Analysis:

A random effects model was applied to analyze the mean values of pulmonary function tests in normal children and adolescents worldwide, as heterogeneity was observed in the data on pulmonary function in children. The pooled mean and its 95% CI were calculated using Jamovi (version 26). The Random Effects Model test calculated the heterogeneity, tau-squared estimate (Tau^2 or τ^2), and I value, which was as high as 97%. This suggests that there is a substantial variability in the values across studies. Random effects model accounted for between and within study variability, providing accurate estimates. Furthermore, Forest Plots visually depicted the distribution and variance across studies for all pulmonary function values.

TABLE – 2 Review table for details of ethnicity, sample size, Pulmonary Functions checked and instrument used of included articles										
SR NO	**Author**	**Year**	**Location**	**Ethnicity**	**Gender**	**Age group**	**Total Sample Size (N)**	**COMBINED - mean height (cms)**	**Pulmonary functions checked**	**Instrument for testing**
1	M H Shamssain [7]	1991	Transkei, africa	Xhosa	Both	6 - 19 years	2000 (M=974, F=1026)	NR	FVC, FEV1	Vitalograph
2	R V Chougule et. al. [8]	1994	Bombay - India	Indian	Both	6 - 15 years	632 (M=354, F=278)	NR	FVC, FEV1, FEF 25% to 75% , PEFR, MVV	Jaeger flow-mate
3	P P Sharma et. al. [9]	1997	Delhi	Indian	Both	10 - 15 years	410 (M=222, F=188)	M = 148.38*, F = 148.56*	FVC, FEV1, 25% FEF, 50% FEF, 75% FEF, PEFR	Portable electronic lung function spirometer (P. K. Morgan limited, UK)
4	V.K. Vijayan et. al. [10]	2000	South India - India	Indian	Both	7 - 19 years	469 (M=246, F=223)	M = 145.62*, F = 137.58*	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, 25% FEF, 50% FEF, 75% FEF, PEFR, MVV	Dry rolling spirometer (Transfer Test Model C P. K. Morgan Ltd. U K)
5	Mary S M et. al. [11]	2000	Hong kong China	Chinese	Both	7 - 19 years	852 (M=392, F=460)	M = 116.4 to 185.9, F = 119.8 to 173.1	FVC, FEV1, 50% FEF	Sensormedics 6200, CA
6	Mohammad Hossein Boskabady et. al. [12]	2002	Masshad, Iran	Iranian	Both	8 - 18 years	336 (M=187, F=149)	M = 150.36, F = 147.3	FVC, FEV1, 25% FEF, 50% FEF, 75% FEF, PEFR,	Spirometer model ST90, Fukuda Sangyo, Japan
7	M Golshan et. al. [13]	2003	Isfahan, Iran	Iranian (persian)	Both	5 - 20 years	1121 (M=683, F=438)	M = 171.10, F = 148.17	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, 25% FEF, 50% FEF, 75% FEF, PEFR	Pneumotachometer (moose PFT, USA) (Hans Rudolph Inc., Kansas, MO, USA)
8	Y. Trabelsi et. al. [14]	2003	Tunisia	Tunisian	Both	6 - 16 years	1114 (M=581, F=533)	M = 140, F = 138	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, PEFR	Spirometer (Japan)
9	David A Arnall et.al. [15]	2009	Navajo, Arizona, Mexico, USA	Navajo	Both	6 - 14 years	558 (M=274, F=284)	M = 136, F = 136	FVC, FEV1, FEV1/FVC, 25% to 75% FEF	Flow-sensing spirometer (Survey tachometer Ferraris Respiratory, 901 Front Street, Louisville, CO)
10	Sandeep Budhiraja et. al. [16]	2010	Ludhiana (North India) - India	Indian	Both	6 - 15 years	600 (M=343, F=257)	T = 141.3 (15.73)	FVC, FEV1, 25% FEF, 50% FEF, 75% FEF, PEFR, MVV	Portable Autospirometer (Superspiro Cat No. SU 6000)
11	Tahera H Doctor et. al. [17]	2010	South Gujarat - India	Indian	Both	8 - 14 years	655 (M=408, F=247)	M = 142.34 (9.67), F = 141.73 (9.56)	FVC, FEV1, FEV1/FVC, PEFR	Spirometer (turbine) (company not mentioned)
12	Meng-chiao Tsai et. al. [18]	2010	Taipei, Taiwan	Chinese	Both	6 - 11 years	309 (M=153, F=156)	T = 134 (12) M = 133.63, F = 133.67	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, PEFR	Exhalyzers, Spiroware, Ecomedics, Switzerland
13	Kui feng et. al. [19]	2011	Heilongjiang, northeast China	Korean Chinese	Both	8 - 18 years	443 (M=226, F=217)	M = 162.59, F = 156.03	FVC, FEV1, 25% to 75% FEF, PEFR	Portable spirometer, Masterlab, 5.10, Jaeger, Wurtzburg, Germany

TABLE – 2 Review table for details of ethnicity, sample size, Pulmonary Functions checked and instrument used of included articles										
SR NO	**Author**	**Year**	**Location**	**Ethnicity**	**Gender**	**Age group**	**Total Sample Size (N)**	**COMBINED - mean height (cms)**	**Pulmonary functions checked**	**Instrument for testing**
14	Mohamed Bougrida et. al. [20]	2012	Constantine, Algeria	Arabian	Both	5 - 16 years	208 (M=107, F=101)	T = 141 (19), M = 143 (21), F = 139 (18)	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, 25% FEF, 50% FEF, 75% FEF, FET(Sec)	ZAN 100, Me Grerate GmbH, Germany
15	Folly Messan et. al. [21]	2013	Benin, Africa	Beninese	Both	11 - 16 years	484 (M=274, F=210)	M = 154.96*, F = 151.74*	FVC, FEV1	Micro-quark spirometer (Cosmed Ltd., Rome, Italy)
16	A. Alfrayh et. al. [22]	2014	Saudi Arabia	Arabian	Both	6 - 18 years	4526 (M=2226, F=2300)	M = 145.9 (17.4), F = 144.5 (14.6)	FVC, FEV1, FEV1/FVC	Spirometer (company not mentioned)
17	Mei Jiang et. al. [23]	2014	Guangzhou, China	Chinese	Both	5 - 15 years	422 (M=226, F=196)	M = 134.4 (16.9), F = 158.6 (4.7)	FVC, FEV1, 25% to 75% FEF, PEFR	Spirometer - Asters Teen, Jaeger Inc. Hochberg, Germany
18	Ewa Rebacz-Maron [24]	2018	Tanzania, Africa	African black	Boy		M = 402	M = 162.89*	FVC, FEV1, FEV1/FVC, PEFR	Micro-plus spirometer (Micro Medical Ltd, Basingstoke, UK)
19	Sara Sadik et.al. [25]	2019	Karachi-Pakistan	Pakistani	Both	7 - 18 years	751 (M=484, F=267)	T = 150.2 (15.8), M = 152.3 (16.7), F = 146.4 (13.3)	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, PEFR	Vitalograph Alpha
20	Ricardo Aristizabal-Duque et.al [26]	2019	Bogota, Colombia, south america	Colombian	Both	6 - 18 years	326 (M=149, F=177)	M = <12 years 131.8 (10.1) & >12 years 163 (8.9), F = <12 years 131.9(10.6) & >12 years 155.3(6.7)	FVC, FEV1, 25% to 75% FEF	Electronic spirometer (Jaeger Vyntus Spiro)
21	Jaksoel C. Silva et. al. [27]	2019	Sao Paulo, Brazil	Mixed, Caucasian	Both	6 - 17 years	348 (M=164, F=184)	T = 147.98*	FVC, FEV1, FEV1/FVC, 25% to 75% FEF, PEFR, MVV	Pneumotechograph - KOKO Sx1000 (nSpire Health, Longmont, CO)
22	Peter Odion et. al. [28]	2024	Lagos, Nigeria	Nigerian - Igbo, Yoruba	Both	6 - 11.80 years	766 (M=359, F=407)	T = 129.35 (10.65), M = 129.49 (10.46), F = 129.23 (10.84)	FEV1, PEFR	ePFM - Asma-1, Vitalograph, UK
	Total number of participants						**16,754 (M = 8,961 F = 7,793)**			

Mean (SD), *pooled mean *(pooled SD)

Sr No	Author	FVC	FEV1	FEV1/FVC	PEFR	FEF 25%-75%	FEF 25%	FEF 50%	FEF 75%	MVV
1	M H Shamssain	M = 2.64*, F = 2.2*	M = 1.31*, F = 1.82*	NR	NR	NR	NR	NR	NR	NR
2	R. V. Chougule et. al.	M = 2.14* (0.10)*, F = 1.81* (0.13)*	M = 1.91* (0.08)*, F = 1.65* (0.12)*	NR	M = 4.66* (0.27)*, F = 4.09* (0.25)*	M = 2.45* (0.23)*, F = 2.20* (0.11)	NR	NR	NR	M = 69.01* (4.29)*, F = 59.61* (2.99)*
3	P P Sharma et. al.	M = 2.49* (0.24)*, F = 1.86 (0.22)*	M = 1.90* (0.25)*, F = 1.84* (0.21)*	NR	M = 4.26* (0.23)*, F = 4.07* (0.27)*	NR	M = 3.48* (0.11)*, F = 3.28* (0.11)*	M = 3.25* (0.08)*, F = 2.83* (0.12)*	M = 1.91* (0.10)*, F = 1.63* (0.04)*	NR
4	V.K. Vijayan et. al.	M = 2.43 (0.07), F = 1.86 (0.05)	M = 2.14 (0.06), F = 1.65 (0.04)	M = 88 (0.35), F = 88.80 (0.33)	M = 5.11 (0.19), F = 3.73 (0.13)	M = 3.04 (0.1), F = 2.42 (0.08)	M = 4.30 (0.16), F = 3.23 (0.12)	M = 3.06 (0.1), F = 2.44 (0.09)	M = 1.62 (0.06), F = 1.39 (0.5)	M = 91.41 (3.65), F = 67.45 (2.41)
5	Mary S. M. et. al.	M = 3.14 (0.95), F = 2.65 (0.62)	M = 2.80 (0.86), F = 2.44 (0.56)	NR	NR	NR	NR	M = 3.95 (1.25), F = 3.77 (0.96)	NR	NR
6	M. H. Boskabady et. al.	M = 2.79 (1.11), F = 2.42 (0.81)	M = 2.47 (0.97), F = 2.19 (0.69)	NR	M = 5.04 (2.12), F = 4.43 (1.46)	NR	M = 1.81 (0.95), F = 1.85 (0.79)	M = 3.5 (1.41), F = 3.39 (1.12)	M = 4.77 (2), F = 4.18 (1.5)	NR
7	M Golshan et. al.	M = 3.31 (1.42), F = 2.88 (0.9)	M = 2.94 (1.27), F = 2.56 (0.80)	M = 88.88 (3.14), F = 88.89 (3.08)	M = 6.56 (3.21), F = 5.73 (1.95)	M = 3.71 (1.65), F = 3.27 (1.12)	M = 5.73 (2.52), F = 5.23 (1.70)	M = 4.06 (1.76), F = 3.76 (1.29)	M = 1.94 (0.97), F = 1.77 (0.75)	NR
8	Y. Trabelsi et. al.	M = 2.37 (0.81), F = 2.21 (0.64)	M = 2.08 (0.69), F = 1.96 (0.55)	M = 87.6 (4.6), F = 89.2 (4.1)	M = 4.41 (1.61), F = 4.10 (1.23)	M = 2.46 (0.78), F = 1.96 (0.69)	NR	NR	NR	NR
9	David A Arnall et.al.	M = 2.60 {1.57-3.95}, F = 2.42 {1.5-3.54}	M = 2.24 {1.42 - 3.48} , F = 2.15 {1.36 - 3.16}	M = 86.8 {78.5 - 95.3}, F = 88.9 {80.3-95.5}	NR	M = 2.67 {1.65 - 4.15}, F = 2.74 {1.67 - 4.18}	NR	NR	NR	NR
10	Sandeep Budhiraja et. al.	T = 2.01 (0.76), M = 2.16, F = 1.8	T = 1.83 (0.67), M = 1.95, F = 1.66	NR	T = 3.40 (1.33), M = 3.36, F = 3.06	NR	T =3.27 (1.3)	T = 2.53 (0.99), M = 2.68, F = 2.37	T = 1.44 (0.63)	T = 68.65 (26.13), M = 72.91, F = 62.97
11	Tahera H Doctor et. al.	M = 2 (0.46), F = 1.91 (0.47)	M = 1.76 (0.38), F = 1.69 (0.4)	M = 88.11 (4.30), F = 88.56 (4.47)	M = 4.74 (0.96), F = 4.47 (1.15)	NR	NR	NR	NR	NR

Table – 3 Review table of Mean and Standard Deviation of various PFT values in studies

Table – 3 Review table of Mean and Standard Deviation of various PFT values in studies

Sr No	Author	FVC	FEV1	FEV1/FVC	PEFR	FEF 25%-75%	FEF 25%	FEF 50%	FEF 75%	MVV
12	Meng-chiao Tsai et. al.	M = 1.76* (0.29)*, F = 1.62* (0.29)*	M = 1.63* (0.28)*, F = 1.56* (0.28)*	M = 92.9* (6.8)*, F = 93.3* (6.57)*	M = 2.83* (0.68)*, F = 3.65* (0.69)*	M = 2.45* (0.56), F = 2.47* (0.58)	NR	NR	NR	NR
13	Kui feng et. al.	M = 3.98* (0.61)*, F = 2.98* (0.40)*	M = 3.67* (0.52)*, F = 2.90* (0.35)*	NR	M = 7.86* (1.38)*, F = 7.44* (0.91)*	M = 4.46* (0.96)*, F = 4.23* (0.70)*	NR	NR	NR	NR
14	Mohamed Bougrida et. al.	T = 2.37 (0.96), M =2.50 (0.81), F = 2.24 (0.81)	T = 2.17 (0.87), M = 2.27 (0.96), F = 2.06 (0.74)	T = 91 (6), M = 90 (6), F = 91 (6)	T = 4.22 (1.51), M = 4.51 (1.71), F = 3.91 (1.2)	T = 2.74 (1), M = 2.8 (1.11), F = 1.63 (0.71)	T = 1.63 (0.67), M = 1.63 (0.71), F = 1.64 (0.62)	T = 3.03 (1.14), M = 3.13 (1.25), F = 2.93 (1.02)	T = 3.93 (1.44), M = 4.18 (1.61), F = 3.66(1.19)	NR
15	Folly Messan	M = 2.59* (0.59)*, F = 2.16* (0.44)*	M =1.96* (0.53)*, F = 1.71* (0.43)*	NR	NR	NR	NR	NR	NR	NR
16	A. Alfrayh et. al.	M = 2.19 (0.98), F = 1.8 (0.92)	M = 1.78 (0.75), F = 1.46 (0.68)	M = 83.9 (17.2), F = 76.5 (30.5)	NR	NR	NR	NR	NR	NR
17	Mei Jiang et. al.	M = 2.2 (0.81), F = 2.06 (0.72)	M = 1.94 (0.70), F = 1.88 (0.64)	NR	M = 4.35 (1.37), F = 4.29 (1.37)	M = 2.20 (0.86), F = 2.34 (0.88)	NR	NR	NR	NR
18	Ewa Rebacz-Maron et. al.	M = 2.42* (0.59)*	M = 2.38* (0.62)*	M = 99.26* (1.63)*	M = 6.31* (1.39)*	NR	NR	NR	NR	NR
19	Sara Sadik et.al.	T = 2.1 (0.74), M = 2.21 (0.75), F = 2.28 (0.75)	T = 2.08 (0.73), M = 2.13 (0.72), F = 1.97 (0.73)	T = 92.9 (4.7), M = 92.93 (4.78), F = 92.89 (4.49)	T = 3.85 (1.17), M = 3.94 (1.23), F = 3.69 (1.06)	T = 2.86 (1.2), M = 2.78 (1.26), F = 2.52 (1.06)	NR	NR	NR	NR
20	Ricardo Aristizabal-Duque et.al	M = <12 years = 2.29 (0.47) & >12 years = 4.26 (0.75), F = <12 years = 2.17 (0.47) &	M = <12 years 1.94 (0.37) & >12 years 3.67 (0.67), F = <12 years 1.87 (0.38) & >12 years 3 (0.44)	NR	NR	M = <12 years 2.14 (0.52) & >12 years 4.09 (0.88), F = <12 years 2.18 (0.51) & >12 years 3.46 (0.87)	NR	NR	NR	NR

Table – 3 Review table of Mean and Standard Deviation of various PFT values in studies

Sr No	Author	FVC	FEV1	FEV1/FVC	PEFR	FEF 25%-75%	FEF 25%	FEF 50%	FEF 75%	MVV
		>12 years 3.46 (0.54)								
21	Jaksoel C. Silva et. al.	T = 2.74* (0.59)*	T = 2.39* (0.5)*	T = 89.03*	T = 5.14* (0.99)	T = 2.94* (0.70)*	NR	NR	NR	T = 86.50* (18.72)*
22	Peter Odion et. al.	NR	T = 1.4 (0.34), M = 1.44 (0.34), F = 1.36 (0.34)	NR	T = 4.01 (0.81), M = 3.85 (0.91), F = 3.93 (0.86)	NR	NR	NR	NR	NR

T = Total, M = Boys, F = Girls, * = pooled mean, ()* = pooled SD, NR = Not recorded, {} = range of mean

Result:

Study Characteristics:

The 22 studies that were included assessed a total of 16,754 (M = 8,961; F = 7,793) healthy children and adolescents. Several basic information, like author, year of publication, ethnicity, sample size, Mean ± SD of height, spirometer used, and Pulmonary functions tested, are shown in Table 2. The age range of the included children ranged from 3 to 19 years. The included studies reported reference values for various spirometry values (FEV_1, FVC, FEV_1/FVC, PEFR, etc). Table 3 portrays the mean and SD values for various pulmonary functions from 22 included articles.

Table – 4 Random-Effects Model and Heterogeneity Statistics for PFT values

PFT Value	N = No of studies	Estimated (pooled) Mean	Standard Error	Z value	Confidence Interval Lower Bound	Confidence Interval Upper Bound	Tau²	I²	H²	p-value
FVC – m	**15**	2.53	0.12	18.4	2.24	2.81	0.284	93.24%	14.78	<0.001
FVC – f		2.16	0.11	20.2	1.95	2.37	0.141	87.73%	8.147	<0.001
FEV1 – m	**16**	2.16	0.14	15.5	1.88	2.43	0.281	94.03%	16.76	<0.001
FEV1 – f		1.92	0.11	17.9	1.71	2.13	0.155	90.05%	10.05	<0.001
PEFR – m	**13**	4.77	0.35	13.8	4.09	5.44	1.476	97.37%	38.057	<0.001
PEFR – f		4.43	0.29	15.2	3.86	5.00	1.036	96.48%	28.40	<0.001
FEF 25%-75% - m	**9**	2.92	0.24	12.3	2.45	3.38	0.461	94.06%	16.84	<0.001
FEF 25%-75% - f		2.56	0.25	10.1	2.06	3.05	0.534	95.91%	24.44	<0.001

PFT – Pulmonary Function Test, FVC – Forced Vital Capacity (L), FEV1 – Forced Expiratory volume in 1st second (L), PEFR – Peak Expiratory Flow Rate (L/min), FEF – Forced Expiratory Flow at 25% - 75% of FVC (L/min), m – boys, f – girls, k – number of studies, SE – Standard Error of mean, Z – Effect size , Tau^2 – Distribution of true effect sizes about the mean, I^2 – heterogeneity - proportion of variance that is true (due to differences about effect size), H^2 - total variance, p-value – level of significance.

Out of 22 studies included for review, only 16 studies which had mean values and SD of PFT values and had low or moderate risk of bias according to QUADAS scale were included in the meta-analysis, so that inconsistent studies will not affect outcome of the result. Out of 22, 15 studies,16 studies, 13 studies and 9 studies fulfilled the criteria for FVC, FEV1, PEFR and FEF 25% - 75%, respectively.

FVC

Table 4 - depicts the meta-analysis of 15 studies using a random-effects model estimated the pooled mean of forced vital capacity (FVC) in boys was greater than girls. Pooled mean was 2.53 L (95% CI: 2.24–2.81; $p < 0.001$) for boys and 2.16 L (95% CI: 1.95–2.37; $p < 0.001$) for girls in FVC.

Heterogeneity was extremely high in both genders; however, it was higher in boys as compared to girls. (boys - $I^2 = 93.24\%$, $p < 0.001$) and (girls - $I^2 = 87.73\%$, $p < 0.001$), indicating substantial variation between studies. The forest plot showed (figure 4) that while some studies reported FVC values close to the pooled mean, only one study Kui-Feng et. al. differed considerably, contributing to the wide heterogeneity. Moreover, the pooled mean [CI] ranged from minimum of 1.76 L [1.46-2.06] for boys and 1.62 L [1.32-1.92] for girls in the study by Meng Chiao Tsai et. al., to maximum of 3.98 L [3.59-4.37] for boys and 2.98 L [2.66-3.30] for girls in the study by Kui-Feng et. al. (Table & Figure – 4A, 4B).

FEV1

Similarly, meta-analysis of 16 studies using a random-effects model estimated the pooled mean of Forced Expiratory Volume in the first second (FEV1) in boys was greater than in girls. Pooled mean was 2.16 L (95% CI: 1.88–2.43; $p < 0.001$) for boys and was 1.92 L (95% CI: 1.71–2.13; $p < 0.001$)
for girls. Heterogeneity was extremely high in both genders; it was higher in boys ($I^2 = 94.03\%$, $p < 0.001$) than girls ($I^2 = 90.05\%$, $p < 0.001$), indicating substantial variation between studies. The forest plot showed that

while some studies reported FEV1 values close to the pooled mean, two studies Kui-Feng et. al. and Peter Odion et. al. differed considerably, contributing to the wide heterogeneity. Moreover, the pooled mean [CI] ranged from minimum of 1.44 L [1.18-1.70] for boys and 1.36 L [95% CI = 1.10-1.62] for girls in the study by Peter Odion et. al. to maximum of 3.67 L [3.31-4.03] for boys and 2.90 L [95% CI = 2.60-3.20] for girls in the study by Kui-Feng et. al. (Table 4 & Figure 5A 5B).

PEFR

Furthermore, the meta-analysis of 13 studies using a random-effects model estimated the pooled mean of Peak Expiratory Flow Rate (PEFR) in boys was 4.77 L/min (95% CI: 4.09 – 5.44; $p < 0.001$) and in girls as 4.43 L/min (95% CI: 3.86–5.00; $p < 0.001$). Heterogeneity was extremely high, it was reported to be almost similar in both genders (boy - $I^2 = 97.37\%$, $p < 0.001$) and (girls - $I^2 = 96.48\%$, $p < 0.001$), indicating substantial variation between studies. The forest plot showed that while most studies reported PEFR values close to the pooled mean, two studies Kui-Feng et. al. and Meng Chiao Tsai et. al. considerably, contributing to the wide heterogeneity. Moreover, minimum pooled mean [CI] of 2.83 L/min [2.37-3.29] for boys and 3.65 L/min [3.19-4.11] for girls in the study by Meng Chiao Tsai et. al. Additionally, the maximum pooled mean [CI] of 7.86 L/min [7.27-8.45] for boys and 7.44 L/min [6.95-7.93] for girls in the study by Kui-Feng et. al. (Table 4 & Figure 6A, 6B).

FEF 25%-75% of FVC

Finally, meta-analysis of 9 studies using a random-effects model estimated the pooled mean Forced Expiratory Flow at 25% to 75% (FEF 25%-75%) in boys as 2.92 L/min (95% CI: 2.45–3.38; $p < 0.001$) and girls 2.56 L/min (95% CI: 2.06–3.05; $p < 0.001$). Heterogeneity was extremely high in both genders (boys - $I^2 = 94.06\%$, $p < 0.001$) and (girls - $I^2 = 95.91\%$, $p < 0.001$), indicating substantial variation between studies. The forest plot showed that while most studies reported FEF 25% to 75% values close to the pooled mean, two studies Kui-Feng et. al., Meng Jiang et. al. and Mohamed Bougrida et. al. differed considerably, contributing to the wide heterogeneity. Moreover, the minimum pooled mean [CI] of 2.20 L/min [1.73-2.67] in the study by Meng Jiang et. al. for boys and 1.63 L/min [1.11-2.15] in the study by Mohamed Bougrida et. al. for girls. And maximum pooled mean [CI] of 4.46 L/min [3.96-4.96] for boys and 4.23 L/min [3.80-4.66] for girls in the study by Kui-Feng et. al. (Table & Figure 7A, 7B).

Figure 4A –Forest plot of Mean and CI of FVC in boys from 15 articles

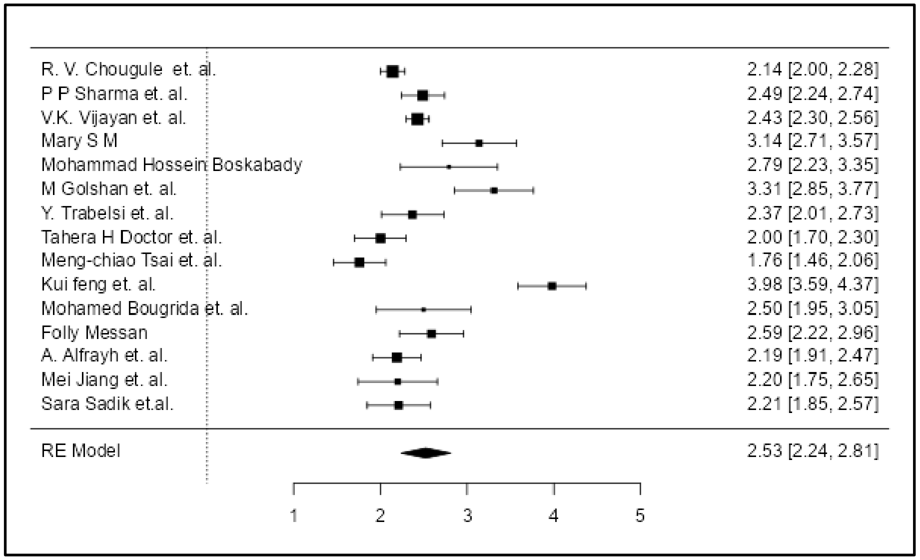


Figure 5A –Forest plot of Mean and CI of FEV1 in boys from 16 articles

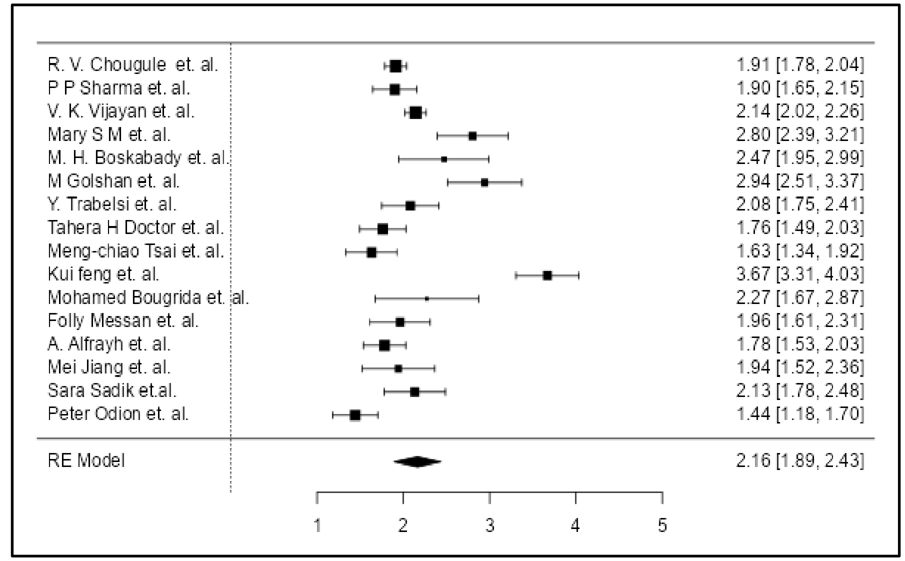


Figure 4B – Forest plot of Mean and CI of FVC in girls from 15 articles

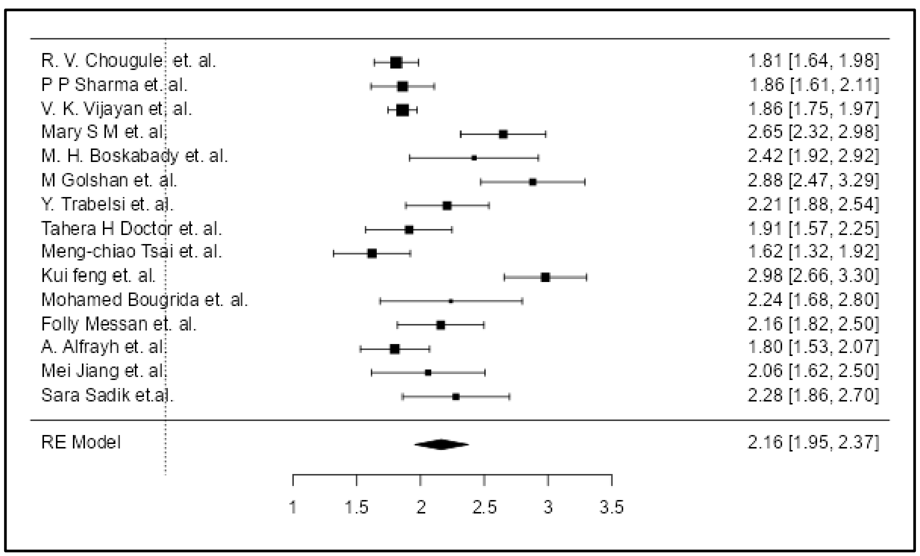


Figure 5B - Forest plot of Mean and CI of FEV1 in girls from 16 articles

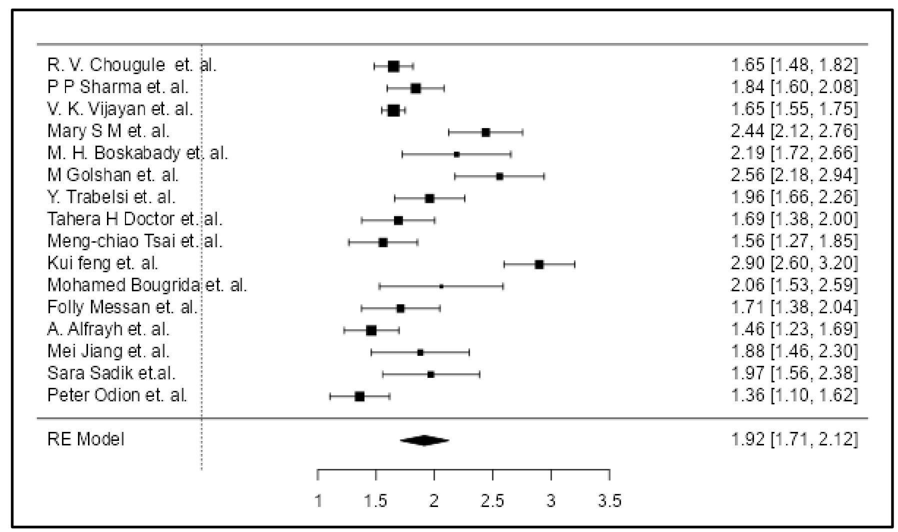


Figure 6A – Forest plot of Mean and CI of PEFR in boys from 13 articles

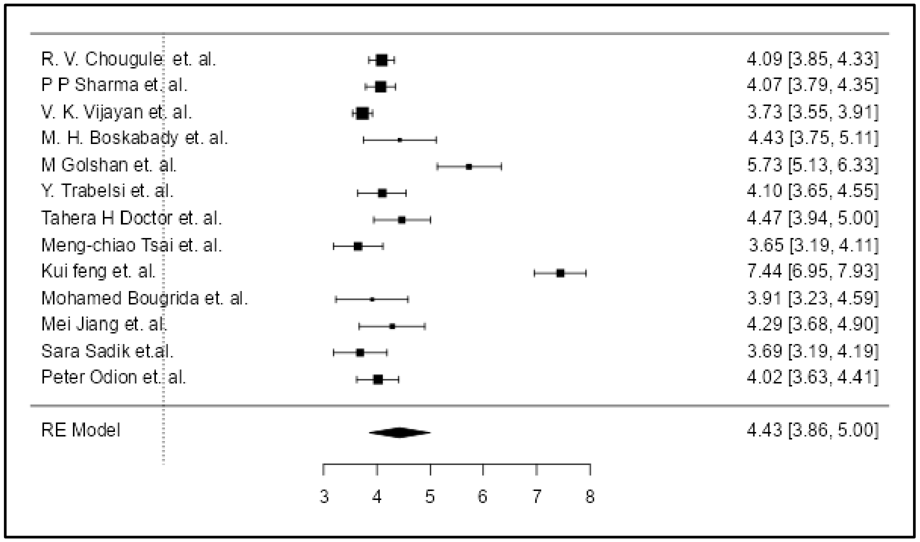


Figure 6B – Forest plot of Mean and CI of PEFR in girls from 13 articles

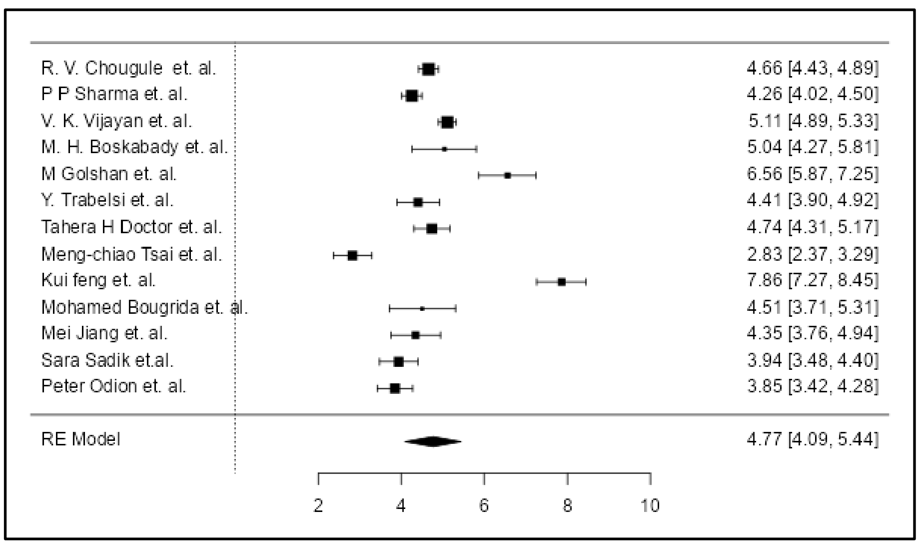


Figure 7A – Forest plot of Mean and CI of FEF 25% - 75% in boys from 9 articles

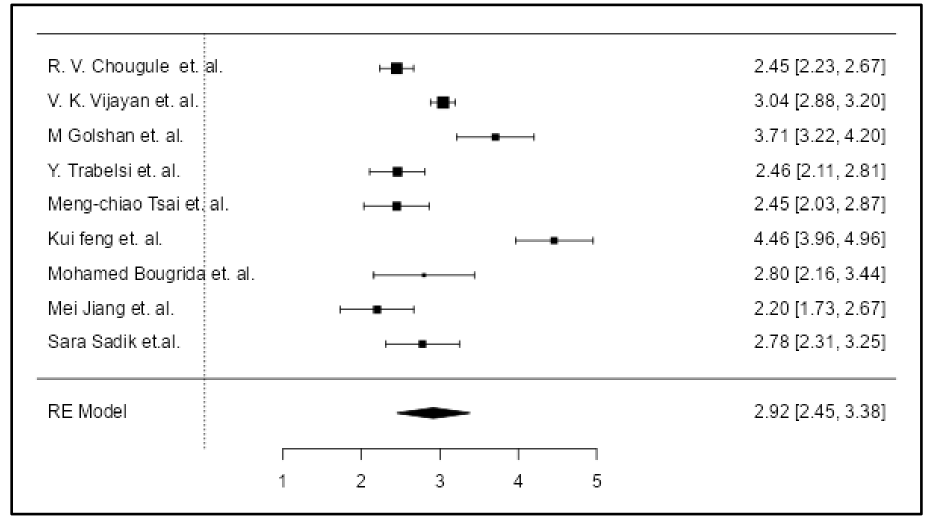
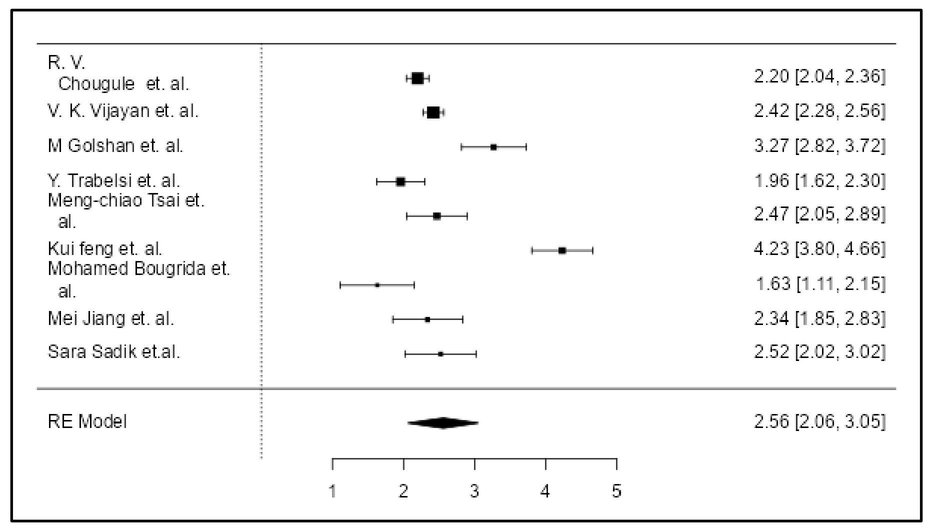


Figure 7B – Forest plot of Mean and CI of FEF 25% - 75% in girls from 9 articles



Discussion

In this systematic review of normative pulmonary function test (PFT) values in children 22 published articles were identified between 1990 and 2024, covering a total of 16,754 (M = 8,961, F = 7,793) children aged between 6 to 19 years. The included studies reported reference values for various pulmonary functions (FEV_1, FVC, FEV_1/FVC, PEFR, etc), The meta-analysis included only 16 studies, which had the lowest risk of bias. Overall, all pulmonary indices varied significantly between populations. Heterogeneity ranged from 87.73% (for FVC in girls) to 97.37% (for PEFR in boys).

The primary reason for demonstrated marked heterogeneity/ variability may be: 1). The strong influence of ethnic composition, like height, weight for age and measurement technique on Pulmonary values. 2). Gender Discrepancies 3). Varying age ranges 4). Differences in methodology 5). Variations in equipments (Jaeger vs. Superspiro vs. dry rolling seal), and 6). sampling (urban vs. semi-urban schools).

Regional and ethnic Variability in Pulmonary Function Values

For all Pulmonary functions, the variability in mean values across studies from different countries ranged from as low as 27% to as high as 252%. Table 8 demonstrates regional analysis revealing marked variability in reported normative PFT values, with Chinese/Taiwanese cohorts showing the greatest variation (up to 252% for FVC). In comparison, Indian studies demonstrated comparatively stable findings (27–50% and variability across indices). Nevertheless, the nearly twofold variation within Indian datasets alone underscores the pressing need for uniform protocols and population-representative equations. In contrast, the African subgroups were more internally consistent but differed substantially when compared across countries. Such discrepancies underline the necessity for region-specific reference equations and standardization of spirometric protocols.

Gender discrepancies

Only one study has examined spirometry in boys exclusively. All other articles have verified spirometry for both sexes. It is observed that for almost all demographic details and pulmonary functions, girls tend to have lower mean values and narrower ranges than their counterparts, irrespective of ethnicity, methodology or testing instrument. Even the pooled mean (figs 4, 5, 6, 7) strikes the same result for all pulmonary indices. This aligns with the theory of Pulmonary physiology, that Pulmonary functions are directly dependent on height, and there is known sex-related differences in lung growth and thoracic development.[29, 30] The variability values calculated in Table 5 are based on combined (male + female) data.

TABLE 8 - Absolute and Relative difference in mean based on region/ethinicity					
Region	**Parameter**	**Range (L or L/s)**	**Absolute Difference of mean**	**Relative Difference of mean (%)**	**Interpretation and reason**
India (n = 5)	FVC	1.96 – 2.49	0.53	**27%**	Moderate variability; • Similar ethnicity • Protocol adherence • Minor methodological differences. • Device and calibration differences. • Variability in age and technique effects.
	FEV_1	1.65 – 2.14	0.49	**30%**	
	PEFR	3.40 – 5.11	1.71	**50%**	
	$FEF_{25-75}\%$	2.20 – 3.27	1.07	**49%**	
China / Taiwan (n = 5)	FVC	1.13 – 3.98	2.85	**252%**	Highest variability; • wide age range • multiple ethnic subgroups (Chinese, Korean Chinese, Taiwanese). • Variability in age adolescent and preschool • instrument heterogeneity. • equipment variability.
	FEV_1	1.06 – 3.67	2.61	**246%**	
	PEFR	2.66 – 7.86	5.20	**195%**	
	$FEF_{25-75}\%$	1.73 – 4.46	2.73	**158%**	
South America (n = 3)	FVC	1.34 – 2.74	1.40	104%	Moderate to high variation; • likely due to mixed ethnic composition. • Wide age range - preschoolers and adolescents.
	FEV_1	1.23 – 2.39	1.16	94%	
	PEFR	2.86 – 5.14	2.28	80%	
	$FEF_{25-75}\%$	1.64 – 2.94	1.30	79%	
Africa (n = 4)	FVC	2.37 – 3.10	0.73	**31%**	Moderate variability; • differing altitudes. • possibly fewer studies reporting mid-flows. • likely influenced by instrument and effort variation. (for PEFR)
	FEV_1	1.56 – 2.17	0.61	**39%**	
	PEFR	3.65 – 6.31	2.66	**73%**	
	$FEF_{25-75}\%$	2.13 – 2.94	0.81	**38%**	
Middle East (Iran, Saudi Arabia)	FVC	2.19 – 3.31	1.12	51%	Moderate variability; • equipment and population differences key.
	FEV_1	1.46 – 2.94	1.48	101%	
Absolute difference = (Mean2 – Mean1), Relative difference = [(Mean2 – Mean1)/Mean1]*100					

Age range Discrepancies

Age is a primary factor influencing pulmonary function in children, with lung function values generally increasing from infancy to adolescence due to lung growth and maturation. Age-specific reference values are crucial because factors like height, sex, and pubertal status interact with age, causing substantial changes in lung and airway development. This means that lung disease may manifest as a reduced rate of lung growth rather than as an outright decline in overall function.[31] The age range mentioned in the review ranges from 6 to 19 years. Hence, as the patterns of lung and airway growth undergo significant changes during puberty, there is a significant variation as age ranges in the review include children (continuously changing lung values) as well as adolescents (growth spurt leads to a sudden increase in lung functions).

Differences in Sample Size

A sufficient sample size in pulmonary function studies is crucial for developing accurate and reliable reference equations, as smaller samples can lead to increased variability and unreliable predicted values. Moreover, larger samples help minimize sampling error, reduce scatter, and provide power to identify genetic or other important factors influencing lung function.[32] However, the sample size was calculated in only 4 studies. In this review, the sample size noted was as low as 208 children (Mohamed Bougrida et. al., 2012) [23] to 4526 children (A. Alfrayh et. al., 2014) [26]. This variation in sample size may affect the normal distribution of data and, thus, the mean may not produce a generalized mean of the whole population.

Variations in methodology

The variation in the methodological processes may have led to a high level of heterogeneity in all pulmonary functions. The type of instrument used may be standardized, but the spirometers for different studies are different; this may affect the predictive values of PFT and lead to discrepancies in the results.

Sampling method is necessary for statistical inferences for the whole population. For most PFT studies (20 studies), sampling methods were not reported. If mentioned (9 studies) sampling techniques were variable for most of the studies. The sample size was calculated in only 4 studies.

In most studies, ATS guidelines were mentioned, but the procedure was not explained in depth. Mouthpiece is an inevitable part of spirometer, as it helps direct the air flow in the device. Even so, use of a mouthpiece for Spirometry was not mentioned in 19 studies; in contrast, only 9 studies mentioned its use. Nose clip is mandatory to prevent escape of air from the nose during PFT maneuvers. Yet the use of nose clip was mentioned only in 12 studies, and 3 studies suggested pinching of the nose by participants; the remaining studies did not mention whether a nose clip was used or not.

Furthermore, the preferred position for performing PFT is in a sitting position as it optimizes pulmonary function values due to the mechanical advantage to the respiratory muscles; however, in the guidelines of a few instruments standing position was used during PFT maneuver.[33] The position of the child was not reported in 6 articles, whereas 22 articles mentioned Spirometry in standing or sitting. It is clearly stated in the ATS guidelines to select the best from a minimum of three trials of the flow-volume loop, yet two studies did not mention the number of attempts that were performed.

Moreover, diurnal variations may affect PFT values by 20%.[34] 21 studies failed to report the time of day when PFT was performed on children. Furthermore, active and passive exposure to smoking has an impact on pulmonary growth and increases the risk of infections and respiratory weakness.[35] It also reduces pulmonary function values in children and adolescents. Only 8 studies that mentioned whether a history of exposure to active or passive smoking was taken for children/adolescents.

These methodological variabilities may be one of the primary factor in variations of the PFT values besides anthropometric and ethnic variables. Nevertheless, unlike later mentioned variables, methodological points like sample size, sampling technique, basic technique of administration, etc., can be easily modified. Hence, by the standardization of methods and techniques for spirometry, the variability in PFT values may be reduced to some extent not only for adults[36] but also for children.

Conclusion

This systematic review underscores the significant variability in normative pulmonary function values among healthy children from various populations and regions. The mean pulmonary function test (PFT) values exhibit considerable heterogeneity, ranging from 85% to 95%, with peak expiratory flow rate (PEFR) and forced expiratory flow at 25–75% ($FEF_{25–75}$%) displaying greater dispersion compared to forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). This variability reflects differences in age, body size, ethnicity, and methodological approaches across studies. Notably, Indian studies revealed a comparatively lower variability (27–50%) than those from East Asian or South American cohorts, indicating more consistent testing protocols, although methodological discrepancies remain.

Despite these regional differences, a consistent trend was observed across studies—boys demonstrated higher mean values and greater variability in FVC and FEV_1 compared to girls, and PFT values have a direct positive correlation with height and age. aligning with established sex-related differences in lung growth and thoracic development as documented in both Indian and international literature.

In summary, the findings highlight that a universal reference equation is inadequate for accurately representing pulmonary function in children from diverse backgrounds. There is a pressing need for region- and sex-specific reference standards derived from large, population-based cohorts utilizing uniform ATS/ERS-compliant methodologies. The establishment of such standardized normative data will improve the precision of spirometric interpretation, minimize the misclassification of respiratory impairment, and enhance clinical and epidemiological evaluations of pediatric lung health.

Clinical Implications:

1. The data provide a comprehensive synthesis of normative pediatric PFT data to guide clinical interpretation and future research.
2. Reference equations that correspond to the patient's age, sex, growth factors, and ethnicity should be used whenever possible by clinicians interpreting pediatric PFTs; in the absence of such equations, GLI (Global Lung Function Initiative) offers a helpful substitute, but it should be used with caution.
3. Inappropriate reference values may lead to misdiagnosis, which may result in an overdiagnosis or underdiagnosis of restrictive or obstructive patterns, with implications for surveillance and therapy.

Recommendations for future research

1. To provide current reference equations, a sizable population-based study using stratified sampling is required, particularly in underrepresented areas.
2. To enable better adjustment and stratification, future research should follow the ATS/ERS spirometry guidelines and record socioeconomic status, environmental exposures, sitting height, pubertal stage, and ethnicity in detail rather than in general terms.
3. Instead of using cross-sectional age/height adjustments, prediction models that take growth trajectories into account should be created. This will more accurately depict the quick physiological changes that occur between youth and adolescence.

Limitations:

1. There are only 22 studies included in this Systematic Review.
2. Articles published only in the English language were included; thus, data of articles from regions that are published in other languages (eg. the European dataset) were not included.
3. A wide range of age groups (6 years to 19 years) of children was included. This may be one of the causes for high variability in the result.
4. Many primary studies had incomplete reporting (lack of anthropometric detail, pubertal status, quality control), which reduced the ability to fully adjust or stratify results.
5. Geographical coverage was uneven – high-quality normative datasets from North and South America and Europe were lacking, limiting generalizability.
6. Possible publication bias - Studies with small samples or outliers, which do not conform to the norm, might not have been published or included in indexes.

Conflict of interest:

The authors have declared that there are no conflicts of interest.

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