# Playful strategy to improve the quality of spirometry and analysis of reference values in a group of schoolchildren from Asunción

Estrategia lúdica para mejorar la calidad de las espirometría y análisis de los valores de referencia en un grupo de escolares de Asunción

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#### **ABSTRACT**

Introduction. Children require special dedication to achieve high quality spirometry. Objective. This work evaluates the frequency of acceptable maneuvers in schoolchildren, the usefulness of incentive gestures to optimize the obtaining of high-quality tests, and performs an analysis of adjustments to several reference equations. Material and Methods. Forced expiratory maneuvers were performed in a group of schoolchildren from Asunción, Paraguay, choosing variables recommended for interpretation in a portable spirometer, to evaluate the frequency of high quality tests. Those who did not achieve acceptable studies were subjected to training with a roll whistle (toy) to evaluate their subsequent performance. The high-quality results were matched to expected values determined by various equations to evaluate adequacy. Results. Of 113 schoolchildren, 58,4% were able to achieve grade A or B maneuvers. After the stimulus with the roll whistle, the frequency of acceptable studies rose to 79,6%. The reference parameters with the best fit were those determined by the Global Lung Initiative (GLI). Conclusion. Playful incentives are an alternative to obtaining acceptable spirometry tests in schoolchildren, which, with the use of GLI parameters, would adjust the clinical management of certain respiratory diseases.

**Key words:** respiratory function tests; spirometry; forced expiratory volume; vital capacity; child

### Cómo citar/How cite:

Álvarez O, Aquino M, González S, Lemir R, Pérez Bejarano D. Playful strategy to improve the quality of spirometry and analysis of reference values in a group of schoolchildren from Asunción. Rev. cient. cienc. salud. 2024; 6: e6142. 10.53732/rccsalud/2024.e6142

Fecha de recepción: 02/04/2024 Fecha de revisión: 20/04/2024 Fecha de aceptación: 31/05/2024

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## **RESUMEN**

Introducción. Los niños requieren especial dedicación para lograr espirometrías de calidad. Objetivo. Este trabajo evalúa la frecuencia de maniobras aceptables en escolares, la utilidad de gestos de incentivo para optimizar la obtención de pruebas de alta calidad y realiza un análisis de ajuste a varias ecuaciones de referencia. Materiales y Métodos. Se realizaron maniobras espiratorias forzadas en un grupo de escolares de Asunción- Paraguay, escogiendo variables recomendadas para la interpretación en un espirómetro portátil, para evaluar la frecuencia de pruebas de calidad. Aquellos que no consiguieron estudios aceptables, fueron sometidos a un entrenamiento con silbato en rollo (juguete) para evaluar el desempeño ulterior. Los resultados de alta calidad fueron pareados a valores esperados determinados por diversas ecuaciones buscando evaluar el grado de adecuación. Resultados. De 113 escolares, el 58,4% pudo conseguir maniobras de grado A o B. Después del estímulo con el silbato en rollo, la frecuencia de estudios aceptables ascendió a 79,6%. Los parámetros de referencia con mejor ajuste fueron aquellos determinados por la Global Lung Initiative (GLI). Conclusión. Los incentivos lúdicos son una alternativa para optimizar la obtención de pruebas de espirometría en escolares, que con el uso de parámetros de GLI adecuarían el manejo clínico de ciertas enfermedades respiratorias.

Palabras clave: pruebas de función respiratoria; espirometría; capacidad vital; volumen espiratorio forzado; niño

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# **INTRODUCCIÓN**

Spirometry, while considered the gold standard for diagnosing and monitoring obstructive pulmonary diseases in children, is not widely utilized in daily medical practice<sup>(1)</sup>. Studies indicate that only 30% of children with asthma and 50% of those hospitalized for asthma receive functional testing during follow-ups<sup>(2,3)</sup>. This overreliance on primary clinical skills in primary care may contribute to the overdiagnosis of bronchial asthma. Objective measures, like spirometry, could play a crucial role in addressing this issue<sup>(4)</sup>.

In addition to the social, economic, and cultural factors influencing prescribing habits, there are two crucial variables to consider in ensuring the reliability of this diagnostic tool. Firstly, there is a need to develop a method for obtaining more accurate forced expiratory maneuvers. Secondly, it's essential to ensure that the measurements and values align with the parameters outlined in the most commonly used reference equations.

Obtaining high-quality forced expiratory maneuvers requires attention, cooperation, and coordination, particularly in certain age groups such as children. It's worth noting that variable rates of acceptable testing are reported in this demographic, emphasizing the critical nature of achieving accurate results in these cases<sup>(5,6)</sup>.

Representativeness is a crucial aspect to consider when establishing reference values for spirometric tests. The concept of having a unified source for these values aims to resolve debates regarding the most suitable parameters for categorizing respiratory diseases across different regions of the world. The Global Lung Function Initiative (GLI), led by the European Task Force, has extracted predictive values from a diverse range of ethnicities, including Caucasians, African-Americans, Asians, and others. This multi-ethnic approach, coupled with a wide age range and the innovative z-score interpretation method in  $\operatorname{GLI}^{(7)}$ , has been the subject of recent research. These studies have shown varying levels of agreement within adult and child populations, potentially due to inadequate representation of certain regions, such as South America, in the universal equation (8,9).

Our study sought to evaluate the feasibility of conducting high-quality spirometry, the effectiveness of incentivizing techniques to enhance its performance, and the compatibility with reference equations in a school-aged population in Asuncion, Paraguay.

# **METHODOLOGY**

A convenience sample of 140 children, from first to sixth grade, was selected from a public school in Asunción, Paraguay, whose parents received an information sheet, a health questionnaire, and a post-informed consent form. The cross-sectional study was conducted between March and April 2011 and was previously approved by the Teaching Committee of the Instituto Nacional de Enfermedades Respiratorias y del Ambiente (INERAM), a health care center of the Public Health Ministry (Paraguay).

Inclusion criteria were children aged 6-11 years who appeared healthy, without symptoms of respiratory diseases or neurological diseases that could prevent testing, and whose parents consented to the test and their inclusion in the study.

Exclusion criteria were a history of preterm birth or low birth weight, chronic respiratory disease, acute respiratory disease in the last four weeks, and home exposure to tobacco. Morbidly obese children were excluded according to WHO references<sup>(10)</sup>. For the purpose of equation-fit analysis, those children who failed to perform the forced expiratory maneuver were excluded.

Age was expressed in absolute numbers. If the kid was 6 months older from birth data, the greater age was recorded. Weight (kg) and height (cm) were measured using weighing scales, respectively. In accordance with the aforementioned tables and in accordance with WHO guidelines for assessing nutritional status, the body mass index (BMI = weight/height $^{(2)}$ ) was also recorded.

To rule out acute viral illnesses on the study day and to confirm the data gathered from the questionnaire, a survey was conducted. The physical examination conducted prior to the test was to find no signs of cardiorespiratory, neuromuscular, or thoracic deformity that might interfere with the subject's ability to exert themselves to their fullest potential.

The functional test was performed by an experienced physician (O.A.) with a portable spirometer (Easy-One, NDD Medical Technologies, Zurich, Switzerland), calibrated before the study with a 3L syringe and attachable to a laptop computer.

The following parameters were evaluated: forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1). The volume-flow and volume-time curves were also recorded as part of the test acceptability evaluation, together with an extrapolated volume of 5% of FVC and a minimum 3-second breath-hold as end-of-test criteria in < 10-year-old children and 6 seconds in those  $\ge$  10-year-olds, in accordance with ATS/ERS requirements<sup>(11)</sup>.

The effectiveness of incentive software (child blowing balloon cartoon, NDD Medical Technologies, Zurich, Switzerland) in achieving quality tests was evaluated. All those who did not get acceptable maneuver quality were asked to perform soft exhalation maneuvers in a brief play period with a blow whistle roll. After a rest period, the relative frequencies of grade A or grade B maneuvers (a 150 ml or 200 ml difference between FVC and FEV1, respectively) obtained before and after the incentive period were recorded. The test was performed standing and with the use of nasal forceps.

For the evaluation of the accuracy or fit of the observed FVC or FEV1 measurements, only post-incentive maneuvers graded A or B were taken. Expected parameters were extracted from the equations of  $GLI^{(12)}$  and from references proposed by  $Zapletal^{(13)}$ ,  $Polgar^{(14)}$ ,  $Polgar^{(15)}$ ,

Comparison of observed and predicted values, as well as the more reliable statistical technique known as the z score, were used to evaluate the fit of equations. The z score measures how close or how far the values obtained are, in terms of standard deviation, from the reference values (the z score is calculated by the ratio of the difference between the measured value and the predicted value with the residual standard deviation). The data was broken down into sex and age categories.

For the descriptive analysis, anthropometric data (gender, age, weight, and height) and functional variables (FVC and FEV1) are described. The scatter plot graph has been used, to evaluate the linear relationship between height and the values of FVC and FEV1 through the coefficient of determination (R2) that provides the model's goodness of fit.

To analyze the statistical difference between the measured value and the expected value of FEV1 and FVC, a t-test for related samples was performed. The same test was employed to analyze the difference between measured FVC and FEV1 and predict values expressed as GLI-2012 z-scores. The SPSS statistical package (v 11.5) was used for inferential analysis. The significance level was set at p<0.05.

The teaching committee of the Instituto Nacional de Enfermedades Respiratorias y Ambientales accepted the protocol's cross-sectional structure and ethical considerations (INERAM).

## **RESULTS**

Out of the 140 schoolchildren chosen, 113 (48 men) participated in the study of acceptability. Due to denial of permission, asthma, or a recent history of an upper respiratory infection, 27 kids were not included (Figure 1).

When applying incentive software, the frequency of acceptable and reproducible grade A and grade B maneuvers was observed in 58.4% of cases (n = 66). Between 6 and 7 years old, the proportion of grade C, D, or F maneuvers was significantly higher. After the

blow, whistle, and roll phases of play motivation, the overall percentage of high-quality spirometric tests was 79.6% (n = 90).

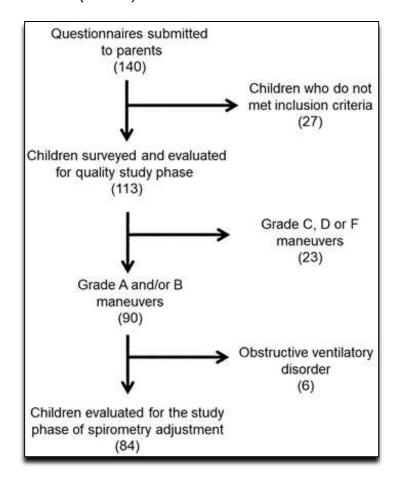


Figure 1. Study flowchart

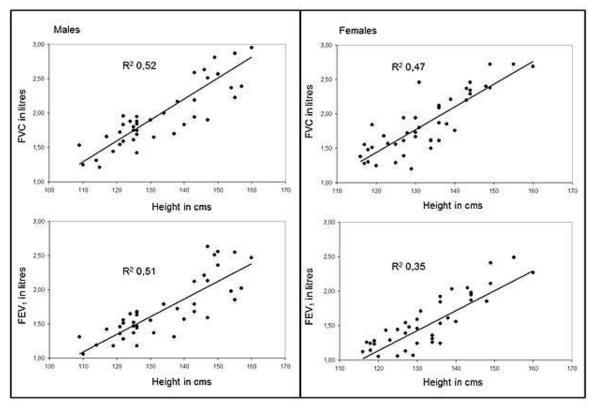
To assess the fit of the equations, 84 children (42 boys and 42 girls) who performed high-quality maneuvers were studied. In Table 1 the anthropometric features and functional test results are presented.

Table 1. Distribution, anthropometric and spirometric data of 84 school children in Paraguay according to three age groups.

Age group (y/o)	6-7		8-9		10-11	
Gender (N)	Males (13)	Females (14)	Males (14)	Females (16)	Males (13)	Females (14)
Height, cm	119,7 ± 5,5	122,3 ± 4,7	130,6 ± 6,4	132,8 ± 4,8	148,1 ± 7,7	142,9 ± 10
Weight, kg	23 ± 2,1	24 ± 4,6	28,1 ± 5,1	29,7 ± 4,3	40,2 ± 9,6	36,8 ± 3,7
IMC	16 ± 1,2	16 ± 0,2	16,4 ± 0,2	16,8 ± 0,2	18,3 ± 0,1	18 ± 0,7
FVC (L)	1,57 ± 0,2	1,49 ± 0,2	1,94 ± 0,4	1,85 ± 0,3	2,40 ± 0,4	2,22 ± 0,4
FEV <sub>1</sub> (L/s)	1,34 ± 0,2	1,21 ± 0,1	1,62 ± 0,3	1,48 ± 0,3	2,05 ± 0,3	1,82 ± 0,4

ISSN: 2664-2891

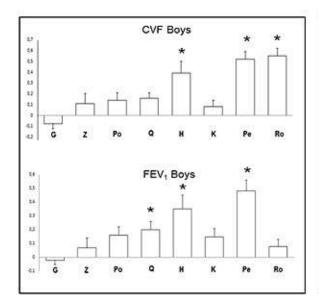
In both sexes, spirometric parameters rise with age and height, with varying degrees of dispersion. A non-uniform distribution may be seen when the relationship between these values and height is plotted, with FEV1 having the most pronounced non-uniformity in females (Figure 2).

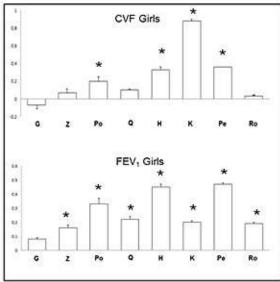


**Figure 2.** Scatter-plot of FVC and FEV1 values related to height in school children of both sexes.

The coefficient of variation, which represents the inter-individual variance of the expiratory maneuvers, was on average 16,4% (range 13,2 to 19,6%) for FVC and 16,7% (range 12,2 to 19,4) for FEV1 for boys. The FVC and FEV1 of the girls in the sample were 14,6% (range 10,3 to 18,3%) and 14,2% (range 11,9 to 18,5%), respectively.

When comparing the values predicted by the Zapletal, Polgar, Quanjer, Hankinson, Knudson, Perez-Padilla, and Rosenthal equations with the values measured in our population, we note that there are significant (p 0.05) scattered differences for the FVC, the FEV1, or both. The values predicted by the GLI did not present differences when compared with the measured parameters (Figure 3).





Mean and standard error of the difference between the observed and expected value for forced vital capacity, expressed (FVC) and forced expiratory volume in one second expressed (FEV1) using the equations of Global Lung Initiative (G), Zapletal (Z), Polgar (Po), Quanjer (Q), Hankinson(H), Knudson (K), Perez-Padilla (Pe) and Rosenthal (R). \*p < 0.05.

**Figure 3.** Differences between Expected and Measured Values According to Most Used Equations in Spirometry in School Children from Paraguay.

Except for the GLI, there are absolute differences of more than 100 ml between the measured values and the values predicted by all of the equations tested (Table 2).

**Table 2.** Agreement between the Observed Values of FVC and FEV1, and Those Expected by the Prediction Equations in schoolchildren

Equations	∆FVC boys	∆FEV1 boys	∆FVC girls	∆FEV1 girls
GLI	-80±116	-20±79	-70±5	80±39
Zapletal	110±221	70±172	70±57	160±61*
Polgar	140±170	160±134	200±140*	330±130*
Quanjer	160±121	20±155*	100±22	220±43*
Hankinson	390±147*	350±137*	330±9*	450±15*
Knudson	80±145	150±145	880±56*	200±51*
Pérez-Padilla	520±71*	480±93*	360±-58*	470±7*
Rosenthal	550±173*	80±130	30±44	190±53*

The mean of the differences was obtained by subtracting the predicted value from the measured value and expressed in milliliters for forced vital capacity, expressed (FVC) and forced expiratory volume in one second (FEV1) using the equations of Global Lung Initiative (GLI), Zapletal, Polgar, Quanjer, Hankinson, Knudson, Perez-Padilla and Rosenthal. \* p< 0,05.

When all of the spirometric variables are reported as GLI 2012 z-scores, the measured variables for both sexes exhibit significant but inconsistent changes when compared to the projected values. The Hankinson and Knudson estimates are the exception.

**Table 3.** Differences between measured FVC and FEV1 and predicted values expressed as GLI-2012 z-scores in school children of Paraguay

Equations	FVC Z-score boys	FEV <sub>1</sub> Z-score boys	FVC Z-score girls	FEV <sub>1</sub> Z-score
Measured 0,47±0,64		0,14±0,47	0,14±0,47	0,14±0,47
Zapletal	0,83±0,27	0,39±0,37*	0,83±0,27	0,39±0,37
Polgar	1,02±0,09	0,87±0,29*	1,02±0,09	0,87±0,29*
Quanjer	1,07±0,20*	1,01±0,31	1,07±0,20	1,01±0,31*
Hankinson	0,87±0,27	0,44±0,70	0,87±0,27	0,44±0,70
Knudson	0,28±1,00	0,38±0,93	0,28±1,00	0,38±0,93
Pérez-Padilla	1,32±0,32	1,26±0,27	1,32±0,32*	1,26±0,27*
Rosenthal	2,97±0,41*	0,45±0,25*	2,97±0,41*	0,45±0,25

Z-scores of measured and predicted values were obtained using GLI (Global Lung Function Initiative) software and are expressed as mean  $\pm$  standard deviation. Forced vital capacity, expressed (FVC) and forced expiratory volume in one second (FEV1). Zapletal, Polgar, Quanjer, Hankinson, Knudson, Pérez-Padilla and Rosenthal. \*p<0,05.

## **DISCUSSION**

The prevalence of asthma, the most common chronic respiratory condition in children, has a substantial adverse impact on the quality of life of children and is a significant driver of healthcare resource utilization<sup>(20)</sup>. Current therapeutic practices for this patient population often fall short of recommended standards, particularly due to the underutilization of spirometry, which is considered the gold standard for diagnosis<sup>(1,21)</sup>. Surprisingly, spirometry is only utilized by a limited percentage of primary care doctors (12%-75%) and pediatricians (25%-50%) across different countries, with a significant lack of confidence in interpreting these test results<sup>(22,23)</sup>. This reliance on clinical history alone may lead to a failure to detect a substantial proportion of obstructive airway disorders, resulting in potential overdiagnosis and unnecessary treatment<sup>(24)</sup>. As a result, it is crucial to recognize the limitations of relying solely on clinical history and to prioritize the adoption of spirometry to improve diagnostic accuracy and reduce the risk of overdiagnosis<sup>(25)</sup>.

There are several reasons why the use of this diagnostic test is limited, such as its cost, difficulty in interpretation, lack of time in the office, equipment availability, and patient difficulties in performing the test<sup>(22)</sup>. To achieve accurate respiratory maneuvers, cooperation and collaboration are necessary. However, this can result in varying percentages of technically acceptable outcomes, particularly in children, who benefit from the use of techniques to optimize forced expiration exercises. Improving spirometry standards in children can be achieved through additional training time and the utilization of incentive computer applications. By investing in these areas, healthcare providers can improve the accuracy and reliability of respiratory assessments in pediatric patients, ultimately leading to better overall care.

There is debate over the data generated by stimulation software. Gracchi and cols. have found that the prior use of these resources can negatively impact the reproducibility and performance of forced expiratory maneuvers<sup>(26)</sup>, while Vilozni and cols. were able to achieve better results when comparing two different animation software<sup>(27)</sup>. In this study, we adhered to the most recent recommendations for spirometry standardization and utilized this resource consistently in our bilingual population<sup>(28)</sup>. Only 58.4% of the people had tests that were acceptable and reproducible across the board and without training prior to the experiment. According to Tomalak et al., only 50.21 percent of the 233 children

Rev. cient. cienc. salud. 2024; 6: e6142 ISSN: 2664-2891

cienc. salud. 2024; 6: e6142

under the age of 10 who participated in the study fully cooperated. The most common reasons for test failure included improper breathing techniques, a lack of a peak in expiratory flow, respiratory effort variables, and even a lack of interest. Only 23,9%, even the ones who were cooperative, were able to exhale for more than three seconds. The maneuvers were performed without any training or computational incentives<sup>(6)</sup>. In 109 spirometric tests conducted on kids between the ages of 6 and 15, Zanconato et al. obtained unacceptable results in 22% of the cases and incorrect interpretations in 21% of the cases. However, prior instruction or rewards before or during the execution are not entirely clear<sup>(29)</sup>. The same spirometer model was used in a sample of 3,133 healthy children between the ages of 4 and 18, and it was discovered that 82.6% of those children met the extrapolated volume and reproducibility criteria. However, when the end-of-test criterion was added, the quality of the spirometry dropped to 39.7%<sup>(30)</sup>. Compared to 92% of tests completed in pulmonary function laboratories, 63% of spirometry tests conducted by patients at home met valid technical criteria<sup>(31)</sup>. This suggests the significance of a technician's or professional's assistance and/or the necessity of a set training period supported by amusing stimuli and/or assistance software, for proprioceptive training and audiovisual feedback, seeking to maximize performance. Van Delden et al. recommend a set of requirements for incentive metaphors—the authors' term for computer programs along with a number of optional games in order to produce high-quality results<sup>(32)</sup>.

A prior training period is not usual before performing spirometry and this aspect leads our experiment to a real practice field with an interesting practical proposal. A game period was used with the blow whistle roll in the sample that was examined here, but only for those who did not pass the test the first time. With this action, the percentage of acceptable and repeatable results rose to 79.6%. The rate of achievement in specific populations may be further optimized by home training recommendations given prior to visiting the pulmonary function laboratory and/or after failing to pass a quality test on the test day. Arets et al. used computer applications to obtain > 90% extrapolated volume and 15.3% forced expiratory time as end-of-test criteria in 446 schoolchildren who, on average, had previously undergone at least two spirometric tests. In other words, the people were already trained<sup>(33)</sup>.

The national literature lacks analyses that effectively align reference parameters with spirometry test results in Paraguayan children, potentially leading to confusion in diagnosing and treating obstructive lung diseases. Among the eight equations tested, the values provided by GLI were deemed the most suitable for this study due to their minimal difference between expected and observed values, which was not statistically significant. Hall et al. considered a z score difference > 0.5 in FVC or FEV1 values between sexes significant when using the Zapletal, Polgar, Quanjer, Pérez-Padilla, and Rosenthal equations<sup>(34)</sup>.

GLI predicted values are obtained by more reliable statistical methods (Generalized Additive Models of Location, Scale, and Shape, or GAMLSS) rather than linear regression models like Rosenthal et al., which is one of the reasons for better adjustment<sup>(35)</sup>. GLI was developed using data from different ethnic groups and a continuous age distribution rather than an age group like Hankinson<sup>(36,37)</sup>.

The FVC and FEV1 values obtained from children in  $France^{(38)}$ , Australia<sup>(34)</sup>, England<sup>(39)</sup>, and sub-Saharan Africa<sup>(40)</sup> are consistent with the GLI reference values, according to two studies<sup>(38,39)</sup>. These prediction equations, however, do not accurately match the spirometric data from children from Taiwan<sup>(41)</sup>, Jordan<sup>(42)</sup> and Brazil<sup>(43)</sup>.

In order to turn auxiliary techniques into trustworthy instruments for decision-making, numerous epidemiological studies on children's lung function have emerged in other nations. The use of the lower limit of normality (LLN) rather than predetermined cut-off points to establish diagnostic thresholds suggests a greater degree of individual adjustment, taking anthropometric and demographic information into account. On the

other hand, using the Z score as a tool for expressing results and a measure of dispersion has the benefit of allowing value comparisons across gender, height, age, and ethnicity<sup>(44)</sup>.

Our study has some limitations. The sample comes from one educational institution in the capital, which makes it difficult to extrapolate the results. It is critical to conduct studies with larger samples that take into account the rural, urban, and ethnic diversity of our nation. The ATS/ERS technical recommendations for spirometric quality have recently been updated, but it should be noted that the technical standard for "forced exhalation" (variation of 0.025-L in 1 second or forced exhalation time of 11-15 seconds, or failure to continue from exhalation to a plateau) is mostly derived from 28 studies in adults 28.

We conclude that: a) most of the schoolchildren perform good forced expiratory behaviors; b) the playful nature of the experiment significantly increases the percentage of participants that perform acceptable and repeatable exercises; and c) GLI reference values are those that best match in this cohort.

Conflict of interest: No conflict of interest.

**Authors' Statement:** The authors approve the final version of the article.

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**Financing:** Autofinanciado.

### REFERENCIAS BIBLIOGRÁFICAS

- Reddel H K, Bacharier LB, Ateman ED et al. Global Inititive for Asthma (GINA) Strategy 2021: executive summary and rationale for key changes. Eur Res J 2021. <a href="https://erj.ersjournals.com/content/59/1/2102730">https://erj.ersjournals.com/content/59/1/2102730</a>
- Bianchi M, Clavenna A, Sequi M, Bortolotti A, Fortino I, Merlino L et al. Spirometri testing in a population of Italian children: age and gender differences. Respir Med. 2012;106(10):1383-1388. <a href="https://doi.org/10.1016/j.rmed.2012.06.005">https://doi.org/10.1016/j.rmed.2012.06.005</a>
- 3. Bianchi M, Clavenna, Sequi M, Bortolotti A, Fortino I, Merlino L, et al. Childhood asthma management pre- and post- incident asthma hospitalization. PLoS One. 2013;8:e76439. https://doi.org/10.1371/journal.pone.0076439

- 4. Aaron SD, Boulet LP, Reddel HK, Gershon AS. Underdiagnosis and Overdiagnosis of Asthma.Am J RespirCrit Care Med. 2018;198(8):1012-1020. https://doi.org/10.1164/rccm.20180 4-0682CI
- Enright PL, Linn WS, Avol EL, Margolis HG, Gong Jr H, Peters JM. Quality of spirometry test performance in children and adolescents: experience in a large field study. Chest. 2000;118(3):665-671. <a href="https://doi.org/10.1378/chest.118.3">https://doi.org/10.1378/chest.118.3</a>
   .665
- Tomalak W, Radlinski J, Latawiec W. The quality of spirometric measurements in children younger than 10 years of age in the light of recommendations. Adv. Respir. Med. 2008;76(6):421–425. https://doi.org/10.5603/ARM.27860

- 7. Quanjer PH, Stanojevic P, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J 2012;40(6):1324-1343 https://doi.org/10.1183/09031936.0 0080312
- 8. Lum S, Bountziouka V, Quanjer P, Sonnappa S, Wade A, Beardsmore C, et al. Challenges in collating spirometry reference data for southasian children: an observational study. PLoS ONE. 2016;11(4):e0154336. https://doi.org/10.1371/journal.pone.0154336
- Caussade S, Contreras I, Villarroel L, Fierro L, Sanchez I, Bertrand P, et al. Valores espirométricos en niños y adolescentes chilenos sanos. Rev. méd. Chile. 2015;143(11):1386-1394. <a href="https://doi.org/10.4067/S0034-98872015001100003">https://doi.org/10.4067/S0034-98872015001100003</a>
- World Health Organization. Growth reference data for 5-19 years /Indicators/BMI-for-age (5-19 years). <a href="https://www.who.int/tools/growth-reference-data-for-5to19-years/indicators/bmi-for-age">https://www.who.int/tools/growth-reference-data-for-5to19-years/indicators/bmi-for-age</a>
- 11. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):219-338. https://doi.org/10.1183/09031936.0 5.00034805
- European Respiratory Society / Global Lung Function Initiative (GLI). GLI calculators for Spirometry, TLCO and Lung Volume. 2021. <a href="http://glicalculator.ersnet.org/">http://glicalculator.ersnet.org/</a>
- Zapletal A. Lung function in Children and Adolescents: Methods, reference values. Prog Respir Res. 1987;22:113-218. <a href="https://doi.org/10.1159/isbn.978-3-318-04125-5">https://doi.org/10.1159/isbn.978-3-318-04125-5</a>
- 14. Polgar G, Promadhat V. Standard values. In: Pulmonary function testing in children: techniques and standards. Philadelphia: W.B. Saunders; 1971. p. 87–212.

- 15. Quanjer PH, Stocks J, Polgar G., Wise M., Karlberg J., and Borsboom G. Compilation of reference values for lung function measurements in children. Eur Res J. 1989;4:1845–261S.
- 16. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. Population. Am J Res Crit Care Med 1999;159(1):179–187. https://doi.org/10.1164/ajrccm.159. 1.9712108
- 17. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in normal maximal expiratory flow-volume curve with growth and aging. Am Rev Respir Dis. 1983;127(6):725–34. https://pubmed.ncbi.nlm.nih.gov/68 59656/
- 18. Pérez-Padilla R, Regalado-Pineda J, Mendoza L, Rojas R, Torres V, Borja-Aburto V, et al. Spirometric variability in a longitudinal study of school-age children. Chest. 2003;123(4):1090-1095. https://doi.org/10.1378/chest.123.4.1090
- 19. Rosenthal M, Bain SH, Cramer D, Helms P, Denison D, Bush A, Warner JO. Lung function in white children aged 4-19 years: I-Spirometry. Thorax. 1993;48(8):794-802. https://doi.org/10.1136/thx.48.8.794
- 20. Ferrante G, La Grutta S. The Burden of Pediatric Asthma. Front Pediatr. 2018;6:186. https://doi.org/10.3389/fped.2018. 00186
- 21. Gaillard EA, Kuehni CE, Turner S, Goutaki M, Holden KA, de Jong C, et al. European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5–16 years. EurRespir J. 2021;58(5):2004173. https://doi.org/10.1183/13993003.04173-2020
- 22. Vanjare N, Chhowala S, Madas S, Kodgule R, Gogtay J, Salvi S. Use of spirometry among chest physicians and primary care physicians in India. npj Prim Care Respir Med. 2016;26:16036.

# https://doi.org/10.1038/npjpcrm.20 16.36

- 23. Dombkowski KJ, Hassan F, Wasilevich EA, Clark SJ. Spirometry use among pediatric primary care physicians. Pediatrics. 2010;126(4):682-7. https://pubmed.ncbi.nlm.nih.gov/20819894/
- 24. Mannino DM, Buist AS, Petty TL, Enright PL, Redd SC. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. Thorax. 2003;58(5):388-93. https://doi.org/10.1136/thorax.58.5.388
- 25. Looijmans-van den Akker I, van Luijn K, Verheij T. Overdiagnosis of asthma in children in primary care: a retrospective analysis. Br J Gen Pract. 2016;66(644):e152-7. https://doi.org/10.3399/bjgp16X683
- 26. Gracchi V, Boel M, van der Laag J, van der Ent CK. Spirometry in young children: should computer-animation programs be used during testing? Eur Respir J 2003; 21: 872–875. <a href="https://doi.org/10.1183/09031936.0">https://doi.org/10.1183/09031936.0</a> 3.00059902
- 27. Vilozni D, Barker M, Jellouschek H, Heimann G, Blau H. An interactive computer-animated system (SpiroGame) facilitates spirometry in preschool children. Am J Respir Crit Care Med. 2001;164(12):2200–2205. https://doi.org/10.1164/ajrccm.164. 12.2101002
- 28. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med. 2019;200(8):e70-e88.

  https://doi.org/10.1164/rccm.201908-1590ST
- 29. Zanconato S, Meneghelli G, Braga R, Zacchello F, Baraldi E. Office spirometry in primary care pediatrics: a pilot study. Pediatrics.

- 2005;116(6):e792-7. https://doi.org/10.1542/peds.2005-0487
- 30. Müller-Brandes C, Krämer U, Gappa M, Seitner-Sorge G, Hüls A, von Berg A, et al. LUNOKID: can numerical American Thoracic Society/European Respiratory Society quality criteria replace visual inspection of spirometry? Eur Respir J. 2014;43(5):1347-56. https://doi.org/10.1183/09031936.0 0058813
- 31. van der Kamp MR, Klaver EC, Thio BJ, Driessen JMM, de Jongh FHC, Tabak M, et al. WEARCON: wearable home monitoring in children with asthma reveals a strong association with hospital based assessment of asthma control. BMC Med Inform Decis Mak. 2020;20(1):192. https://doi.org/10.1186/s12911-020-01210-1
- 32. van Delden R, Plass Oude Bos D, de With V, Vogel K, Klaassen R, Zwart, N, et al. SpiroPlay, a Suite of Breathing Games for Spirometry by Kids & Experts. ACM Publishing. 2020. <a href="https://doi.org/10.1145/3410404.34">https://doi.org/10.1145/3410404.34</a> 14223
- 33. Arets HG, Brackel HJ, van der Ent CK. Forced expiratory manoeuvres in children: do they meet ATS and ERS criteria for spirometry? Eur Respir J. 2001;18(4):655-60. https://doi.org/10.1183/09031936.0 1.00204301
- 34. Hall GL, Thompson BR, Stanojevic S, Abramson MJ, Beasley R, Coates A, et al. The Global Lung Initiative 2012 reference values reflect contemporary Australasian spirometry. Respirology. 2012;17(7):1150–1151. https://doi.org/10.1111/j.1440-1843.2012.02232.x
- 35. Palamarchuk P. Elaboración de curvas de referencia normales de espirometría en niños uruguayos mediante modelos GAMLSS. [Tesis de grado]. Universidad de la República. Uruguay. 2017. https://hdl.handle.net/20.500.1200

- 36. Quanjer PH, Hall GL, Stanojevic S, Cole T, Stocks J. Age-and height-based prediction bias in spirometry reference equations. Eur Respir J. 2012;40(1):190-197. https://doi.org/10.1183/09031936.0 0161011
- 37. Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, et al. Reference ranges for spirometry across all ages: a new approach. Am J Respir Crit Care Med. 2008;177(3):253-60. https://doi.org/10.1164/rccm.200708-12480C
- 38. Nève V, Machuron F, Behal H, Howsam M, Methlin CM, Delille C, et al. Global Lung Initiative spirometry references in healthy 3-15-year-old French children. ERJ Open Res. 2019;5(3):00023-2019. https://doi.org/10.1183/23120541.00023-2019
- 39. Bonner R, Lum S, Stocks J, Kirkby J, Wade A, Sonnappa S. Applicability of the global lung function spirometry equations in contemporary multiethnic children. Am J Respir Crit Care Med. 2013;188(4):515–516. https://doi.org/10.1164/rccm.20121 2-2208LE
- 40. Arigliani M, Canciani MC, Mottini G, Altomare M, Magnolato A, Vanda Loa Clemente S. Evaluation of the Global Lung Initiative 2012 reference values

- for spirometry in African children. Am J Respir Crit Care Med. 2017;195(2):229–236. https://doi.org/10.1164/rccm.201604-0693OC
- 41. Chang SM, Tsai HJ, Tzeng JY, Kuo-Wei Yeh, Li-Chen Chen, Shen-Hao Lai, et al. Reference equations for spirometry in healthy Asian children aged 5 to 18 years in Taiwan. World Allergy Organ J. 2019;12(11):100074.

  https://doi.org/10.1016/j.waojou.20 19.100074
- 42. Al-Qerem W. Spirometry reference equations for children from a Middle Eastern population. Int J ClinPract. 2021;75(10):e14598. https://doi.org/10.1111/ijcp.14598
- 43. Jones MH, Vidal PCV, Lanza FC, França de Melo Franco Silva DC, Pitrez PM, Bigliardi de Freitas Olmedo AP, et al. Reference values for spirometry in Brazilian children. J Bras Pneumol. 2020;46(3):e20190138. https://doi.org/10.36416/1806-3756/e20190138
- 44. Ben Salah N, Bejar D, Snène H, Ouahchi Y, Mehiri N, Louzir B. The Z-score: A new tool in the interpretation of spirometric data. Tunis Med. 2017;95(8-9):767-771. <a href="https://latunisiemedicale.com/index.php/tunismed/article/view/3289">https://latunisiemedicale.com/index.php/tunismed/article/view/3289</a>