

Global Lungs Initiative

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A European Respiratory Society/American Thoracic Society (ERS/ATS) Task Force was funded in 2009 to establish improved lung function reference values. The task force chairs are Janet Stocks, Xaver Baur, Graham Hall, and Brian Culver.

The group has met over the past two years at the ERS and ATS meetings, with an extraordinary amount of work occurring between meetings. An editorial group including Janet Stocks, Xaver Baur, Graham Hall, Philip Quanjer, and Sanja Stanojevic was formed to publish appropriate material on the Global Lungs Initiative (GLI) website and disseminate a newsletter. The Steering Committee includes the following members: Janet Stocks and Xaver Baur (ERS), Graham Hall (Australian & New Zealand Society of Respiratory Science), Bruce Culver (ATS), Jinping Zheng and Mary Ip (Asian Pacific Society of Respiriology), Sanja Stanojevic, Tim Cole, Paul Enright, John Hankinson, and Philip Quanjer.

Attendance at the GLI meetings has brought representatives from all areas of the globe, including pulmonary function technologists, researchers, physicians, and manufacturers, together to review, discuss, and provide updates on the task force progress.

As of the fall 2010, over 50 groups were sharing data with the GLI related to reference values in multiple populations across the world. Papers have already been published from the data analyzed, and many more are forthcoming. This work is building a platform for reference values globally. The GLI has provided an explanation with working examples for software engineers to use when incorporating forthcoming regression equations into software. Manufacturers have been welcomed and included in the GLI process since the onset of the task force.

New findings from the data analysis have been presented at each GLI meeting. The initial focus is on spirometry. Phase 1 of the project has resulted in the following information:

- A paper was published regarding the changes related to age and FEV₁/FVC: Quanjer PH, Stanojevic S, Stocks J, Hall GL, *et al.* Changes in the FEV₁/FVC ratio during childhood and adolescence: an intercontinental study. *Eur Respir J* 2010;36:1391-1399.
- Specific difficulties in analyzing the current data include the lack of recording ethnicity; so many results had to be excluded and a limited age range was available for many studies, leaving a paucity of data for the very old and very young.
- In the Caucasian population, there is no evidence that secular trends have influenced lung function over the past three decades, probably reflecting the relative socioeconomic stability over this period in Europe, North America, and Australia, the countries from which the majority of these data were derived. This may be different in developing countries.
- Of great importance is the understanding of an appropriate sample size to validate a reference equation properly; a sample size of 300 (150 males, 150 females) is required. Similarly, reference equations based on sample size <300 are likely to show spurious differences from other equations purely due to sampling error. (See Quanjer

PH, Stocks J, Cole TJ, Hall GL, Stanojevic S. Influence of secular trends and sample size on reference equations for lung function tests. *Eur Respir J* 2011;37:658-664.)

- With the exception of the elderly, there does not appear to be any need to collect further spirometry reference data in white subjects.

The GLI group has demonstrated that use of 80% predicted as a cut off is only applicable in a narrow age range in adults. This is a critical issue related to the GOLD standards and interpretation of lung function results.

Phase 2 of the project is designed to investigate the quality control criteria for the studies and their influence on the data. The review of adult studies has been led by John Hankinson, PhD. It has been expressed that an experienced human eye was far superior to computerized over-reads, which may be misleading. Results from this study will be published and could influence further changes to the ATS/ERS spirometry guidelines. The same process will be applied in pediatric studies.

The Stanojevic “all-age” equations had been incorporated by many of the manufacturers as of May 2011. Although the Stanojevic equations are restricted to Caucasian populations, they are based on exactly the same format as now being used for the GLI equations. Consequently, any manufacturer who has implemented the Stanojevic equations will easily be able to upgrade to the GLI equations as soon as these have been approved by the main respiratory societies and peer-reviewed for publication. Using all-age equations will bridge the breaks in age changes that can often result in misinterpretation of the results and misdiagnosis. Unfortunately, data received to date from the Indian subcontinent were too disparate, with unusually large coefficients of variation, particularly in children. No data are available from sub-Saharan Africa and most large Asian countries.

The GLI task force is investigating a method to establish a safe repository for the data that could make it available to other researchers in the future. This will require development of a data sharing policy, identification of a location for the data repository, and establishment of a protocol for sharing and using these data.

A new project has been proposed to review reference values for DLCO measurements.

This is likely one of the most important projects undertaken in pulmonary function testing. I would encourage each of you to access and review the data published to date and watch for subsequent articles to be published as the project continues. Reference values are a critical component of accurate interpretation of pulmonary function data and subsequent clinical decisions.

Additional References

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- Stanojevic S, Wade A, Stocks J. Reference values for lung function: past, present and future. *Eur Respir J* 2010; 36: 12-19. **Author’s Note:** Good overview including explanation of Z-scores.

For additional information, visit the [GLI](#) website.