Longitudinal assessment of lung function decline in the occupational setting

Carrie A. Redlich[a] *and Susan M. Tarlo*[b]

Purpose of review
Spirometry is performed in the work setting as part of medical surveillance of workers with potentially respiratory hazardous work exposures, to identify early disease and evaluate the effectiveness of preventive interventions. However, many clinicians are not familiar with workplace medical surveillance and how to evaluate longitudinal spirometry over time.

Recent findings
A recent American Thoracic Society technical standards report addressed issues related to performing spirometry in the work setting, including the interpretation of longitudinal lung function. Important considerations in assessing longitudinal lung function are reviewed. Recent studies evaluating the impact of selected occupational exposures on longitudinal lung function are reviewed.

Summary
Recent longitudinal studies of exposed workers have identified novel occupational respiratory diseases such as flavoring-related lung disease, and advanced our understanding of more familiar exposures such as mineral dusts. Clinicians will increasingly need to be able to evaluate longitudinal spirometry, including thresholds that trigger further evaluation.

Keywords
annual decline FEV_1, FEV_1, longitudinal spirometry, medical surveillance, occupational health, spirometry, workplace

INTRODUCTION: LONGITUDINAL SPIROMETRY – WHEN AND HOW

Pulmonary function variables assessed from spirometry have been used in the diagnosis and management of respiratory diseases for over 150 years. In addition, spirometry is widely used in research to identify lung function changes over time that may be associated with aging, genetic factors, disease progression, medication effects, environmental exposures and other factors. The methodology is well established, and when performed correctly the results show good reproducibility. Standards for the performance of spirometry have been published in a combined official American Thoracic Society and European Thoracic Society (ATS/ERS) statement in 2005. These standards include requirements for calibration of equipment, use of appropriate comparison reference values, corrected for age, sex and height, need for repeat efforts and criteria for determining reproducibility of the tests and interpretation strategies. When spirometry is performed in accredited pulmonary function laboratories using these criteria, there can be confidence in the results.

However, spirometry is also often performed outside of pulmonary function laboratories, for diagnosis or follow-up of patients in medical office settings (primary care or specialist), for workplace surveillance of employees or for research purposes. Although the ATS/ERS guidelines [1,2] have mainly been directed to test performance in pulmonary function laboratories, the same criteria would ideally be met when these tests are performed in other settings. However, there are differences that may cause difficulties. First, the training of those performing the tests may be different: a nurse or an

[a]Pulmonary Section and Occupational and Environmental Medicine, Department of Medicine, Yale School of Medicine, New Haven, Connecticut, USA and [b]Department of Medicine and Dalla Lana School of Public Health, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada

Correspondence to Carrie A. Redlich, MD, MPH, Professor of Medicine, Yale Occupational and Environmental Medicine Program, Yale School of Medicine, 135 College Street, Room 366, New Haven, CT 06510, USA. Tel: +1 203 785 6434; fax: +1 203 785 7391; e-mail: carrie.redlich@yale.edu

Curr Opin Allergy Clin Immunol 2015, 15:145–149
DOI:10.1097/ACI.0000000000000153

1528-4050 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

KEY POINTS

- Spirometry is performed in the work setting as part of medical surveillance of workers with potentially respiratory hazardous work exposures, to identify early disease and also to evaluate the effectiveness of preventive interventions.
- Important aspects of workplace spirometry are discussed, including approaches to identify excessive loss of lung function over time. There are several approaches to determine if a decline in FEV_1 over time is excessive. Easiest is to determine whether the observed decline in FEV_1 from initial baseline spirometry to follow-up is >15%, taking into account age-related change in FEV_1. Alternatively, available software can be used to determine annual decline in FEV_1 using the limit of longitudinal decline approach or linear regression.
- Workplace exposures associated with accelerated decline in lung function include mineral dusts, silica, metals, organic materials and butter flavorings.

assistant in a primary care setting or workplace, or a research assistant in a research study may perform these tests with minimal training. Another important aspect of performing spirometry in an occupational setting, as recently addressed in an ATS Technical Standards Report [3▪▪], is consideration of appropriate reference values (because a workplace for example in the United States may have a large proportion of workers who are Hispanic or of African-American ethnicity). Another important aspect that was addressed is the issue of longitudinal changes in spirometry, expanding on the recommendations from the ATS/ERS guidelines.

Clinically, assessing longitudinal changes in spirometry has been useful for an individual patient, in conjunction with symptoms and other markers, as a indicator to objectively determine changes in pulmonary disease over time. For patients with chronic obstructive lung disease (COPD), the severity of airflow limitation has been used to categorize the severity of disease, based on the presence of flow limitation demonstrated by a reduced forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio and a severity rating based on the postbronchodilator FEV_1. Repeat spirometry over time can be used to monitor progression of COPD. For patients with asthma, repeat spirometry while the patients are taking their usual asthma medication provides an objective component to longitudinal follow-up, also recognizing that variable airflow limitation is a feature of asthma, and therefore the results at each time point, even with medications, may not be representative of overall control. Nevertheless, an aim of asthma control is to reduce airflow variability, and therefore, the longitudinal pattern may allow some assessment of this in addition to the immediate response. For patients with restrictive lung diseases, a diagnosis cannot be made on the basis of spirometry without additional lung volumes and diffusing capacity, but once a diagnosis has been made, serial spirometry can be useful to assess progressive changes in FVC that may relate to disease progression or responses to treatment, and this has been used as a primary end point in major research studies assessing the efficacy of treatment [4]. Correct interpretation of these longitudinal changes requires consideration of the technical performance of the test, the adequacy and reproducibility of the patient performance, and knowledge of other factors that can affect the test such as changes in test equipment, changes in reference values used and change in patient factors such as weight and respiratory muscle function that can affect lung volumes.

In primary care management, there has been emphasis on the performance of spirometry in smokers, as the results may provide an incentive to quit smoking [5] in addition to smoking cessation advice, and recent guidelines have addressed the performance of spirometry in the primary care setting [6]. Similarly, for the many asthmatic patients followed in primary care, spirometry can add to optimum management when well performed and interpreted.

USE OF SPIROMETRY AS PART OF A MEDICAL SURVEILLANCE PROGRAM

In the occupational setting, spirometry is mainly performed as part of a medical surveillance program to aid in the early detection of respiratory diseases resulting from work exposures, and also to evaluate whether preventive measures in place are effective [3▪▪,7]. Initial posthire preplacement spirometry testing in conjunction with the assessment of respiratory symptoms and history, may identify a worker unable to meet an increase in ventilatory demand that the job requires. Such pre-placement spirometry may also provide information to determine whether the worker should be advised to avoid such placement in jobs that may carry risk of work-related asthma from exposure to respiratory irritants or sensitizers [8▪▪]. For those who do work in such environments, medical surveillance with serial assessment of spirometry, respiratory questionnaires and in some circumstances, immunologic testing and/or chest imaging is often performed with the aim of early detection of respiratory disease, as recently reviewed [7,9].

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Spirometry that is performed as part of a workplace spirometry program requires consideration of factors beyond those medical providers typically consider when evaluating individual patients as described in the recent ATS Technical Standards [3▪▪]. These include clarifying the reason for performing spirometry, exposures of concern, the frequency of spirometry testing, regulatory and workplace-mandated requirements, other workplace testing such as respiratory questionnaires or chest imaging and clarifying criteria that will trigger further medical evaluation. Appropriate lines of communication of relevant information between the clinician, patient and employer should be clarified prior to spirometry testing, as well as the occupational health professional with overall responsibility for the workplace spirometry program. Each worker's spirometry data should be evaluated in the context of known work exposures and the other available surveillance information such as symptom questionnaire and prior testing [3▪▪].

Also important is the aggregate analysis of the spirometry and other data on the group of workers, including work factors such as job, location or tasks. Such aggregate analysis of the group of workers can identify associations between work exposures and lung function, and also assess the effectiveness of interventions to better focus preventive efforts [3▪▪,7]. However, such analysis is commonly not performed. A recent survey of 198 institutions with laboratory animal care facilities in the United States (19.2% response rate) found that medical surveillance of laboratory animal workers was mandated by 58% of the organizations. However, only 7% of the organizations reported analyzing surveillance results for the group of workers [10].

As noted in the recent ATS technical standards statement [3▪▪], some aspects in the occupational setting warrant special consideration. First, manual workers are often fitter than the general population and at the onset of a job can have greater than 'normal' lung function parameters based on reference values for age, height and sex. For this reason, serial measurements are especially important to detect a decline in function that may still fall within the 'normal predicted' value and which therefore may not be flagged for further clinical assessment unless compared with earlier results. Conversely, results from a single time of testing may falsely be considered to be abnormally low if ethnic background is not considered and appropriate reference values not used. The complexity of the issue of reference values in people originating from different geographic regions has been illustrated in part by a study looking at global lung function differences [11]. An advantage of having multiple serial spirometry results is that the effects of any ethnic differences are not expected to play a role in causing progressive decline in function over time.

EVALUATION OF LUNG FUNCTION CHANGE OVER TIME

The FEV_1 is the primary measurement used to assess lung function change over time in the work setting. Several factors that impact spirometry testing should be considered, including aging-related changes in lung function, testing quality and variability, and testing frequency and years of follow-up. Lung function (FEV_1, FVC) increases during childhood until reaching a maximum around age mid-20s to mid-30s, after which it declines over time, about 25–30 ml/year in nonsmokers [12]. Factors such as cigarette smoking and weight gain [13], in addition to occupational exposures, can contribute to excessive loss in lung function over time [3▪▪], best evaluated by using FEV_1. Given that typical variability in spirometry testing can range from about 5 to 10% with repeat testing, such variability has to be considered in establishing a threshold for abnormal rate of decline in lung function when evaluating an individual worker. Less testing variability, more years of follow-up and more frequent spirometry testing improve the detection of true decline in FEV_1 over time. Because of the healthy worker effect, workers can have above normal lung function. Thus, an accelerated decline in FEV_1 may be able to detect early loss of lung function before lower limit of normal (LLN) for FEV_1 or FVC is reached.

With exposures that cause more acute lung diseases, such as occupational asthma and constrictive bronchiolitis, short-term declines in lung function of 15% or less, comparing individuals' results with their prior testing, may be significant, especially when evaluating these changes in relationship to symptoms and work or other exposures [3▪▪]. Longitudinal evaluation of lung function can also be used to evaluate the impact of preventive measures in these work settings. Respiratory surveillance in such industries should evaluate workers lost to follow-up, because there is potential for the healthy worker effect, as has recently been shown in studies of textile workers [14▪] and workers exposed to occupational asthmagens [15].

There are several approaches used to evaluate longitudinal change in lung function and decide whether a decline in FEV_1 is excessive [3▪▪]. The simplest way is to consider a 15% decline from baseline FEV_1 taking into account expected age-related loss as excessive. Easy-to-use software is available, such as SPIROLA (Spirometry Longitudinal Data Analysis), which can calculate a limit of longitudinal

1528-4050 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

decline, based on spirometry quality and variability [16]. If the current FEV_1 falls below the lower limit of decline threshold, then the observed decline in FEV_1 may be excessive.

SELECTED OCCUPATIONAL EXPOSURES ASSOCIATED WITH ACCELERATED LOSS OF LUNG FUNCTION

Work-related exposures are known to contribute to accelerated loss of lung function and the development of COPD [17▪▪]. Recent studies are characterizing the effects of specific exposures and work settings on longitudinal lung function.

Silica, mineral and metal dusts

Accelerated lung function decline has been shown in longitudinal occupational cohort studies of workers exposed to silica and mineral dusts [18▪,19], coal dust [17▪▪,20▪], as well as steel workers [21] and aluminum smelter workers [22]. Several recent publications have highlighted the recurrence of more severe coal dust lung disease, including rapidly progressive loss of lung function [23,24▪].

The effects of another important work exposure, welding fumes, on longitudinal lung function has also been under investigation. Haluza *et al.* [25] recently evaluated the effects of welding fumes on lung function in 1982 nonquartz-exposed workers in Austria, primarily welders ($n = 1326$) over a period of 9 years [19]. Excessive decline in FEV_1 was significantly associated with duration of exposure to welding fumes and heavy smoking. These findings are consistent with prior studies showing that welding fumes are associated with increased risk of COPD [26]. Workers exposed to hard metals and isocyanates in this study [25] also showed excessive annual decline in FEV_1.

Cummings *et al.* [27] recently evaluated the effectiveness of workplace changes to prevent indium lung disease, a newly described lung disorder involving pulmonary alveolar proteinosis in workers exposed to indium-tin oxide, a metal alloy used in electronics. Among 41 workers employed for 8 years with at least two spirometry tests, 12 (29%) had excessive decline in FEV_1 during employment on the basis of LLN criteria, but more recent hires had fewer spirometric abnormalities, suggesting some improvement in exposure controls.

Organic exposures: cotton and wood dusts

Textile dusts in the clothing industry can cause asthma and chronic lung disease, reviewed by Lai and Christiani [14▪]. Longitudinal analyses of lung function in textile workers have expanded knowledge of the chronic effects of exposure in these workers and the effectiveness of preventive interventions [14▪]. In an updated analysis of the Shanghai Textile Workers study, cotton workers had an excessive annual decline in FEV_1 compared with silk workers at 15, 20 and 25 years of follow-up [14▪,28,29]. Cross-shift drop in FEV_1, years worked in cotton mills and high level of endotoxin exposure were predictive of annual decline in FEV_1 [14▪,29,30]. At the most recent 30-year follow-up of the Shanghai Textile Workers study, cessation of exposure to cotton dust with retirement led to improvement in annual FEV_1 [31].

Similarly to cotton dust, exposure to wood dust can also cause cross-shift declines in FEV_1 and asthma. However, it has been unclear whether chronic wood dust exposure also causes accelerated FEV_1 decline over time [22]. In a recent study [22] of 817 woodworkers in Denmark, cross-shift declines in FEV_1 did not predict chronic lung function changes, and there was no excessive decline in lung function compared with controls at 6-year follow-up. Other longitudinal studies of wood dust exposed workers have also generally not shown an excessive decline in lung function [17▪▪] , although a healthy worker effect could obscure findings.

Chemicals: flavorings and pesticides

Medical surveillance of workers exposed to butter and other flavorings over the past 5–10 years has led to the recognition of flavoring-related constrictive bronchiolitis in different industries that produce and use butter flavoring [32]. Surveillance studies [33,34] of workers exposed to butter flavor (diacetyl as well as its substitute 2,3-pentanedione) have demonstrated excessive declines in FEV_1 and FVC and identified potential early cases of constrictive bronchiolitis. Workforce surveillance data from flavoring industries have also identified targets for improved preventive efforts [7,35,36].

In addition to occupational longitudinal cohort studies longitudinal studies of general populations where periodic spirometry was performed, such as the Vlaardingen Study or Framingham Heart Study, have also been used to evaluate work exposures that predict accelerated decline in FEV_1. Recent further analysis of the Vlaardingen study population, showed that exposure to pesticides, based on job-exposure matrix, was associated with accelerated decline in FEV_1 (6.9 ml/year) [37]. In the Framingham Heart Study population, participants with more dust exposure had an excess rate of decline in FEV_1 (4.5 ml/year) compared to those with less dust exposure [38].

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

CONCLUSION

Longitudinal spirometry is an important component of workplace respiratory surveillance, enabling early detection of respiratory disease resulting from work exposures and also facilitating the assessment of the effectiveness of preventive measures. An expanding number of workplace exposures including mineral dusts, silica, metals, organic materials and specific chemicals such as diacetyl have been associated with accelerated decline in lung function. Medical surveillance, including preemployment, annual spirometry and questionnaire, is also recommended in workers exposed to agents that can cause asthma. Evaluation of repeated medical surveillance data should include an assessment of decline in FEV_1 over time. Aggregate analysis of the spirometry and other data on the group of workers is also important. Such analysis can identify associations between work exposures and lung function, and also assess the effectiveness of exposure controls.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Miller MR, Crapo R, Hankinson J, *et al.* General considerations for lung function testing. Eur Respir J 2005; 26:153–161.
2. Miller MR, Hankinson J, Brusasco V, *et al.* Standardisation of spirometry. Eur Respir J 2005; 26:319–338.
3. ■■ Redlich CA, Tarlo SM, Hankinson JL, *et al.* Official American Thoracic Society technical standards: spirometry in the occupational setting. Am J Respir Crit Care Med 2014; 189:983–993.

This recent ATS technical standard provides guidance on the performance and interpretation of spirometry performed in the work setting.

4. King TE Jr, Bradford WZ, Castro-Bernardini S, *et al.* A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. N Engl J Med 2014; 370:2083–2092.
5. Ischaki E, Litsiou E, Saltagianni V, *et al.* Early COPD diagnosis during a smoking cessation (SC) program increases smoking cessation rates. Eur Respir J 2014; 44 (Suppl 58):1406.
6. Coates AL, Graham BL, McFadden RG, *et al.* Spirometry in primary care. Can Respir J 2013; 20:13–21.
7. Weissman DN. Medical surveillance for the emerging occupational and environmental respiratory diseases. Curr Opin Allergy Clin Immunol 2014; 14:119–125.
8. ■■ Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med 2014; 370:640–649.

This article provides a useful up-to-date review on occupational asthma.

9. Szram J, Cullinan P. Medical surveillance for prevention of occupational asthma. Curr Opin Allergy Clin Immunol 2013; 13:138–144.
10. Stave GM, Darcey DJ. Prevention of laboratory animal allergy in the United States: a national survey. J Occup Environ Med 2012; 54:558–563.
11. Quanjer PH, Stanojevic S, Cole TJ, *et al.* Multiethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J 2012; 40:1324–1343.
12. Lee PN, Fry JS. Systematic review of the evidence relating FEV_1 decline to giving up smoking. BMC Med 2010; 8:84.
13. Sood A, Petersen H, Meek P, Tesfaigzi Y. Spirometry and health status worsen with weight gain in obese smokers but improve in normal-weight smokers. Am J Respir Crit Care Med 2014; 189:274–281.
14. ■ Lai PS, Christiani DC. Long-term respiratory health effects in textile workers. Curr Opin Pulm Med 2013; 19:152–157.

Up-to-date review on the respiratory health effects of cotton dust and endoxin.

15. Dumas O, Le Moual N, Siroux V, *et al.* Work related asthma. A causal analysis controlling the healthy worker effect. Occup Environ Med 2013; 70:603–610.
16. NIOSH. Spirometry Monitoring Technology, SPIROLA software. Available at: http://www.cdc.gov/niosh/topics/spirometry/spirola.html. [Accessed 1 January 2015].
17. ■■ Omland O, Wurtz ET, Aasen TB, *et al.* Occupational chronic obstructive pulmonary disease: a systematic literature review. Scand J Work Environ Health 2014; 40:19–35.

Rigorous systematic review of the occupational COPD literature, cross-sectional and longitudinal studies, organized by study type and exposures.

18. ■ Bruske I, Thiering E, Heinrich J, *et al.* Respirable quartz dust exposure and airway obstruction: a systematic review and meta-analysis. Occup Environ Med 2014; 71:583–589.

Thorough systematic review on the effects of silica exposure on airways disease.

19. Hochgatterer K, Moshammer H, Haluza D. Dust is in the air: effects of occupational exposure to mineral dust on lung function in a 9-year study. Lung 2013; 191:257–263.
20. ■ Lewis L, Fishwick D. Health surveillance for occupational respiratory disease. Occup Med (Lond) 2013; 63:322–334.

Thorough review of the respiratory medical surveillance literature, including surveillance for occupational asthma and COPD.

21. Wang ML, McCabe L, Hankinson JL, *et al.* Longitudinal and cross-sectional analyses of lung function in steel workers. Am J Respir Crit Care Med 1996; 153 (6 Pt 1):1907–1913.
22. Johnsen HL, Hetland SM, Benth JS, *et al.* Dust exposure assessed by a job exposure matrix is associated with increased annual decline in FEV_1: a 5-year prospective study of employees in Norwegian smelters. Am J Respir Crit Care Med 2010; 181:1234–1240.
23. Stansbury RC, Beeckman-Wagner LA, Wang ML, *et al.* Rapid decline in lung function in coal miners: evidence of disease in small airways. Am J Ind Med 2013; 56:1107–1112.
24. ■ Petsonk EL, Rose C, Cohen R. Coal mine dust lung disease. New lessons from old exposure. Am J Respir Crit Care Med 2013; 187:1178–1185.

Up-to-date synthesis of the recent literature on coal mine dust disease.

25. Haluza D, Moshammer H, Hochgatterer K. Dust is in the air. Part II: effects of occupational exposure to welding fumes on lung function in a 9-year study. Lung 2014; 192:111–117.
26. Boggia B, Farinaro E, Grieco L, *et al.* Burden of smoking and occupational exposure on etiology of chronic obstructive pulmonary disease in workers of Southern Italy. J Occup Environ Med 2008; 50:366–370.
27. Cummings KJ, Suarthana E, Edwards N, *et al.* Serial evaluations at an indium-tin oxide production facility. Am J Ind Med 2013; 56:300–307.
28. Shi J, Mehta AJ, Hang JQ, *et al.* Chronic lung function decline in cotton textile workers: roles of historical and recent exposures to endotoxin. Environ Health Perspect 2010; 118:1620–1624.
29. Wang X, Zhang HX, Sun BX, *et al.* Cross-shift airway responses and long-term decline in FEV_1 in cotton textile workers. Am J Respir Crit Care Med 2008; 177:316–320.
30. Christiani DC, Wang XR, Pan LD, *et al.* Longitudinal changes in pulmonary function and respiratory symptoms in cotton textile workers. A 15-yr follow-up study. Am J Respir Crit Care Med 2001; 163:847–853.
31. Lai P, Hang JQ, Zhang FY, *et al.* 0031 lung function improvement is sustained after work cessation in Shanghai cotton and silk textile workers. Occup Environ Med 2014; 71 (Suppl 1):A3.
32. Kreiss K. Occupational causes of constrictive bronchiolitis. Curr Opin Allergy Clin Immunol 2013; 13:167–172.
33. Kreiss K. Work-related spirometric restriction in flavoring manufacturing workers. Am J Ind Med 2014; 57:129–137.
34. Kreiss K, Fedan KB, Nasrullah M, *et al.* Longitudinal lung function declines among California flavoring manufacturing workers. Am J Ind Med 2012; 55:657–668.
35. Cummings KJ, Boylstein RJ, Stanton ML, *et al.* Respiratory symptoms and lung function abnormalities related to work at a flavouring manufacturing facility. Occup Environ Med 2014; 71:549–554.
36. Kanwal R, Kullman G, Fedan KB, Kreiss K. Occupational lung disease risk and exposure to butter-flavoring chemicals after implementation of controls at a microwave popcorn plant. Public Health Rep 2011; 126:480–494.
37. de Jong K, Boezen HM, Kromhout H, *et al.* Association of occupational pesticide exposure with accelerated longitudinal decline in lung function. Am J Epidemiol 2014; 179:1323–1330.
38. Liao SY, Lin X, Christiani DC. Occupational exposures and longitudinal lung function decline. Am J Ind Med 2015; 58:14–20.

1528-4050 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.