The Value of Periodic Spirometry for Early Recognition of Long-Term Excessive Lung Function Decline in Individuals

Eva Hnizdo, PhD

Objective: To establish the value of workplace spirometry monitoring methods for early recognition of long-term excessive lung function decline in individuals. **Methods:** Sensitivity, specificity, and positive likelihood ratio were calculated to determine the predictive value of the linear regression slope and limits of longitudinal decline for early prediction of long-term excessive forced expiratory volume in 1 second (FEV_1) decline (> 90 mL/yr established over 9 to 11 years) in ongoing spirometry monitoring programs (firefighters and construction workers) and a historical program (paper-pulp mill workers). The longitudinal limits account for the expected FEV_1 within-person variability. **Results:** The longitudinal limits achieved clinical "usefulness" (positive likelihood ratio 10 or higher) from the fourth to fifth year of follow-up, whereas the linear regression slope was less useful. The usefulness depended on data precision and measurement frequency. **Conclusion:** The limits of longitudinal decline are more useful for early recognition of long-term excessive FEV_1 decline than the linear regression slope.

Low lung function is an important predictor of morbidity from chronic obstructive pulmonary disease (COPD), mortality from COPD and cardiovascular disease (CVD), and all-cause mortality.[1–6] In addition, excessive lung function decline established over a 5-year follow-up is associated with increased risk of COPD morbidity, COPD and CVD mortality, and all-cause mortality, even in those whose lung function level is within the limits of normal.[5,6] The increased risk is observed in men, women, never-smokers, and those younger than 45 years.[5,6]

Excessive lung function decline can reflect an underlying respiratory condition, increasing abdominal obesity, general loss of fitness, CVD or other adverse health conditions.[7,8] In COPD and asthma, chronic inflammation in the lung tissue leads to progressive lung tissue degradation that may start many years before it can be detected by radiology, lung function test, or other markers.[9,10] A single lung function test can identify individuals whose lung function is abnormal based on population-based criteria of normality, usually the lower fifth percentile based on healthy nonsmokers of the same sex, race, and height (ie, the lower limit of normal [LLN]). Nevertheless, in relatively healthy worker populations, some workers with a "normal" lung function level may display excessive lung function decline,[11] whereas individuals with forced expiratory volume in 1 second (FEV_1) below the LLN may follow a normal trajectory with age.[5,6]

From the Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, W Va.

This work was supported by a funding through the National Institute for Occupational Safety and Health intramural program.

The findings and conclusions in this report are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention. Mention of a specific product or company does not constitute endorsement by the Centers for Disease Control and Prevention.

The author declares no conflict of interest.

Address correspondence to: Eva Hnizdo, PhD, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, 1095 Willowdale Rd, Morgantown, WV 26505 (ehnizdo@cdc.gov).

DOI: 10.1097/JOM.0b013e3182664811

Prevention of excessive lung function decline is possible in occupational settings when periodic spirometry is combined with intervention, such as workplace respiratory protection and occupational exposure control, lifestyle changes such as smoking cessation or regular exercise, or medical treatment.[12–17] Nevertheless, some questions still remain unanswered. How soon and how reliably can periodic spirometry identify individuals with excessive lung function decline? What screening criteria are most effective in predicting long-term excessive decline? How do the answers to these questions depend on the frequency of testing and longitudinal data precision?

Often in practice, the decision about whether a decline in two lung function measurements observed over time is excessive and is based on the absolute decline in FEV_1 or forced vital capacity (FVC) exceeding a certain critical value (eg, 90 mL/yr). This is analogous to fitting a linear regression model to the data points and making a decision on whether the estimated rate of decline exceeds a critical value (eg, 90 mL/yr). This method of evaluation has limitations during the early (1 to 8) years of follow-up when the data are sparse, as it does not account well for the inherent longitudinal FEV_1 data variability. An important consideration in periodic spirometry interpretation is the within-person variability in the longitudinal FEV_1 measurements, which in healthy worker populations are mostly related to biological fluctuation in lung function and the quality of the spirometry tests. To account for the FEV_1 variability, especially during the early years of follow-up, the limits of longitudinal decline that assume a certain fixed level of within-person variation have been proposed. The American Thoracic Society (ATS) recommends that an annual decline greater than 15% should not be considered normal. Nevertheless, because the year-to-year measurements mostly reflect the within-person variation, applying the ATS annual limit is not very useful in predicting a long-term excessive decline in worker population.[18] Also, because the predictive value of periodic spirometry increases with increasing duration of follow-up,[18] a longitudinal limit based on the 15% criterion and expected age-related decline is recommended for longer-term evaluation in occupational settings by the American College of Occupational and Environmental Medicine (ACOEM).[16] Because the limit based on the 15% criterion assumes relatively large within-person variation in FEV_1, it has low sensitivity (SE).[18–20] To increase the SE while maintaining adequate specificity (SP), a more flexible longitudinal limit, which reflects the precision of existing longitudinal spirometry data, has been proposed.[18–20]

To illustrate the issue, Fig. 1 shows longitudinal FEV_1 data for a real person whose decline in FEV_1 is excessive in relation to the limit of longitudinal decline (LLD) and the age-related LLN that corresponds to the lower fifth percentile for a healthy nonsmoker of the same sex, race, and height. To be useful, the limit of longitudinal decline should be sufficiently robust, but have an adequate ability to predict long-term adverse outcomes, including long-term excessive decline, at an early stage.

The objective of this article is to evaluate the predictive value of the methods proposed for early recognition of individuals at risk of developing long-term excessive lung function decline. For that purpose, we studied data from at-risk worker populations with varying precision and varying frequency of longitudinal spirometry. The information from this study is pertinent to prevention in ongoing workplace monitoring programs including those in this study.[17,21]

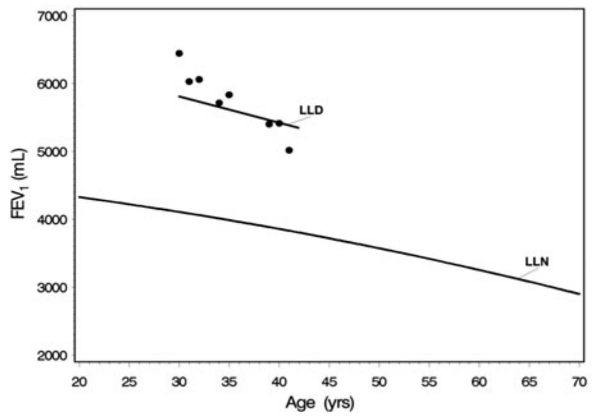

FIGURE 1. Longitudinal FEV_1 data for a real person whose lung function is normal based on the cross-sectional criteria of LLN, which represents the lower fifth percentile in healthy nonsmokers, but the relative LLD classifies the person as having excessive FEV_1 decline. FEV_1, forced expiratory volume in 1 second; LLD, limit of longitudinal decline; LLN, lower limit of normal.

MATERIAL AND METHODS

Populations Studied

We studied data from three large spirometry-based monitoring programs of workers (firefighters, paper-pulp mill workers, and construction workers) potentially exposed to respiratory hazards. The programs started from 1988 onward and are ongoing in the firefighters and construction workers; the ATS spirometry testing standards current at that time were used. The paper-pulp mill workers' annual monitoring involved a standardized respiratory symptoms questionnaire and spirometry testing using standardized protocol and volume-based spirometers. Spirometry tracings were reviewed by one experienced reviewer.[22] The firefighters' annual spirometry was done by trained technicians using a volume-based spirometer over the period included in this study (1989 to 2000); a worsening spirometry quality from 2001 to 2005 precluded us from using those data.[21] In the construction workers, monitoring is done on a triannual basis, mostly by commercial van services or health clinics that reportedly adhere to current ATS standards.[17] The studied data were previously described with respect to spirometry quality and longitudinal data precision.[17,21,23] Individuals with spirometry follow-up longer than 8 years and at least four longitudinal spirometry tests were selected for this study.

In addition, a subcohort of "healthy" nonsmokers was selected from the paper-pulp mill workers who reported never to have smoked, and not having asthma or symptoms consistent with chronic bronchitis, or wheezing. This cohort was used to derive longitudinal limits based on FEV_1 within-person variation and mean rate of decline observed in healthy never-smokers.

The study was approved by the National Institute for Occupational Safety and Health institutional review board.

Data Analysis

For each cohort, we calculated descriptive statistics for the cross-sectional and longitudinal spirometry data. US population reference equations were used to calculate the predicted FEV_1 and FVC values.[24] Using the longitudinal data, we evaluated how soon and how well the different proposed methods predict the long-term excessive decline in FEV_1.

Longitudinal Evaluation—Determination of Long-term Excessive Decline

To determine whether individuals' long-term decline in FEV_1 is excessive, we estimated the rate of FEV_1 decline (mL/yr) by fitting the linear regression model with FEV_1 as a dependent variable and the intercept and age as independent variables, to each subject's all longitudinal data. A rate of decline in excess of a critical value of 90 mL/yr was categorized as excessive. The 90 mL/yr decline is likely to lead to clinically significant airflow impairment[25] and importantly FEV_1 rate of decline greater than 90 mL/yr can be detected as excessive after 8 years of follow-up depending on the longitudinal data precision.[18] For practical purposes, slopes estimated over 8 to 11 years of follow-up can be considered to have sufficient reliability and we can also assume that the relationship is linear.[18] The relative rate of decline (%/yr), relative to the baseline FEV_1 value and a relative critical value comparable with a rate of decline greater than 90 mL/yr were also estimated.

Longitudinal Evaluation—Determination of an Excessive Decline at a Particular Time

We applied the linear regression model and the longitudinal limits to the spirometry data collected over increasing duration of follow-up to determine if and at what specific follow-up time (ie, year) would the methods classify the FEV_1 decline as excessive.

A. Decline estimated by *linear regression model* and compared with a critical value. For each person, short-term rates of FEV_1 decline were estimated by fitting the regression model (the same as described for long-term evaluation) to longitudinal FEV_1 data collected up to each year of follow-up (ie, years 1 through 8). If the rate of decline estimated up to the specific year was greater than a critical value of 90 mL/yr, it was considered to be excessive.
B. Decline evaluated using limits of longitudinal decline. The limits are designed to determine whether the decline from the baseline FEV_1 value (or mean of two values if second value was higher) to a specific follow-up time is within a critical limit set by a longitudinal limit that takes into account the expected within-person variation in longitudinal FEV_1 and age-related decline. If the decline in FEV_1 exceeds the limit, the decline is considered excessive. Because the purpose of this article is to evaluate usefulness of the limits previously described in detail,[16,18] only their principle is outlined. Three types of relative longitudinal limits were evaluated:

1. ACOEM recommends a longitudinal normal limit (LNL_{ACOEM}) based on the ATS recommended year-to-year decline limit of 15% and the predicted age-related decline over years.[16] The limit is defined in terms of a critical value below which a longitudinal measurement should not fall from the baseline FEV_1 value (FEV_{1b}), as follows:

$$LNL_{ACOEM} = FEV_{1b}(1 - 0.15) - (\text{pred. } FEV_1 \text{ at baseline} - \text{pred. } FEV_1 \text{ at follow-up}) \quad [1]$$

2. The flexible relative limit of longitudinal decline (LLD_r) represents the upper 95% confidence limit for the group's average relative rate of decline b_r (relative to FEV_{1b}) and the follow-up time t measured in years, and is defined as follows:

$$LLD_r = t \times b_r + (1.645 \times s_{wr} \times 1.41), \quad [2]$$

where s_{wr} is the relative within-person standard deviation that accounts for the average longitudinal FEV_1 data variability in the monitoring program. The constant 1.41 represents a fixed effect of two repeated measurements as $1.41 = \sqrt{12(p-1)}/\sqrt{p(p+1)}$, where $P = 2$.[18,26] For the purposes of this study, we estimated s_{wr} as the relative pairwise within-person variation calculated using annual within-person differences in FEV_1 summed over all the individuals and years of follow-up in a program.[18] The ACOEM limit is comparable with LLD_r when the average within-person variation is approximately 6% and annual decline is approximately 1%.

3. The relative limit of longitudinal decline based on the FEV_1 variability observed in nonsmokers (LLD_r-NS) was calculated using equation (2) and the within-person variation and the mean rate of decline estimated for the healthy nonsmokers' subcohort.

The critical value below which the FEV_1 measured at a follow-up time t should not fall from the baseline FEV_{1b} value is then calculated as $FEV_1 = FEV_{1b} - [FEV_{1b} \times (LLD_r \text{ or } LLD_r\text{-NS})/100]$. Software for monitoring of longitudinal data precision and for longitudinal evaluation by these limits is available on the Internet.[27]

Measures of Predictive Ability of the Excessive Decline Criteria

The predictive ability of the four longitudinal criteria, that is, how well and how soon they can identify individuals with long-term excessive decline, was measured using the SE, SP, and positive likelihood ratio (LR+) statistics, evaluated over the years of follow-up.[28] SE is the proportion of individuals identified by a longitudinal limit as having excessive decline at a specific follow-up time who have long-term excessive decline. SP is the proportion of individuals not identified by a longitudinal limit as having excessive decline at a specific follow-up time who do not have long-term excessive decline. The LR+ combines SE and SP [LR+ = SE/(1 − SP)] and indicates overall usefulness of the tests balancing SE and SP. LR+ is the proportion of positive test results in those who have longer-term excessive decline, divided by the proportion of positive test results in the absence of long-term excessive decline. Generally, a LR+ value of 10 or higher indicates that a test is clinically useful.[28]

RESULTS

Descriptive statistics for the three cohorts and a subcohort of "healthy" never-smokers who satisfied the selection criteria are presented in Table 1. The firefighters' monitoring program started in 1988 and is ongoing. By 2010, there were 4527 firefighters with at least two spirometry measurements, and of these 965 satisfied the selection criteria. The construction program started in 1990 and is ongoing. By 2009, there were 2771 workers with at least two spirometry measurements, and of these 460 satisfied the selection criteria. The paper-pulp mill monitoring was conducted from 1988 through 2000 in several plants, 11 of which were identified to have sufficient data[23]; 6440 workers had longitudinal data and of these 1286 satisfied the selection criteria and 345 of these were never-smokers. Because very few female firefighters and construction workers satisfied the selection criteria, for comparability we excluded women from the study.

Table 1 shows that the baseline lung function in firefighters was comparable with never-smokers, but the rate of decline was, however, higher. The construction workers were comparable with the paper-pulp mill workers, except for the longitudinal decline and variability, which appeared higher. The relative within-person variation ranged from 3.8% in nonsmokers to 6.0% in the construction workers. Because the relative statistic adjusts for FEV_1 size, it provides a more comparable measure than the absolute one.

Table 2 shows the values of the three longitudinal limits (LNL_{ACOEM}, LLD_r, and LLD_r-NS) for increasing years of follow-up (1 to 8). The limits represent the percent decline from the baseline

TABLE 1. Characteristics (Mean [SD] or No. [%]) of the Three Occupational Cohorts and the Never-Smokers Subcohort

Characteristic at Baseline or Calculated Over Follow-Up	Firefighters (n = 965)	Paper-Pulp Mill Workers: All (n = 1286)	Paper-Pulp Mill Workers: Never Smokers (n = 345)	Construction Workers (n = 460)
Age (yr)	36.3 (9.3)	36.4 (8.4)	33.7 (9.1)	35.4 (8.8)
Follow-up time (yr)	9.3 (0.5)	9.5 (0.7)	8.2 (1.6)	9.5 (0.8)
Height (cm)	180.4 (6.2)	177.9 (6.4)	178.4 (6.4)	177.9 (6.8)
Weight (kg)	87.2 (11.8)	87.2 (15.4)	78.2 (9.9)	86.1 (15.5)
Body Mass Index (kg/m^2)	26.8 (3.2)	27.6 (4.4)	24.5 (2.4)	27.4 (4.5)
Smokers (%)	≈5*	60.6	0.0	NA†
Cross-sectional evaluation at baseline				
FEV_1 (L)	4.39 (0.64)	4.11 (0.68)	4.33 (0.60)	4.10 (0.7)
FEV_1% predicted	98.9 (11.7)	95.5 (12.8)	98.9 (11.2)	95.7 (14.2)
FVC (L)	5.46 (0.77)	5.09 (0.80)	5.30 (0.73)	5.19 (0.83)
FVC% predicted	98.7 (11.0)	94.9 (11.7)	97.6 (10.8)	97.7 (12.8)
FEV_1/FVC (%)	80.5 (5.7)	80.9 (5.8)	82.0 (5.8)	79.1 (7.6)
Longitudinal evaluation for more than 8 years				
FEV_1 rate of decline (mL/yr)	39.6 (29.5)	45.2 (32.2)	34.3 (33.5)	48.7 (50.1)
FEV_1 rate of decline (%/yr)	0.9 (0.7)	1.1 (0.8)	0.8 (0.8)	1.2 (1.2)
Within-person variation (mL)	175.0	153.0	149.9	200.0
Within-person variation (%)	4.5	4.3	3.8	6.0
Long-term decline > 90 mL/yr (no., %)	46 (4.8)	106 (8.2)	18 (5.2)	80 (17.4)
Long-term decline > 2.1 %/yr (no., %)‡	54 (5.6)	99 (7.7)	11 (3.2)	77 (16.7)

*In 2009, only 5% of the firefighters reported smoking tobacco.
†Smoking information was not sufficient to estimate prevalence.
‡Relative decline of 2.1%, 2.2%, 2.1%, and 2.2% were used respectively for the four programs to adjust for the FEV_1 size.
NA, not available because of insufficient data; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

TABLE 2. The Value of the Relative Longitudinal Limits Over 1 to 8 Years of Follow-Up. The Limits Represent the % Decline From the Baseline FEV_1 Value. The ACOEM Limit Is Fixed. The Flexible Limit (LLD_r) Is Based on Each Program's Data Variability and Mean Rate of Decline and Is Thus Specific for Firefighters, Pulp-Paper Mill Workers, Construction Workers, and the Healthy Never-Smokers (LLD_r-NS)

		Flexible LLD_r Limit as % of FEV_1 Decline From Baseline			
Follow-Up Year	ACOEM Limit as % of FEV_1 Decline From Baseline	Firefighters	All Pulp-Paper Mill Workers	Construction Workers	LLD_r-NS*
1	15.0	11.3	11.1	15.0	9.6
2	16.1	12.2	12.2	16.1	10.4
3	17.2	13.1	13.3	17.2	11.2
4	18.3	14.0	14.4	18.3	12.0
5	19.4	14.9	15.5	19.4	12.7
6	20.5	15.8	16.6	20.5	13.6
7	21.6	16.7	17.1	21.6	14.3
8	22.7	17.6	18.8	22.7	15.1

*On the basis of healthy never-smokers selected from the pulp-paper mill workers.
FEV_1, forced expiratory volume in 1 second; LLD, limit of longitudinal decline.

FEV_1 value, with increasing years of follow-up. The ACOEM limit was calculated using equation 1 and is thus fixed for all the cohorts. The flexible limit, LLD_r, was calculated for each monitoring program and for the never-smokers using equation 2. The input parameters in equation 2 were years of follow-up (t), and each program's mean relative FEV_1 rate of decline (%/yr) and relative within-person variation (%) as shown in Table 1.

Figures 2 A–D show the SE, SP, and LR+ statistics and the fraction identified as having excessive decline for each year of follow-up, for four methods of assessment: the longitudinal limits (LNL_{ACOEM}, LLD_r, and LLD_r-NS) and the regression slope (Slope), for the firefighters' cohort. The solid line indicates at what year the test becomes clinically useful ($LR \geq 10$). For example, Fig. 2A shows that LNL_{ACOEM} reached clinical usefulness from the fourth year of follow-up. In comparison, Fig. 2B shows that LLD_r reached clinical usefulness from the fifth year, but with almost doubled SE. On the contrary, the regression slope reached clinical usefulness from the seventh year because of the high fraction of excessive declines and very low SP during the initial years. Figures 3 and 4 show the validity statistics for the paper-pulp mill and construction worker cohorts, respectively. For the construction cohort (Fig. 4), the LR+ and SE statistics indicate similar performance for LNL_{ACOEM} and LLDr; both became useful from the fifth year with similar SE. The reason for this is that the within-person variation for the construction cohort was 6% (Table 1) and thus the LNL_{ACOEM} and LLDr limits had similar values (Table 2). For both cohorts, the regression slope and LLD_r-NS were not useful in predicting long-term excessive decline; their performance decreased with decreasing longitudinal data precision.

DISCUSSION

In occupational settings, periodic spirometry can be useful in primary, secondary, or tertiary prevention.[16] The study set out to investigate questions relevant in the secondary and tertiary prevention. How soon is it possible to identify excessive lung function decline reliably? Which methods are useful for screening for the potential excessive decliners? How do the answers depend on the longitudinal data precision and the frequency of testing?

Generally, the LR+ value of 10 indicates that a test is clinically useful in predicting a disease or condition in a person.[28] In our study, the test (ie, periodic spirometry evaluated using the regression slope or a longitudinal limit) was used to screen for individuals with excessive lung function decline who are at risk of developing longer-term excessive FEV_1 decline. These individuals may then be targeted for prevention, which may include retesting to confirm the results, intervention on occupational or life-style risk factors, or medical intervention.[16,17]

The results show that because of low SP, the linear regression slope (Slope) does not have a good predictive value for early identification of individuals who developed long-term excessive decline (Figs. 2 to 4). In comparison, the relative longitudinal limits (LLD_r and LNL_{ACOEM}), which reflect data variability, reached usefulness from the fourth to fifth year of follow-up. Generally, the relative limit LLD_r had higher SE than LNL_{ACOEM} with comparable LR+ values. Depending on longitudinal data precision, LLD_r identified almost 40% to 60% of those with longer-term excessive decline from the fifth year of follow-up. The LLD_r-NS limit based on healthy nonsmokers' parameters had the highest SE but at the cost of low SP, and the LR+ values indicate poor usefulness as a screening tool. Nevertheless, usefulness of these limits depends on the spirometry quality, longitudinal data precision, and the population.

The firefighter cohort represents a relatively healthy workforce with low tobacco consumption but exposure to respiratory hazards, which may be reflected in the higher mean rate of FEV_1 decline (39.6 mL/yr) and higher rate of longer-term excessive decliners (5.6%) than observed in the never-smokers (Table 1). Annual spirometry and the average within-person variation in FEV_1 of 4.5% indicate relatively precise longitudinal data, which is reflected in the more precise longitudinal limit LLD_r (Table 2). The ACOEM limit (LNL_{ACOEM}) identified less than 5% as having excessive decline each year (Fig. 2A), with LR+ reaching above 10 on the fourth year with SE around 20%. In comparison, LLD_r identified approximately 5% individuals as having excessive decline each year (Fig. 2B), with LR+ reaching above 10 on the fifth year with SE around 60%, twice as high as for LNL_{ACOEM} at that point. LLD_r-NS reached clinical significance from the fifth year with SE of about 70% (Fig. 2C) but LR+ remained flat with increasing follow-up. The linear regression slope performed poorly, reaching LR+ above 10 at the seventh year (Fig. 2D).

The paper-pulp mill workers' programs represented annual spirometry and good data precision (average within-person variation of 4.3%), but a less-fit workforce than the firefighters (mean rate of

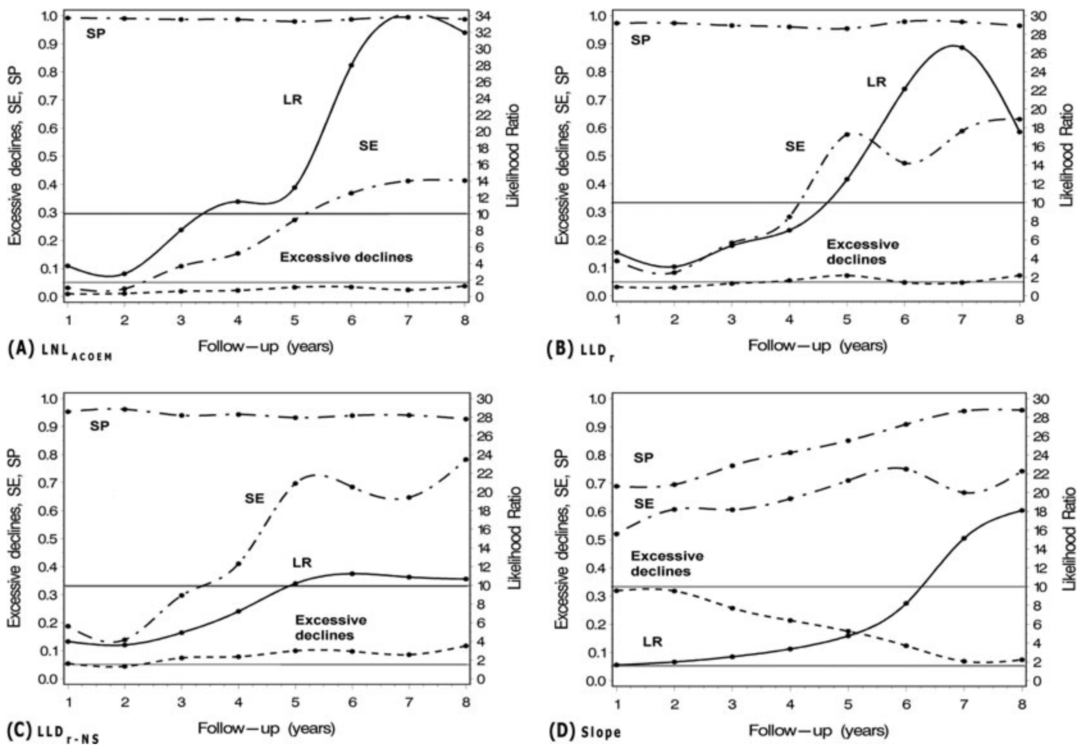

FIGURE 2. Predictive statistics (SE [dash-dot line], SP [dash-dot line], LR+ [solid line], and the fraction identified as having excessive decline [dash line]) for the ACOEM limit LNL_{ACOEM} (chart A), the relative limit LLD_r (chart B), the relative limit based on never-smokers' parameters LLD_r-NS (chart C), and the regression slope "Slope" (chart D), for the firefighter cohort. LLD, limit of longitudinal decline; LNL, longitudinal normal limit; LR+, positive likelihood ratio; SE, sensitivity; SP, specificity.

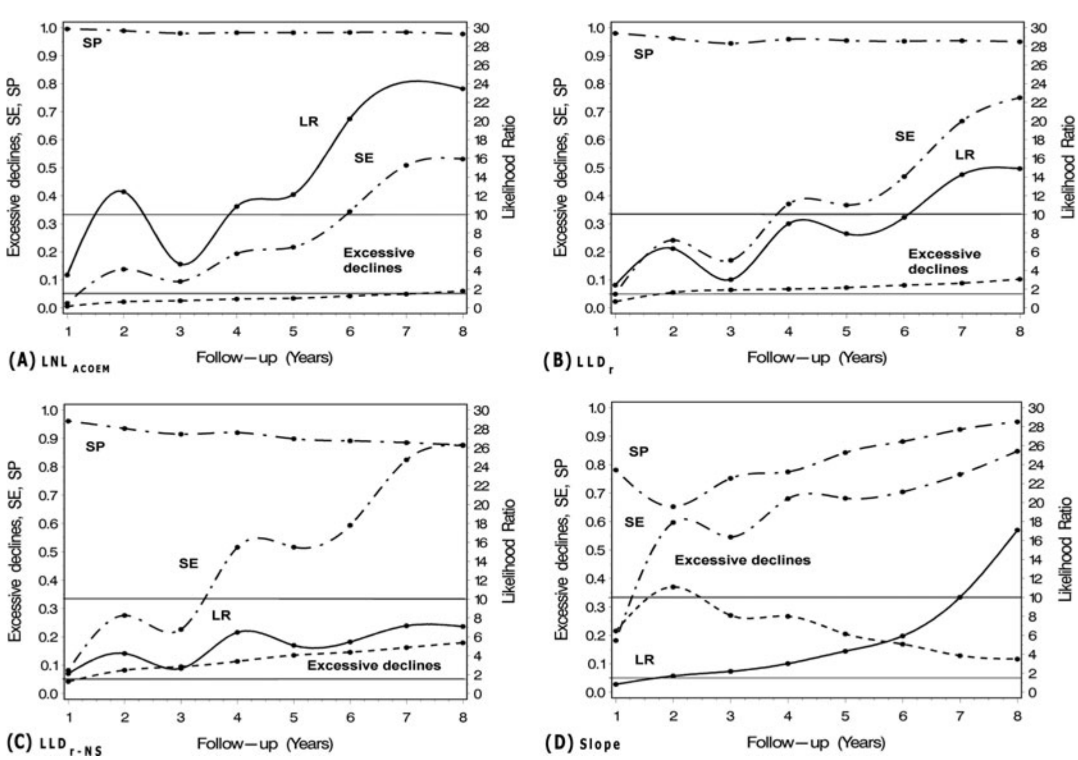

FIGURE 3. Predictive statistics (SE [dash-dot line], SP [dash-dot line], LR+ [solid line], and the fraction identified as having excessive decline [dash line]) for the ACOEM limit LNL_{ACOEM} (chart A), the relative limit LLD_r (chart B), the relative limit based on never-smokers' parameters LLD_r-NS, (chart C), and the regression slope "Slope" (chart D), for the paper-pulp mill workers. LLD, limit of longitudinal decline; LNL, longitudinal normal limit; LR+, positive likelihood ratio; SE, sensitivity; SP, specificity.

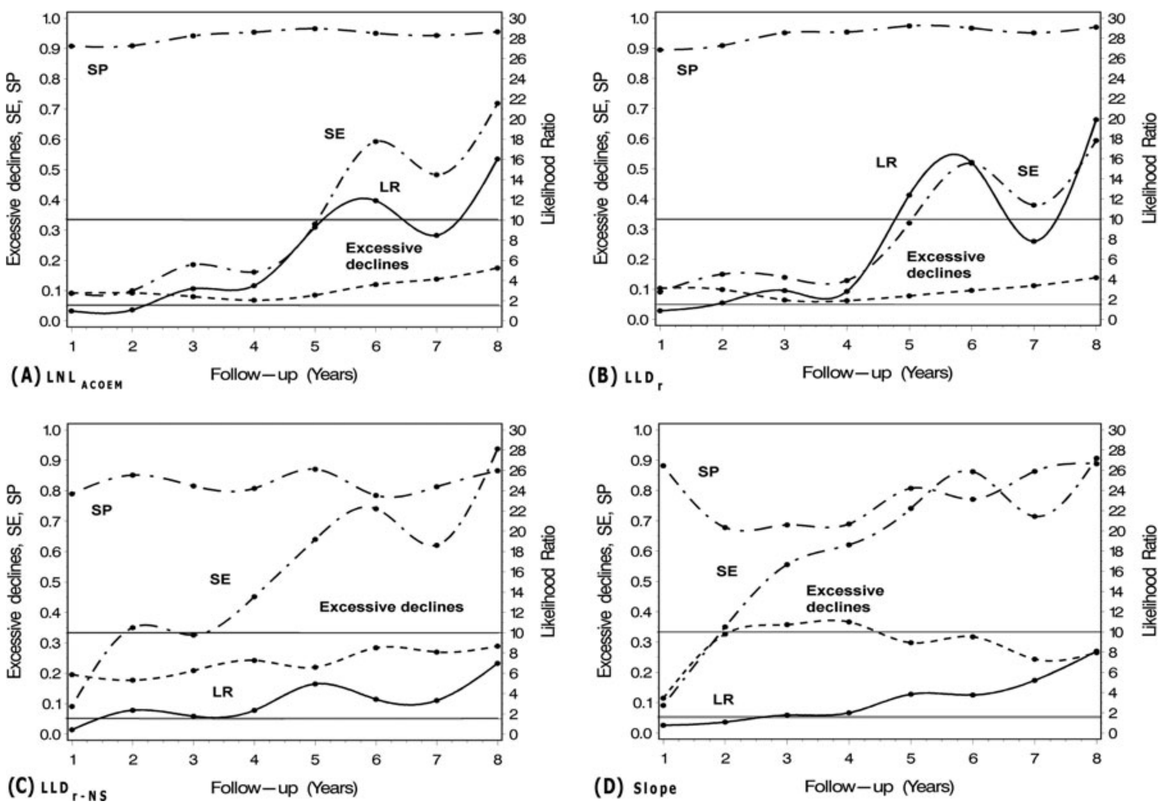

FIGURE 4. Predictive statistics (SE [dash-dot line], SP [dash-dot line], LR+ [solid line], and the fraction identified as having excessive decline [dash line]) for the ACOEM limit LNL_{ACOEM} (chart A), the relative limit LLD_r (chart B), the relative limit based on never-smokers' parameters LLD_r-NS, (chart C), and the regression slope "Slope" (chart D), for the construction workers cohort. LLD, limit of longitudinal decline; LNL, longitudinal normal limit; LR+, positive likelihood ratio; SE, sensitivity; SP, specificity.

FEV_1 decline of 45.2 mL/yr and frequency of excessive decliners, 8.2%, Table 1). The predictive statistics displayed a similar pattern as for the firefighters' cohort (Fig. 3).

The construction workers represent programs with less frequent testing (triannually) and less precise longitudinal data (mean relative within-person variation of 6%). The workers had the highest rate of FEV_1 decline (49.5 mL/yr) and highest percentage of longer-term excessive decliners (17.4%). Nevertheless, both limits of LLD_r and LNL_{ACOEM} (of similar values, Table 2), reached "usefulness" from the fifth year, whereas LLD_r-NS and the regression slope performed poorly. The drop at the seventh year may reflect the smaller sample due to triannual testing.

The performance of the longitudinal limits was best in the firefighter cohort that had annual spirometry and relatively precise longitudinal FEV_1 data. Nevertheless, even in the construction workers where spirometry was conducted by van services on a triannual basis and the longitudinal data had relatively high average within-person variation (6%), both LLD_r and LNL_{ACOEM} performed reasonably well, reaching clinical usefulness from the fifth to sixth year of follow-up, identifying about 60% of individuals with long-term excessive decline from the sixth year.

In practice, to create a flexible robust limit, we can let the relative within-person variation s_{wr} range from about 4% to 6% to reflect the likely range of variability observed in workplace monitoring programs, which corresponds to an annual limit of approximately 10% to 15%.[18] With good spirometry quality and a healthy worker population, we can assume within-person variation of approximately 4%.[21] When spirometry quality is less good, 6% is more appropriate and spirometry quality should be improved. The flexible limit LLD_r allows us to consider the likely nature of the work-related outcome (large effect over short period of time vs chronic effect as investigated in our study) and the likely cost associated with the outcome's effects on the individual and the society. To effectively prevent potentially large work-related respiratory health effects occurring within a short period (eg, a year), the periodic spirometry quality and data precision need to be high. This can be achieved by stringent quality review. The longitudinal limits should also be applied to maintain acceptable longitudinal spirometry data precision by reviewing spirometry quality in measurements that fall below the longitudinal limits, or by retesting.[21]

Limitations of the study stem from the fact that we used existing data where spirometry quality was not specifically reviewed as it would be in an epidemiological investigation or at an individual's assessment by a health care provider. The predictive ability of the periodic spirometry interpreted using the longitudinal limit was evaluated as a screening tool. In practice, usefulness of the method would be likely enhanced by considering additional information about a person.

CONCLUSION

In at-risk worker populations, periodic spirometry and the relative longitudinal limits can be effective screening tools for identifying individuals with excessive decline in FEV_1 from about the fourth to fifth year of follow-up. Both the flexible longitudinal limit LLD_r and the ACOEM limit became useful from about the fourth to fifth year, but the LLD_r limit had more acceptable SE with comparable LR+ values when the longitudinal data were more precise. The effectiveness of the longitudinal limits is determined by the existing longitudinal FEV_1 data precision, which is mostly determined by spirometry quality and frequency of measurements. On the contrary, the linear regression slope, or other methods that compare decline with a critical value that does not account for data variability, and the limit based on healthy never-smokers data (LLD_r-NS) are not useful for individual screening because of their low SP. In conjunction with this article, we have created a Web-based interactive calculator that can be used to evaluate longitudinal FEV_1 data using the earlier-mentioned longitudinal limits.[27]

ACKNOWLEDGMENT

The author thanks the Phoenix Fire Department, Occupational Medical Consulting for CIANBRO, and the Tulane Medical School Pulmonary Disease Section for sharing their data, and the graphic support by Parmjit Singh.

REFERENCES

1. 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;58:388–393.
2. Tockman MS, Pearson JD, Fleg JL, et al. Rapid decline in FEV_1. A new risk factor for coronary heart disease mortality. *Am J Respir Crit Care Med*. 1995;151:390–398.
3. Mannino DM, Davis KJ. Lung function decline and outcomes in an elderly population. *Thorax*. 2006;61:472–477.
4. Mannino DM, Reichert MM, Davis KJ. Lung function decline and outcomes in an adult population. *Am J Respir Crit Care Med*. 2006;173:985–990.
5. Baughman P, Marott JL, Lange P, Andrew M, Hnizdo E. Health outcomes associated with lung function decline and respiratory symptoms and disease in a community cohort. *COPD: J Chronic Obstructive Pulmonary Dis*. 2011;48:103–113.
6. Baughman P. *An Epidemiological Assessment of Lung Function Decline as a Predictor of Morbidity and Mortality, Doctoral Dissertation*. Morgantown, WV: West Virginia University; 2011.
7. Lange P. Spirometric findings as predictors of survival. *Thorax*. 2011;66:1–2.
8. Lange P, Nyboe J, Jensen G, Schnohr P, Appleyard M. Ventilatory function impairment and risk of cardiovascular death and of fatal or non-fatal myocardial infarction. *Eur Respir J*. 1991;4:1080–1087.
9. Hogg JC, Pierce RA. Remodeling of peripheral lung tissue in COPD. *Eur Respir J*. 2008;31:913–914.
10. Vestbo J, Rennard S. Chronic obstructive pulmonary disease biomarker(s) for disease activity needed—urgently. *Am J Respir Crit Care Med*. 2010;82:863–869.
11. Hankinson JL, Wagner GR. Medical screening using periodic spirometry for detection of chronic lung disease. *Occup Med.* 1993;8:353–361.
12. Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med*. 2002;166:675–679.
13. Musk AW, Peters JM, Bernstain L, Rubin C, Monroe CB. Pulmonary function in firefighters: a six-year follow-up in the Boston fire department. *Am J Indust Med*. 1982;3:3–9.
14. Pahwa P, Senthilselvan A, McDuffie HH, Dosman JA. Longitudinal decline in lung function measurements among Saskatchewan grain workers. *Can Respir J*. 2003;10:135–141.
15. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Anto JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2007;458–463.
16. Townsend MC. Evaluating pulmonary function change over time in the occupational setting. ACOEM evidence-based statement. *J Occup Environ Med*. 2005;47:1307–1316.
17. Hnizdo E, Berry A, Hakobyan A, Beeckman-Wagner L-A, Catlett L. Worksite wellness program for respiratory disease prevention in heavy construction workers. *J Occup Environ Med*. 2011;53:274–281.
18. Hnizdo E, Glindmeyer HW, Petsonk EL. Workplace spirometry monitoring for respiratory disease prevention: a method review. *Int J Tuberc Lung Dis*. 2010;14:1–10.
19. Wang M, Petsonk EL. Repeated measures of FEV_1 over six to twelve months: what change is abnormal? *J Occup Environ Med*. 2004;46:591–595.
20. Wang ML, Vashia BH, Petsonk LE. Interpreting periodic lung function tests in individuals. The relationship between 1- to 5-year and long-term FEV_1 changes. *Chest*. 2006;130:493–499.
21. Hnizdo E, Hakobyan A, Fleming J, Beeckman-Wagner L. Spirometry-based medical monitoring: spirometry quality vs. data precision. *J Occup Environ Med*. 2011;53:1205–1209.
22. Glindmeyer H, Lissack T. A network approach to national respiratory health care. In: Rubin M, eds. *Computerization and Automation in Health Facilities*. Boca Raton, FL: CRC Press, Inc; 1984:1–16.
23. Hnizdo E, Yu L, Freyder L, Lefante J, Glindmeyer HW. Precision of longitudinal lung function measurements—monitoring and interpretation. *Occup Environ Med*. 2005;62:695–701.
24. Hankinson JL, Odenkrantz JR, Fedan KB. Spirometric reference values from a smaple of the general US population. *Am J Respir Crit Care Med*. 1999;159:179–187.
25. Buist AS, Vollmer WM. The use of lung function tests in identifying factors that affect lung growth and aging. *Stat Med*. 1988;7:11–18.
26. Schlesselman JJ. Planning a longitudinal study: II. Frequency of measurement and study duration. *J Chron Dis*. 1973;26:553–558.
27. Spirometry Longitudinal Data Analysis (SPIROLA) software. Available at: http://www.cdc.gov/niosh/topics/spirometry/spirola.html. Accessed August 13, 2012.
28. Gallagher EJ. Clinical Utility of likelihood ratios. *Ann Emerg Med*. 1998;31:391–397.