Excessive Longitudinal FEV_1 Decline and Risks to Future Health: A Case–Control Study

Mei Lin Wang, MD, MPH,[1†] Bipin H. Avashia, MD,[2‡] John Wood, MS,[1§] and Edward L. Petsonk, MD, FCCP[1*¶]

Background *Accelerated loss of forced expiratory volume in 1 s (FEV_1) in an individual is considered an indicator of developing lung disease.*

Methods *We investigated longitudinal FEV_1 slopes, calculated by simple linear regression, and adverse health outcomes after 10–30 years, among 1,428 chemical plant workers. Cases were defined by FEV_1 slopes below 5th percentile values for the cohort. Cases were matched with controls (107 pairs) for race, gender, smoking status, year of birth, age, height, and calendar year at first test. Matched pair statistics were used for comparisons.*

Results *Cases had a higher proportion, compared to controls, of diagnosis of COPD or emphysema (17.8% vs. 1.9%, $P = 0.0002$), medication use for respiratory diseases (24.3% vs. 4.7%, $P < 0.0001$), dyspnea (15% vs. 3.7%, $P = 0.0042$), and wheezing or rhonchi on examination (10.3% vs. 1.9%, $P = 0.0225$).*

Conclusions *Chemical plant workers who experienced accelerated FEV_1 declines experienced four to nine times as many adverse health conditions over 10–30 years.* Am. J. Ind. Med. 52:909–915, 2009.

KEY WORDS: spirometry; pulmonary disease; chronic obstructive; mass screening; excessive FEV_1 decline

INTRODUCTION

Serial monitoring of lung function change is recommended to detect airflow limitation in its early stage, when interventions are most likely to be successful [Hankinson and Wagner, 1993; NHLBI/WHO workshop, 2001] For this to be an effective health conserving strategy, such testing must provide reasonably accurate identification of individuals who are at risk for developing symptoms, illnesses, and increased mortality from cardiovascular and non-malignant respiratory disease, and thus permit appropriate targeting of interventions [Sherman et al., 1992; Carta et al., 1995; Tockman et al., 1995; Burchfiel et al., 1996; Beeckman et al., 2001]. The purpose of the current study is to better define the long-term risks for specific adverse health outcomes among individuals who are experiencing accelerated lung function declines.

We examined existing plant medical records among a group of chemical plant workers who participated in the company-sponsored medical monitoring program and had demonstrated accelerated forced expiratory volume in 1 s (FEV_1) losses (cases), and matched referent employees with relatively stable lung function (controls). Documentation in the medical record of adverse health outcomes was extracted for the most recent 4-year testing period, including

[1]Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention, Morgantown, West Virginia
[2]Medical Department, Institute Plant, Institute, West Virginia
The findings in this report have not been formally disseminated by NIOSH or the Institute Plant of West Virginia, and should not be construed to represent any agency policy or determination.
[†]Epidemiologist.
[‡]Physician.
[§]Statistician.
[¶]Senior Medical Officer.
Contract grant sponsor: NIOSH.
*Correspondence to: Edward L. Petsonk, NIOSH, Mail Stop H-G900.2, 1095 Willowdale Road, Morgantown, WV 26505. E-mail: elp2@cdc.gov

Accepted 31 August 2009
DOI 10.1002/ajim.20764. Published online in Wiley InterScience (www.interscience.wiley.com)

respiratory symptoms and signs, medication use, and diagnosed lung or heart disease.

METHODS

Approval for performance of the study was received from the NIOSH Human Subjects Review Board. The data for this analysis were obtained from an ongoing health-monitoring program at a large chemical plant.

Participants and Spirometry Testing

As previously described, a total of 1,884 participants with at least five valid results over 10 or more years between 1973 and 2003 were included in the study database [Wang et al., 2006]. Only workers who had medical records available (N = 1,428) were eligible for inclusion in this case–control study. Spirometry testing was performed annually by trained nurses at the on-site medical department according to American Thoracic Society standards current at the time of the test. In the years before professional standards were published, spirometry was supervised by academic researchers who were familiar with spirometry techniques and procedures. The head nurse spent 1-week training in spirometry at Tulane University; she then initiated the program and trained the other nurses. In 1978, the medical director collaborated with NIOSH in starting a NIOSH-approved spirometry course. Thereafter, all nurses were trained through that course. Quality was checked by the nurse technicians during testing, and reviewed by the medical director during the annual physical examination. Spirometry quality feedback was consistently provided to technicians by the head nurse and the medical director. Daily volume calibration checks were performed using a 3 L syringe. A leak check was also done each day prior to testing. Initially, spirometry results were all hand calculated using a back extrapolation time zero technique. Starting in 1978, software packages calculated results and provided quality feedback to the technicians. The testing posture was standing before March 1988; and was sitting afterward.

Four different models of volume spirometers were used in testing for various periods of time over the 30 years. Between 1973 and 1987, testing was performed with a Jones Pulmonaire spirometer with a Datamite microprocessor (Jones Instrument, Oak Ridge, IL). Between 1988 and 1996, testing was done using an InfoMed model 5100-0020 device. The NIOSH HF5 system with an Ohio rolling seal spirometer was used from 1997 to 2002, and an OMI (Occupational Marketing, Houston, TX) since 2003.

The original test results, including the graphic outputs, were part of the individual medical records; the best values of FVC and FEV_1 for each test session were entered into an electronic spirometry database. The values of lower limit of normal (LLN) for spirometry indexes were calculated using the Hankinson equation [Hankinson et al., 1999] The patterns of abnormal spirometry results were categorized as follows: (1) Obstructive: $FEV_1/FVC < LLN$, $FVC > LLN$, and $FEV_1 < LLN$; (2) Restrictive: $FEV_1/FVC > LLN$ and $FVC < LLN$; and (3) Mixed: $FEV_1/FVC < LLN$ and $FVC < LLN$.

Definition of Cases and Matched Controls

Individual longitudinal FEV_1 slopes (ml/year) were calculated by simple linear regression for each study worker (N = 1,428). The distribution of FEV_1 slopes for the entire cohort stratified by race (white and black) and gender (male and female) was computed using the SAS univariate procedure. Cases were defined as individuals whose FEV_1 slope was below the gender and race specific 5th percentile value (−65 ml/year for white and −56 ml/year for black males, and −50 ml/year for females, both white and black). Paired controls were identified as non-case employees who could be fully matched with a case for race, gender, smoking status, birth cohort, age at baseline, height, and calendar year of first test. Non-smoker refers to individuals who never reported smoking cigarettes. Ex-smokers include those who reported they had quit smoking at both the initial and final test. Quitters were those who smoked at their initial test but reported at their final test that they no longer smoked. Smoker refers to those who reported current smoking at their initial and final tests. Controls were matched with cases by quartiles of baseline age: <26, 26–32, 33–40, and >40. Matching on the calendar year of first spirometry testing was also determined by the quartile distribution: 1973–1974, 1975–1976, 1977–1982, and 1983–1991. The median value of birth year (calendar year 1946) was used to define two birth cohorts for matching. Baseline height was categorized into tertiles for matching purposes. The matching process was performed with SAS macro language, using the SAS® v9.0 software package [SAS, 2003].

Health Information From Medical Records

One of the authors (BHA) reviewed all medical department records that were available for each individual during the 4 years prior to his or her last spirometry test, including both annual health surveys and any other medical examinations, without knowledge of the spirometry decline status. Health information was abstracted on medication use, respiratory symptoms and signs, and lung or heart disease diagnoses. The following variables were noted:

1. Medication taken for hypertension, sinus or allergy, cardiac, or respiratory conditions.

2. Respiratory system diagnoses for COPD or emphysema, upper respiratory tract infection (URI), bronchitis, sinus conditions, asbestosis or asbestos-related X-ray changes, and cardiac conditions (angina, bypass surgery, myocardial infarction). The medical diagnoses were based either on the results of medical examinations or on reports by the workers of doctor-diagnosed conditions.
3. Respiratory symptoms (cough, phlegm, hemoptysis, dyspnea on effort or walking on level ground, attacks of asthma or hay fever, difficulty wearing or using respirators in the plant) or findings (wheezing, rhonchi, crackles or rales on examination).
4. Job descriptions at the initial and final tests, including department number (workplace unit coding), job title, and year of last job transfer.

Data Analysis

Significance of differences for group comparisons of demographic and spirometry parameters between cases and controls was analyzed using the Student's *t*-test. The percentage of abnormal spirometry results was calculated and compared between cases and controls for the spirometry measurements at the initial and final tests, respectively. Significance of differences in the proportion of abnormal spirometry results was tested by Chi-square tests. Workplace exposure to methylisocyanate (MIC) and phosgene was determined by Department and Unit coding. Significance of differences in frequencies of health outcomes including reported medication use, respiratory symptoms and signs, and lung or heart disease diagnoses; and workplace exposure to MIC and phosgene was tested by matched pair Chi-square tests (McNemar's Test or Exact McNemar's Test) [Cody and Smith, 1997].

RESULTS

The cases and the matched controls were drawn from the cohort of 1,428 workers who participated for at least 10 years in the employer-sponsored health monitoring program. The cohort included 1,163 (81%) and 125 (8.8%) white males and females, 120 (8.4%) and 20 (1.4%) black males and females; 43% had never smoked cigarettes, 16% were continuous smokers, and 20% were ex-smokers at the initial test, while 22% quit smoking during follow-up. There were 18,731 pulmonary function measurements in total, with each participant providing an average of 13 valid spirometry results (range, 5–23). The follow-up interval between each participant's first and last test averaged 19 years, ranging from 10 to 30 years.

The overall mean of individual FEV_1 slopes was −29 ml/year. Cases were defined as individuals with FEV_1 slopes below the gender and race specific 5th percentile values; this resulted in 71 cases. However, only 64 cases could be included in this case–control analysis (3 cases did not have matched controls and 4 cases had missing medical records). Controls (N = 88) were matched with cases (N = 64) by race, gender, smoking status, birth cohort, age at baseline, height, and calendar year of first test. The matching process resulted in one case matched with one or two controls, and conversely, one control could be matched with one or two cases. The ratio for case versus control was 1:1 for 21 cases and 1:2 for 43 cases. In other words, for 21 cases, each case has one matched control, while for 43 cases; each case has two matched controls. A total of 107 case–control pairs (1:1 matching pairs) was obtained and included in the data analysis.

Among cases and controls, the percentage of current, ex-, and never smokers was 58%, 14%, and 28% at baseline; and 28%, 47%, 25% at the last test, respectively—about 30% of subjects quit smoking during follow-up.

Table I shows the group comparisons between cases and controls of demographics, spirometry indices, the percentage of abnormal spirometry results, and workplace exposure. There were no statistically significant differences found at baseline. At their final examination, cases had a greater proportion of abnormal spirometry results (70.3% vs. 23.9%, $P < 0.0001$), gained more weight than controls ($P < 0.05$), and tended to smoke more cigarettes, although this was not statistically significant. The mean FEV_1 slope was −80 ml/year for cases and −11 ml/year for controls ($P < 0.0001$). Figure 1 demonstrates the distribution of FEV_1 slopes by cases versus controls. The proportion of participants who had any workplace exposure to MIC and/or phosgene was similar.

Matched pair comparisons between cases and controls for long-term health outcomes are illustrated in Figures 2–4. Figure 2 shows that a higher proportion of the medical records from cases indicated medication use (67.3% vs. 47.7%, $P = 0.0082$) and particularly medications for respiratory disease (24.3% vs. 4.7%, $P < 0.0001$) compared to controls. A higher proportion of cases also had diagnoses of COPD or emphysema (17.8% vs. 1.9%, $P = 0.0002$) (Fig. 3) and there was a trend toward more cardiac diagnoses (10.3% vs. 3.7%, $P = 0.0923$). Figure 4 shows that dyspnea on exertion or walking on level ground (15.0% vs. 3.7%, $P = 0.0042$) and wheezing or rhonchi on examination (10.3% vs. 1.9%, $P = 0.0225$) were more common among cases compared to controls.

DISCUSSION AND CONCLUSION

Physicians often recommend that individuals who are exposed to respiratory hazards perform periodic spirometry, to monitor lung health. When an individual is identified with

TABLE I. Group Comparisons of Demographic and Spirometry Indices at the Initial and the Final Follow-Up, and Workplace Exposure by Case Status

Grouping	All subjects, N = 152	Cases, N = 64	Controls, N = 88
At the initial test			
Mean age, year (SD)	36.1 (8.1)	36.5 (8.2)	35.9 (8.0)
Height, inch (SD)	69.9 (2.6)	69.8 (2.5)	70.0 (2.7)
Weight, lb (SD)	188.1 (31.5)	191.2 (35.8)	185.8 (27.9)
Mean pack-years (SD)	10.2 (10.4)	11.6 (11.1)	9.2 (9.7)
Mean FEV_1, L (SD)	3.67 (0.73)	3.80 (0.78)	3.59 (0.69)
Mean FVC, L (SD)	4.87 (0.84)	4.99 (0.85)	4.78 (0.81)
^Spi-abnormal, n (%)	45 (29.6)	16 (25.0)	29 (33.0)
At the final			
Mean age, year (SD)	53.8 (7.6)	53.1 (8.0)	54.4 (7.2)
Weight, lb (SD)	209.3 (43.8)	218.6 (52.0)	202.6 (35.6)*
Mean pack-years (SD)	18.5 (16.4)	21.1 (17.0)	16.7 (15.9)
Mean FEV_1, L (SD)	3.05 (0.86)	2.36 (0.87)	3.26 (0.67)**
Mean FVC, L (SD)	3.95 (0.93)	3.53 (0.91)	4.26 (0.81)**
FEV1 slope, L/year (SD)	−0.040 (0.038)	−0.080 (0.020)	−0.011 (0.014)**
Spi-abnormal, n (%)	66 (43.4)	45 (70.3)	21 (23.9)**
Workplace exposure to MIC and phosgene			
Exposure = yes, n (%)	34 (22.4)	14 (21.9)	20 (22.7)

^Spi-abnormal, abnormal spirometry results.
*$P < 0.05$.
**$P < 0.0001$.

a rapid rate of lung function decline; both the physician and the affected individual need an understanding of the health implications of the decline, in order to assess the potential costs and benefits of various interventions. In the current study, we used a case–control approach to investigate long-term health among chemical plant workers who had shown accelerated FEV_1 declines while participating in an employer-sponsored medical monitoring program. Previous results from a cohort study in the same population indicated that FEV_1 measurements were affected by age, gender, race, height, weight gain, smoking, and the type of spirometer used [Wang et al., 2005, 2009]. In the current study, 64 individuals were designated as cases because they had demonstrated FEV_1 slopes below the values at the 5th percentile of the distribution of FEV_1 slopes over the mean of 19 years follow-up in the cohort. These cases were matched with 88 controls for race, gender, smoking status, year of birth, age at baseline, height, and calendar year of first test. The matching process was performed using SAS® macro language; and resulted in 107 pairs (1:1 matching) that could be included in the data analysis.

At baseline, there were no statistically significant differences between cases and controls for demographic and spirometry indices. The individuals with accelerated

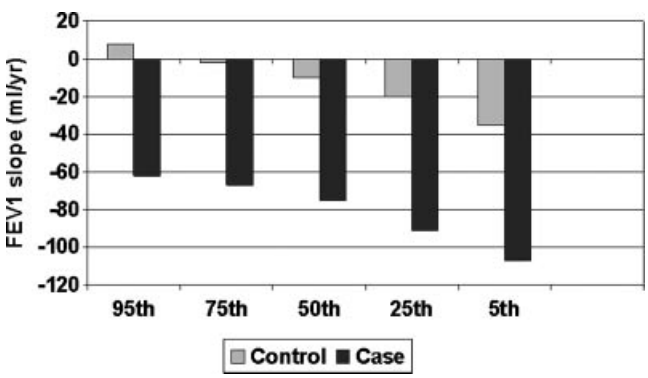

FIGURE 1. Distribution of FEV_1 slope (ml/year) by cases versus controls.

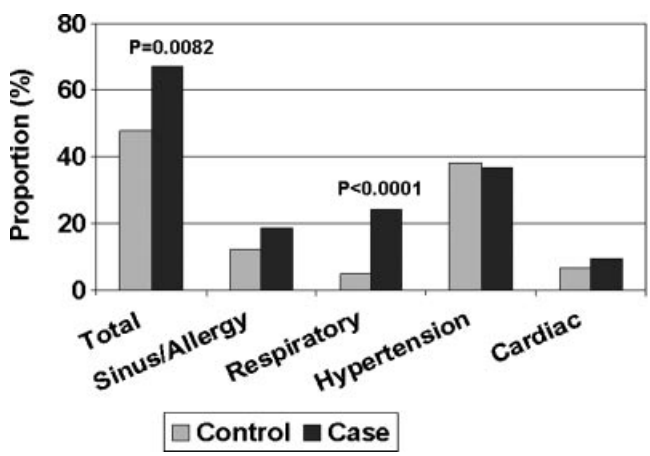

FIGURE 2. Matched pair case–control comparison of medication use, N = 107 pairs.

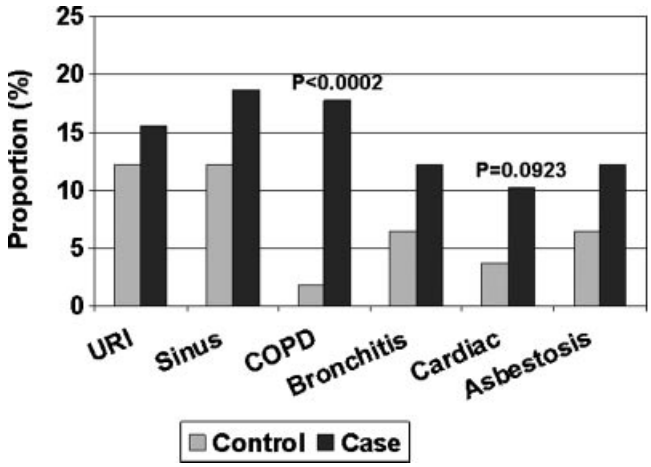

FIGURE 3. Matched pair case–control comparison of diagnoses, N = 107 pairs. URI = upper respiratory infection; cardiac = angina, bypass, and MI.

lung function declines had a markedly increased risk of adverse long-term health outcomes compared to the matched controls, as documented in plant medical records during the last 4 years of follow-up. Cases had approximately nine times the proportion of diagnoses of COPD and three times the proportion of cardiac diagnoses compared to the matched controls. Symptoms of shortness of breath were recorded four times more frequently, and wheezing on examination and the use of medication for respiratory tract problems were both documented five times as often. The average age at follow-up was 53 years. Interestingly, the cases mainly developed a restrictive pattern of spirometric abnormality, reflecting similar declines in both FEV_1 and FVC. In the absence of a measure of absolute lung volume in this study, however, it is unclear if this pattern is associated with air trapping or true restriction.

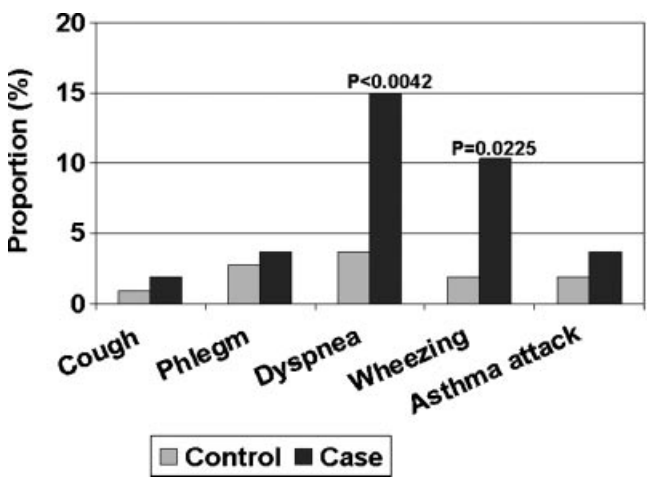

FIGURE 4. Matched pair case–control comparison of symptoms and findings, N = 107 pairs. Dyspnea = Dyspnea on effort or walking on level ground.

The results from this case–control study are consistent with several previous investigations. Excessive longitudinal decline in FEV_1 among US coal miners has been associated with adverse long-term health outcomes including mortality. The rapid FEV_1 declines experienced by some coal miners were associated with subsequent increases in respiratory symptoms, illnesses, and mortality from cardiovascular and non-malignant respiratory disease [Wang et al., 1996; Beeckman et al., 2001; Sircar et al., 2007]. A report by Ryan et al. [1999] indicated that the rate of decline in FEV_1 was a predictor of survival independent of FEV_1 level. Mannino et al. [2006] analyzed data from a large longitudinal, population-based study (n = 15,536); the results indicated that rapid decline in the FEV_1 was associated with a higher risk of death and COPD hospitalization.

In this study, although smoking status was one of the matching items, during follow-up cases smoked on average about 1.1 more pack-years of cigarettes than controls and also gained significantly more weight (16 lb) (Table I). Both weight gain and cigarette smoking appeared to contribute to excessive loss of lung function (Table I), which is consistent with a number of recent longitudinal studies [Wang et al., 1997, 2005].

The proportion of cases and controls who had worked in areas with potential exposure to either methyl isocyanate or phosgene was similar (Table I). However, our previous cohort analysis (N = 1,884) from this plant had identified a significant adverse effect of chemical exposures on the odds of an employee experiencing rapid FEV_1 decline [Wang et al., 2009]. In that earlier study, we used a random effects model approach to identify rapid decliners whose FEV_1 slope showed a significant ($P < 0.05$) decline, after adjusting for all the significant co-variables. We were able to identify a group of workers exposed to chemicals in the plant and a group of workers who had no known potential exposure to workplace respiratory hazards based on limited employment histories. The proportion of ''rapid decliners'' in the exposed group was five times greater than in the putatively non-exposed group ($P = 0.0037$ by Chi-square test). The lack of an apparent exposure effect using the case–control approach in the current study may be attributed to fewer subjects and the inability to account for various chemical exposures other than MIC and phosgene. In the current study, a majority of both cases and controls had potential exposures to multiple chemicals while only a small proportion had no known workplace exposures to chemicals.

This study has several strengths. Spirometry was performed annually according to professional standards in a relatively large (1,428 participants) generally healthy working population, with 18,731 pulmonary function measurements, a minimum 10 and an average 19 years of follow-up. The case–control design permitted estimation of the risk to individuals for several important outcomes.

Medical records were reviewed without knowledge of the spirometry decline status, reducing the possibility of observer bias. There are also a number of weaknesses of the study. Three cases could not be fully matched to controls, and four other cases did not have complete medical records. Information was not available about either the duration or level of potentially hazardous workplace exposures. Medical diagnoses were based upon all medical examinations (including both annual health surveys and any other medical visits) provided in the plant medical department during the last 4 years of employment, and when reported by the workers as doctor-diagnosed, may not have been independently verified. Because only 4 years of medical records were reviewed for cases and controls, the specific timing of onset of the adverse health conditions could not be determined.

In this study, cases and controls were matched in the calendar year of first test, because FEV_1 results obtained from different models of volume spirometers may affect the estimates of longitudinal decline in FEV_1. The ''spirometer effects'' likely reflect many factors which can change over time when longitudinal pulmonary function measurements are made in actual practice. The magnitude of the effect of spirometer type on FEV_1 measurements may be impacted by differences in technicians and methods used to perform the tests over the 30 years, as well as by differences in spirometer software measurement algorithms, automated feedback to the technician during testing, and calibration procedures used for each spirometer. Also, the testing posture was changed from standing to sitting in March 1988; standing posture is expected to result in a slightly larger FEV_1, however matching by the calendar year of first test should reduce the effect of the change in testing posture.

Recent research findings, professional guidelines, and public domain software have become available to improve the accuracy of medical monitoring programs in the identification of apparently healthy individuals who are experiencing accelerated lung function declines [Wang and Petsonk, 2004; Townsend, 2005; Wang et al., 2006; Hnizdo et al., 2007; NIOSH, 2008]. Interventions directed at preserving lung health may be difficult to effectively implement, and costly to the individual and/or the employer [Vandenplas et al., 2003]. Both the responsible physician and the affected individual need an understanding of the health implications of the declines, in order to assess the potential costs and benefits of various interventions. This study expands the scientific basis for monitoring respiratory health using spirometry, by providing quantitative estimates of the increase in adverse health conditions (from four- to ninefold) that were observed among a group of working age individuals whose long-term FEV_1 slope was below the race- and gender-specific 5th percentile values of the distribution of FEV_1 slopes in the entire cohort.

REFERENCES

Beeckman LF, Wang ML, Wagner GR, Petsonk EL. 2001. Accelerated declines in FEV_1 and subsequent increased respiratory symptoms, illnesses, and mortality in coal miners. Am J Respir Crit Care Med 163: 633–639.

Burchfiel CM, Marcus EB, Sharp DS, Enright PL, Rodriguez BL, Masaki KH, Hwang LJ, Curb JD. 1996. Characteristics associated with rapid decline in forced expiratory volume. Ann Epidemiol 6:217–227.

Carta P, Aru G, Barbier MT, Avataneo G, Casula D. 1995. Dust exposure, respiratory symptoms, and longitudinal decline of lung function in young coal miners. Occup Environ Med 53:312–319.

Cody RP, Smith JK. 1997. Applied statistics and the SAS programming language, 4th edition. New Jersey: Prentice-Hall, Inc. Upper Saddle River, p 81–83.

Hankinson J, Wagner GR. 1993. Medical screening using periodic spirometry for detection of chronic lung disease. Occup Med State Art Rev 8:353–361.

Hankinson J, Odencrantz JR, Fedan KB. 1999. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 159:179–187.

Hnizdo E, Sircar K, Yan T, Harber P, Fleming J, Glindmeyer HW. 2007. Limits of longitudinal decline for the interpretation of annual changes in FEV_1 in individuals. Occup Environ Med 64:701–707.

Mannino DM, Reichert M, Davis KJ. 2006. Lung function decline and outcomes in an adult population. Am J Respir Crit Care Med 173:985–990.

NHLBI/WHO Workshop Summary. 2001. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 163:1256–1276.

NIOSH Safety and Health Topic: Spirometry Monitoring Technology. 2008. Available at http://www.cdc.gov/niosh/topics/spirometry/spirola.html (accessed 15 April 2008).

Ryan G, Knuiman MW, Divitini ML. 1999. Decline in lung function and mortality: The Busselton Health Study. J Epidemiol Community Health 53:230–234.

SAS. 2003. SAS/STAT User's Guide, version 9. Cary, NC: SAS Institute, Inc.

Sherman CB, Xu X, Speizer FE, Ferris BG, Jr., Weiss ST, Dockery DW. 1992. Longitudinal lung function decline in subjects with respiratory symptoms. Am Rev Respir Dis 146:855–859.

Sircar K, Hnizdo E, Petsonk EL, Attfield MD. 2007. Decline in lung function and mortality: Implications for medical monitoring. Occup Environ Med 64:461–466.

Tockman MS, Pearson JD, Fleg JL, Metter EJ, Kao SY, Rampal KG, Cruise LJ, Fozard JL. 1995. Rapid decline in FE V_1: A new risk factor for coronary heart disease mortality. Am J Respir Crit Care Med 151: 390–398.

Townsend MC. 2005. ACOEM evidence-based statement: Evaluating pulmonary function change over time in the occupational setting. American College of Occupational and Environmental Medicine. J Occup Environ Med 47:1307–1316.

Vandenplas O, Toren K, Blanc PD. 2003. Health and socioeconomic impact of work-related asthma. Eur Respir J 22:689–697.

Wang ML, Petsonk EL. 2004. Repeated measures of FEV_1 over six to twelve months: What change is abnormal? J Occup Environ Med 46:591–595.

Wang ML, Petsonk EL, Attfield MD, Short SR, Beeckman LF, Bonnett B, Hankinson JL. 1996. Miners with clinically important declines in FE V_1: Analysis of data from the U.S. National Coal Study. Appl Occup Environ Hyg 11:989–995.

Wang ML, McCabe L, Petsonk EL, Hankinson JL, Banks DE. 1997. Weight gain and longitudinal changes in lung function in steel workers. Chest 111:1526–1532.

Wang ML, Avashia B, Petsonk EL. 2005. Factors affecting the recognition of excessive FEV_1 decline: Analysis of 30 years of data from an industry-based monitoring program [abstract]. Am J Respir Crit Care Med 71:A440.

Wang ML, Avashia BH, Petsonk EL. 2006. Interpreting periodic lung function tests in individuals: The relationship between 1- to 5-year and long-term FEV_1 changes. Chest 130:493–499.

Wang ML, Avashia BH, Petsonk EL. 2009. Interpreting longitudinal spirometry: Weight gain and other factors affecting the recognition of excessive FEV_1 decline. Am J Ind Med 52:782–789.