Interpreting Screening Questionnaires

Specific Respiratory Symptoms and Their Relationship to Objective Test Results

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Objective: To better delineate the relationship between responses to screening respiratory symptom questionnaires and various pulmonary function test results. **Methods:** Spirometry, methacholine challenge, standardized questionnaires, smoking, medical, and work histories were recorded at initial and 5-year follow-up surveys among 411 participants. Percent-predicted forced expiratory volume in 1 second ($ppFEV_1$), 5-year FEV_1 decline, and proportion of methacholine responders (% hyper-responders) were compared with questionnaire responses utilizing generalized estimating equations modeling and analysis of variance. **Results:** Significant associations were found between $ppFEV_1$ and cough, phlegm, dyspnea, or ever wheezing; between greater percentage of hyper-responders and dyspnea with wheezing, ever/persistent wheezing, or history of asthma/hay fever; and between accelerated FEV_1 decline and new onset dyspnea with wheezing, phlegm, or persistent wheeze. **Conclusions:** Particular respiratory symptoms reported on screening questionnaires are associated with specific physiologic abnormalities, enhancing questionnaire utility in workplace health surveillance.

Standardized respiratory symptom questionnaires were first developed for use in epidemiological studies, to investigate the relationships between exposures (eg, dust, smoking) and chronic respiratory disorders.[1] Questionnaires are also frequently used in medical screening and health monitoring for individuals with potential exposure to respiratory hazards.[2,3] In the context of workforce screening, rather than studying effects of exposures, questionnaires are used to accurately identify a subset of individuals with either early disease or a high likelihood of its future occurrence, to efficiently target clinical evaluations and preventive actions.[4] Individuals who inhale hazardous substances in the workplace may develop various inflammatory disorders of the respiratory tract. The interpretation of symptoms reported during health surveillance is based on knowledge of the recognized toxicities of workplace hazards, as well as the operating characteristics of the specific questionnaire items.[5,6] For example, mucous hypersecretion can cause symptoms of cough and phlegm, airway inflammation can generate wheezing and chest tightness, while dyspnea on exertion may result from both airflow obstruction and interstitial lung disorders.[7] To assess validity for items that reflect respiratory health, outcomes based on questionnaires should be compared with objective measures of respiratory dysfunction. Nevertheless, previous studies of the relationships between respiratory symptoms and measures of lung function and non-specific airway responsiveness have yielded complex findings.[8–10] To further investigate these relationships, the current study analyzed respiratory symptoms reported on standardized questionnaires in a group of blue-collar workers. The objective was to describe differences in lung function results between individuals reporting and those not reporting specific respiratory symptoms, and thereby assist occupational health providers in understanding the association of specific symptom outcomes with reduced ventilatory lung function, accelerated functional decline, and/or increased non-specific airway responsiveness.

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METHODS

Approval for performance of the study was received from the West Virginia University Institutional Review Board, and all volunteers gave written informed consent prior to participating. Subject selection and methods have been described in detail,[11,12] and are reviewed briefly below.

Participants

Miners were recruited from three large Appalachian underground bituminous coal mines. Non-mining workers were recruited in the same region from nine public and private employers with no history of adverse respiratory exposures. A total of 478 volunteers were recruited from May 1985 to July 1987.

Spirometry Testing

Spirometry was performed at the work site immediately prior to the work shift at 6-month intervals for 5 years. Testing was conducted using an 8L water-sealed survey spirometer with an attached microprocessor (Eagle II, Warren E. Collins, Braintree, Massachusetts), using the standards of the American Thoracic Society 1978 Snowbird workshop.[13]

Of the 478 participants, a total of 411 who had completed both the initial and final questionnaires and performed 3 to 12 valid spirometry tests over approximately 5 years were included in this analysis (199 underground coal miners, and 212 working non-miners).

Questionnaire

A standardized self-administered respiratory symptom questionnaire, based on the British Medical Research Council (1976), was used at both the initial and 5-year follow-up surveys. An occupational history and additional questions on tobacco use were included.

Symptom outcomes were defined based on the questionnaire responses as follows: cough: cough less than six times/d; chronic cough: cough at least six times/d most days for at least 3 months during the year; phlegm: phlegm brought up from the chest in the morning, during the day, or at night; chronic phlegm: phlegm most days for at least 3 months during the year; dyspnea: shortness of breath when hurrying on level ground or walking up a slight hill; wheeze: chest ever sounds wheezing or whistling; persistent wheeze: wheezing most days or nights each week; dyspnea with wheezing:

attacks of shortness breath with wheezing; asthma history: ever had asthma; and hay fever history: ever had hay fever.

Methacholine Tests

For all participants whose FEV_1 was at least 80% predicted, an abbreviated methacholine inhalation challenge protocol was performed at the initial and final surveys.[14] Subjects with reproducible FEV_1 declines of 15% or greater at any point in the protocol were classified as methacholine responders (hyperresponders [HR] = Yes) at that survey. If declines were less than 15% after five vital capacity inhalations of the highest concentration (25 mg/ml) of methacholine aerosol, the individual was classified as having normal nonspecific bronchial responsiveness (HR = No).

Data Analysis

Statistical analysis was performed using the SAS personal computer version 8.0 software package (SAS, Inc, Cary, NC).[15] The percentage of predicted value of FEV_1 ($ppFEV_1$) was calculated based on the individual's race, gender, age, and height using the equation of Hankinson and coworkers.[16] Longitudinal rate of change of FEV_1 (FEV_1 slope in milliliters per year) was computed for each individual across the repeated measurements using simple linear regression.

Group comparisons: Cross-sectional group comparisons were performed among those who did or did not (Yes-No) report each of the symptom outcomes at the initial and/or the final surveys: for comparisons of percentage of methcholine responders, the chi-squared test was performed; for comparisons of mean percent predicted FEV_1, *t* test was used.

Analysis of covariance: To evaluate the relationship between longitudinal patterns of symptoms and the longitudinal FEV_1 change (FEV_1 slope), analysis of covariance (SAS GLM procedure) was performed. The longitudinal pattern of each symptom outcome at both the initial and final survey was defined as: (1) Continuing symptom (Yes-Yes); (2) New onset symptom (No-Yes); (3) Symptom regression (Yes-No); and (4) Symptom absence (No-No). For each symptom outcome, the SAS GLM procedure was used to determine the significance of differences in mean FEV_1 slopes among the four groups with different longitudinal patterns adjusting for the average age at the mid-point of follow-up, mean pack-years of smoking, and average $ppFEV_1$ (recorded at the initial and 5-year follow-up surveys).

Multiple logistic regression analysis using Generalized Estimating Equations (GEE): To further investigate the relationship of specific symptom outcomes and the objective test results (spirometry and methacholine tests) the GEE technique (SAS GENMOD procedure) was used, analyzing the repeated responses for each symptom outcome (yes/no at both the initial and final surveys). Explanatory variables included age at initial survey, mining status (yes/no), and the time-dependent variables of smoking status (current, ex-, and never), HR status (yes/no), and $ppFEV_1$, with values corresponding to the time of each survey. The model structure was based on a binomial distribution, logit link function, and exchangeable 'working correlation'. The models examined linear time trends and terms for interactions between smoking and mining, and smoking and HR.

RESULTS

The study participants represented a working population and included 389 white men (95%), with 28% current smokers and 27% exsmokers at the initial survey. The 411 participants provided 3756 valid spirometry measurements, with an average of nine tests per person (range 3–12) over a mean 4.9 years. Table 1 shows the demographic characteristics, spirometry indexes, and methacholine challenge test results at the initial and 5-year follow-up surveys. At the initial survey, the miners had worked an average 18 years underground, whereas among the non-miners work tenure averaged 21 years. The 67 workers excluded from the study included individuals with incomplete data, those who were unable to perform repeatable spirometry, and also persons whose initial FEV_1 values were less than 80% predicted.

Figure 1 shows the prevalence of respiratory symptoms at the initial and 5-year follow-up surveys. The prevalence was similar on both surveys ranging from 15% to 30% for cough, phlegm, dyspnea, wheeze, and hay fever history; and from 5% to 10% for persistent wheeze, dyspnea with wheezing, and asthma history. Figure 2 presents the group comparisons of HR by symptom outcomes at the initial and the 5-year follow-up surveys. Both dyspnea with wheezing and asthma history were highly associated with a methacholine response (>60% HR = Yes, $P < 0.0001$); followed by persistent wheeze, wheeze, hay fever history, chronic phlegm, phlegm, and cough. Group comparisons of $ppFEV_1$ by symptom outcomes are shown for the initial (Figure 3A) and follow-up (Figure 3B) surveys. Dyspnea, wheeze, and persistent wheeze were most highly associated with a reduced level of $ppFEV_1$; followed by chronic phlegm, chronic cough, phlegm, cough, dyspnea with wheezing, and asthma history. The results at the initial and the follow-up surveys were similar, but not identical. Table 2 shows the results of the analysis using a GEE model of the association between the symptom outcomes and test results expressed by odds ratios. Being a methacholine responder increased the odds of reporting hay fever history (1.7), persistent wheeze (2.1), dyspnea with wheezing (2.7), and asthma history (4.8). Each 10% reduction in $ppFEV_1$ increased the odds

TABLE 1. Study Population Demographics, Spirometry and Methacholine Test Results

	Initial survey	Final survey
Age (years)	39.1 (9.1, 19–64)*	44.0 (9.2, 22–70)
Height (inch)	70.1 (2.7, 62.0–78.0)	
Smoking (pack-yrs)	10.6 (15.1, 0.0–83.2)	13.2 (17.6, 0.0–94.3)
FEV_1 (ml)	4116 (719, 1570–6410)	3803 (714, 1880–6090)
FVC (ml)	5120 (843, 2650–7230)	4812 (845, 2370–7250)
% predicted FEV_1†	97.5 (11.7, 44–133)	93.0 (12.5, 52–138)
% predicted FVC	96.8 (11.0, 56–130)	92.9 (11.7, 56–128)
FEV_1 Slope (ml/yr)	−57 (55, −282–359)	
HR‡ = Yes, n/N	104/386 (26.9%)	92/308 (29.9%)

*Mean (SD, range).
†Percent predicted by Hankinson equation.
‡HR = Yes indicates methacholine responder.

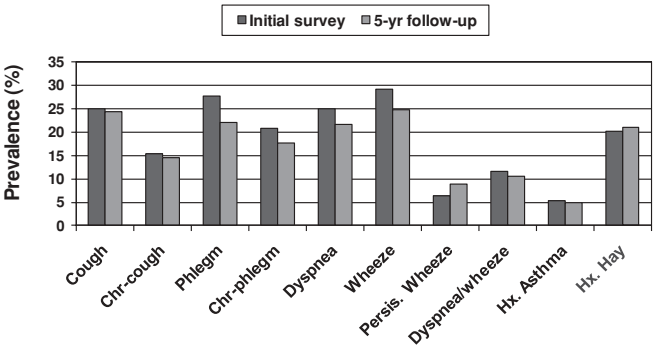

FIGURE 1. The prevalence of respiratory symptoms at the initial (N = 411) and the 5-yr follow-up (N = 363) surveys. See text for definitions of symptom categories.

of reporting cough, phlegm, dyspnea, and wheeze by 20% to 40%. Each of the symptom outcomes seemed to associate more clearly with one or the other of the objective tests.

To further investigate the association of symptoms and lung function, responses were grouped into symptom scores, on the basis of the number of symptoms reported by each participant that were associated in the GEE model with either HR (for asthma) or reduced $ppFEV_1$ [for Chronic obstructive pulmonary disease (COPD)]. Increases in the asthma symptom score were significantly associated with HR, though few participants had more than two of the symptoms. (Table 3) No consistent pattern of abnormalities was associated with the COPD symptom score.

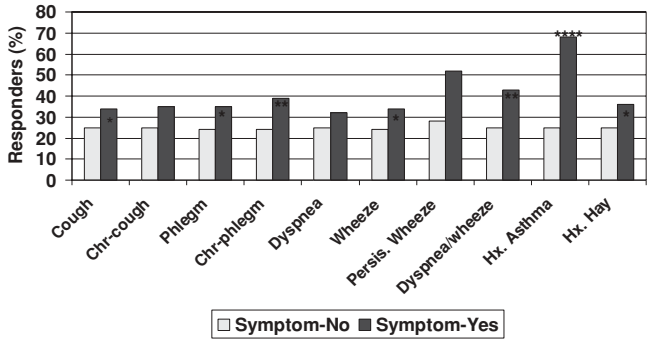

FIGURE 2. (A) Percentage of methacholine responders by symptoms reported at initial survey, N = 386, $^{****}P < 0.0001$; $^{**}P < 0.01$; $^{*}P < 0.05$.

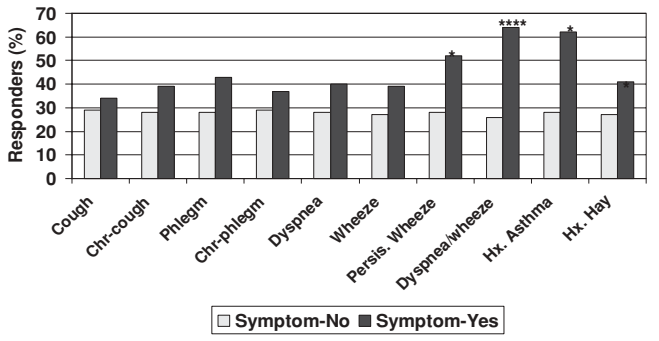

FIGURE 2. (B) Percentage of methacholine responders by symptoms reported at 5-year follow-up, N = 308, $^{****}P < 0.0001$; $^{**}P < 0.01$; $^{*}P < 0.05$.

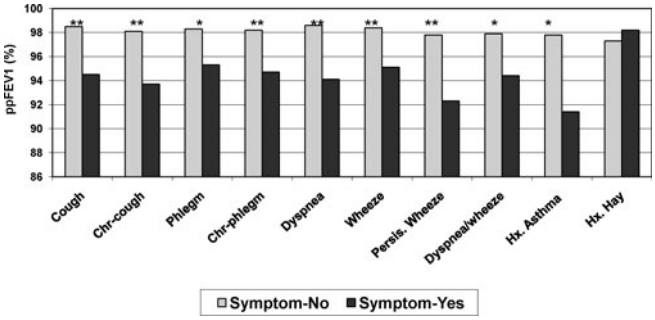

FIGURE 3. (A) Mean percent predicted FEV_1 by symptoms reported at initial survey, N = 411, $^{**}P < 0.01$; $^{*}P < 0.05$.

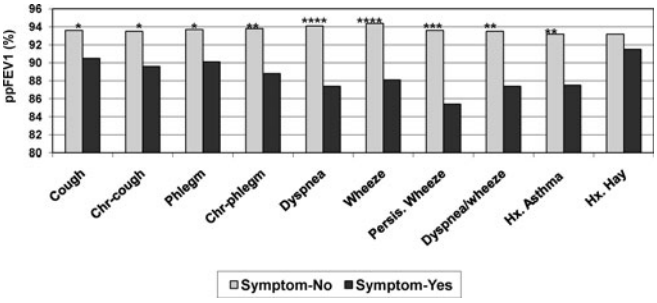

FIGURE 3. (B) Mean percent predicted FEV_1 by symptoms reported at 5-year follow-up, N = 363, $^{****}P < 0.0001$; $^{***}P < 0.001$; $^{**}P < 0.01$; $^{*}P < 0.05$.

Figure 4 illustrates the significance of differences in FEV_1 slope by longitudinal symptom patterns. For the group with absent symptoms, the 5-year FEV_1 slopes averaged −57 ml/yr. Mean FEV_1 declines were significantly greater with the new onset of phlegm (−86), persistent wheeze (−89), and dyspnea with wheezing (−94). Groups that reported continuing symptom outcomes (Yes at both initial and final surveys) for phlegm and persistent wheeze also had steeper FEV_1 slopes (−71 and −64 ml/yr, respectively) than the corresponding group with absent symptoms.

DISCUSSION AND CONCLUSIONS

Standardized respiratory symptom questionnaires have historically been used in epidemiological studies of occupational, environmental, life-style, and other factors to investigate the causes, distribution, and evolution of symptoms in populations.[17,18] Recently, attention has focused on the use of questionnaire-based outcomes to assess clinical status and quality of life in individuals enrolled in therapeutic trials.[19,20] Brief standardized respiratory symptom questionnaires are also widely used in periodic assessments of apparently healthy workers exposed to respiratory hazards. Although occupational lung diseases can occasionally develop over a matter of months,[21] most exposed workers have symptoms over a period of years before the onset of disabling impairment. Occupational health providers seek to identify at-risk individuals and offer timely referrals for further evaluations and preventive interventions. To assure effective and efficient surveillance, decisions are based on the consistency of the symptoms reported with those anticipated from recognized job hazards, as well as the operating characteristics of the specific questionnaire items.[4]

In the current study, health outcomes based on self-reported respiratory symptoms were analyzed from a study of 411 blue-collar workers. We investigated the association between specific symptom

TABLE 2. Odds Ratios for Objective Test Results from GEE Models of Symptom Outcomes

	Odds Ratio (95% CI)	
Symptom items	**Methacholine responder (Y/N)**	**ppFEV$_1$ (%) (−10 units)**
Cough	1.1 (0.7–1.6)	1.2 (1.0–1.5)
Chronic cough	1.2 (0.7–2.1)	1.3 (1.0–1.7)*
Phlegm	1.2 (0.8–1.8)	1.2 (0.9–1.4)
Chronic phlegm	1.2 (0.8–1.9)	1.3 (1.0–1.6)*
Dyspnea	1.1 (0.7–1.7)	1.3 (1.1–1.7)**
Wheeze	1.3 (0.9–2.0)	1.2 (1.0–1.5)*
Persistent wheeze	2.1 (1.1–4.0)*	1.2 (0.8–1.9)
Dyspnea with wheezing	2.7 (1.7–4.5)****	1.2 (0.9–1.6)
Asthma history	4.8 (2.4–9.5)****	1.4 (1.0–2.1)*
Hay fever history	1.7 (1.2–2.4)**	1.0 (0.8–1.2)

****$P < 0.0001$; **$P < 0.01$; *$P < 0.05$.
GEE models: Symptom(Y/N) = baseline age, smoking status, mining status, HR,% predicted FEV$_1$, time.

TABLE 3. Association of Baseline Symptom Scores and Lung Function Results

Asthma symptom score†	N = for symptoms/methacholine	HR = Y N = 386 n (%)	FEV$_1$slope ≥60 ml/yr n (%)	FEV$_1$slope ≥90 ml/yr n (%)
0	278/266	62 (23)*	124 (45)	71 (26)
1	99/89	25 (28)	46 (47)	23 (23)
2	25/23	11(48)	11 (44)	7 (28)
3	5/5	3(60)	1 (20)	0
4	4/3	3(100)	1 (25)	0
COPD symptom score‡				
0	205/196	38 (19)*	95 (46)	58 (28)
1	103/96	36 (38)	46 (45)	24 (23)
2	57/50	13 (26)	21 (37)	7 (12)
3	29/28	10 (36)	14 (48)	6 (21)
4	11/16	7 (44)	7 (41)	6 (35)

†Asthma symptom score = persistent wheeze + dyspnea with wheezing + asthma history + hay fever history.
‡COPD symptom score = Chronic cough + chronic phlegm + dyspnea + wheeze.
*$P < 0.01$ for trend by Cochran-Mantel-Haenszel Statistics.

outcomes and objective test results (spirometry and methacholine challenge tests) with the goal of assisting health professionals who utilize respiratory questionnaires for periodic-health screening of working individuals. The proportion of methacholine responders was found to be significantly increased among participants who reported shortness of breath with wheezing, wheeze, persistent wheeze, chronic phlegm, or a history of asthma or hay fever. The GEE model results also suggested that specific symptoms reported by workers during periodic screening appear to have distinct functional implications (Table 2).

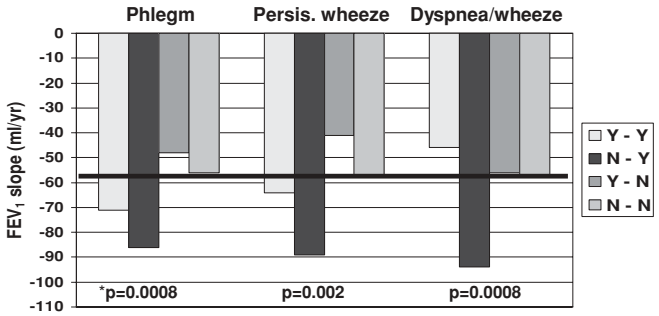

FIGURE 4. FEV$_1$ slope by longitudinal pattern of responses to specific questionnaire symptom items. FEV$_1$ slope adjusted for age, smoking, and percent predicted FEV$_1$. The line "—" = overall average slope. *P value refers to longitudinal pattern of "N-Y" vs. "N-N" groups.

The findings are consistent with previous population-based studies that recognized an association between the presence of airway hyper-responsiveness to methacholine or histamine and self-reported or physician-diagnosed asthma or wheezing symptoms.[5,10,22–24] Among individuals exposed to occupational sensitizers such as western red cedar dust or methylene diphenyl diisocyanate, the proportion of methacholine responders is increased in those who report asthma or asthma–like symptoms.[25,26] In both occupational and community populations about half of individuals who demonstrate airway hyper-responsiveness do not report respiratory symptoms, although follow-up studies demonstrate that asymptomatic hyper-responsiveness increases the risk of subsequent symptom development.[27,28]

A number of previous studies have observed that reports of certain symptoms on questionnaires including cough, chronic cough, and/or chronic phlegm, shortness of breath and wheeze are related to a reduced ppFEV$_1$ and also an excessive decline in FEV$_1$.[29–34] Consistent with these previous reports, participants in the current study who developed the new onset of respiratory symptoms during follow-up, particularly persistent wheeze, phlegm, and dyspnea with wheezing, lost more lung function than those who did not.

The current study has several strengths. Standardized and contemporary approaches were used for periodic assessment of

symptom and lung function outcomes among a group of over 400 generally healthy blue-collar workers, similar to occupational medical screening programs. There was good participation and follow-up. The modeling results provide useful quantitative information about the association of specific symptoms with particular lung function abnormalities. The study also has several limitations. Many participants were exposed to dust during the study and experienced both respiratory symptoms and accelerated lung function loss, but none were exposed to recognized sensitizers. The study population was generally healthy and had a low prevalence of clinically important abnormalities, which reduced the power to estimate the operating characteristics of the symptom outcomes. An attempt was made to improve questionnaire performance by combining symptoms related to each outcome into a score, but this did not greatly improve performance of the individual items. Of the 478 volunteers, 67 were excluded from the analysis for various reasons, and the prevalence of two symptoms was elevated in the excluded versus included participants (dyspnea: 42% vs. 25%, $P = 0.0067$. and wheeze: 43% vs. 29%, $P = 0.0319$). Although deemed necessary, the exclusions may have affected the power of the study to detect associations with these symptoms. Finally, in the current study, no attempt was made to associate the observed physiologic abnormalities with specific causes, such as occupational dust exposures or tobacco smoking.

In summary, although outcomes from self-completed questionnaires are considered "subjective," specific respiratory symptom outcomes are significantly correlated with particular objective lung function testing results. The new onset of certain symptoms (dyspnea with wheeze, persistent wheeze, or regular phlegm production) was associated with a significantly accelerated 5-year FEV_1 decline. A significantly increased percentage of methacholine responders were found among participants reporting shortness of breath with wheezing, wheeze, persistent wheeze, or chronic phlegm, as well as those with a history of asthma or hay fever. Finally, a lower level of FEV_1 was seen among those reporting cough, chronic cough, phlegm, chronic phlegm, wheeze, persistent wheeze, or dyspnea. These results support the utility of responses to specific respiratory symptom questionnaire items in medical monitoring programs. Health care providers can use these results when evaluating recognized hazards and specific symptoms reported to better identify individuals who may benefit from further evaluation and/or interventions to prevent development of clinically important lung diseases related to exposures.

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