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Original Research

Spirometric pattern transitions in a World Trade Center occupational cohort on longitudinal surveillance

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ABSTRACT

Background: Many workers and volunteers who participated in the rescue and recovery of the World Trade Center (WTC) disaster site in 2001–2002 manifest a heterogeneous group of chronic lower airway diseases, with variable spirometric patterns on longitudinal surveillance. We examined systematically the observed transitions among those spirometric patterns and assessed their association with BMI and occupational WTC exposure intensity.

Methods: We selected 10,810 Mount Sinai WTC General Responders' Cohort members with at least three acceptable quality periodic spirometries (n = 56,312) performed between July 2002 and November 2019. We defined three spirometric patterns: (1) normal: prebronchodilator first-second forced expiratory volume (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio > lower limit of normal (LLN); (2) obstruction: prebronchodilator FEV_1/FVC ratio<LLN; (3) low FVC: FVC < LLN and FEV_1/FVC > LLN. We built a multi-state Markov-like model to analyze probabilities of transition between those three spirometric patterns.

Results: Low FVC is the most frequent abnormal spirometric pattern in the WTC workers. Substantial stationary probabilities of stability (0.88) were observed for normal, and less so for low FVC (0.73) and obstructive (0.65) pattern. At least 80 % of the observed transitions involved the normal and low FVC patterns, and both higher WTC exposure intensity (early arrival at the site), and body mass index (BMI) were predictors of transitions to low FVC in this cohort.

Conclusion: Low FVC is relatively stable, and both WTC exposure intensity and BMI are independently and significantly associated with transitions to it. Transitions to obstruction are generally infrequent among the WTC workers and have greater instability.

1. Introduction

A substantial proportion of workers and volunteers who participated in the rescue, search, recovery, and service restoration at the World Trade Center (WTC) disaster site in 2001–2002 manifest a heterogeneous group of chronic lower airway diseases [1].

Several longitudinal surveillance programs exist in the United States, where a high variability in spirometric patterns is apparent. Longitudinal surveillance often focuses on rates of expiratory flow (most often first-second forced expiratory flow, FEV_1) decline [2–4]. In the spectrum of chronic airway diseases, and in the context of occupational longitudinal respiratory surveillance, transitions are observed between spirometric patterns. Such transitions may reflect different disease states but could also be due to technical deficiencies or unevenness in spirometry performance.

Spirometric pattern transitions have been studied specifically in cohorts at elevated risk for chronic obstructive pulmonary disease (COPD) [5] and for limited periods of time, but not in the WTC occupational

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cohorts. In the WTC occupational cohorts, the most frequently observed abnormal spirometric impairment pattern is a reduced forced vital capacity (low FVC) [6–9]. Our aim in this study was to quantify and examine systematically the observed transitions among spirometric patterns and their main determinants over a 17-year interval in the largest occupational WTC cohort with longitudinal surveillance spirometry data.

2. Methods

Subjects and Study procedures: Study participants are members of the World Trade Center General Responders' Cohort (WTC GRC), an open cohort of workers and volunteers who performed rescue, search, recovery, and service restoration duties at the WTC disaster site after the terrorist attack of September 11th, 2001, and are enrolled on longitudinal screening and surveillance since July 2002 at Mount Sinai Medical Center, in New York. We included subjects examined until November 2019.

Screening and recruitment tools have been described in detail in previous publications [10–12]. A baseline screening evaluation included questionnaires on respiratory and other symptoms and WTC-related and unrelated occupational exposures [12], physical examination, laboratory testing (including a complete blood count, lipid and chemistry panel, and urine analysis), spirometry, and, on alternate visits, chest radiographs. With intervals generally varying between 12 and 18 months, subsequent ("monitoring") health surveillance visits included a similar evaluation, and clinical services were offered since December 2002 for individualized diagnostic and treatment services [7,8]. We excluded participants from the current analysis if they: (1) had no assessment of WTC exposure status, weight and height measurements or smoking status; (2) did not have a minimum of 3 visits; and/or (3) did not provide informed consent to participate in research studies. Additionally, we excluded from this analysis monitoring visits lacking spirometry data.

Spirometry was performed using a single device type, the EasyOne® portable flow spirometer (ndd Medizintekhnik, Zurich, Switzerland) [13]. Bronchodilator response (BDR) was assessed at least once in each subject (most often at the baseline visit), by repeating spirometry 15 min after administration of 180 μg of albuterol via metered dose inhaler and a disposable spacer. Clinically significant BDR was defined as a change in pre-bronchodilator (pre-BD) FEV_1 or FVC by at least 12% and 200 ml after bronchodilator administration. Predicted values for spirometric measurements were calculated for each subject based on reference equations from the third phase of the National Health and Nutrition Examination Survey (NHANES III) [14]. All testing, quality assurance, ventilatory impairment pattern definitions, bronchodilator response presence, and interpretative approaches followed American Thoracic Society recommendations [15]. To be included in data analyses, spirometric maneuvers had to be (1) acceptable, including absence of artifacts and a back extrapolation volume <5% of FVC or 150 ml; (2) reproducible (based on a computer quality grade [13] of A or B, or C if at least 5 trials had been obtained, (3) a forced exhalatory time of at least 6 s [9,16].

Our outcome of interest was the set of transition probabilities between pre-BD spirometric patterns. We defined the latter as follows: (1) normal: pre-BD FEV_1, FVC, and FEV_1/FVC ratio at or above their respective lower limit of normal (LLN) values; (2) airflow obstruction: pre-BD FEV_1/FVC ratio<LLN; (3) low FVC: FVC<LLN and FEV_1/FVC>LLN [16–18]. Airflow obstruction was defined using pre-BD spirometry measures due to the limited frequency of BDR testing after the participants' initial or baseline visit. Given its high and increasing prevalence in this cohort [9], we focused on transitions to and from the low FVC pattern (also referred to in the medical literature as pseudorestrictive or nonspecific impairment pattern) [9,16,19,20]. In secondary analyses, we examined the agreement of that definition with that of preserved ratio impaired spirometry (PRISm), with a definition similarly requiring FEV_1/FVC>LLN but requiring instead FEV_1<LLN.

Our exposure of interest was self-reported arrival at the WTC disaster site within 48 h, a generally accepted indicator of higher occupational exposure to dust, gases, and fumes at the site, based on limited environmental measurements, and associations with adverse respiratory outcomes [7,9,21–23]. Given the high prevalence [9] and adverse respiratory health impact [24,25] of overweight and obesity in this and other [26] occupational WTC cohorts, we also examined the association between body mass index (BMI, in kg/m^2), measured at baseline and at each surveillance visit, and transition between spirometric patterns.

Covariates assessed at the baseline examination included age on 11-September-2001 (grouped into 5-year intervals), gender, ethnicity/race (Latino of any race, non-Latino White, non-Latino of other races), height, cumulative WTC exposure duration (both continuous or dichotomous, <60 vs. ≥60 days), pre-WTC occupation (categorized into: protective services; construction; building cleaning and maintenance, and electrical, telecommunications, and other installation and repair group [BCM&IRG]; and all others). Covariates assessed at any visit included: height, weight (and BMI), highest recorded diastolic blood pressure (cutpoint 90 mm Hg), highest recorded serum glucose (whether fasting or not, cutpoint 200 mg/dl), highest serum triglycerides (whether fasting or not, cutpoint 300 mg/dl), highest peripheral blood eosinophil count (BEC, cutpoint 300/μl) [27], highest peripheral blood neutrophil count (cutpoint 6000/μl), and lowest HDL cholesterol (cutpoints 40 and 50 mg/dl for men and women, respectively), and both smoking status (current, former, or never smoker), and smoking intensity (in pack-years). A subject was considered a never smoker if (s)he had smoked less than 20 packs of cigarettes (or 12 oz. of tobacco) in a lifetime, or less than 1 cigarette/day (or 1 cigar/week) for one year. A minimum of 12 months without tobacco use was required to deem a subject a former smoker [28]. We used low HDL, hyperglycemia and -triglyceridemia, and diastolic hypertension as surrogate indicators of probable metabolic syndrome (MetSyn), categorized dichotomously based on the presence of 2–4 indicators [9].

The Mount Sinai Program for the Protection of Human Subjects Research approved this investigation (PPHS, HS17-01098). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies [29].

Statistical analyses: Continuous variables are described as mean with standard deviation (SD) or median with interquartile range (IQR), and categorical variables as counts and proportions, as appropriate. We used standardized differences (StD) [30] to compare the characteristics of the Mount Sinai WTC GRC members included and excluded from this study, with values of 0.2, 0.5, and 0.8 representing small, medium, and large differences, respectively. We generated multi-state Markov-like models [5] for subjects with at least 3 visits (2 transitions) to estimate probabilities of transition among spirometry patterns. To investigate the association between WTC exposure or BMI and transitions between spirometry patterns we calculated odds ratios (OR) for the odds of transition between abnormal spirometric patterns relative to the odds of transition to normal spirometry.

Odds ratios with 95 % confidence intervals (CI) were produced using generalized estimating equations (GEE) considering multiple transitions per subject and adjusted (after appraising confounder relationships) [31] for age on November 9, 2001, gender, ethnicity/race, time-varying smoking status categories (with an interaction term with smoking intensity), highest recorded peripheral blood neutrophil and eosinophil counts, MetSyn, and pre-WTC occupational category. Previous work has described possible effect modification by gender on the association between WTC disaster exposure and low FVC [9], so these odds ratios were additionally stratified by gender to evaluate effect modification on the multiplicative scale and the relative excess risk due to interaction (RERI) on the additive scale [32,33]. Additional *post hoc* sensitivity analyses were performed by (1) adjusting GEEs for any evidence of bronchodilator response, (2) testing associations with WTC cumulative exposure duration, (3) testing an alternative definition of obstructive impairment as pre-bronchodilator $FEV_1/FVC<0.70$, and (4) calculating *E*-values—expressed as a point estimate and confidence interval (CI)— to measure the minimum association on the odds ratio scale that an unmeasured confounder would have to have in order to nullify significant associations reported herein [34,35], and (5) examining in this cohort the Pearson correlation between FEV_1 and FVC, and the simple and Cohen's agreement between the definition of low FVC and that of preserved ratio impaired spirometry (PrISM), with the latter as the reference. All analyses were performed using SAS v. 9.4 (SAS, Inc., Cary, NC).

3. Results

Among 23,218 subjects enrolled between June 2002 and November 2019 in the Mount Sinai WTC General Responders' Cohort, 10,810 had at least three (and a total of 56,312) visits with adequate quality spirometry and met our inclusion criteria for these analyses (Fig. 1). The earliest and latest visit with spirometry occurred, respectively, on July 16, 2002 and November 22, 2019. Compared with the subjects excluded from this study (n=12,408, see **Table OS1**) for having fewer than three high-quality spirometries, those included were younger, had a higher prevalence of high peripheral blood neutrophil and eosinophil counts, hypertriglyceridemia, and probable MetSyn, but most differences were small and the two groups were generally quite similar. **Table OS2** shows that spirometry quality requirements for inclusion in the study resulted, as expected, in a decrease in the proportion of studies with low FVC impairment, an increase in the proportion of normal spirometry patterns, and almost no change in the proportion of obstructive pattern results.

Table 1 summarizes the demographic, exposure, and clinical characteristics of participants in the current study. Their mean age on September 11, 2001 was 39 (SD 9) years, and 85 % were male. Subjects' initial visits occurred a mean of 6 (SD 5) years after the disaster, and they had a median of 5 (IQR 3–7) visits. The mean baseline BMI was 30 (SD 5) kg/m^2. The prevalence of overweight and obesity classifications at the first visit (42 % and 40 % respectively) changed slightly at the most recent (to 41 % and 46 %, respectively), with the proportion of subjects with normal BMI ($\leq$25 kg/m^2) decreasing by about 2 %. As previously reported in this cohort [9,16], most subjects were never smokers at the baseline visit (60 %), and the cross-sectional prevalence of current smoking had decreased from 14% to 8% at the most recent visit.

Table 2 shows the counts and proportions of the three different spirometry patterns at the first or baseline visit, and all the visits. As previously reported [7–9,36], when spirometry was abnormal, low FVC was substantially more frequent than airflow obstruction. Since 90 % of the spirometry patterns in this cohort were either normal or low FVC (Table 2), the correlation between FEV_1 and FVC was, as expected, highly significant (Pearson r=0.95, $p<0.001$). Similarly, the low FVC and PrISM definitions had a high simple agreement (90%), and a good or substantial Cohen's κ statistic (0.71, 95 % CL 0.70, 0.72), with positive and negative predictive value of 88 % and 90 %, respectively.

The multi-state Markov-like model produced probabilities of

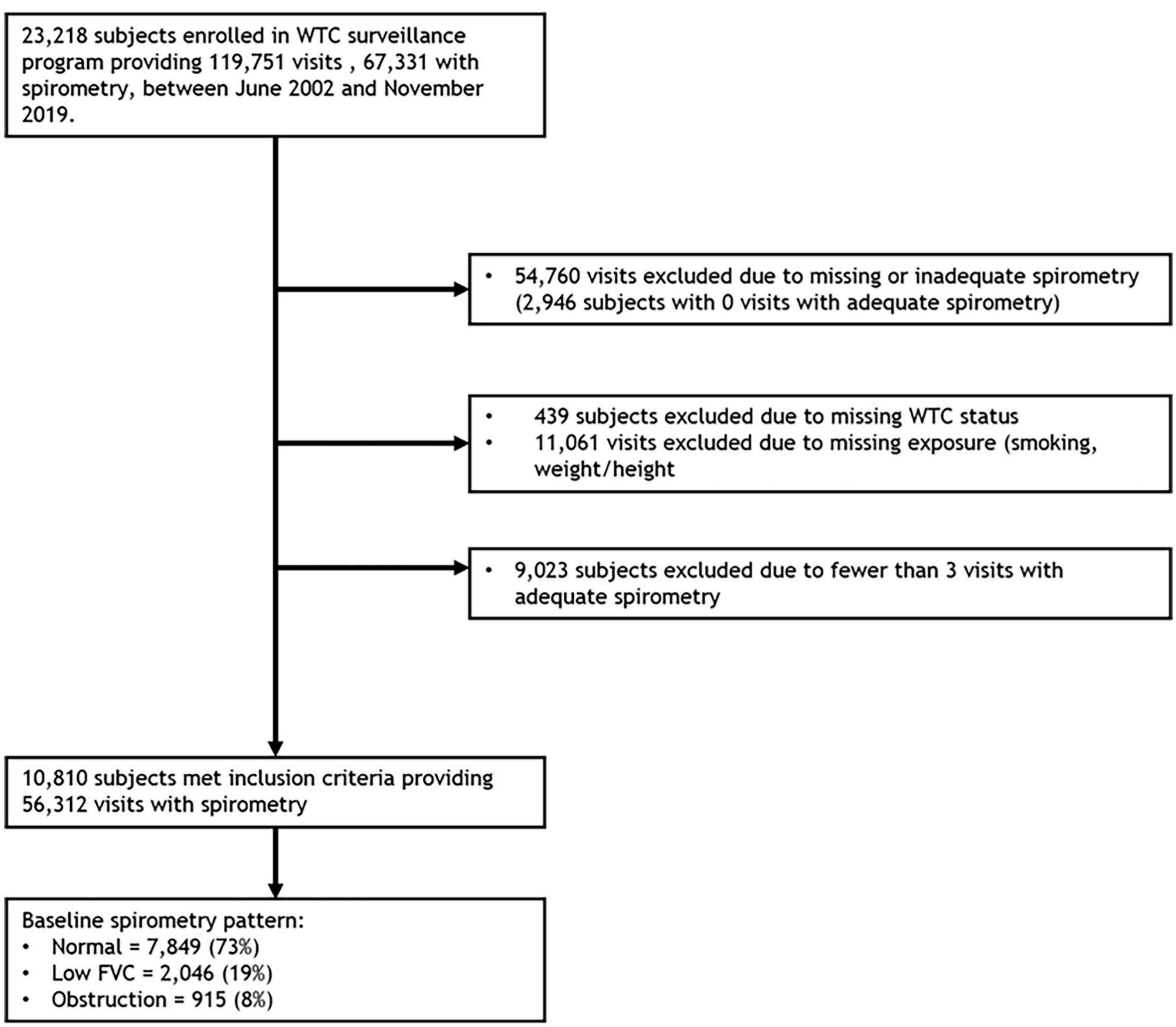

Fig. 1. Flow chart of study participant selection.

Table 1
Baseline characteristics of 10,810 WTC rescue and recovery workers with at least one baseline and two longitudinal surveillance spirometries.

Characteristic	Mean or count	SD or %
Male sex	9229	85.4
Age on September 11, 2001	39	9
Age at initial visit	44	9
Ethnicity/race		
Non-Latino/White	5663	56
Latino/any race	2879	29
Non-Latino/other race	1508	15
Height (in)	69	4
BMI (kg/m^2)	29.6	5.0
Cumulative WTC exposure duration (days)	83	74
Arrival at WTC site within 48 h (P48hr)	6924	64
Smoking status at baseline		
Current smoker	1347	13
Former smoker	2735	27
Never smoker	6226	60
Missing data	502	
Peripheral blood eosinophil count (ever≥350/μl)	2169	21
Peripheral blood neutrophil count (ever≥6000/μl)	2943	28
Hyperglycemia (ever≥200 mg/dl)	860	8
High-density lipoprotein (ever too low)[a]	3550	36
Hypertriglyceridemia (ever≥300 mg/dl)	2508	24
Probable MetSyn (2–4 indicators present)	3563	33

[a] <50 and 40 mg/dl for women and men, respectively.

Table 2
Spirometric patterns observed in Mount Sinai WTC General Responders Cohort members (n = 10,810) on longitudinal surveillance, who also had a minimum of three good quality spirometries (total, 56,312) between 2002 and 2019.

Spirometric pattern	At first visit	All visits
	n (%)	n (%)
Normal	7849 (73)	37,872 (69)
Low FVC	2046 (19)	12,653 (22)
Obstruction	915 (8)	4787 (9)
	10,810	56,312

transitioning between spirometric patterns. As shown in Fig. 2, spirometry visits with normal results had the highest probability of remaining in the same pattern (0.88), with less stability observed for both low FVC (0.73) and obstruction (0.65). Subjects transitioning away from airflow obstruction had a higher probability of transitioning to normal spirometry (0.22) than to low FVC pattern (0.13). This was also true for subjects transitioning out of low FVC spirometry pattern, who had a higher probability of transitioning to normal spirometry (0.25) than to the obstructive pattern (0.03). The stability of the normal spirometry pattern is further demonstrated by the low probability of transition to low FVC (0.11) or obstruction (0.02) patterns. Examining two transitions ahead (representing a longer lag period), revealed very similar results (data not shown).

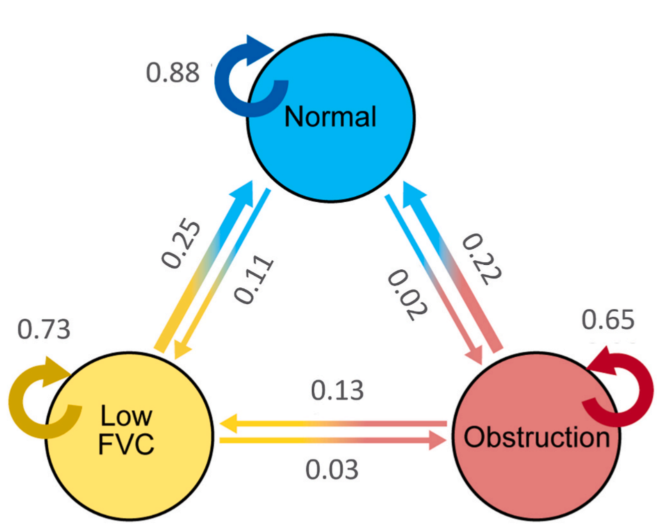

Fig. 2. Probabilities of transition between spirometric patterns in 10,810 WTC rescue and recovery workers with at least one baseline and 2 longitudinal surveillance evaluations, 56,312 in total.

BMI was measured as a time-varying exposure in the GEE models and was used to assess associations between odds of transition to incident abnormal spirometric patterns versus transition to (or remaining with) normal spirometry. In this analysis, change in BMI was associated with any transition to the low FVC spirometry pattern versus any transition to normal spirometry, or versus any transition to obstruction: for every 1 kg/m^2 increase in BMI, the odds of a participant having a transition to low FVC spirometry increased by 8% (OR_{adj} 1.08, 95 % CI 1.07–1.09) compared to normal or 10% (OR_{adj} 1.10, 95 % CL, 1.08–1.12) compared to airflow obstruction (Table 3). BMI was minimally associated with transition to obstructive versus normal spirometric pattern. When modeling transition to low FVC spirometry versus transition to obstruction, a 1 kg/m^2 increase in BMI was associated with a 10% increase in the odds of transition to low FVC spirometry versus any airflow obstruction (OR_{adj} 1.10, CI 1.08–1.12). Interactions between BMI and gender were not statistically significant and effect estimates were very small on both the multiplicative and additive scales.

We also assessed the association between higher WTC occupational exposures, indicated by arrival at the disaster site within 48 h of the terrorist attack (versus arrival after 48 h) and spirometry transitions. Early arrival at the WTC site was associated with increased probability of transition to low FVC pattern (OR_{adj} 1.19, 95 % CL 1.07–1.31) and airflow obstruction (OR_{adj} 1.21 95 % CL 1.00–1.46), Table 3. Moreover, gender modified the estimated effect of early WTC arrival on transition to low FVC, although statistical interaction was not demonstrated (p for interaction = 0.76) [33]. Early arrival at the disaster site was associated with a 74% increase in the odds of transitioning to low FVC (versus any transition to normal) among men (OR_{adj} 1.74, 95 % CI 1.45–2.14) vs. 19% among women (OR_{adj} 1.19, 95 % CI 1.06–1.32). There was no evidence of effect-measure modification on the additive scale.

In sensitivity analyses, we adjusted for any bronchodilator response as a covariate in both the BMI and WTC exposure models and found no appreciable change to any effect estimates. We also investigated associations with cumulative WTC exposure duration, both as a continuous variable and a dichotomous variable (with 60 days as a cut off) and found no association by itself with spirometry pattern transitions. Further, we assessed the interaction between WTC arrival within 48 h and exposure duration >60 days and found no important deviations from the results presented in Table 3. Using an alternative diagnostic criterion for airflow obstruction (pre-bronchodilator $FEV_1/FVC<0.70$)

Table 3
Adjusted models of associations of body mass index (BMI) and World Trade Center exposure (arrival at the site within 48 h, P48hr) with transitions to obstruction (1) or low FVC (2) spirometric pattern (including transition to itself, i.e., stability), with transition to normal as reference. In (3) the model examined any transition to low FVC pattern with transition to obstruction as the reference.

	Pattern transition model[a]	BMI			P48hr		
		OR_{adj}[a]	*LL*	*UL*	*OR_{adj}*[a]	*LL*	*UL*
1	To obstruction	0.98	0.96	1.00	1.21	1.00	1.46
2	To low FVC	1.08	1.07	1.09	1.19	1.07	1.31
3	Obstruction- > Low FVC	1.10	1.08	1.12	1.03	0.84	1.26

[a] Adjusted for age on September 11, 2001, gender, ethnicity/race, time-varying smoking status categories (with an interaction term with smoking intensity), highest recorded blood neutrophil count, highest recorded blood eosinophil count, MetSyn, and pre-WTC occupational category.

yielded very similar results to those reported using the LLN (data not shown). The association between BMI and transition to low FVC versus any transition to normal spirometry had an *E*-value of 1.24 (CI 1.22). The *E*-value around the association between WTC exposure and low FVC was 1.41 (CI 1.20) for women and 1.97 (CI 1.67) for men.

4. Discussion

In this WTC occupational cohort with good quality surveillance spirometric data, spirometry impairment patterns are relatively stable between longitudinal surveillance visits, and higher WTC-related occupational exposure and BMI are associated with their transitions. The normal pattern was clearly predominant in this population during the 17-year study period, and it had a high probability of stability. The studied abnormal patterns were comparatively less stable. Transitions from obstruction to normal or vice versa may be evidence of reversible obstruction, perhaps reflecting asthma, for which there was some evidence of increased incidence within the first two years after the occupational WTC exposures [8,37]. Low FVC has also been associated with asthma and airway disease in some studies [38]. This study demonstrates the substantial stability of this pattern, higher than previously demonstrated in the smaller longitudinal study by Iyer et al. [39]. Low FVC likely reflects diverse pathophysiological states [19], as cluster analyses in this [40] and other cohorts [41] have already suggested. As this study again demonstrated, low FVC in the WTC GRC is modestly associated with our crude indicator of higher occupational exposure level [9] and strongly with BMI but is also strongly modified by gender [9,40]. Focused studies will be required to elucidate the interrelation of these factors. Lastly, we confirmed for the first time in this cohort an excellent correlation and good agreement between our primary definition of low FVC and that of PrISM.

Given its well-known adverse respiratory health effects, smoking was not a primary exposure of interest in the present study but was included as a covariate in all the models, showing significance, for instance, in the transition from low FVC to airflow obstruction (data not shown). As expected, low FVC and normal pattern prevalence would have been respectively over- and underestimated (**Table OS2**) had we not applied the test quality requirements. As previously reported, transitions to COPD during the study period were infrequent among the WTC workers [36] and this pattern has considerable potential instability [42], expected with the large predominance of mild and moderate COPD [36], and suggesting the need to require its consistency with repeated testing over time before arriving at that diagnosis in this cohort [43].

Spirometry is a fundamental tool to assess respiratory health, and an association between reduced vital capacity and decreased survival and worse prognosis was proposed by its inventor more than a century and a half ago [44]. Surveillance spirometry remains a key approach to primary and secondary prevention of occupational respiratory diseases [2,3], but longitudinal spirometry is increasingly regarded as key to the general population, given limitations with prediction equations, and the multitude of factors that influence lung development and injury through life [45]. In this context, experiences from large cohorts such as the WTC GRC can provide insights into what to expect at the population and individual level.

Considering the association between WTC exposure and low FVC and the E-values hereby reported, we were unable to find a covariate with a strong enough association with the exposure and the outcome to completely nullify their association. Low FVC, on the other hand, is an impairment pattern in search of clearer and likely multiple causal associations [19,40,41]. The association between BMI and low FVC is more complicated and, as suggested [19], should not be considered a simple epiphenomenon. It is associated with metabolic syndrome and systemic inflammation. Since waist circumference or other markers of inflammation were unavailable, we used a proxy metabolic syndrome indicator, leaving the possibility for uncontrolled confounding. Given our reported E-values, we do not believe that those potential confounders, themselves confounded by other variables, such as post-traumatic stress disorder [46,47] and other factors, are likely to completely explain our reported results. This holds for the E-values of the effect estimates of the associations between WTC exposure in both genders and low FVC, or fixed obstruction versus transition to normal, but not the confidence intervals suggesting lack of precision due to small event sizes and further stratification by gender.

Our study has several strengths. It reports on one of the largest single center longitudinal spirometry programs in the United States, which provides an opportunity to examine in realistic terms the performance of a surveillance program in a population at risk of adverse health effects. This population was aged from their early 40s to their early 60s over the span of the program, an age range when critical changes in lung function may occur in relation to the cumulative effect of environmental (including tobacco) and occupational exposures and other risk factors. The program has utilized the same device and protocol and, despite the strong male sex predominance characteristic of the WTC responder cohorts, and unlike cohorts such as the New York City firefighters', it includes a substantial number of female responders. It also examines a cohort with a prevalence of overweight and obesity that has exceeded those of the U.S. population, as obesity is increasingly recognized as a risk factor for adverse respiratory health outcomes. Finally, the cohort exhibits a consistently high and increasing prevalence of low FVC as a respiratory disease state, substantially more prevalent than obstruction, and increasingly recognized as being associated with significant morbidity in its own right [19].

Despite its real and potential value, occupational surveillance spirometry poses several logistical and technical challenges, which our results demonstrate. Continuous attention to technical performance and clear analytical criteria, such as we reported, would help obtain useful information. As our studies were performed before 2019, they did not follow the 2019 update of the recommendations of the American Thoracic and European Respiratory Societies [48], or the most recent Global Lung Initiative race-blinded prediction equations [49]. Subjects included in our analysis were slightly younger on average and had a higher prevalence of elevated peripheral blood eosinophil and neutrophil counts, and metabolic syndrome indicators compared to those excluded, but those differences were modest and unlikely to explain the reported findings. Of note, the *post hoc* evaluation of the excluded individuals and spirometries did not suggest an important difference in results.

In conclusion, in the largest WTC occupational surveillance cohort with spirometric data, we estimated the stability of spirometric patterns, and the probabilities of transitions among those patterns as well as their associated risk factors. We confirmed the significant, albeit modest impact of WTC exposures on transitions to low FVC pattern, which is further compounded by obesity in a population already known to have a state-level average and sharply declining cross-sectional current cigarette smoking prevalence.

CRediT authorship contribution statement

Jonathan Weber: Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Zitong Zhang:** Writing – review & editing, Methodology. **John T. Doucette:** Writing – review & editing, Supervision, Methodology. **Akshay Sood:** Writing – review & editing, Methodology, Conceptualization. **Juan C. Celedón:** Writing – review & editing, Methodology, Conceptualization. **Rafael E. de la Hoz:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Rafael E. de la Hoz reports financial support was provided by National Institute for Occupational Safety and Health. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2025.108170.

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