



Original Research

The development of frailty trajectories in world trade center general responders and the association with World Trade Center Exposure



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ABSTRACT

Background: As the World Trade Center (WTC) General Responder Cohort ages, it is imperative to study their aging process and identify factors that can be targeted for interventions.

Objectives: Our goal was to utilize a previously developed WTC Clinical Frailty Index (CFI) to identify distinct frailty trajectories and associated factors in this cohort.

Design: A latent class mixed model evaluated frailty trajectories using WTC CFIs. Multinomial regression models were used to assess associations between frailty trajectory and sociodemographic and WTC characteristics.

Setting: We utilized data collected during routine WTC monitoring visits from 2004 until 2021.

Participants: The participants were WTC general responders.

Measurements: Relative risk ratios (RRR) assessed associations with a 95 % confidence interval (CI).

Results: Three distinct linear frailty trajectories were identified: high CFI (indicating higher frailty), low CFI, and progressively increasing CFI. Compared with the low CFI group, females were more likely to be in the high CFI and progressively increasing CFI groups (RRR 1.66, 95 %CI 1.46, 1.90; RRR 1.32, 95 %CI 1.15, 1.53, respectively). Education beyond high school and elevated income were protective against high CFI and progressively increasing CFI groups. Individuals that self-identified as Hispanic had an elevated RRR for the high CFI group (RRR 1.17, 95 %CI 1.04, 1.31). Occupation on 9/11, such as construction and maintenance and repair, as well as high/very high WTC exposure were significantly associated with both the high CFI and progressively increasing CFI groups.

Conclusions: Several sociodemographic and WTC variables were associated with more hazardous frailty trajectories in WTC general responders. This work is beneficial to informing and directing future interventions for those at higher-risk for more hazardous frailty progression.

1. Introduction

After the events of September 11, 2001 and subsequent clean-up and recovery efforts of the fallen World Trade Center (WTC) towers and other sites, researchers have endeavored to understand the lasting effects of the significant environmental exposures and physiological trauma to those who participated in these efforts as general responders. Aerodigestive diseases along with mental health conditions, such as post-traumatic stress disorder, have subsequently been found to be common in this WTC general responder population [1]. Newer research

has highlighted a concern for a higher risk of cognitive impairment [2,3]. Along with this elevated burden of disease, general responders who are a part of the WTC Health Program (WTHP) are aging (median age of 60 in 2023) and are at an increased risk for a host of aging-related conditions [4]. Thus, there is a growing need to understand how aging-related diseases influence the health of the general responder population, as well as to understand the potential role of WTC exposures in augmenting these aging-related conditions. Our research group has begun to address this need by evaluating frailty, a syndrome commonly seen in the older population, in WTC general responders.

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Frailty is characterized by the accumulation of deficits associated with dysregulation in multiple physiological systems. This multisystem dysregulation makes it difficult to return to a homeostatic state after stress or an insult and increases one's vulnerability to poor health outcomes [5–7]. Thus, frailty is associated with adverse events including falls, hospitalizations, and even death [6]. One frailty measurement previously utilized by our group in the WTC General Responder Cohort (WTCGRC) is the Frailty Index [8]. The Frailty Index model is a well-validated approach to measure frailty and is an assessment of one's accumulated functional and health deficits, presented as a ratio to the total potential deficits, with a higher proportion of deficits indicating a higher frailty [8–10]. While the specific deficits and sample populations can vary, a recent meta-analysis showed that the Frailty Index was significantly associated with mortality [10]. We recently developed a WTC Clinical Frailty Index (CFI) using routinely collected clinical data from general responders 40 years of age and older who had at least one WTC follow-up surveillance or monitoring visit between 2012 and 2017. Variables from the physical examination and health-related questionnaires were systematically evaluated for inclusion into the final model [11]. The final WTC CFI was 30 items and included deficits such as diabetes, fair/poor self-rated health, difficulty climbing several flights of stairs, and abnormal heart examination [8]. Frailty in WTC general responders as determined by the WTC CFI was found to be associated with a higher WTC exposure severity as well as all-cause mortality [8].

Frailty is increasingly being recognized as a dynamic syndrome. Frailty can change over time with varying rates of change [12]. The benefits of characterizing frailty over time include identifying individuals who may be on a poor trajectory (that is those with accelerated progression of frailty severity with age), as well as understanding the risk factors associated with distinct patterns of trajectories [13]. Previous investigations have worked to identify particularly hazardous frailty trajectories in the geriatric population, including those associated with higher mortality [14–16]. One population-based cohort study additionally found steep frailty trajectories to be associated with increased visits to the emergency room and hospital [17]. Although the methodologies vary, risk factors for these types of poor frailty trajectories include female sex, lower educational achievement, obesity, and living alone [13,15,18]. Given the high burden of disease in the aging WTC general responders, it is important to understand if there are WTC-specific factors such as the WTC exposure severity or job performed in the clean-up and recovery efforts at the WTC site, as well as general responder sociodemographic characteristics that may alter frailty trajectory in this population. This knowledge may enable further evaluation of interventions with the goal of mitigating poor trajectories [19,20]. Thus, the aim of this study was to use the previously developed WTC CFI to determine frailty trajectories in WTC general responders and evaluate factors associated with these trajectories.

2. Methods

2.1. Study sample and WTC CFI

The WTCGRC has been previously described [8,21]. Briefly, general responders are those who participated in the rescue and recovery activities at the WTC site after the events of September 11, 2001. General responders who enrolled in the WTC follow-up are followed for yearly health surveillance or monitoring visits [21]. During these monitoring visits with a healthcare professional, a physical examination along with a survey with demographic and health-related questions, named the Interviewer-Administered Medical Questionnaire (IAMQ), are completed. Additional information routinely ascertained includes a Self-Administered Mental Health Questionnaire (SAMHQ), which is collected starting from the second monitoring visit.

We utilized the previously developed WTC CFI to evaluate frailty trajectories in WTC general responders (Supplemental Table 1) [8]. The WTC CFI is derived from 30 items that are taken from clinical data rou-

tinely obtained during yearly monitoring visits. A WTC CFI score of 0.25 or higher indicated frailty. The current study calculated the WTC CFI from longitudinal data collected during WTC follow-up monitoring visits that took place between 2004 and 2021. Additional covariates evaluated in our frailty trajectory models included education, race/ethnicity, income, WTC exposure severity, and occupation on 9/11. Occupation on 9/11 was categorized as protective services (protective service and military specific occupations), construction, maintenance and repair (building, grounds cleaning, and maintenance; and electrical, telecommunications, and other installation and repair occupations), and other [22]. WTC exposure severity was a previously defined composite variable based on questions from a survey performed at the WTC follow-up initial visit [21,23]. It compiles questions related to a general responder's time spent at the WTC site, their exposure to dust/debris, and their participation in the cleanup efforts and categorizes them into levels based on severity of exposure (low, medium, high, and very high) [23,24].

All data used in this study were collected from WTC follow-up general responders who previously consented to have their WTC monitoring data used for research. The Institutional Review Board (IRB) of Icahn School of Medicine at Mount Sinai approved this current study.

2.2. Statistical analyses

We used a latent class mixed model to construct frailty trajectory groups using WTC follow-up data from WTC follow-up general responders from 2004 to 2021. WTC follow-up general responders with at least one monitoring visit were included. Visits were excluded if they were missing more than 3 WTC CFI measures. There were no exclusion criteria based on age. To create the model, we estimated the WTC CFI for each included individual general responder at each yearly monitoring visit using an average score of the 30 items after an appropriate binary categorization was applied (Supplemental Table 1) [8]. Then, we modeled individual frailty trajectories using these estimated WTC CFIs at all follow-up monitoring visits and grouped subsets of the WTC general responders into group frailty trajectories based on similarities of the individual trajectories [25]. We evaluated different numbers of frailty trajectory groups and selected the appropriate number (three) based on parsimony as well as both the Akaike (AIC) and Bayesian (BIC) Information Criteria, widely utilized methods for model selection (Supplemental Figure 1) [26]. To accommodate repeated estimated WTC CFIs for multiple monitoring follow-up visits, the latent class mixed model included a random intercept and random slope per individual. To decide group selection, the model reported each individual general responders' probability of belonging to each trajectory group. The highest individual probability was used to classify general responders into the appropriate frailty trajectory group. Based on the shape of the identified frailty trajectories, we named the classes as low CFI (LCFI), high CFI (HCFI), and progressively increasing CFI (PICFI). Using linear terms and cubic splines, we also assessed the fit of linear and non-linear time trends for the group frailty trajectories respectively. The AIC and BIC were used to select the number of classes and the overall fit of the model (Supplemental Table 2 and Supplemental Figure 2). Based on these values and the overall fit, a linear model was chosen.

The outcome of interest was WTC CFI trajectory group (LCFI, HCFI, or PICFI). The independent variables included sociodemographic (age at 9/11, sex, highest education level, race/ethnicity, and income) and WTC-specific variables (occupation on 9/11, WTC exposure severity, and time since 9/11).

We also used a multinomial regression model to examine associations between WTC CFI trajectory membership, treated as a categorical variable, and sociodemographic variables (sex, education, race/ethnicity, income) and WTC-specific variables (WTC exposure severity and occupation on 9/11). The following are the reference groups utilized for each variable: sex (reference male), education (reference high school or less), race/ethnicity (reference non-Hispanic white), income (reference less than \$30,000), WTC exposure severity (reference

low), and occupation on 9/11 (reference protective services). Each regression model was adjusted for other covariate sociodemographic and WTC-specific variables. A supplemental analysis evaluated the WTC CFI trajectories and their association adjusting for age at 9/11. In all models, the LCFI trajectory served as the reference group, and coefficients were interpreted as the change in the relative risk ratio (RRR) among WTC general responders assigned to a given trajectory versus the LCFI trajectory. A 95 % confidence interval (CI) was utilized. All analyses were conducted using R (version 4.0.2) with the latent class mix models (lcmm) R package utilized for modelling [25,27].

3. Results

This analysis included 16,571 WTC general responders with a total of 66,293 observations (that were unique WTCHP monitoring visits) between October 2004 and January 2021. General responders were included if they had one or more monitoring visits during this time frame. Descriptive characteristics are also provided for general responders with one visit versus multiple visits (Supplemental Table 3). The characteristics between these two groups were largely similar.

All individuals were subsetted into three linear WTC CFI trajectories (Fig. 1), as suggested by the parsimony criterion, AIC and BIC (Supplemental Figure 1). To support our decision to utilize the linear time WTC CFI trajectories, performance metrics were evaluated with the linear model found to perform better (Supplemental Table 2 and Supplemental Figure 2). The HCFI group demonstrated an elevated CFI at a younger age with a slope of 0.00153 CFI unit/year. The LCFI group showed a low CFI at an early age with a slight increase in CFI over time (0.00063 CFI unit/year). The slope was the steepest (0.00309 CFI unit/year) in the PICFI group that had a modest CFI at a younger age with a progressive increase with age.

Table 1 presents sociodemographic and WTC-specific variables in each WTC CFI trajectory. More individuals completed schooling beyond high school in the LCFI group compared to the other two groups

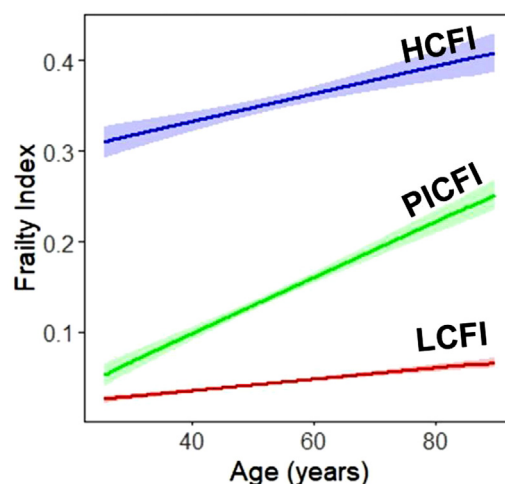


Fig. 1. Frailty Trajectories for World Trade Center General Responders based on World Trade Center Clinical Frailty Index. HCFI: High Clinical Frailty Index Group (slope of 0.00153 CFI unit/year), PICFI: Progressively Increasing Clinical Frailty Index Group (0.00309 CFI unit/year), and LCFI: Low Clinical Frailty Index Group (0.00063 CFI unit/year).

(79 % compared with 71 % in the PICFI group and 59 % in the HCFI group). While the majority of WTC general responders in each group self-identified as non-Hispanic white, 32 % of those that self-identified as Hispanic had a HCFI compared with 22 % in the LCFI and 25 % in the PICFI groups. In the HCFI group, more individuals had incomes less than \$30,000 (22 % versus 4.8 % in the LCFI group and 10 % in the PICFI group). Interestingly, the percentage of individuals increased with increasing income level in the LCFI group. Occupation on 9/11 also varied between WTC CFI trajectory groups. Sixty-three percent of

Table 1
Cohort Characteristics at Time of Entrance to the World Trade Center Health Program.

Variable (N)	Low WTC CFI Trajectory (347,431)	High WTC CFI Trajectory (27,559)	Progressively Increasing WTC CFI Trajectory (19,920)
Age (years) at 9/11, mean (SD)	38 (8)	40 (8)	40 (9)
Sex, %			
Female	12	20	16
Male	88	80	84
Education, %			
High School or Less	21	41	29
More than High School	79	59	71
Race/Ethnicity, %			
Non-Hispanic Black	14	13	14
Hispanic	22	32	25
Non-Hispanic Other	2.8	2.4	2.8
Non-Hispanic White	62	53	58
Income Category, %			
Less than \$30,000	4.8	22	10
\$30,000–60,000	27	32	31
\$60,000–80,000	30	23	29
More than \$80,000	38	22	30
Frailty Index, median (Q1, Q3)	0.03 (0, 0.07)	0.37 (0.26, 0.47)	0.17 (0.10, 0.23)
Occupation on 9/11, %			
Construction	14	35	22
Protective Services	63	30	46
Other	15	23	21
Maintenance and Repair	8.1	12	11
Severity of WTC Exposure, %			
High/Very High	23	21	22
Intermediate	63	67	64
Low	15	12	14
Time Since 9/11, mean (SD)	13.5 (3.9)	13.2 (3.8)	13.4 (3.8)

CFI: Clinical Frailty Index, WTC: World Trade Center, Q: quartile, SD: standard deviation.

Table 2

Relative Risk Ratios Comparing the High WTC CFI Trajectory and Progressively Increasing WTC CFI Trajectory Classes with the Low WTC CFI Trajectory Class.

	High WTC CFI Trajectory			Progressively Increasing WTC CFI Trajectory		
	Relative Risk Ratio	95 % Confidence Interval		Relative Risk Ratio	95 % Confidence Interval	
Sex						
Female Sex	1.66	1.46	1.90	1.32	1.15	1.53
Male Sex	Ref	–	–	Ref	–	–
Education						
More than High School	0.66	0.59	0.73	0.80	0.72	0.90
High School or Less	Ref	–	–	Ref	–	–
Income Category						
\$30,000–60,000	0.43	0.36	0.51	0.69	0.57	0.85
\$60,000–80,000	0.37	0.31	0.44	0.70	0.57	0.86
More than \$80,000	0.31	0.26	0.37	0.59	0.48	0.73
Less than \$30,000	Ref	–	–	Ref	–	–
Race/Ethnicity						
Non-Hispanic Black	1.01	0.88	1.17	0.96	0.83	1.12
Hispanic	1.17	1.04	1.31	1.11	0.98	1.25
Non-Hispanic Other	0.91	0.69	1.20	0.98	0.74	1.31
Non-Hispanic White	Ref	–	–	Ref	–	–
Pre-9/11 Occupation on 9/11						
Construction	4.17	3.67	4.74	2.12	1.84	2.45
Other	2.45	2.16	2.77	1.84	1.61	2.10
Maintenance and Repair	2.64	2.25	3.10	1.86	1.56	2.21
Protective Services	Ref	–	–	Ref	–	–
Severity of WTC Exposure						
High/Very High	1.82	1.55	2.13	1.20	1.03	1.41
Intermediate	1.41	1.23	1.62	1.05	0.91	1.20
Low	Ref	–	–	Ref	–	–

WTC: World Trade Center, CFI: Clinical Frailty Index.

WTC general responders in the LCFI group had a job title of “protective services” which was higher than the HCFI (30 %) or the PICFI (46 %) groups. The “construction” job title was seen more frequently in the HCFI group (35 %) compared with the LCFI group (14 %) and the PICFI group (22 %). The severity of WTC exposure and time since 9/11 were similar between WTC CFI classes.

A multinomial regression model was utilized to examine sociodemographic and WTC-specific variables and their association between WTC CFI trajectory classes (Table 2). Compared with the LCFI group, being female was associated with an elevated RRR in both the HCFI (RRR 1.66, 95 %CI 1.46, 1.90) and PICFI (RRR 1.32, 95 %CI 1.15, 1.53) groups. Having an educational level greater than high school was protective in both HCFI and PICFI groups versus the LCFI group (RRR 0.66, 95 %CI 0.59, 0.73 and RRR 0.80, 95 %CI 0.72, 0.90, respectively). Additionally, having an income level over \$30,000 were associated with a lowered RRR for both the HCFI and PICFI groups. Those identifying as Hispanic compared to Non-Hispanic White general responders had a higher RRR for the HCFI compared to the LCFI group (RRR 1.17, 95 %CI 1.04, 1.31). While a higher RRR was also seen for those identified as Hispanic in the PICFI group, statistical significance was not reached (RRR 1.11, 95 %CI 0.98, 1.25).

Interestingly, having a “construction” job compared with a “protective services” job had 4 times (RRR 4.17, 95 %CI 3.67, 4.74) and 2 times (RRR 2.12, 95 %CI 1.84, 2.45) higher risks for the HCFI and PICFI groups, respectively. The other jobs, “other” and “maintenance and repair,” also had significantly elevated RRRs for both the HCFI and PICFI classes compared with the LCFI class. Finally, individuals who had a high/very high WTC exposure severity compared with a low WTC exposure level had a RRR of 1.82 (95 %CI 1.55, 2.13) for being in the HCFI group and a RRR of 1.20 (95 %CI 1.03, 1.41) for being in the PICFI group when compared with the LCFI group.

A secondary multinomial regression model was completed that additionally adjusted for age at 9/11. The associations are largely the same. When age was included in the model, the association between the PICFI trajectory and self-identifying as Hispanic was strengthened (RRR 1.16, 95 %CI 1.03, 1.32; Supplemental Table 4).

4. Discussion

Our study showed three distinct frailty trajectories in the WTCGRC: low, high, and progressively increasing suggesting that the WTC CFI is a robust marker of aging that captured the multidimensional and dynamic nature of frailty over time and is a suitable measure to investigate frailty trajectories. The HCFI and PICFI classes may suggest more hazardous trajectories in that the slopes of these classes were steeper than that of the LCFI class. Moreover, the HCFI class demonstrated an elevated WTC CFI exceeding the theoretical cutoff of frailty (that is an FI estimate of 0.25) even at a relatively young age [8]. While the PICFI class had a modest CFI at a younger age approaching that of the LCFI class, a rapidly progressive increase in the frailty trajectory was observed with age. The risk factors for these two hazardous trajectories were largely the same and included female sex, lower levels of education and income, a construction-type occupation on 9/11, and an elevated WTC exposure level. Interestingly, self-identifying as Hispanic was also associated with the HCFI group. This study provides important insight into possible subgroups of the WTCGRC that may be at higher risk of rapid progression towards worsening frailty and thus candidates for early healthy aging interventions.

In our cohort, we found that women were more likely to belong to the more hazardous WTC CFI trajectories. Previous studies that have clustered frailty trajectories and evaluated group association had heterogeneous findings in the association between the female sex and a more hazardous or “worse” frailty trajectory [18,28,29]. This frailty trajectory analysis expands upon our previous work developing the WTC CFI in this population which showed a higher risk for frailty in women compared with men (incidence rate ratio of 1.33), and it echoes findings from a 2017 meta-analysis that examined sex differences in frailty in community-dwelling adults over the age of 65 years [8,30]. The idea of the “male-female health survival paradox,” in which women are found to live longer even with increased frailty has been previously proposed [30,31]. While it is not fully known why this occurs, the higher number of non-life threatening chronic conditions that women develop compared to men may be contributory [32]. An example illustrative of this

idea in the WTCGRC is a 2016 study that found an increased risk of asthma and gastroesophageal reflux in women [33]. Thus, further work is needed to understand how this paradox, particularly regarding the association between a more hazardous trajectory and mortality, may differentially affect female and male WTC general responders.

Another important finding from this current study is the increased risk of a high WTC CFI trajectory in general responders who identified as Hispanic compared with non-Hispanic White individuals. Few studies have extensively evaluated the association between race/ethnicity and frailty. In these studies, the Hispanic population has a variable association with frailty; however, there is heterogeneity in the study populations [34–37]. For example, in a recent study using the Multiethnic Cohort, Latino women (odds ratio 1.44, 95 % CI 1.31–1.59) but not Latino men (odds ratio 1.03, 95 % CI 0.90–1.29) had increased odds of frailty after adjusting for age, educational status, marital status, and social economic factors [34]. Whereas another study from 2021 that used data from the National Health and Aging Trends Study found increased odds of frailty in the Hispanic population after adjusting for age, sex, income, and geographical region of the country [35]. Our finding adds to this literature by indicating that self-identifying as Hispanic may selectively influence frailty trajectory particularly in WTC general responders who have higher CFI estimates at an earlier age (i.e., those in the HCFI class). However, the lack of a statistically significant association between self-identifying as Hispanic and the PICFI trajectory when not adjusting for age at 9/11 suggests that the risk conferred may be different depending on the type of frailty trajectory. This is valuable because it highlights the complex interplay between identified factors in this study as well as likely other factors, including culture and social support [13].

Our study also evaluated other risk factors including educational status, occupation on 9/11, and WTC exposure. For educational status, we found higher education attainment to be protective against hazardous frailty trajectories (HCFI and PICFI) in the WTC general responders. This finding is consistent with a recent systematic review which showed a benefit of education on the rate of change towards worsening frailty [13]. Uniquely, our study found that certain types of occupation on 9/11 increased risk for both HCFI and PICFI trajectories. Although, there is limited literature evaluating the role of occupation on frailty trajectories, one study observed an association between occupational class and frailty trajectory and hypothesized that physical and physiological hazards of one's occupation can have a long-term impact [38–40]. Our data support this theory given the events of the 9/11 attack and the subsequent clean-up and recovery occurred over 20 years prior, and yet we are still seeing variations in frailty trajectory associated with occupation performed by WTC general responders. Other studies have shown differences in frailty trajectories in late-life based on employment history [41,42]. Manual labor-type jobs have been associated with frailty; this is similarly observed in our study of WTC general responders who had a construction occupation on 9/11 [43,44]. However, it should be noted that little is known regarding the WTCGRC and their occupations after the completion of clean-up and recovery efforts at WTC. While certain occupations on 9/11 appear to confer a greater risk to hazardous frailty trajectory, further research is needed to better understand how the responders' more recent work histories may have affected frailty. Finally, our study found a link between the severity of WTC exposure, particularly high/very high levels, and hazardous frailty trajectories. Our previous study also found an association between point estimates of WTC CFI and WTC exposure severity, with a higher risk associated with high/very high exposure level compared to intermediate exposure level [8]. While the WTC exposure was unique and unlike the composition of common environmental pollutants, several studies have highlighted the possible impact of the environment on frailty. In a 2019 survey of Chinese adults aged 65 or older, PM2.5 as well as long-term air pollution were found to be associated with frailty [45]. Others have shown a similar association between frailty and air pollution and phthalates [46–48]. Taken together, it could be hypothesized that the high-degree of environmental

toxicant exposure at the WTC site may be contributory to the acceleration towards worsening frailty in WTC general responders.

Various strategies have been employed to evaluate frailty trajectories including linear mixed models, random effect models, and generalized estimating equations [13]. For this study, we utilized mixture models due to: (1) the ability to handle large datasets, as we have with the WTCGRC, (2) the robustness and stability in providing parameter estimates with post-fit accuracy measures, and (3) the flexibility in evaluating both linear and non-linear trajectories. Stow et al. also used latent growth mixture modeling in a group of adults aged 75 years and older and found three distinct frailty trajectories with a rapidly rising trajectory most associated with mortality [14]. This modelling strategy has the benefit of accommodating challenges such as missing data or repeated variables, and it may be useful for outcome prediction and intervention planning [49,50].

Our study has several limitations that should be noted. First, this is a retrospective analysis, and thus other factors that may play a role in frailty development were not readily available for consideration. However, future research on frailty trajectories in the general responder population could expound upon the risk factors identified in this study to evaluate additional and related candidate social, occupational, and health factors, as described in the literature [13]. Importantly, it would also be beneficial for future work to evaluate the interactions between these risk factors. While the WTC CFI in general responders prior to 2004 is unknown, it is likely that the HCFI group had an elevated frailty index prior to 9/11. Thus, the associations seen in specific sociodemographic (sex, education, income) and WTC (occupation on 9/11, WTC exposure severity) covariates in this group compared to the LCFI group may be more difficult to interpret. As such, the impact and causal influence of 9/11 environmental exposures on the frailty trajectory in the HCFI group are not fully identified. However, the association of 9/11 environmental exposures with the PICFI group compared to the LCFI group, both of which had similar WTC CFIs in 2004, lends support to this association. Second, individuals were included in the analysis only if they had sufficient data to calculate WTC CFI estimates, and thus this may have created some bias in our analyzable cohort. Moreover, while there are a number of validated and operationalized frailty definitions, there is currently no consensus definition. As such, different frailty measures have been used to study frailty trajectories in the literature [51]. Our findings were derived using a deficit accumulation FI model; however, it is not known whether the results may differ if a physical frailty based definition is applied. Furthermore, future studies that include a post-prediction inference to the WTC CFI may account for analytic variability of latent class mix models and contribute to improved characterization of WTC general responders who experience frailty. Finally, the WTCGRC as well as the WTC exposures that they encountered are unique, and thus the generalizability of our findings may be limited.

5. Conclusion

We identified several risk factors that are associated with a more hazardous frailty trajectory in general responders who participated in the clean-up and recovery efforts at the WTC site after the attack on September 11. These risk factors include being female, self-identifying as Hispanic, higher WTC exposure, and doing construction work at the WTC site. The identification of these factors may be used clinically to develop and implement early healthy aging interventions focused on these high-risk groups.

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Declaration of competing interest

Hannah Thompson, Roberto Lucchini, Michael Crane, Ghalib Bello, Ahmad Sabra, Erin Thanik, Susan Teitelbaum, William Hung, Elena Colicino, Katherine Ornstein, and Fred Ko have no conflicts of interest to disclose.

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Supplementary materials

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References

- Jordan HT, Osahan S, Li J, Stein CR, Friedman SM, Brackbill RM, et al. Persistent mental and physical health impact of exposure to the September 11, 2001 World Trade Center terrorist attacks. *Environ Health* 2019;18(1):12. doi:10.1186/s12940-019-0449-7.
- Santiago-Colon A, Daniels R, Reissman D, Anderson K, Calvert G, Caplan A, et al. World trade center health program: first decade of research. *Int J Environ Res Public Health* 2020;17(19). doi:10.3390/ijerph17197290.
- Clouston SAP, Hall CB, Kritikos M, Bennett DA, DeKosky S, Edwards J, et al. Cognitive impairment and World trade centre-related exposures. *Nat Rev Neurol* 2022;18(2):103–16. doi:10.1038/s41582-021-00576-8.
- Li Z, Zhang Z, Ren Y, Wang Y, Fang J, Yue H, et al. Aging and age-related diseases: from mechanisms to therapeutic strategies. *Biogerontology* 2021;22(2):165–87. doi:10.1007/s10522-021-09910-5.
- Chen X, Mao G, Leng SX. Frailty syndrome: an overview. *Clin Interv Aging* 2014;9:433–41. doi:10.2147/CIA.S45300.
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013;381(9868):752–62. doi:10.1016/S0140-6736(12)62167-9.
- Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013;14(6):392–7. doi:10.1016/j.jamda.2013.03.022.
- Bello GA, Ornstein KA, Lucchini RG, Hung WW, Ko FC, Colicino E, et al. Development and validation of a clinical frailty index for the World Trade Center General responder cohort. *J Aging Health* 2021;33(7–8):531–44. doi:10.1177/0898264321997675.
- Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;1:323–36. doi:10.1100/tsw.2001.58.
- Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and meta-analysis. *Age Ageing* 2018;47(2):193–200. doi:10.1093/ageing/afx162.
- Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr* 2008;8:24. doi:10.1186/1471-2318-8-24.
- Buchman AS, Wilson RS, Bienias JL, Bennett DA. Change in frailty and risk of death in older persons. *Exp Aging Res* 2009;35(1):61–82. doi:10.1080/03610730802545051.
- Welstead M, Jenkins ND, Russ TC, Luciano M, Muniz-Terrera G. A systematic review of frailty trajectories: their shape and influencing factors. *Gerontologist* 2021;61(8):e463–ee75. doi:10.1093/geront/gnaa061.
- Stow D, Matthews FE, Hanratty B. Frailty trajectories to identify end of life: a longitudinal population-based study. *BMC Med* 2018;16(1):171. doi:10.1186/s12916-018-1148-x.
- Verghese J, Ayers E, Sathyan S, Lipton RB, Milman S, Barzilay N, et al. Trajectories of frailty in aging: prospective cohort study. *PLoS One* 2021;16(7):e0253976. doi:10.1371/journal.pone.0253976.
- Alvarez-Bustos A, Carnicero-Carreño JA, Sanchez-Sanchez JL, Garcia-Garcia FJ, Alonso-Bouzon C, Rodriguez-Manas L. Associations between frailty trajectories and frailty status and adverse outcomes in community-dwelling older adults. *J Cachexia Sarcopenia Muscle* 2022;13(1):230–9. doi:10.1002/jcsm.12888.
- Chamberlain AM, Finney Rutten LJ, Manemann SM, Yawn BP, Jacobson DJ, Fan C, et al. Frailty trajectories in an elderly population-based cohort. *J Am Geriatr Soc* 2016;64(2):285–92. doi:10.1111/jgs.13944.
- Hsu HC, Chang WC. Trajectories of frailty and related factors of the older people in Taiwan. *Exp Aging Res* 2015;41(1):104–14. doi:10.1080/0361073X.2015.978219.
- Smith E, Holmes L, Larkin B. Health trends among 9/11 responders from 2011 to 2021: a review of World trade center health program statistics. *Prehosp Disaster Med* 2021;36(5):621–6. doi:10.1017/S1049023x21000881.
- Mears MJ, Aslaner DM, Barson CT, Cohen MD, Gorr MW, Wold LE. Health effects following exposure to dust from the World Trade Center disaster: an update. *Life Sci* 2022;289:120147. doi:10.1016/j.lfs.2021.120147.
- Dasaro CR, Holden WL, Berman KD, Crane MA, Kaplan JR, Lucchini RG, et al. Cohort profile: world Trade Center Health Program General responder Cohort. *Int J Epidemiol* 2017;46(2):e9. doi:10.1093/ije/dyv099.
- Woskie SR, Kim H, Freund A, Stevenson L, Park BY, Baron S, et al. World trade center disaster: assessment of responder occupations, work locations, and job tasks. *Am J Ind Med* 2011;54(9):681–95. doi:10.1002/ajim.20997.
- Wisnivesky JP, Teitelbaum SL, Todd AC, Boffetta P, Crane M, Crowley L, et al. Persistence of multiple illnesses in World Trade Center rescue and recovery workers: a cohort study. *Lancet* 2011;378(9794):888–97. doi:10.1016/S0140-6736(11)61180-X.
- Shapiro MZ, Wallenstein SR, Dasaro CR, Lucchini RG, Sacks HS, Teitelbaum SL, et al. Cancer in general responders participating in World Trade Center health programs, 2003–2013. *JNCI Cancer Spectr* 2020;4(1):pkz090. doi:10.1093/jncics/pkz090.
- Proust-Lima C, Philipps V, Lique B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. *J Stat Softw* 2017;78(2):1–56. doi:10.18637/jss.v078.i02.
- Neath AA, Cavanaugh JE. The Bayesian information criterion: background, derivation, and applications. *WIREs Computational Statistics* 2012;4(2):199–203. doi:10.1002/wics.199.
- R Core Team R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2021.
- Fustinoni S, Santos-Eggimann B, Henchoz Y. Trajectories of phenotypical frailty over a decade in young-old community-dwelling adults: results from the Lc65+ study. *J Epidemiol Community Health* 2022;76(3):216–22. doi:10.1136/jech-2021-216633.
- Guo Y, Ng N, Hassler S, Wu F, Miao Jonasson J. Frailty trajectories in Chinese older adults: evidence from the China health and retirement longitudinal study. *Innov Aging* 2024;8(1):igad131. doi:10.1093/geroni/igad131.
- Gordon EH, Peel NM, Samanta M, Theou O, Howlett SE, Hubbard RE. Sex differences in frailty: a systematic review and meta-analysis. *Exp Gerontol* 2017;89:30–40. doi:10.1016/j.exger.2016.12.021.
- Jenkins ND, Hoogendijk EO, Armstrong JJ, Lewis NA, Ranson JM, Rijnhart JJM, et al. Trajectories of frailty with aging: coordinated analysis of five longitudinal studies. *Innov Aging* 2022;6(2):igab059. doi:10.1093/geroni/igab059.
- Park C, Ko FC. The science of frailty: sex differences. *Clin Geriatr Med* 2021;37(4):625–38. doi:10.1016/j.cger.2021.05.008.
- Jiang J, Icitovic N, Crane MA, Dasaro CR, Kaplan JR, Lucchini RG, et al. Sex differences in asthma and gastroesophageal reflux disease incidence among the World Trade Center Health Program General Responder Cohort. *Am J Ind Med* 2016;59(9):815–22. doi:10.1002/ajim.22634.
- Wu AH, Setiawan VW, Stram DO, Crimmins EM, Tseng CC, Lim U, et al. Racial, ethnic, and socioeconomic differences in a deficit accumulation frailty index in the Multiethnic Cohort Study. *J Gerontol A Biol Sci Med Sci* 2022. doi:10.1093/gerona/glac216.
- Usher T, Buta B, Thorpe RJ, Huang J, Samuel LJ, Kasper JD, et al. Dissecting the racial/ethnic disparity in frailty in a nationally representative cohort study with respect to health, income, and measurement. *J Gerontol A Biol Sci Med Sci* 2021;76(1):69–76. doi:10.1093/gerona/glaa061.
- Espinoza SE, Jung I, Hazuda H. Lower frailty incidence in older Mexican Americans than in older European Americans: the San Antonio Longitudinal Study of Aging. *J Am Geriatr Soc* 2010;58(11):2142–8. doi:10.1111/j.1532-5415.2010.03153.x.
- Woods NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. *J Am Geriatr Soc* 2005;53(8):1321–30. doi:10.1111/j.1532-5415.2005.53405.x.
- Elo IT. Social class differentials in health and mortality: patterns and explanations in comparative perspective. *Annu Rev Sociol* 2009;35(1):553–72. doi:10.1146/annurev-soc-070308-115929.
- Stolz E, Mayerl H, Waxenegger A, Rasky E, Freidl W. Impact of socioeconomic position on frailty trajectories in 10 European countries: evidence from the Survey of Health, Ageing and Retirement in Europe (2004–2013). *J Epidemiol Community Health* 2017;71(1):73–80. doi:10.1136/jech-2016-207712.
- Benzeval M, Green MJ, Leyland AH. Do social inequalities in health widen or converge with age? Longitudinal evidence from three cohorts in the West of Scotland. *BMC Public Health* 2011;11:947. doi:10.1186/1471-2458-11-947.
- Lu W, Benson R, Glaser K, Platts LG, Corna LM, Worts D, et al. Relationship between employment histories and frailty trajectories in later life: evidence from the English Longitudinal Study of Ageing. *J Epidemiol Community Health* 2017;71(5):439–45. doi:10.1136/jech-2016-207887.
- Gardiner PA, Mishra GD, Dobson AJ. The effect of socioeconomic status across adulthood on trajectories of frailty in older women. *J Am Med Dir Assoc* 2016;17(4):372 e1–3. doi:10.1016/j.jamda.2015.12.090.
- Iavicoli I, Leso V, Cesari M. The contribution of occupational factors on frailty. *Arch Gerontol Geriatr* 2018;75:51–8. doi:10.1016/j.archger.2017.11.010.
- van der Valk AM, Theou O, Wallace LMK, Andrew MK, Godin J. Physical demands at work and physical activity are associated with frailty in retirement. *Work* 2022;73(2):695–705. doi:10.3233/WOR-210859.
- Hu K, Keenan K, Hale JM, Borger T. The association between city-level air pollution and frailty among the elderly population in China. *Health Place* 2020;64:102362. doi:10.1016/j.healthplace.2020.102362.
- Shin J, Choi J. Frailty related to the exposure to particulate matter and ozone: the Korean Frailty and aging cohort study. *Int J Environ Res Public Health* 2021;18(22). doi:10.3390/ijerph18221796.

- [47] Guo YF, Ng N, Kowal P, Lin H, Ruan Y, Shi Y, et al. Frailty risk in older adults associated with long-term exposure to ambient PM2.5 in 6 middle-income countries. *J Gerontol A Biol Sci Med Sci* 2022;77(5):970–6. doi:[10.1093/gerona/giac022](https://doi.org/10.1093/gerona/giac022).
- [48] Kim H, Lee S, Jung YI, Hong YC. Association between phthalate exposure and frailty among community-dwelling older adults: a repeated panel data study. *Int J Environ Res Public Health* 2021;18(4). doi:[10.3390/ijerph18041985](https://doi.org/10.3390/ijerph18041985).
- [49] Nguena Nguetack HL, Page MG, Katz J, Choiniere M, Vanasse A, Dorais M, et al. Trajectory modelling techniques useful to epidemiological research: a comparative narrative review of approaches. *Clin Epidemiol* 2020;12:1205–22. doi:[10.2147/CLEP.S265287](https://doi.org/10.2147/CLEP.S265287).
- [50] Lennon H, Kelly S, Sperrin M, Buchan I, Cross AJ, Leitzmann M, et al. Framework to construct and interpret latent class trajectory modelling. *BMJ Open* 2018;8(7):e020683. doi:[10.1136/bmjopen-2017-020683](https://doi.org/10.1136/bmjopen-2017-020683).
- [51] Hoogendijk EO, Dent E. Trajectories, transitions, and trends in frailty among older adults: a review. *Ann Geriatr Med Res* 2022;26(4):289–95. doi:[10.4235/agmr.22.0148](https://doi.org/10.4235/agmr.22.0148).