FINAL PROGRESS REPORT

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Project Title:

The Aging Process of WTC Responders: Assessment and Consequences of Frailty

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Grant Number:

U01OH012068

FAIN:

U01OH012068

Project starting and ending dates:

09/01/2020 - 08/31/2022

Date the final report was completed:

09/30/2022

Contents

List of Terms and Abbreviations

BMI	Body Mass Index
Clinical-FI	Clinical Frailty Index
CCE	Clinical Center of Excellence
CRC	Clinical Research Coordinator
EAQ	Exposure Assessment Questionnaire
FI	Frailty Index
FRIDs	Fall risk increasing drugs
GERD	Gastroesophageal reflux disease
GRDC	General Responder Data Center
GS	Grip Strength
IAMQ	Interviewer Administered Medical Questionnaire
IER	Immigrant and Employee Rights Section
IQR	inter quartile range
ISMMS	Icahn School of Medicine at Mount Sinai
LCMM	Latent Cluster Mixed Model
OAD	Obstructive airway disease
PE	Physical exam
PTSD	Post-traumatic stress disorder
QOL	Quality of Life
SAMHQ	Self-Assessed Mental Health Questionnaire
URD	Upper respiratory disease
WS	Walking speed
WTC	World Trade Center
WTCHP	World Trade Center Health Program
WTC-GRC	World Trade Center General Responder Cohort

ABSTRACT:

Project Title**:**
The Aging Process of WTC Responders: Assessment and Consequences of Frailty

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Although the WTC general responder cohort (WTC-GRC) is aging (average age=56), the WTC Health Program (WTCHP) does not routinely collect data on aging-related syndromes. In particular, frailty is a syndrome characterized by increased vulnerability to adverse events including mortality, morbidity, disability, and hospitalizations. Therefore, the overarching aim of this study is to assess whether previous WTC exposure leads to premature age-related deterioration in physiological function. We will develop a WTC-specific Clinical Frailty Index (FI) based on clinically observable signs and symptoms of aging regularly examined within WTCHP surveillance. We will carry out analyses using the repository of WTC-GRC health monitoring data that has been collected at the Mount Sinai Clinical Center of Excellence (CCE) since 2002. Additionally, we will recruit individuals from the WTC-GRC who are followed at the Mount Sinai Clinical CCE to collect new measures of cognitive function, grip strength, weight loss, physical activity, exhaustion and walking speed, which will improve the accuracy of the WTC Clinical-FI.

We will first establish a validated frailty cutoff for a WTC-specific Clinical-FI using newly collected measures of cognition, grip strength, walking speed, unintentional weight loss, physical activity, and exhaustion (Aim 1). We will assess the influence of WTC exposure severity on the development of frailty in WTC general responders (Aim 2) and the association of WTC exposure (and other potential risk factors) with frailty trajectories (Aim 3). In an exploratory Aim we will assess the influence of frailty on other age-related syndromes and key consequences. Identifying modifiable risk factors for premature aging has the potential to impact the entire WTCHP, which is an aging cohort and at higher risk for negative consequences. Our broader focus on aging and frailty serves as a paradigm shift in the WTCHP from exposure and trauma-related injury. Results of this study will be instrumental in improving the capacity of the WTCHP to monitor and care for aging responders through partnership with Geriatrics and Palliative Care programs at ISMMS, including the development of future intervention research on the effectiveness of specific multifactorial preventive programs.

SECTION 1 OF THE FINAL PROGRESS REPORT

Significant or Key Findings:
Our first aim was to establish a validated frailty cutoff for a WTC-specific Clinical-FI using newly collected measures of cognition, grip strength, walking speed, unintentional weight loss, physical activity, and exhaustion. To achieve this goal, we developed a frailty index using existing data collected for WTC respondents and conducted in-person frailty assessments on participants. Using data drawn from WTC general responders, a 30-item clinical frailty index, WTC Clinical-FI, was developed according to the cumulative deficit model of frailty. The validity of the resulting index was initially assessed using all-cause mortality as an endpoint. We began enrolling general responders from the Mount Sinai CCE in Feb 2021, during the COVID pandemic, for in–depth frailty and aging assessments. We successfully enrolled more than 120 responders and conducted in-person or telephone frailty phenotype assessments and followed patients at high risk for falls. We validated a cutoff for the WTC Clinical-FI which can be used for frailty assessment based on routinely collected assessment data.

Our second aim was to assess the influence of WTC exposure severity on the development of frailty among WTC general responders. To test this association, we examined the association between WTC exposure severity and clinical frailty assessments in an adjusted logistic regression analysis. Over 25% of the 7,679 participants, median age 58.3 years (IQR 9.3), who had any visit to the WTC clinical program from 2017 to 2019, were frail. Frailty increased with age, WTC exposure, and by occupation type (e.g., higher risk among construction worker).

The third aim was to identify subpopulations with distinct frailty trajectories among WTC general responders and examine the association of WTC exposure (and other potential risk factors) with frailty trajectories. To conduct this aim we used latent class growth mixture models of individuals with 3 or more WTC-Clinical FI assessments to characterize frailty trajectories and examine association between trajectories and WTC exposure status and occupation type. We identified three distinct patterns of change in frailty over time. WTC general responders with higher age, working in construction, and higher-intermediate WTC level of exposure had higher rate of increase in frailty over time.

We originally planned to recruit 500 responders to validate WTC Clinical-FI and conduct in person aging assessments. We were unable to achieve this goal given the onset of the COVID-19 pandemic in New York City and the lack of in-person WTC visits for responders at the Mount Sinai clinic. Despite this setback, we successfully recruited 123 general responders and followed 17 of them for falls risk. We used previously collected General Responder Data Center (GRDC) data to examine frailty trajectories and reviewed routinely collected patient medication and comorbidity data to characterize the patient frailty experience. In 2022 we received a new 4-year grant that will allow us to continue to expand this work focused on assessing frailty among WTC general responders and developing new interventions to support healthy aging.

Our research suggests that frailty and its related conditions are prevalent among the WTC-GRC despite their younger age. Such a significant level of frailty among a non-geriatric population is not surprising given the high level of disease burden documented among WTC responders. These findings underscore the urgent need for routine systematic assessments of structured aging-related indicators in the WTC-GRC, the majority of whom will be over 65 by 2030. We have successfully developed a clinical frailty index specifically for WTC general responders which can be deployed in routine follow-up in the WTCHP. Monitoring frailty in the WTC-GRC will allow for identification of individuals at risk for further decline based on both accumulated deficits and physiological change and will expand the capacity of WTCHP to monitor and care

for aging responders, and will enable the development of future intervention research on the effectiveness of specific multifactorial preventive programs focused on healthy aging. Moreover, our broader focus on aging and frailty serves as a paradigm shift in the WTCHP from exposure and trauma-related injury.

Translation of Findings:
A vital takeaway message from this research is that the aging WTC-GRC has high burden of frailty and aging-related conditions. In order to support the health care of aging WTC general responders, further research needs to focus on efforts to target modifiable factors that promote healthy aging. Our study has set the initial stage for the proper monitoring of the aging processes in the WTC-GRC through rigorous validation and implementation of state of the art tools in aging research. Specifically, this study has enabled us to develop a new tool (i.e., WTC Clinical-FI that leverages data routinely collected via the WTCHP) to assess frailty among WTC general responders and therefore assess their increased vulnerability over time. Moreover, these data will allow us to target general responders at higher risk for poor outcomes and consequently alleviate aging-related syndromes in this older and high-risk population. Therefore, findings from this completed and ongoing frailty investigations in the WTC-GRC will be instrumental in improving the capacity of the WTCHP to monitor and care for members as they age for years to come. Besides the direct implications for WTC responders, findings from this study has contributed to our understanding of how occupational and environmental exposures can induce premature aging. Thus, frailty is an important outcome to assess when conducting medical surveillance after future disasters where workers are exposed to potentially neurotoxic chemicals and/or experience post-disaster mental health problems.

Research Outcomes/Impact:
The main outcome from this project is that WTC general responders may be at especially high risk for aging-related syndromes and related consequences. The results from this study suggest that further work must be completed to routinely screen WTC responders for aging-related outcomes and that interventions will need to be developed to better support WTC responders as they get older.

The recommendation most relevant to occupational safety and health is that frailty should be an included condition when implementing medical monitoring and surveillance after future disasters. Exposure to neurotoxic agents such as metals, solvents, pesticides, and fine particulate matter is common in many workplaces. The effects of these toxicant exposures on frailty have not been previously studied and may often be overlooked. This may be especially relevant as workers postpone retirement and as our work suggests, is relevant to certain workplace settings.

SECTION 2 OF THE FINAL PROGRESS REPORT

Scientific Report

Background:

Rescue and recovery workers (responders) involved in the emergency response and cleanup following the 2001 World Trade Center (WTC) disaster were exposed to high levels of toxicants and intense psychological trauma.[1] Exposure to occupational and environmental hazards can accelerate aging processes.[2] Ergonomic constraints during working years are associated with musculoskeletal disorders and disability after retirement,[3] and physically demanding occupations can decrease quality of life (QOL) in old age.[4] Exposure to solvents affects the workers' cognitive functions long after exposure cessation,[5] Further, psychosocial stressors during working life can induce long-term negative impacts on physical and mental health.[6,7] In the years following the 2001 WTC disaster, the WTC Health Program (WTCHP) implemented health surveillance for monitoring and treatment of WTC-related health consequences among responders.[8] About one half of responders have developed respiratory symptoms after 9/11, including asthma, sinusitis, abnormal spirometry, sarcoidosis, and multiple comorbidities.[9] Approximately one third have developed mental health conditions such as post-traumatic stress disorder and depression. Additionally, standardized incidence ratios for all-cancer-sites combined, thyroid, prostate, soft tissue and combined hematopoietic cancer are higher than expected rates.[10] These findings underscore the need for routine systematic assessment of age-related indicators in the cohort. Yet, the WTCHP does not collect information on early aging among the cohort members, many of whom have already reached a critical turning point in aging. The current cohort's median age is 56 years; 80% are aged 50 or over and 30% are above 61 years.

Frailty is a recognized syndrome among older adults resulting from cumulative declines across multiple physiological symptoms.[11] It is characterized by an individual's increased vulnerability to adverse events (including mortality, morbidity, disability, and hospitalizations[12,13]) occurring after exposure to stressors.[14] Because it can have a serious impact on QOL, frailty assessment is now recommended in routine clinical examination among older adults.[14] Two approaches to measuring frailty are: (1) the Frailty Phenotype,[13] based on the presence of specific clinical signs, symptoms and physiology and (2) the Frailty Index model,[15] which conceptualizes frailty as the accumulation of functional and health deficits resulting from (and indicative of) a diminishing ability to maintain normal function/homeostasis.[16] With this '*deficit accumulation'* model, frailty is measured by computing the proportion of deficits in multiple domains of health and well-being: disability, functional impairment, health conditions, and comorbidities. Because this index is computed from clinically-observable health deficits, it is often referred to as a Clinical Frailty Index (or Clinical-FI). A higher Clinical-FI score indicates the presence of a greater proportion of aging-related health conditions in an individual.[17] The frailty phenotype and index are two different approaches for operationalizing the concept of frailty.[18] The phenotype is designed to allow stratification into clear-cut categories of non-frail, pre-frail and frail, while the FI is designed to be a continuous measure (though it can be dichotomized using empirical cutoffs). And unlike the phenotype which utilizes a predefined set of 5 criteria, the FI can be constructed from a large variety of deficits. Because it offers a large degree of latitude in the variables used in its construction, the FI approach is especially suitable for the WTC cohort, who have had repeated health-related assessments with information managed by the WTCHP Data Center. By adapting this tool specifically for the WTC responders, and refining its stratification ability with the measurement of the frailty phenotype via key physiological assessments (i.e., unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity), we will produce an instrument that can be deployed in routine follow-up in the WTCHP. Monitoring frailty in this

cohort will allow for identification of individuals at risk for further decline based on both accumulated deficits and physiological change and will enable health professionals to comprehensively capture and intervene upon health deficits in this population at-risk for aging-related consequences.

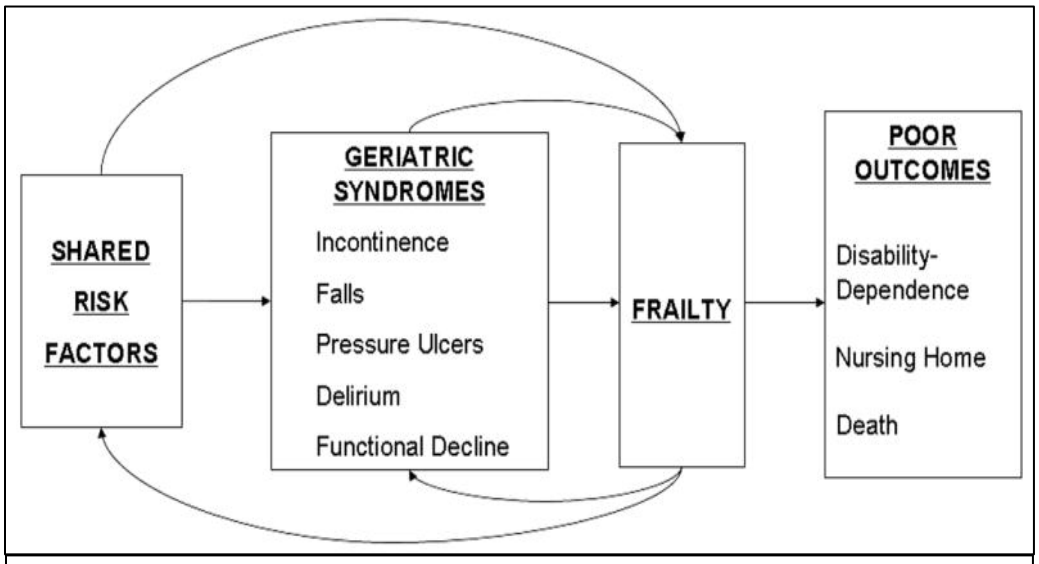


Figure 1: Conceptual framework of frailty and geriatric syndromes

Frailty is a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems,[18] [19,20] and has long been recognized by clinicians and caregivers as a warning sign for functional and cognitive decline, chronic illnesses, and mortality.[21] Frailty is often considered a geriatric or "age-related" syndrome," one of many clinical conditions seen among older persons that does not fit into discrete disease categories.[22] Many of the most common conditions cared for by geriatricians, including delirium, dizziness, syncope and urinary incontinence, are classified as geriatric syndromes. Although heterogeneous, these syndromes involve multiple organ systems and have substantial impact on QOL and disability.[13] We posit that frailty is associated with other aging-related syndromes, including disability and falls,[15,22-25] based on Inouye's conceptual framework of frailty and geriatric syndromes (**Figure 1**).[22] Falls and fall-related injuries are an especially important target for intervention among older adults, as they are common (approximately one in three older Americans fall each year) and lead to a number of adverse consequences including injuries, reduction in QOL, increased hospitalizations,[26,27] and increased mortality.[28] Even when falls do not result in physical injury, they can cause individuals to become fearful of falling, with consequent restrictions on mobility and physical fitness, which in turn increase risk of falling.[29]

The WTC cohort is especially at risk for premature aging, due to previous exposure to environmental toxicants and intense psychological trauma. Frailty can be reduced or delayed with exercise, protein-calorie supplementation, vitamin D, and reduction of polypharmacy.[14] Therefore, for the purposes of optimally managing individuals with a higher degree of vulnerability, frailty can and should be identified at an early stage. The WTCHP does not routinely collect structured information to specifically assess the aging processes. This is a relevant need since the current cohort's median age is close to 60 years. The development of a WTC-specific frailty index is critical for us to: (i) identify individuals with a higher degree of vulnerability to age-related

syndromes; and (ii) examine association between WTC exposure and frailty risk and prevent further clinical deterioration.

Study Aims

The overarching aim of this study was to assess whether previous WTC exposure leads to premature age-related deterioration in physiological function. We will develop a WTC-specific 'WTC Clinical-FI,' based on clinically observable signs and symptoms of aging regularly examined within the WTCHP health surveillance. We will carry out analyses on the repository of WTC-GRC health monitoring data that has been collected at the Mount Sinai Clinical Center of Excellence (CCE) since 2002.[9] Additionally, we will recruit individuals from the WTC-GRC who are followed at the Mount Sinai Clinical CCE to collect new measures of cognitive function, grip strength, weight loss, physical activity, exhaustion and walking speed, which will improve the accuracy of the WTC Clinical-FI. We ***hypothesized*** that WTC exposure increases the development and rate of aging processes.

AIM 1: To establish a validated frailty cutoff for a WTC-specific Clinical-FI using newly collected measures of cognition, grip strength, walking speed, unintentional weight loss, physical activity, and exhaustion.
AIM 2: To assess the influence of WTC exposure severity on the development of frailty among over 9000 WTC responders.
AIM 3: To identify subpopulations with distinct frailty trajectories among WTC responders and examine the association of WTC exposure (and other potential risk factors) with frailty trajectories.
Exploratory AIM 4: To assess the influence of frailty on age-related syndromes and consequences. One age related condition is polypharmacy, defined as the use of multiple medications, which are associated with poor functional outcomes and falls. We explored the association of frailty with polypharmacy and also specifically the use of medications that increases falls risk.

Methodology

Study population:

The study population includes members of the WTC-GRC who are routinely seen for monitoring and treatment at the Icahn School of Medicine at the Mount Sinai Clinical CCE. The WTC-GRC enrolled persons who participated as employees or volunteers in the rescue, recovery, and cleanup efforts at the WTC site after 9/11/2001 on the basis of eligibility criteria including type of duties, site location, and dates and hours worked.[9] The protocol for the monitoring program, which began in July 2002, includes an exposure assessment questionnaire, self-administered physical and mental health questionnaires, and a physical examination, laboratory tests, spirometry, and a chest radiograph. Routine WTC monitoring visits, scheduled every 12–18 months, are performed by WTC-GRC clinical centers located at several sites in the New York Metropolitan Area, including the Mount Sinai CCE. The Mount Sinai CCE is the largest CCE of the WTCHP, and the Mount Sinai WTC cohort is fully representative of the entire GRC cohort.

Study enrollment:

The study used data routinely collected from the site and also enrolled patients for new data collection. Study Inclusion criteria were: (i) enrollment in the WTCHP; (ii) previous consent to be contacted for research purposes; and (iii) age 50 or above at the time of their appointment.

Exclusion criteria were: (i) inability to understand and provide written informed consent; and (ii) inability to speak and understand English

We used 2 methods for study recruitment: (1) WTC-GRC members who have consented to be contacted for research were identified by the General Responder Data Center (GRDC) at Mount Sinai per its standard protocols. A list of these individuals with contact information were provided to the study team. The study team emailed eligible individuals (including an opt out option). If an individual did not opt out, the study team contacted these individuals by phone to seek consent and schedule assessments for those who consented. (2) A Clinical Research Coordinator (CRC) was onsite at the WTCHP clinic approximately 3 days per week when onsite hosts were scheduled (varied depending on COVID-19). A recruitment flyer was hung in the clinic introducing the research, and noting that patients should ask clinic staff if they are interested. Interested individuals were directed to the CRC, who consented patients to be in study. In total, 60 patients were recruited in the clinic and 63 were recruited via email. Participants were enrolled between February 2021 and November 2021.

Study assessments:
An experienced CRC conducted all assessments including those for the frailty phenotype measures (Grip Strength [GS], Walking Speed [WS], unintentional weight loss, physical activity, and exhaustion) as well as cognitive function. Weakness was measured via hand grip strength (GS), assessed using the Jamar hand dynamometer, following the standardized South Hampton method.[30] We measured walking speed in meters/second as assessed via the Short Physical Performance Battery (SPPB)[31]. Because of COVID-19, we also assessed frailty using the FRAIL (Fatigue, Resistance, Ambulation, Illnesses & Loss of Weight) Scale,[32] a validated 5-item telephone-based assessment to screen frailty. Additionally, we collected the following measures: cognitive function (Montreal Cognitive Assessment) [33,34] functional dependence, fall occurrence, fear of falling, and risk of falls. A telephone and email option was also made available to complete survey instruments. Data from the questionnaires and physical exam (collected during the WTCHP monitoring visits) that are necessary to compute the WTC Clinical-FI were obtained from the GRDC. Seventeen enrolled participants determined to be at high risk for falls were given a calendar to track falls, and were contacted for follow up by the CRC via telephone at 3 months follow-up (See assessments Table below).

Table 1: Frailty study assessments

	Domain	**measure**
FRAILTY	1. Weight loss	JHU Frailty
	2. Exhaustion	JHU Frailty
	3. Physical activity	JHU Frailty
	4. Weakness	Grip Strength
	5. Walking speed	Walking speed
	Overall frailty measure	Frail scale
FALLS	Falls risk	STRIDE Falls assessment
	Fear of falling	Falls Efficacy Scale
	Falls experience	Falls Log
COGNITION		MOCA
		Callahan dementia screener

FUNCTION		ADLs and IADLs
HOSPITALIZATIONS		Self-report

Statistical approach:
For AIM 1, we computed frailty phenotype using the approach outlined by Fried et al (2001).[13] The frailty phenotype is composed of 5 criteria. The presence of each criterion is assigned a score of 1, yielding an integer-valued total score with possible range 0-5. An individual scoring 3 or above is considered frail. A score in the range 1-2 is considered intermediate or pre-frail. In this study, we used a dichotomized version of the frailty phenotype, with scores ≥3 considered frail, and <3 considered non- or pre-frail. We computed a WTC-specific Clinical-FI using WTCHP responses available to the GRDC, according to the protocol outlined by Searle et al[35] for constructing frailty indices. With the standardized cutoffs from the frailty phenotype (≥3 [frail] vs. <3 [non- or pre-frail]), we derived a WTC cohort-specific cut-point for the WTC Clinical-FI. Frailty phenotype measures for the responders allowed designation of these subjects as frail or not, which was used as a gold standard. With WTC Clinical-FI treated as a continuous predictor, ROC (receiver operating characteristic) analysis,[36] implemented in the R package OptimalCutPoints[37] was used to derive a WTC Clinical-FI cut-point that established an optimal sensitivity/specificity tradeoff with respect to the gold standard. This cut-point was used among all responders with and without addition of new measures. We also examined frailty cut-point among those individuals identified with cognitive impairment.

For AIM 2, 9/11 WTC exposure severity was quantified using responses to a questionnaire completed by all WTCHP enrollees. At the time of enrollment, all enrollees completed the Exposure Assessment Questionnaire (EAQ) which is designed to evaluate the extent of exposure to pollutants prior to, and while working on the rescue and recovery effort. Responses from the EAQ were used to design a 9/11 Exposure Severity Index that can assess the extent and severity of exposure.[38] The Exposure Severity Index has four levels of exposure: low, intermediate, high, and very high. These categories were defined based on a cohort member's duration of work on the WTC cleanup effort, exposure to the dust cloud on 9/11, and whether or not they worked on the debris pile[38]. For this study, we merged the 'high' and 'very high' exposure categories into one category. With the cutoff derived from Aim 1, we were able to more accurately stratify cohort members into 'frail' and 'non-frail' status using their Clinical-FI scores. We assessed the association of exposure severity with frailty status, adjusting for potentially confounding cohort characteristics. Using logistic regression, we tested the association of frailty status (dependent variable) and exposure severity, adjusting for age, sex, race/ethnicity, education, pre-9/11 occupation, smoking status and WTCHP enrollment period (independent variables). We repeated this analysis using the continuous version of the WTC Clinical-FI (a value ranging between 0 and 1, representing the proportion of items on which an individual has deficits).

To map out and analyze the trajectories of frailty in the WTC cohort (AIM 3), we used longitudinal data collected on cohort members from 2002 to 2017. We focused on subjects with 3 or more visits since 2002, with non-missing values on the variables required for computation of the WTC Clinical-FI, and covariates of interest. We used latent class growth mixture models to model the patterns of change in WTC Clinical-FI measurements over time. The association of estimated trajectories with various risk factors (demographics, WTC exposure severity, pre-9/11 occupation, smoking status, etc.) was assessed.

Finally, an exploratory analysis was conducted to assess the influence of frailty on age-related syndromes and consequences. We examined polypharmacy, defined as the use of multiple

medications, and its relationship with frailty because polypharmacy is associated with age-related outcomes of poor function, falls, and hospitalizations, and polypharmacy and medication use presents a potentially modifiable risk factor for aging. We assessed the influence of frailty on polypharmacy. WTC-related certified conditions (considered to be directly related to exposures from WTC work) were grouped into 14 certification categories. We excluded low frequency certification categories, leaving the following: anxiety disorder, cancer, depression, gastroesophageal reflux disease (GERD), obstructive airway disease (OAD), post-traumatic stress disorder (PTSD) and upper respiratory disease (URD). Self-reported medication count was determined from the IAMQ Medication History section. The exact question posed to respondents was: "Are you currently taking any prescription, non-prescription or herbal medications?" If they answered 'Yes', then the interviewer prompted them to list medications, including alternative, herbal, homeopathic or other medicines. For this exploratory analysis, medication count was determined by counting the number of medications listed by the respondent. Polypharmacy was defined as having 5 or more medications.

For fall-risk inducing drugs, we identified those matching generic and brand names under 5 classes of fall-risk inducing drugs: benzodiazepines, first generation antihistamines, long-acting hypoglycemic, skeletal muscle relaxants and tertiary tricyclic antidepressants which were previously defined as associated with an increase in the risk of falls. We assessed the relationship of polypharmacy with the following cohort characteristics: age, sex, race/ethnicity, enrolment year, 9/11 exposure severity, pre-9/11 occupation, smoking status, alcohol consumption, BMI, self-reported conditions (history of sleep apnea, diabetes, hypertension), WTC certified conditions (anxiety disorder, cancer, depression, GERD, OAD, PTSD, URD), self-reported functional limitations, and WTC Clinical-FI. For cohort characteristics that were continuous values (age, WTC Clinical-FI), the relationship with polypharmacy was assessed via Wilcoxon rank sum test comparing distributions of these variables between the polypharmacy and "no-polypharmacy" groups. The remaining characteristics were discrete in nature, and Pearson's Chi-squared test was used to assess the relationship of each with polypharmacy. Multivariable logistic regression models were used to assess the association of following variables with polypharmacy: age, sex, race/ethnicity, enrolment year, 9/11 exposure severity, pre-9/11 occupation, smoking status, alcohol consumption, BMI, self-reported conditions (history of sleep apnea, diabetes, hypertension), WTC certified conditions (anxiety disorder, cancer, depression, GERD, OAD, PTSD, URD), self-reported functional limitations, and WTC Clinical-FI (re-computed to exclude polypharmacy).

RESULTS

Aim 1: Construction of the WTC Clinical-FI

A large pool of potentially age-related indicators from the available data collected by the WTCHP was screened for inclusion in the index. These candidate indicators were obtained from the Interviewer Administered Medical Questionnaire (IAMQ), the Self-Assessed Mental Health Questionnaire (SAMHQ), and the physical examination, all of which are administered in every monitoring visit. Candidate items from the IAMQ and SAMHQ include responses to questions about clinical signs and symptoms potentially related to aging (e.g., difficulty hearing, history/onset of diabetes, pneumonia, etc. from the IAMQ; difficulty climbing stairs, and problems with short-term memory from the SAHMQ). Candidate items from the physical examinations include assessments of eyes, ears, heart, and general appearance. The pool of candidate items was screened systematically, following a widely used protocol by Searle et al[35] for constructing frailty indices. This protocol considers that an item/variable is appropriate for inclusion in a frailty index if it is associated with health status and if the prevalence of deficits on this variable increases

with age.[35,39] Therefore, each candidate item was coded as a binary value indicating the presence or absence of a deficit, and the correlation between age and the prevalence of deficits on the item was computed. For example, the candidate item: *self-rated health* asks responders to rank their health using a 5-point Likert scale: *Excellent*, *Very Good*, *Good*, *Fair*, *Poor*. To determine if this item was appropriate for inclusion in our WTC Clinical-FI, we coded it as a binary value where a response of *Fair*/*Poor* was considered as a 'deficit' score of 1, and a response of *Excellent*/*Very Good*/*Good* was assigned a non-deficit score of 0. Then, we calculated the prevalence of deficits (i.e., proportion of individuals with a 'deficit' on this item) for each age in our sample and the correlation of deficit prevalence with age. If the correlation was at least 0.4 (moderate correlation), the item was considered appropriate for inclusion in our WTC Clinical-FI. This procedure was repeated for all candidate items and a total of 30 items were selected, spanning multiple domains of health and well-being (**Table 2**).

Table 2: WTC Clinical-FI Items

Items included in frailty index	Source	Coding Map
1 Ever had pneumonia	IAMQ	0: No, 1: Yes
2 Ever had diabetes	IAMQ	0: No, 1: Yes
3 Persistent fatigue	IAMQ	0: No, 1: Yes
4 Unexplained weight loss	IAMQ	0: No, 1: Yes
5 Difficulty urinating	IAMQ	0: No, 1: Yes
6 Inability to taste	IAMQ	0: No, 1: Yes
7 Difficulty swallowing	IAMQ	0: No, 1: Yes
8 Change in bowel habits	IAMQ	0: No, 1: Yes
9 Coughing after you lie down or eat	IAMQ	0: No, 1: Yes
10 Difficulty hearing	IAMQ	0: No, 1: Yes
11 Concurrent medications (polypharmacy)	IAMQ	0: 0–5, 1: 6+
12 Self-rated health	SAMHQ	0: Excellent/Very good/Good 1: Fair/poor
13 Difficulty performing moderate activities, e.g., moving table, pushing a vacuum cleaner, bowling, or playing golf	SAMHQ	0: No, not at all/Yes, a little 1: Yes, a lot
14 Difficulty climbing several flights of stairs	SAMHQ	0: No, not at all/Yes, a little 1: Yes, a lot
15 In past month, accomplished less than you would like	SAMHQ	0: No, 1: Yes
16 In past month, were limited in the kind of work or other activities you could perform	SAMHQ	0: No, 1: Yes
17 In past month, accomplished less due to emotional problems	SAMHQ	0: No, 1: Yes
18 In past month, did work less carefully than usual due to emotional problems	SAMHQ	0: No, 1: Yes
19 How much does pain interfere with normal work	SAMHQ	0: Not at all/a little/moderately 1: Quite a bit/extremely
20 In past month, how often felt calm/peaceful	SAMHQ	0: All or most of the time 1: Some or little of the time/none of the time

21	In past month, how often felt lots of energy	SAMHQ	0: All or most of the time
22	In past month, how often felt downhearted	SAMHQ	0: Some or little of the time/none of the time 1: All or most of the time
23	In the past month, how often has physical health/emotional problems interfered with social activities	SAMHQ	0: Some or little of the time/none of the time 1: All or most of the time
24	Frequency of short-term memory problems (e.g., forgetting keys)	SAMHQ	0: Not at all/a little bit/moderately 1: Quite a bit/extremely
25	In past month, frequency of difficulty concentrating	SAMHQ	0: Not at all/a little bit/moderately 1: Quite a bit/extremely
26	Abnormal eye exam	PE	0: No, 1: Yes
27	Abnormal ear exam	PE	0: No, 1: Yes
28	Abnormal extremities exam	PE	0: No, 1: Yes
29	Abnormal heart exam	PE	0: No, 1: Yes
30	Abnormal physician-assessed general appearance	PE	0: No, 1: Yes

These domains overlap with those from other frailty indices (e.g., the 70-item Frailty Index by Rockwood et al., 2005[17]). We examined the correlation between our WTC Clinical-FI and age. Using an adjusted Cox proportional hazards model, we found that WTC Clinical-FI was a significant independent predictor of mortality in our cohort. Using a dichotomized composite frailty score (derived from a composite of the frailty phenotype [i.e., Johns Hopkins University frailty tool] score and FRAIL scale among WTC responders), we derived a cutoff for WTC Clinical-FI. A cutoff of .27 was chosen as the value of WTC Clinical-FI that maximizes Youden's J-statistic (sensitivity + specificity - 1), with respect to discriminating between 'frail' and 'not frail/robust health' status. Approximately 30% of subjects were found to be frail/pre-frail using the cutoff as shown in **Figure 2.**

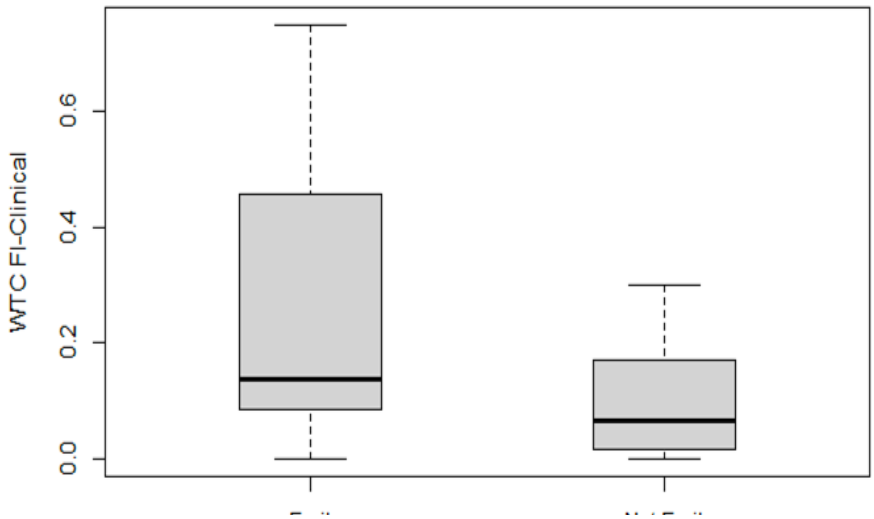


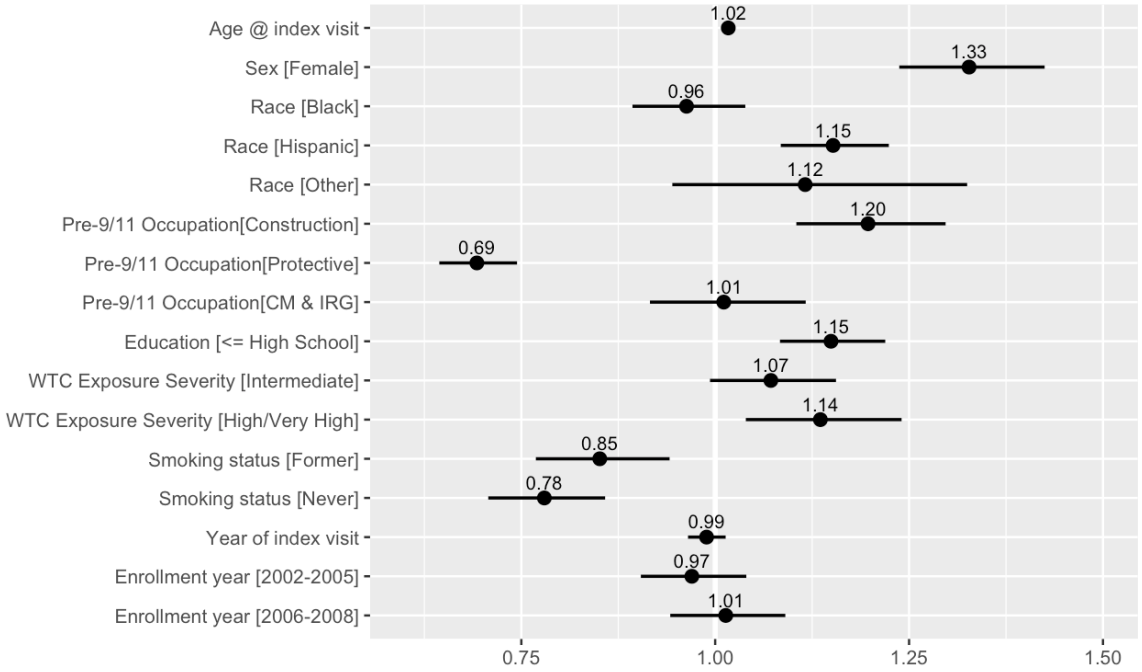
Figure 2: WTC Clinical–FI by cutoff

Aim 2: Association of frailty with WTC exposure

We assessed the association of WTC Clinical-FI with various cohort characteristics. **Figure 3** below summarizes the incidence rate ratios (and 95% CIs) for the continuous variables (age and year of index visit) and for non-baseline categories of the categorical variables (race, education, WTC exposure severity, sex, smoking status, pre-9/11 occupation, and enrollment year). Baseline (referent) categories for nominal variables were as follows: race: *white*; education: *>high school*; WTC exposure severity: *low exposure*; sex: *female*; smoking status: *current smoker*: pre-9/11 occupation: *other occupation*; enrollment year: *>2008*.

These results indicate that multiple demographic and risk factors are associated with clinical frailty. In particular, we found that those with high/very high WTC exposure severity had higher frailty, relative to those with low exposure severity (p = .005). Those in the *protective occupation* category (e.g., law enforcement and emergency medical services) up to and at the time of 9/11 had significantly lower frailty (p < .0001) compared to those in the *other* category (i.e., all other occupations outside of construction, protective, cleaning/maintenance and installation/repair services). And relative to this *other occupations* category, those in the construction-related occupations had higher frailty (p < .0001). Males in this cohort had higher frailty relative to females (p < .0001), as did Hispanics relative to whites (p < .0001). Relative to (self-reported) current smokers, former smokers, and those who reported never having smoked had significantly lower frailty (p = .002 and p < .0001, respectively). Those less educated (high school education or less) had significantly higher frailty (p < .0001) relative to those with greater than high school education.

In the study sample, the median survival time (measured from index visit date) was 4.2 years, and the censoring rate was 98.8%. In a Cox Proportional Hazards model, WTC Clinical-FI showed a strong association with all-cause mortality (p < .0001), after adjustment for the following potential confounders: age, sex, race/ethnicity, pre-9/11 occupation, education, smoking status, and WTCHP enrollment year.



Aim 3: Assessment of frailty trajectories

Three distinct frailty trajectories in WTC general responders were identified using Latent Cluster Mixed Model (LCMM). **(Figure 4)** All 3 trajectories demonstrated an increase in WTC Clinical-FI score with increasing age. The "low FI" group (indicted by a red line) had low WTC Clinical-FI score at all ages that gradually increased over time. The "sustained increase FI" group (green line) had low WTC Clinical-FI score at younger ages that rapidly increased over time. The "high FI" group (blue line) had high WTC Clinical-FI score across all ages (even in youth) that moderately increased over time. As shown in Figure 4 below, all trajectories showed an increase with age. Three distinct frailty trajectories were identified – "low FI" (red), "sustained increase FI" (green), and "high FI" (blue) using LCMM.

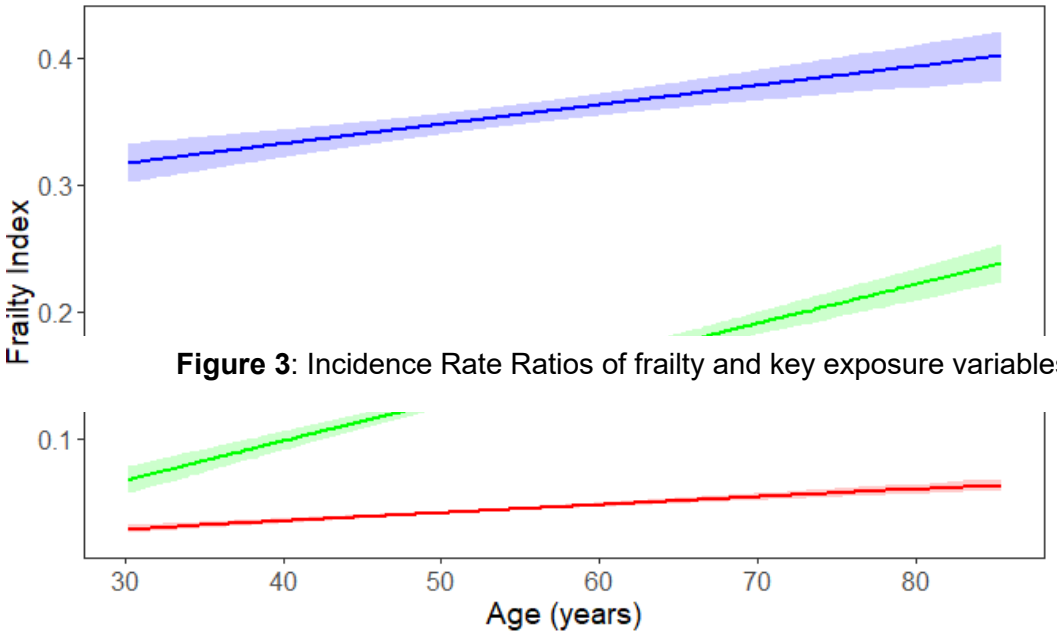


Figure 3: Incidence Rate Ratios of frailty and key exposure variables

Figure 4. Frailty trajectories in WTC general responders.

- "red" group ("low FI") has low frailty index at all ages with gradual increase over time (reference level)
- "green" group ("sustained increased FI") has low frailty index at younger ages that increased drastically during years
- "blue" group ("high FI") has highest frailty index estimates even in youth with moderate increasing trend over time

The level of WTC exposure severity was associated with frailty trajectories using a multinomial regression model. **(Figure 5)** In comparing "high FI" group to "low FI" group, high/very high WTC exposure severity (RR 1.82, 95% CI, 1.55 to 2.13) and intermediate WTC exposure severity (RR 1.41, 95% CI, 1.23 to 1.62) were associated with frailty trajectories. In the "sustained increase FI" group, frailty trajectory was associated with high/very high WTC exposure severity (RR 1.20, 95% CI, 1.03 to 1.41) but not with intermediate WTC exposure severity (RR 1.05, 95% CI, 0.91 to 1.20).

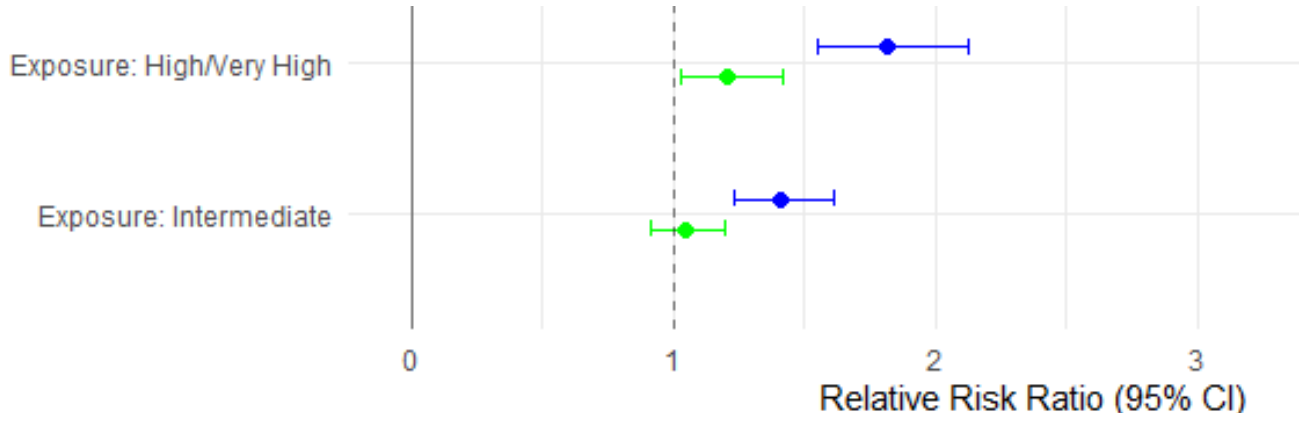


Figure 5: Multinomial regression on frailty trajectories and WTC exposure.

Exploratory Aim 4: Assessment of the influence of frailty on age-related syndromes

For this analysis, we selected WTC-GRC members who had at least one follow-up clinical monitoring visit (where they gave consent to use the data collected on them) between 2017 and 2019 and who were aged 50+ years at the time of the visit. Further, we excluded those with missing values on one or more variables required for the analyses. A total of 6,966 WTC general responders were included in this exploratory analysis. (see **Table 3** for cohort characteristics) The median age was 58 years old (Interquartile range 54 and 63); 86% were male with 62% of the cohort identified as white, 14% were black and 21% were Hispanic. Approximately 39% of responders were initially enrolled in the WTCHP from 2002-2005, 24% from 2006-2008, and 38% from 2009 to present. For severity of WTC exposure, 14% had low exposure, 63% had intermediate exposure and 23% had high or very high exposure. In the cohort, occupation prior to 9/11/2001 varied, including 20% in construction categories, 53% in protective category (including police, workers from law enforcement agencies). Chronic disease was prevalent in the cohort with 21% with diabetes, 56% with hypertension, 39% had sleep apnea, 20% had cancer diagnosis, 38% with gastroesophageal reflux disease, 27% with obstructive airway disease and 46% with upper airway disease. In addition, 4.8% had depression, 8.4% reported post-traumatic stress disorder and 3.9% had anxiety disorder. Obesity, defined as body mass index at 30 or over, was prevalent with 49% of the cohort. For self-reported health, 33% reported that their health was fair or poor, 43% reported that their physical health affected their work or regular daily activities, 22% reported that pain interfered with their normal work (including work outside the home or housework) quite a bit or extremely; and 18% reported that they had quite a bit or extremely, trouble with their short-term memory.

Regarding medication use, mean number of medications was 6.1. Polypharmacy, defined as taking five or more medications, was present in 55% of the cohort, with 21% taking 10 or more medications (**Figure 6**). Factors associated with polypharmacy **(Table 4)** included age (OR 1.08; 95% CI 1.07, 1.09) and female sex (OR 1.23; 95% CI 1.03, 1.47). Being overweight (BMI between 25 and 30) and obesity were associated with polypharmacy when compared to those with BMI

under 25 with an odds ratio of 1.50 (95% CI 1.24, 1.81) and 1.92 (95% CI 1.60, 2.32), respectively. Chronic conditions associated with polypharmacy included cancer (OR 1.30, 95% CI 1.12, 1.50), GERD (OR 1.71, 95% CI 1.47, 1.99), obstructive airway disease (OR 2.24, 95% CI 1.91, 2.62) and upper airway disease (OR 1.85, 95% CI 1.60, 2.14). Anxiety, depression and PTSD were not associated with polypharmacy. Frailty index by deficit count was independently associated with polypharmacy with an OR 1.15 (95% CI 1.13, 1.17).

For the use of fall risk increasing drugs (FRIDs), 7.6% of the cohort used any FRIDs. Frailty index was independently associated with the use of FRIDs, **(Table 5)** with an odds ratio of 1.11 (95% CI 1.09, 1.13) after adjusting for covariates. Other factors associated with use of FRIDs included female sex (OR 1.64, 95%CI 1.27, 2.08), race/ethnicity (black and Hispanic were less likely to be on FRIDs compared with white with OR of 0.53 (95% CI 0.38, 0.74) and 0.64 (95% CI 0.50, 0.82), respectively), smoking status with current and former smoker more likely to be on FRIDs when compared to those who never smoked with OR of 1.55 (95% CI 1.09, 2.19) and 1.30 (95% CI 1.05, 1.60), respectively. Chronic conditions associated with the use of FRIDs included anxiety disorder (OR 1.66, 95% CI 1.16, 2.33), depression (OR 2.85, 95% CI 2.03, 4.02), and PTSD (OR 1.72, 95% CI 1.28, 2.31).

As polypharmacy has its associated adverse effects, we examined the polypharmacy patterns in this aging cohort. We found that polypharmacy was prevalent in WTC-GR population and a substantial portion of WTC-GRC took five or more medications, and a fifth of them took ten or more medications. As polypharmacy increases the risk of interactions and adverse effects from medications, improving the use of medications through judicious review of medications that are no longer needed or whether the potential harms from these medications exceed the benefits from taking them would be important. Consistent with prior literature, polypharmacy is found to be associated with frailty, with each deficit on the frailty index corresponding to a 20% increase in the likelihood of having polypharmacy. Given the potential bidirectional relationship between frailty and polypharmacy, examining whether reduction of polypharmacy could yield benefits in modifying frailty trajectory could be important**.**

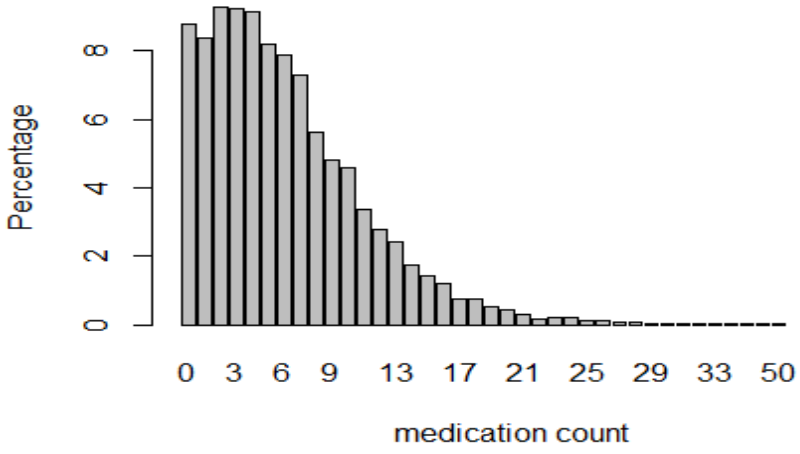


Figure 6: Distribution of number of medications in the cohort

Table 3: Patterns of polypharmacy across cohort characteristics			
	Medication Count		
Variable	<5, N = 3,125	>=5, N = 3,841	p-value[1]
Age at the time of the visit			<0.001
Median (IQR)	57 (53, 61)	59 (55, 65)	
Gender			<0.001
• Female	357 (38%)	588 (62%)	
• Male	2,768 (46%)	3,253 (54%)	
Race/ Ethnicity			0.3
• White	1,978 (45%)	2,373 (55%)	
• Black	422 (45%)	519 (55%)	
• Hispanic	634 (43%)	846 (57%)	
Other	91 (47%)	103 (53%)	
Enrollment Year			0.002
• 2002-2005	1,148 (43%)	1,536 (57%)	
• 2006-2008	732 (44%)	926 (56%)	
• 2009-Present	1,245 (47%)	1,379 (53%)	
Exposure Severity			0.8
• Low	451 (46%)	540 (54%)	
• High/Very High	703 (44%)	888 (56%)	
• Intermediate	1,971 (45%)	2,413 (55%)	
Pre-9/11 Occupation			<0.001
• Construction	585 (42%)	794 (58%)	
• Protective	1,788 (49%)	1,876 (51%)	
Smoking Status			<0.001
• Never Smoker	2,077 (48%)	2,215 (52%)	
• Current Smoker	199 (47%)	224 (53%)	
• Former Smoker	849 (38%)	1,402 (62%)	
Alcohol Status			<0.001
• None/Non-Drinker	664 (35%)	1,258 (65%)	
• Less Than One Drink Per Week	1,865 (48%)	2,019 (52%)	
• More Than One Drink Per Week	596 (51%)	564 (49%)	
BMI			<0.001
• <25	450 (53%)	394 (47%)	
• 25-30	1,340 (49%)	1,391 (51%)	
• >30	1,335 (39%)	2,056 (61%)	
Sleep Apnea			<0.001
• No Apnea	2,414 (57%)	1,830 (43%)	
• Apnea	711 (26%)	2,011 (74%)	
Diabetes			<0.001

• No	2,807 (51%)	2,664 (49%)	
• Yes	318 (21%)	1,177 (79%)	
Hypertension			<0.001
• No	1,886 (62%)	1,152 (38%)	
• Yes	1,239 (32%)	2,689 (68%)	
Anxiety Disorder			<0.001
• No	3,065 (46%)	3,628 (54%)	
• Yes	60 (22%)	213 (78%)	
Cancer			<0.001
• No	2,627 (47%)	2,976 (53%)	
• Yes	498 (37%)	865 (63%)	
Depression			<0.001
• No	3,076 (46%)	3,558 (54%)	
• Yes	49 (15%)	283 (85%)	
GERD			<0.001
• No	2,494 (58%)	1,810 (42%)	
• Yes	631 (24%)	2,031 (76%)	
Obstructive Airway Disease			<0.001
• No	2,771 (55%)	2,286 (45%)	
• Yes	354 (19%)	1,555 (81%)	
PTSD			<0.001
• No	3,024 (47%)	3,359 (53%)	
• Yes	101 (17%)	482 (83%)	
Upper Respiratory Disease			<0.001
• No	2,256 (60%)	1,478 (40%)	
• Yes	869 (27%)	2,363 (73%)	
Self reported General Health			<0.001
• Excellent/Very Good/Good	2,597 (55%)	2,096 (45%)	
• Fair/Poor	528 (23%)	1,745 (77%)	
Accomplish less because of physical health			<0.001
• No	2,265 (57%)	1,712 (43%)	
• Yes	860 (29%)	2,129 (71%)	
Health limiting moderate activities			<0.001
• Not Limited At All/ Limited A Little	2,920 (50%)	2,959 (50%)	
• Limited A Lot	205 (19%)	882 (81%)	
Pain limits work			<0.001
• Not At All/A Little Bit/Moderately	2,736 (50%)	2,689 (50%)	
• Quite A Bit/Extremely	389 (25%)	1,152 (75%)	
Reports Short term memory problems			<0.001
• Not At All/A Little Bit/Moderately	2,732 (48%)	2,952 (52%)	

• Quite A Bit/Extremely	393 (31%)	889 (69%)	
WTC Frailty Index (Deficit Count)			<0.001
Median (IQR)	2.0 (1.0, 5.0)	6.0 (3.0, 10.0)	
[1]Wilcoxon rank sum test; Pearson's Chi-squared test			

Table 4: Association of polypharmacy with frailty			
Characteristic	OR[1]	95% CI[1]	p-value
At The Time Of Visit	1.08	1.07, 1.09	<0.001
Gender			
• Female	---	---	
• Male	0.81	0.68, 0.97	0.018
Race/ Ethnicity			
• White	---	---	
• Black	0.95	0.80, 1.12	0.5
• Hispanic	0.97	0.84, 1.13	0.7
• Other	1.07	0.76, 1.50	0.7
Enrollment Year			
• 2002-2005	---	---	
• 2006-2008	0.91	0.79, 1.06	0.2
• 2009-Present	1.10	0.96, 1.26	0.2
Exposure Severity			
• Low	---	---	
• High/Very High	0.85	0.71, 1.03	0.10
• Intermediate	0.92	0.78, 1.09	0.3
Pre-9/11 OCC			
• Residual (not construction/protective) (Ref)	---	---	
• Construction	0.73	0.60, 0.88	0.001
• Protective	1.30	1.10, 1.53	0.002
Smoking Status			
• Never Smoker (Ref)	---	---	
• Current Smoker	0.75	0.59, 0.96	0.022
• Former Smoker	1.14	1.01, 1.30	0.035
Alcohol Status			
• None/Non-Drinker (Ref)	---	---	
• Less Than One Drink Per Week	0.82	0.72, 0.94	0.004
• More Than One Drink Per Week	0.76	0.64, 0.91	0.003
BMI			
• <25 (Ref)	---	---	
• 25-30	1.50	1.24, 1.81	<0.001
• >30	1.92	1.60, 2.32	<0.001
WTC Conditions			

Anxiety Disorder	1.07	0.76, 1.52	0.7
Cancer	1.30	1.12, 1.50	<0.001
Depression	1.22	0.82, 1.85	0.3
GERD	1.71	1.47, 1.99	<0.001
Obstructive Airway Disease	2.24	1.91, 2.62	<0.001
PTSD	1.15	0.86, 1.54	0.3
Upper Respiratory Disease	1.85	1.60, 2.14	<0.001
WTC Frailty Index (Deficit Count)	1.15	1.13, 1.17	<0.001
[1]OR = Odds Ratio, CI = Confidence Interval			

Table 5: Association of the use of Fall Risk Increasing Drugs (FRIDs) with frailty

Characteristic	OR[1]	95% CI[1]	p-value
Age At The Time Of The Visit	0.99	0.97, 1.00	0.065
Gender			
• Male	0.61	0.48, 0.79	<0.001
Race/Ethnicity			
• White (Ref)	---	---	
• Black	0.53	0.38, 0.74	<0.001
• Hispanic	0.64	0.50, 0.82	<0.001
• Other	0.49	0.23, 0.94	0.046
Enrollment Year			
• 2002-2005 (Ref)	---	---	
• 2006-2008	1.39	1.08, 1.79	0.009
• 2009-Present	1.51	1.20, 1.91	<0.001
Exposure Severity			
• Low (Ref)	---	---	
• High/Very High	1.27	0.92, 1.78	0.15
Intermediate	1.11	0.84, 1.50	0.5
Pre-9/11 Occ			
• Residual (Ref)	---	---	
• Construction	0.60	0.44, 0.80	<0.001
• Protective	0.90	0.70, 1.17	0.4
Smoking Status			
• Never Smoker (Ref)	---	---	
• Current Smoker	1.55	1.09, 2.19	0.013
• Former Smoker	1.30	1.05, 1.60	0.014
Alcohol Status			
• None/Non-Drinker (ref)	---	---	
• Less Than One Drink Per Week	0.84	0.68, 1.04	0.11
• More Than One Drink Per Week	0.88	0.65, 1.19	0.4
BMI			

• <25 (Ref)	---	---	
• 25-30	0.90	0.67, 1.22	0.5
• >30	0.75	0.56, 1.01	0.054
WTC conditions			
Anxiety Disorder	1.66	1.16, 2.33	0.004
Cancer	1.15	0.91, 1.45	0.2
Depression	2.85	2.03, 4.02	<0.001
GERD	1.29	0.99, 1.68	0.056
Obstructive Airway Disease	0.99	0.78, 1.25	>0.9
PTSD	1.72	1.28, 2.31	<0.001
Upper Respiratory Disease	1.11	0.84, 1.45	0.5
WTC Frailty Index (Deficit Count)	1.11	1.09, 1.13	<0.001
[1]or = Odds Ratio, Ci = Confidence Interval			

CONCLUSIONS

Identifying modifiable risk factors for premature aging, such as the exposure to chemicals and stressors experienced after 9/11, has a relevant impact for the WTCHP. Our study will ensure proper monitoring of the aging processes in the WTCHP cohort through the rigorous validation and implementation of state-of-the-art tools. The WTC Clinical-FI is a new instrument that leverages the data collected via the WTCHP. Now validated, the WTC Clinical-FI is available for periodical assessment in the entire WTC cohort. By developing a new instrument for use in the cohort and identifying high-risk individuals, researchers will be able to develop and test the effectiveness of a personalized multifactorial intervention on frail individuals from the WTC cohort. Besides the implications for WTC responders, this study may inform our understanding of how other occupational and environmental exposures can induce premature aging. Globally, the number of older persons is expected to more than double by 2050.[40] Therefore, the worldwide increase in the population of older adults and the constant aging of the workforce will require rigorous aging and frailty assessment as operationalized by this study. Our ultimate goal is to develop and test the effectiveness of a personalized multifactorial intervention on frail individuals from the WTC cohort at higher risk for aging-related consequences as identified by the indicators assessed in this study. We are embarking on a new study now aimed to promoting healthy aging in this population.

PUBLICATIONS AND PRESENTATIONS

1. Bello GA, Ornstein KA, Lucchini RG, Hung WW, Ko FC, Colicino E, Taioli E, Crane MA, Todd AC. Development and Validation of a Clinical Frailty Index for the World Trade Center General Responder Cohort. J Aging Health. 2021 Aug-Sep;33(7-8):531-544. doi: 10.1177/0898264321997675. Epub 2021 Mar 12. PMID: 33706594.
2. “Polypharmacy in World Trade Center (WTC) General Responders” American Geriatrics Society poster presentation, Orlando, FL. May 2022.
3. Symposium: Promoting Health Aging of World Trade Center Responders, Gerontological Society of America, Annual Meeting, Nov 2-6, 2022, Indianapolis, IN
4. Frailty trajectories among World Trade Center general responders, Oral Presentation, Gerontological Society of America, Annual Meeting, Nov 2-6, 2022, Indianapolis, IN
5. Frailty and age-related conditions among World Trade Center general responders, Oral Presentation, Gerontological Society of America, Annual Meeting, Nov 2-6, 2022, Indianapolis, IN
6. Polypharmacy and frailty among World Trade Center general responders, Oral Presentation, Gerontological Society of America, Annual Meeting, Nov 2-6, 2022, Indianapolis, IN

Publications in Preparation:

1. Hung et al., Polypharmacy in World Trade Center (WTC) General Responders, in preparation
2. Ko et al., Frailty trajectories among WTC General Responders, in preparation
3. Thompson et al., Frailty And Its Association With Obesity In The World Trade Center Responder Cohort: A Pilot Study.

INCLUSION/EXCLUSION REPORT

Racial categories	Not Hispanic or Latino		Hispanic or Latino		Unknown/Not Reported Ethnicity		Total
	Female	Male	Female	Male	Female	Male	
Black or African American	0	0	0	0	0	0	0
White	19	45	0	0	0	0	64
Other	0	0	0	13	0	0	13
Unknown or Not reported	0	0	0	0	0	23	23
Total	19	45	0	13	0	23	100

Note: Cells under 10 were reported as 0 in this IER, as cells under 10 cannot be reported per General Responder Data Center cell size guidelines. Removed individuals were included in the unknown/not reported race/ethnicity male cell (n=23). There were a total of 12 Black/African American participants, which we were unable to report in this format due to the breakdown by sex.

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