Association of PTSD Dose with Cardiovascular Disease Risk in Multi-Ethnic WTC Heart Cohort: 13 Year Follow Up

Alfredo Morabia, MD, PhD
Professor of Epidemiology
Barry Commoner Center
Queens College/CUNY

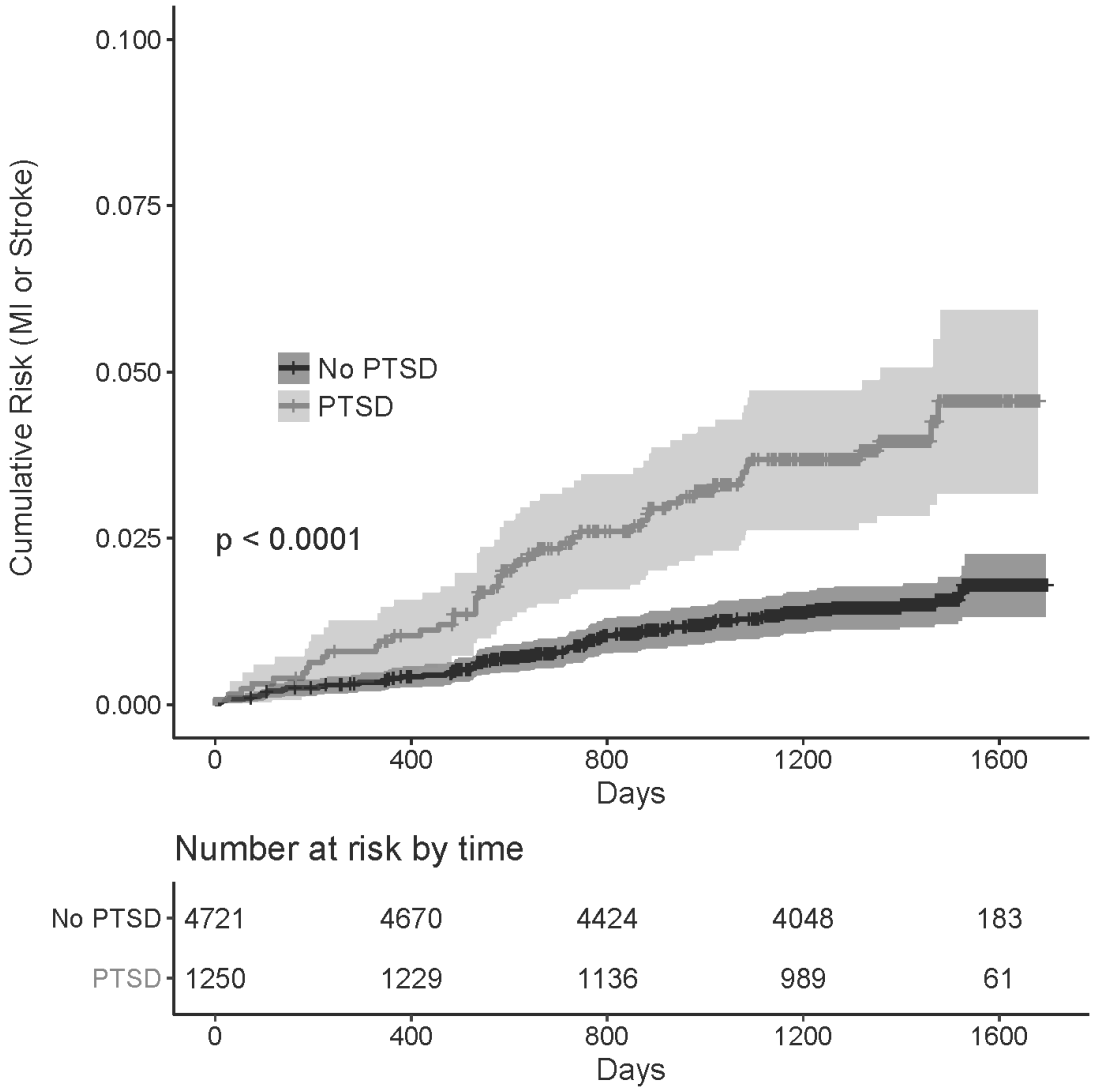
Project ID: 13759707

Funding Support

- September 26, 2011- September 25, 2014: This study was supported by grants 939ZLZB 2526 2011 75-11-0946 (Dr Morabia) by the Center for Disease Control/ NIOSH and Prevention/ National Institute for Occupational Safety and Health.

- July 1, 2014 - June 30, 2017: This study was supported by grant 5U01OH010722-02 (Dr Morabia) by the Center for Disease Control/ NIOSH and Prevention/ National Institute for Occupational Safety and Health.

- July 1, 2022 – June 30, 2026: This study was supported by grant U01OH012265-01-00 (Dr Morabia) by the Center for Disease Control/ NIOSH and Prevention/ National Institute for Occupational Safety and Health.



Remch et al *Circ Cardiovasc Qual Outcomes*. 2018

Prior Work

- Launched in 2012-2013 to specifically assess the risk of CVD of 6481 first-responders involved in the 2001 policing and cleaning activities

- WTC-Heart is nested within the WTC-Health Program and the retention rate at the last completed follow-up round (June 2016) was 91%

- Between 2012 and 2016, female and male first responders who developed WTC-related self-reported PTSD had about 2x the risk of CVD than those who did not develop PTSD

- Because of the small number of cases after 4 years the estimated association was imprecise in women (n=21) and could not be assessed in workers of color

Numbers of MI/Strokes				
Men	**PTSD**	**No PTSD**	**HR**	**aHR**
MI	23	38	2.29	2.22
Stroke	19	27	2.71	2.76
MI or Stroke	41	61	2.51	2.46
Women				
MI	4	5	1.96	
Stroke	3	4	2.08	
MI or Stroke	7	9	2.06	
All				
MI	27	43	2.24	2.22
Stroke	22	31	2.61	2.51
MI or Stroke	48	70	2.46	2.35
Men, No Depression				
MI or Stroke	14	52	2.19	1.88

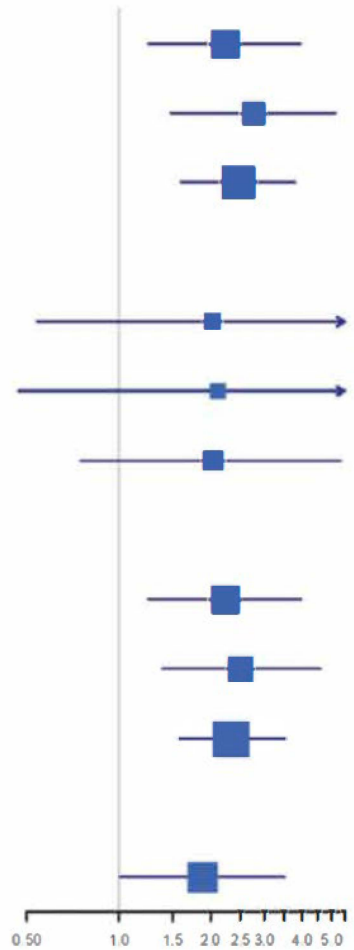


Figure 3. Age-adjusted hazard ratio (HR) and adjusted* HR (aHR) for post-traumatic stress disorder (PTSD) and pooled incident (including recurrent) myocardial infarctions and strokes in the World Trade Center–Heart cohort (n=5971)—New York, 2012 to 2016.
*Adjusted for use of a respirator and for recognized cardiovascular risk factors: age, blood pressure, total cholesterol, body mass index, tobacco use, and, when relevant, sex. MI indicates myocardial infarction.

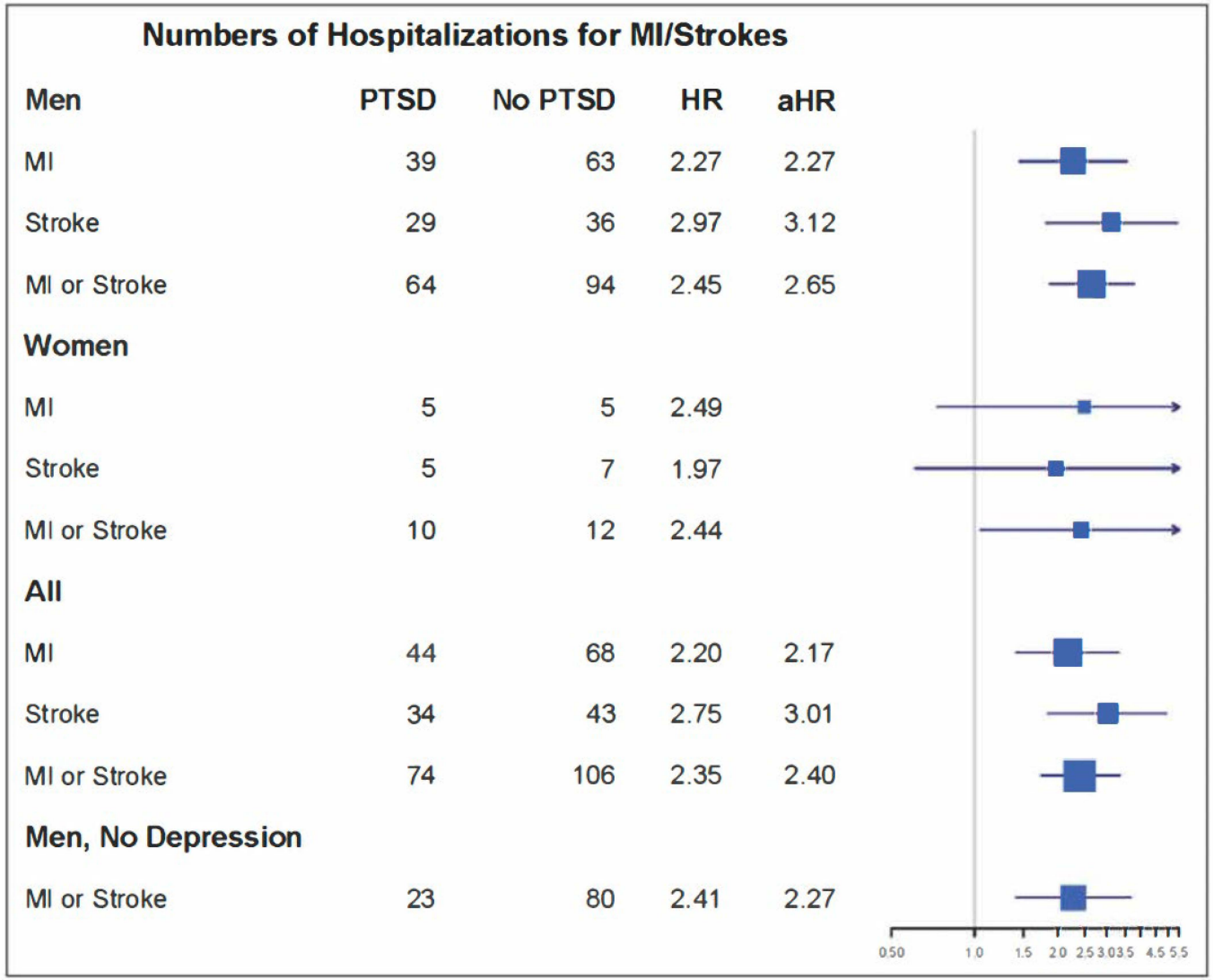


Figure 4. Age-adjusted hazard ratio (HR) and adjusted* HR (aHR) for post-traumatic stress disorder (PTSD) and hospitalizations for pooled (including recurrent) myocardial infarctions and strokes in the World Trade Center–Heart cohort (n=5484)—New York, 2012 to 2016.

*Adjusted for use of a respirator and for recognized cardiovascular risk factors: age, blood pressure, total cholesterol, body mass index, tobacco use, and, when relevant, sex. MI indicates myocardial infarction.

Aims of the Current Phase

Aim 1. To analyze the long-term relationship between PTSD symptom burden and Cardiovascular Disease (CVD)

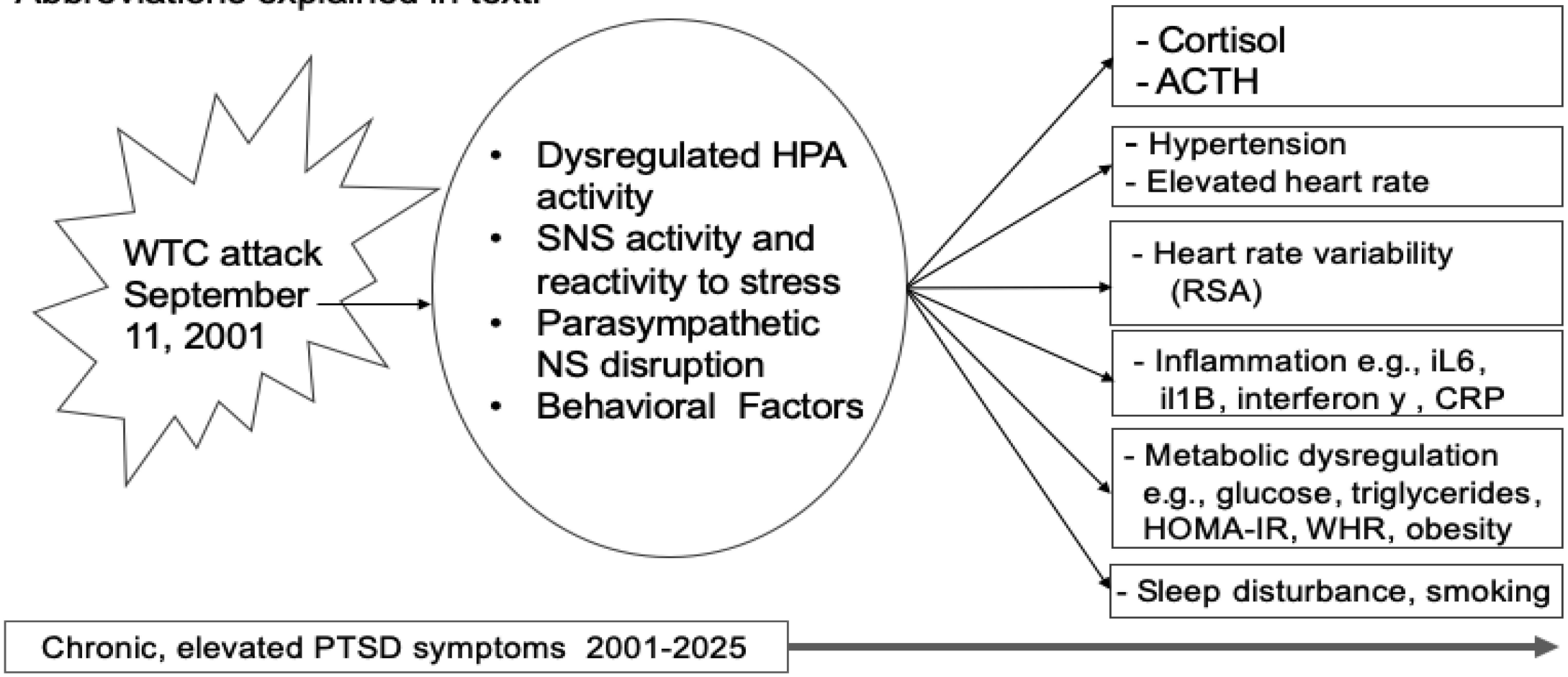
> **Aim 1a.** To assess the causal effect of PTSD symptom burden on CVD
> **Aim 1b**. To assess differences by ethnic groups

Aim 2. To identify differences in biological correlates of PTSD that reflect putative systemic and chronic dysfunction associated with poor health

Cardiovascular Disease in First Responder Populations

- First responders are susceptible to chronic PTSD, depression, and their related CVD risk factors
- Among WTC-Heart first-responders, the prevalence of PTSD is 3 to 5 times higher than in the general population and the risk of incident cardiovascular diseases among men and women in their fifties is about 10 times higher than expected in the general population.
- WTC first-responders who developed PTSD because of their involvement in the removal of the debris of the WTC complex suffered from CVD at twice the rate of those who did not develop PTSD
- In the WTC Registry, WTC first-responders and civilians who reported higher, chronic levels of PTSD from 9/11 through 2017 had a two-fold increased cardiovascular *mortality*, relative to those reporting lower symptoms over the same follow up period[7]
- In our previous work, WTC-Heart dust exposure (e.g., from the thick dust cloud and debris) was unrelated to CVD risk

Figure 1: Progression of trauma exposure to the WTC attack to CVD via chronic, elevated PTSD symptoms associated with chronic dysregulation in HPA axis, SNS, PSNS and behavioral responses as assessed by downstream blood markers, physiology ad behavior. Abbreviations explained in text.



PTSD and Cardiovascular Disease

The available evidence suggesting that post-traumatic stress disorder (PTSD) of occupational origin causes cardiovascular diseases (CVD), including from our prior NIOSH funded work, allows for limited causal inference because it fails to take into consideration:

1. The time-varying effects of both PTSD symptoms and conventional CVD risk factors

2. The magnitude of the misclassification resulting from self-reported symptoms of PTSD

3. Whether there is a dose-response effect of PTSD symptoms on CVD risk (e.g., as reflected by commonly observed longitudinal symptom trajectories: chronic, delayed onset, remitted, vs never PTSD)

4. The biological correlates of three PTSD symptom trajectory groups: chronic, remitted and never PTSD. In addition, the COVID-19 pandemic represents a second common exposure in NYC residents, which might influence the association between WTC-related PTSD and CVD

CVD: Primary Diagnosis Upon Admission

- I00-I99 Diseases of the circulatory system
-
- I00-I02 Acute rheumatic fever
- I05-I09 Chronic rheumatic heart diseases
- I10-I16 Hypertensive diseases
- I20-I25 Ischemic heart diseases
- I26-I28 Pulmonary heart disease and diseases of pulmonary circulation
- I30-I52 Other forms of heart disease
- I60-I69 Cerebrovascular diseases
- I70-I79 Diseases of arteries, arterioles and capillaries
- I80-I89 Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified
- I95-I99 Other and unspecified disorders of the circulatory system
-
- I20 Angina pectoris
- I21 Acute myocardial infarction
- I22 Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I23 Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within the 28 day period)
- I24 Other acute ischemic heart diseases
- I25 Chronic ischemic heart disease
-
-
- I60 Nontraumatic subarachnoid hemorrhage
- I61 Nontraumatic intracerebral hemorrhage
- I62 Other and unspecified nontraumatic intracranial hemorrhage
- I63 Cerebral infarction
- I65 Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
- I66 Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
- I67 Other cerebrovascular diseases
- I68 Cerebrovascular disorders in diseases classified elsewhere
- I69 Sequelae of cerebrovascular disease

Current Work

Table 1: Prevalence of PTSD at baseline and numbers of CVD events by race-ethnicity between 1/2012 and 1/2023 among 6481 responders.					
	Men		Women		
Race-ethnicity	PTSD %		PTSD %		
White	760		115		
Black/ AA	194		69		
Hispanic	518		223		
Total	1472		407		
PTSD % - endorsed PTSD in visit between 2002-2012 (prior to cohort)					

Data Sources (N = 6481)

- World Trade Center Health Program Visit Data
- National Death Index
- Statewide Planning and Research Cooperative System (SPARC)
- Sub-Study: Icahn School of Medicine at Mount Sinai Biomarkers

Icahn School of Medicine at Mount Sinai Biomarkers

- Volunteers recruited in follow-up rounds
- Measures include:
  - Cortisol, adrenocorticotropic hormone, hypertension, heart rate, heart rate variability, Interleukins 6 and 1B, interferon γ, C-reactive protein, glucose, triglycerides, homeostatic model assessment of insulin resistance, waist-hip ratio, body mass index, sleep quality, and smoking.
- Stratified by PTSD symptom trajectory
  - Never PTSD, Chronic PTSD, Delayed Onset PTSD, Remitting PTSD, Recurring PTSD based on 15 assessments

Sample at baseline

- Total Sample 6481
- 315 deaths confirmed by NDI
- Re-contacting every year since 2023

Table 3. Demographics of the Sample at Baseline

	Subcategory	N (%)
Gender	Male	5261(82.84)
	Female	1090(17.16)
	Non-Hispanic	4401(70.05)
	Hispanic/Latino(a)	1882(29.95)
Race/	White/Caucasian	3399(53.52)
Ethnicity	Black or African American	980(15.43)
	Other Race	1477(23.26)
	Unknown Race	495(7.79)
	<$30,000	609(12.22)
Income	$31,000-$60,000	1511(30.31)
	$60,000-$80,000	1377(27.62)
	>$80,000	1488(29.85)
	< HS graduate	478(7.53)
	HS graduate	1204(18.96)
Education	<BA/BS	2494(39.27)
	BA/BS/Graduate School	1985(31.25)
	Unknown	190(2.99)

Table 4. Descriptive Statistics

	Category	N (%)
Characteristics	Probable PTSD at first cohort visit (2012)	607(19.39)
	Depression symptoms at first cohort visit (2012)	295(9.59)
	Deaths confirmed NDI (all cause)	315(4.86)
	CVD events	672(10.37)
	Smoking at baseline	792(37.59)
Dust Exposure	Low	858(14.29)
	Intermediate	3838(63.91)
	High	1119(18.63)
	Very High	190(3.16)
Psychological Exposure	Life in danger during 9/11 attacks	1887(42.16)
	Recovered Human Remains	2647(60.85)

Descriptive Statistics

- Average days at site 79 or ~2.5 months (SD = 72.7)
  - Range 1 – 584 (longest approximately 19.5 months)
- Construction, sanitation workers, emergency responders including 1415 police officers in cohort

Acknowledgements

- Paola Angel Study Coordinator
- Yan Guo Data Manager
- Interviewers: Dahlia Abbas, Cassidy King, Nigersultana Rinky

- WTC Health Program at Mount Sinai
- WTC Health Program at Northwell
- WTC Data Center
- Statewide Planning and Research Cooperative System (SPARC) for New York State

Selected References

- Cohen HW, Zeig-Owens R, Joe C, et al. Long-term Cardiovascular Disease Risk Among Firefighters After the World Trade Center Disaster. JAMA Netw Open. Sep 2019;2(9):e199775. doi:10.1001/jamanetworkopen.2019.9775
- Daskalakis NP, Cohen H, Nievergelt CM, et al. New translational perspectives for blood-based biomarkers of PTSD: From glucocorticoid to immune mediators of stress susceptibility. Exp Neurol. Oct 2016;284(Pt B):133-140. doi:10.1016/j.expneurol.2016.07.024
- Giesinger I, Li J, Takemoto E, Cone JE, Farfel MR, Brackbill RM. Association Between Posttraumatic Stress Disorder and Mortality Among Responders and Civilians Following the September 11, 2001, Disaster. JAMA Netw Open. 02 2020;3(2):e1920476. doi:10.1001/jamanetworkopen.2019.20476
- Passos IC, Vasconcelos-Moreno MP, Costa LG, et al. Inflammatory markers in post-traumatic stress disorder: a systematic review, meta-analysis, and meta-regression. Lancet Psychiatry. Nov 2015;2(11):1002-12. doi:10.1016/S2215-0366(15)00309-0
- Remch M, Laskaris Z, Flory J, Mora-McLaughlin C, Morabia A. Post-Traumatic Stress Disorder and Cardiovascular Diseases: A Cohort Study of Men and Women Involved in Cleaning the Debris of the World Trade Center Complex. Circ Cardiovasc Qual Outcomes. Jul 2018;11(7):e004572. doi:10.1161/CIRCOUTCOMES.117.004572