Heart Disease and Stroke among WTC Health Registry Cohort

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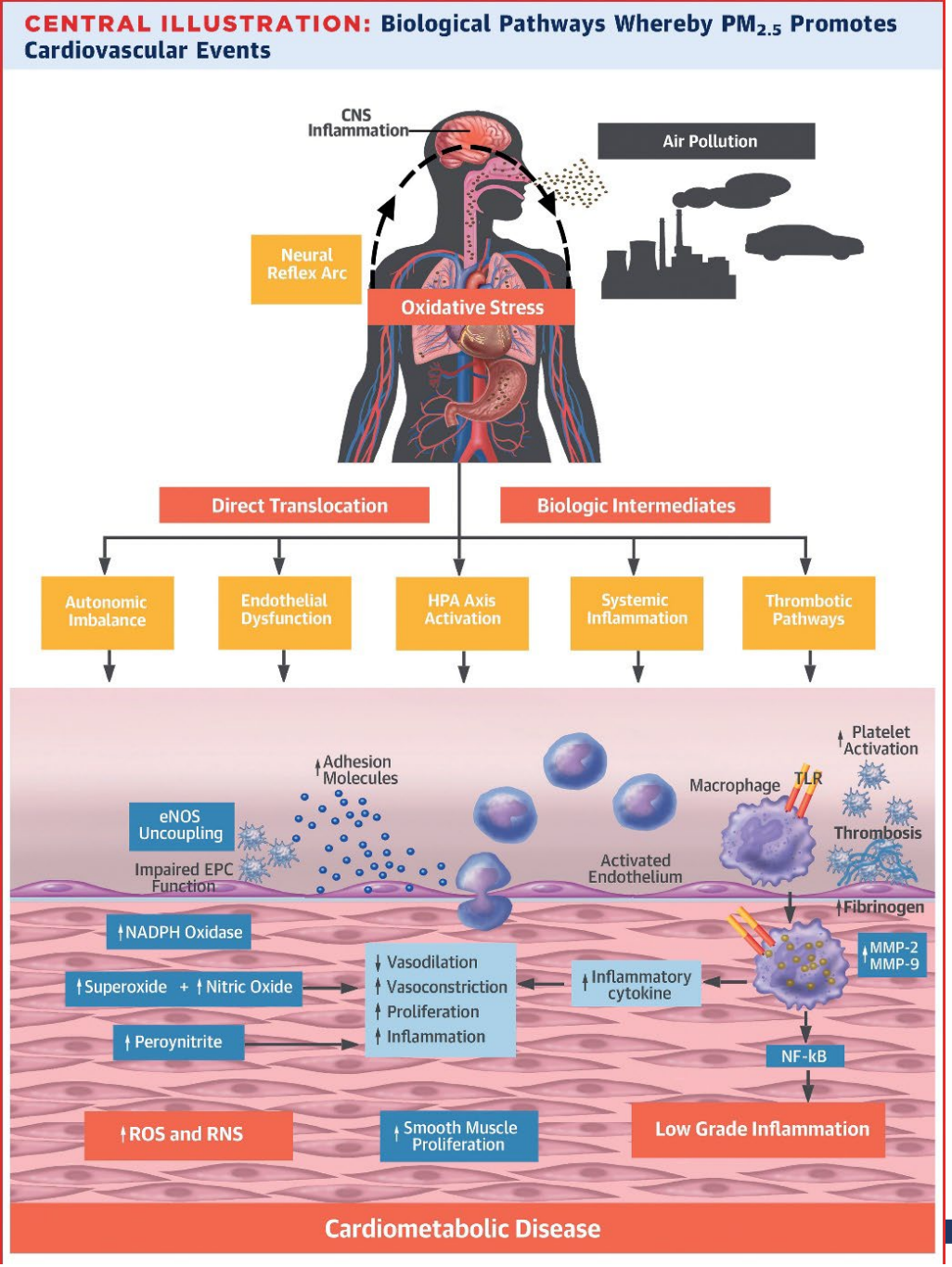
NIOSH PI Meeting, November 13, 2024

WORLD TRADE CENTER HEALTH REGISTRY

NYC Health

Outline

- Plausible WTC exposures for coronary heart disease and strokes
- World Trade Center Health Registry (WTCHR)
- Measurement of 9/11 exposures
- Findings on coronary heart disease (Jordan, 2011; Jordan, 2013; Alper, 2017)
- Findings on stroke (Yu, 2018; Yu, 2021)
- Strengths and limitations
- Preliminary findings on GERD and heart attack
- Recommendations for future research



Air pollution and cardiovascular disease

- Particulate Matter (PM) $_{2.5\mu m}$ is primary component of air pollution associated with:

Cardiovascular Mortality

Myocardial Infarction (MI)

Heart Failure

Hypertension and Insulin Resistance

Cerebrovascular Disease (Stroke)

- Significant associations for $PM_{2.5\mu m}$ and $PM_{10\mu m}$ regardless of lag between exposure and event (admission to hospital for stroke)
- Studies that separated ischemic and hemorrhagic were overall significant for ischemic but not hemorrhagic

Shah et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis, BMJ 2015.

Rajagopalan, S. et al. J Am Coll Cardiol. 2018; 72(17):2054-70

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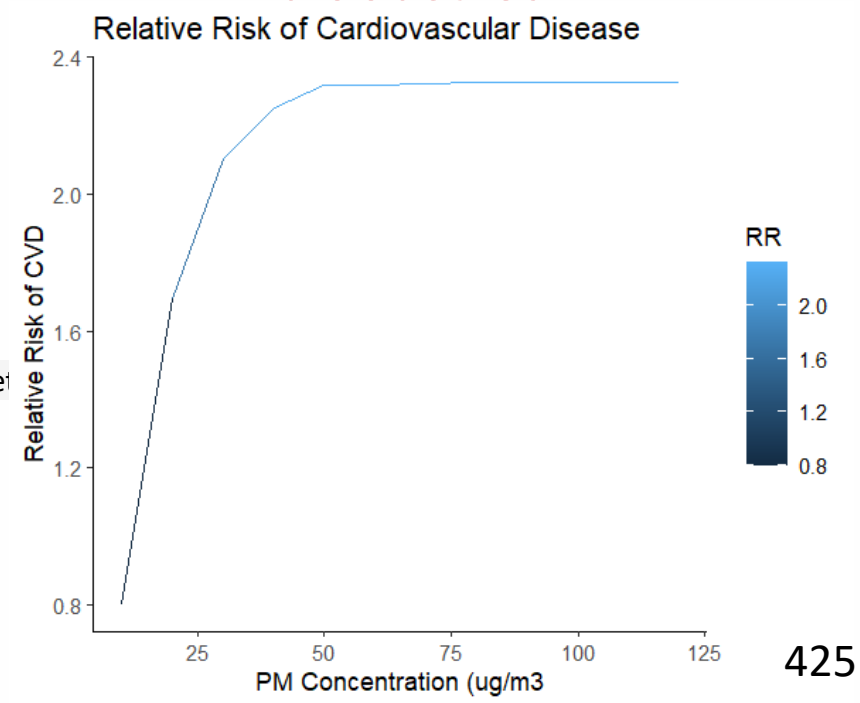
PM2.5µm takes awhile to settle, can travel a great distance and can locate in both alveolar regions of lungs and bloodstream

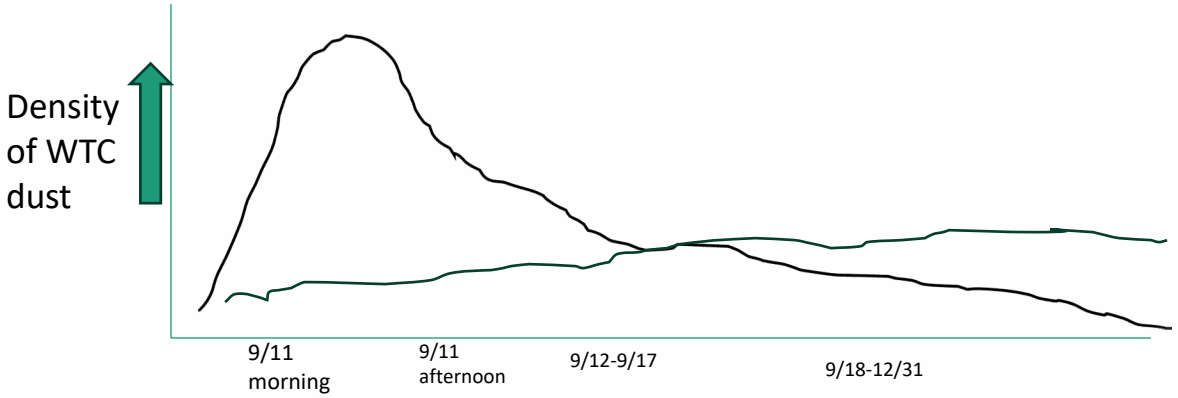


Adapted from Rajagopalan S et al 2018

425 µg/m3

The relative risk of cardiovascular disease is related to the density of ambient particular matter PM $_{2.5um}$ in the air

The maximum concentration of particulate matter in the dust cloud from collapse of buildings was estimated to be 100,000 µg per cubic meter which lasted about 5-6 hours. 2 to 4% of WTC dust by weight was $PM_{2.5µm}$ composed of 80 – 90% gypsum and calcite



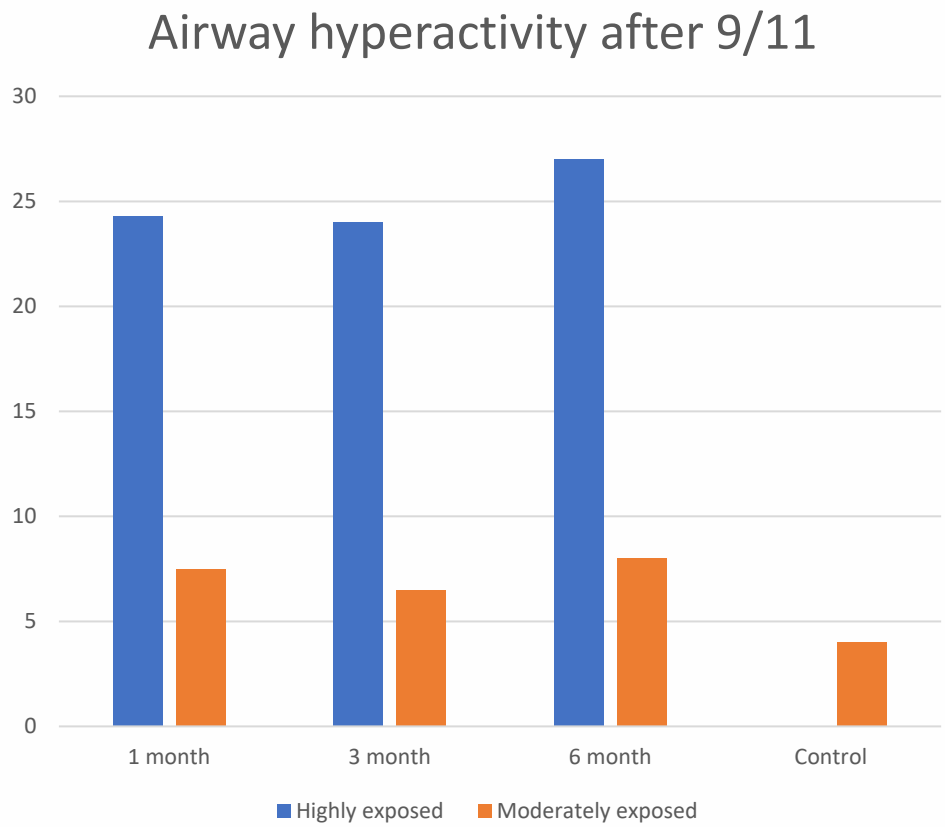
Density of PM highest on morning of 9/11 after WTC 1 and 2 collapse. Indoor dust increased as dust settled and entered surrounding buildings

Aspirated WTC dust has physiological effects

Supernatent biochemical indicators of lung injury	Measure	WTC pooled dust 100ug	Residual oil fly ash (ROFA) 100ug
Protein	ug/mL	161.4	297.5
LDH	U/L	33.7	93.2
Albumin	ug/mL	21.3	39.2
Cell numbers			
Macrophages	10^4	20	29
Neutrophils	10^4	1.5	13
Eosinophils	10^4	0.02	0.18
Lymphocytes	10^4	0.2	0.4
Hyperresponsiveness to Metacholine		High	Medium

Mice aspirated with WTC dust and comparison material

Adapted from Gavett et al. World Trade Center fine particulate matter causes respiratory tract hyperresponsiveness in mice, 2003

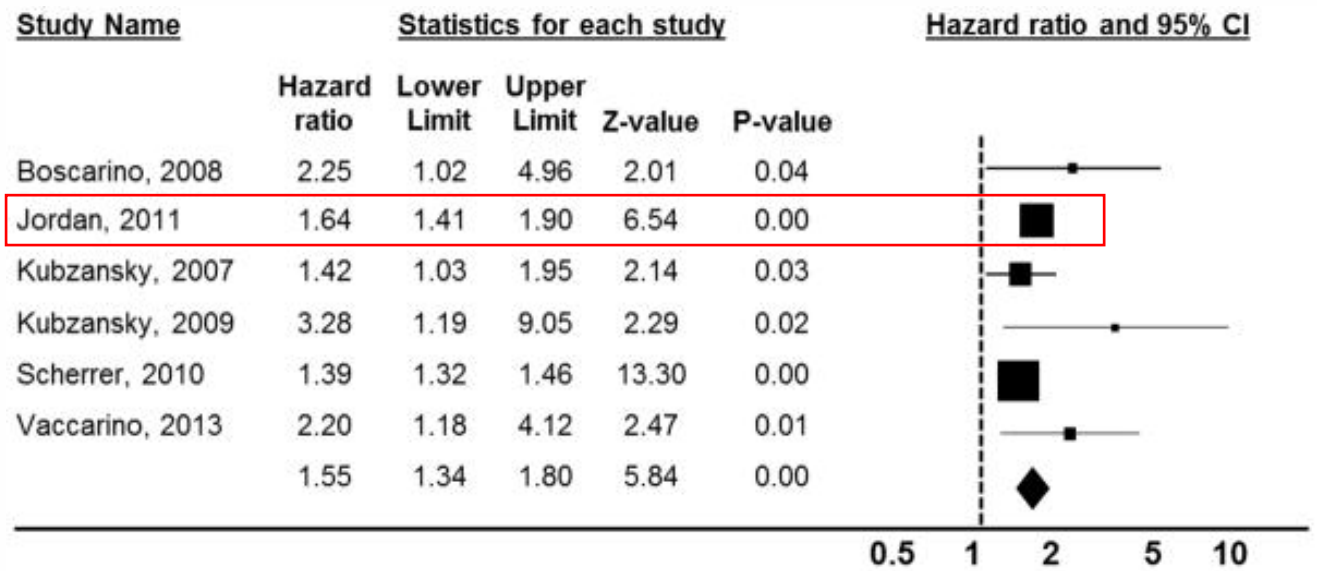


Banauch et al, Persistent hyperactivity and reactive airway dysfunction in firefighters at the World Trade Center, 2003

Posttraumatic Stress Disorder and Risk for Coronary Heart Disease: A Meta-analytic Review – Edmondson et al 2013

- Meta analysis of 6 selected studies (inc. Jordan,2011) found a pooled HR of 1.55 for PTSD and coronary heart disease and with depression in the model an HR 1.27

- **Post-traumatic stress disorder (PTSD) has had a consistent prevalence of around 10% in the WTCHR cohort**



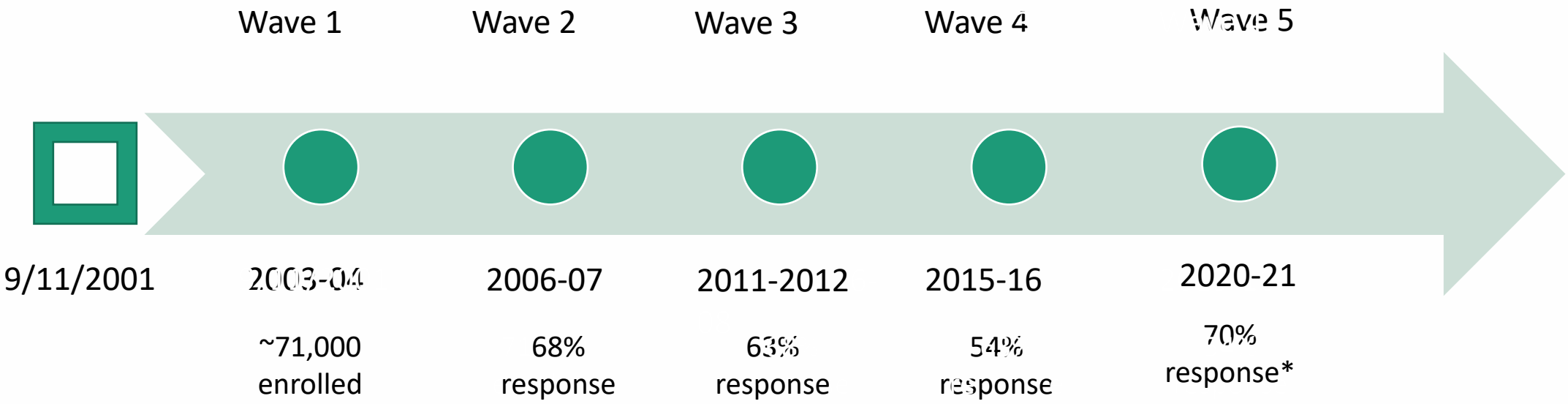
Forest plot of the association of PTSD to incident CHD

Note: The area of each square is proportional to the study's weight in the meta-analysis, and each line represents the confidence interval around the estimate. The diamond represents the aggregate estimate, and its lateral points indicate confidence intervals for this estimate.

World Trade Center Health Registry (WTCHR)

- Enrolled 71,435 in 9/11 exposure longitudinal study in 2003-2004
- Eligibility groups included rescue/recovery and other 9/11 workers, residents, occupants of buildings and passersby, children under 18 on 9/11
- 4 follow-up surveys (latest 2021)
- Published nearly 200 scientific articles on findings related to 9/11 health effects

Timeline

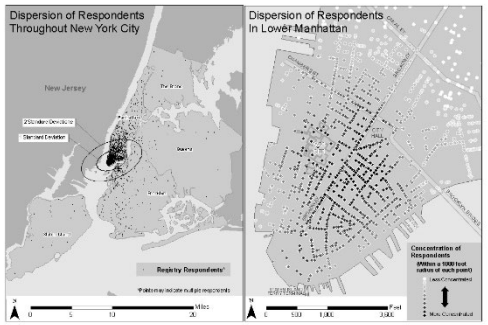


*Response rate based on enrollees who had completed at least three prior surveys

Dust and Debris Cloud Measure

On September 11th, [were you/was SUBJECT] outdoors within a dust or debris cloud resulting from the collapse of the World Trade Center towers?

1	YES	
2	NO	[SKIP TO Ex4]
DON'T KNOW		[SKIP TO Ex4]
REFUSED		[SKIP TO Ex4]



Geocoded data was used to restrict those within two ellipses of WTC site

The next series of questions asks about the dust and debris cloud on September 11, 2001. These questions refer to the cloud in Lower Manhattan that resulted from the collapse of the WTC Towers. We asked similar questions during the initial WTCHR interview, but we want to obtain additional information about your dust and debris cloud experience.

24 **On September 11, 2001, were you in the dust and debris cloud that resulted from the collapse of the WTC Towers?**

- ☐ 1 Yes
- ☐ 2 No → SKIP to Question 26

a. On September 11, 2001, when were you first caught in the dust and debris cloud?

- ☐ 1 After the first tower began to collapse but before the collapse of the second tower.
- ☐ 2 Less than 1 hour after the collapse of the second tower.
- ☐ 3 More than 1 hour after the collapse of the second tower.

25 **When you were in the dust and debris cloud on September 11, 2001, which of the following did you experience?**

a. I could not see more than a couple of feet in front of me.
- ☐ 1 Yes
- ☐ 2 No

b. I had trouble walking or finding my way because the dust was so thick.
- ☐ 1 Yes
- ☐ 2 No

c. I had to find shelter like under a car or in a doorway.
- ☐ 1 Yes
- ☐ 2 No

d. I was covered from head to toe with dust and debris.
- ☐ 1 Yes
- ☐ 2 No

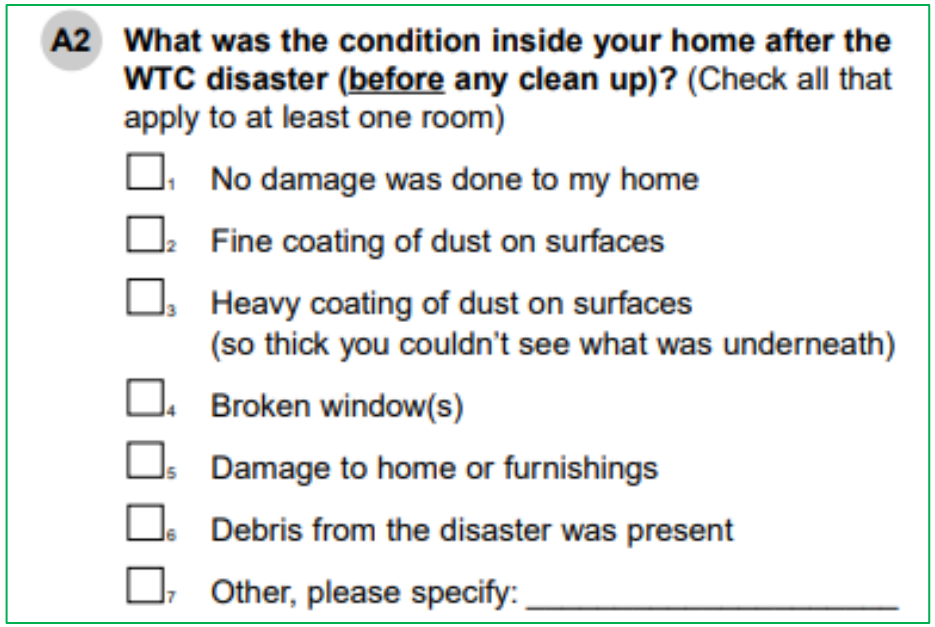
e. I could not hear anything.
- ☐ 1 Yes
- ☐ 2 No

- Waves 1 & 2 questions used to develop a derived variable with 3 categories: None, Some, Intense

Wave 1 Wave 2

Dust coating and damage to home or workplace

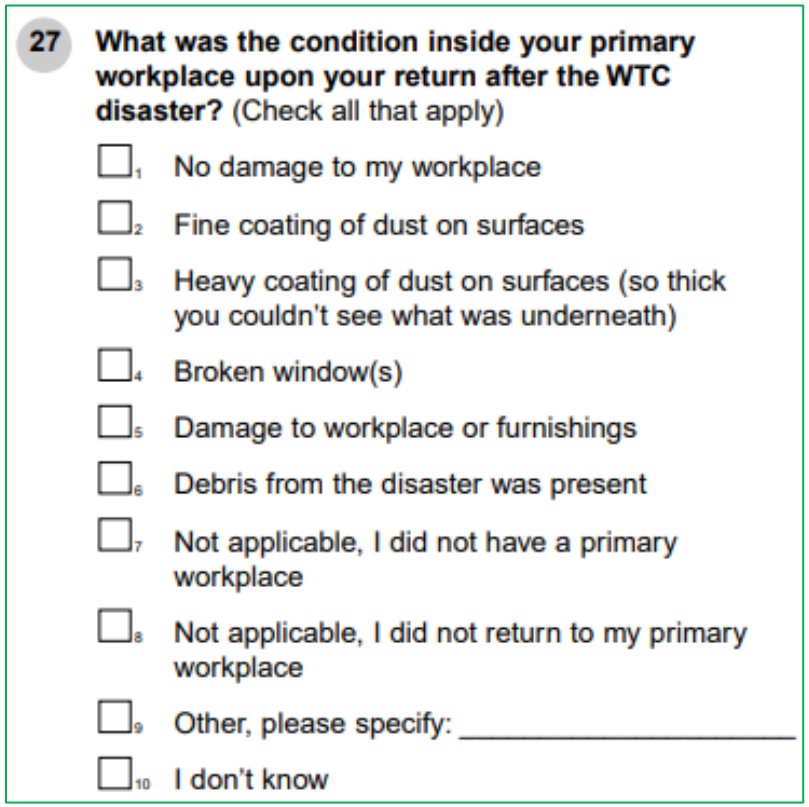
- Wave 2



A2 **What was the condition inside your home after the WTC disaster (before any clean up)?** (Check all that apply to at least one room)

- ☐ 1 No damage was done to my home
- ☐ 2 Fine coating of dust on surfaces
- ☐ 3 Heavy coating of dust on surfaces (so thick you couldn't see what was underneath)
- ☐ 4 Broken window(s)
- ☐ 5 Damage to home or furnishings
- ☐ 6 Debris from the disaster was present
- ☐ 7 Other, please specify: _____

- Wave 2



27 **What was the condition inside your primary workplace upon your return after the WTC disaster?** (Check all that apply)

- ☐ 1 No damage to my workplace
- ☐ 2 Fine coating of dust on surfaces
- ☐ 3 Heavy coating of dust on surfaces (so thick you couldn't see what was underneath)
- ☐ 4 Broken window(s)
- ☐ 5 Damage to workplace or furnishings
- ☐ 6 Debris from the disaster was present
- ☐ 7 Not applicable, I did not have a primary workplace
- ☐ 8 Not applicable, I did not return to my primary workplace
- ☐ 9 Other, please specify: _____
- ☐ 10 I don't know

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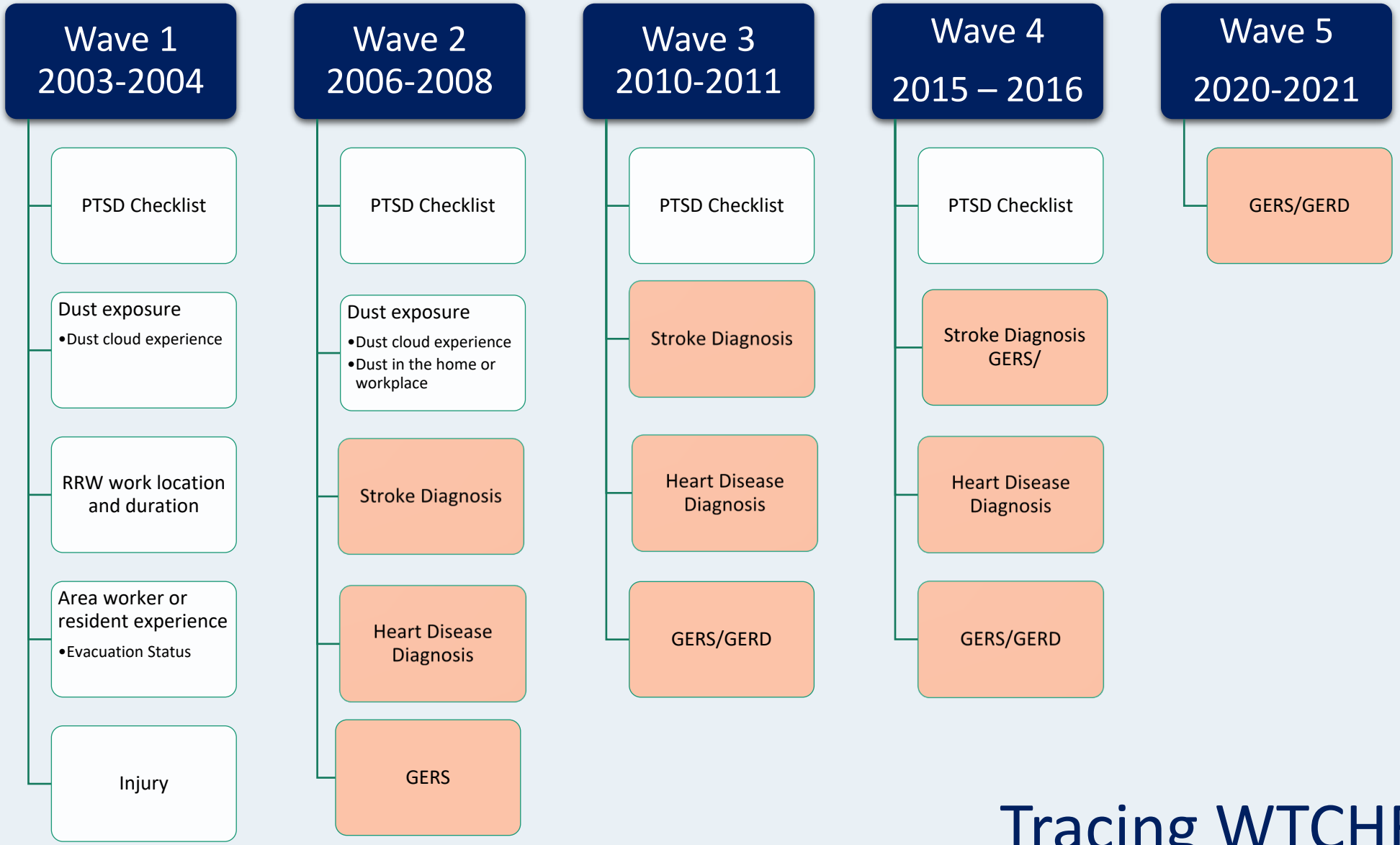
PTSD Measure

- PTSD Checklist-Specific (PCL-S) included in W1-W4 surveys
  - 17 –item symptom scale with reference to events on 9/11/2001
- Corresponded to PTSD symptoms in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV); DSM-V in Wave 5
- Sum the endorsed symptoms to create PCL score 17-85
  - **Probable PTSD defined as PCL score >44** (Blanchard, 1996)

Injury Measure

- WTCHR enrollees reported injuries sustained on 9/11
- Types of injuries
  - Cut, abrasion or puncture wound
  - Sprain or strain
  - Burn
  - Broken bone or dislocation
  - Concussion or head injury
- Severity of injury was based on number of types of injuries reported
- No information from Wave 1 on whether treated, hospitalized or long-term effects



Tracing WTCHR Exposure and Outcome Variables

Heart Disease

Methods for Heart Disease Studies

Jordan et al 2011

- Longitudinal survival analysis with **self-report** heart attack, angina and other heart disease
- Person years of observation from 2003/04 to 2008
- Stratified by sex
- Adjusted by age, race/ethnicity, education, marital status, hypertension, diabetes

Jordan et al 2013

- Longitudinal survival analysis, person years of observation from 2003/04 to first **hospitalization** or 12/31/2010
- Hospitalization based on matching with NYS Statewide Planning and Research Cooperative System (SPARCS)
- Stratified by sex
- Used categorical exposure to evaluate linear trends

Jordan 2011 Exposure Definitions

Population	Exposure
	9/11 Dust Cloud Exposure
	intense
	some
	none
	Injury on 9/11
	yes
	no
	PTSD at enrollment
Wave 2 participants	yes
	no
	Time of arrival
	9/11, on pile
	9/11, other WTC site
Rescue Recovery Workers/Volunteers	9/12-9/17
	9/18-6/2002
	Damage to Home
	Heavy Layer of Dust +/- Damage
Lower Manhattan Area Residents	Damage without heavy layer of dust
	no damage
	Damage to Workplace
	Heavy Layer of Dust +/- Damage
Lower Manhattan Area Workers	Damage without heavy layer of dust
	no damage

Table 1. Definitions of Overall Levels of Exposure to the World Trade Center Disaster and Its Aftermath[1]

Rescue/recovery workers
• High—Was present in Manhattan south of Chambers Street between the time of the first plane impact and noon on 9/11 (encompassing the WTC towers' collapse) *and* at least one of the following:
○ Worked on the dust and debris pile on 9/11 and/or
○ Worked for >90 days starting before September 18, 2001
• Low—Met all of the following conditions
○ Began work on or after September 18, 2001, *and*
○ Did not work on pile *and*
○ Worked fewer than 30 days *and*
○ Was not present south of Chambers Street between the first plane impact and noon on 9/11
• Intermediate—Neither high nor low
Residents of lower Manhattan, area workers, and commuters or passersby on 9/11.
• High—Reported at least two 9/11-related injuries and, if a lower Manhattan resident, did not evacuate home
• Low—Reported no injuries related to 9/11 and, if a lower Manhattan resident, also evacuated home
• Intermediate—Neither high nor low

Jordan 2013 Exposure: key differences from 2011

- Modified exposure hierarchy for Rescue Recovery Workers and Survivors into Low, Intermediate, and High exposure groups
- Injury is included as a factor for Survivor exposure

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Association of dust exposure and self-reported heart disease varied by gender (Jordan, 2011)

Table 3
Associations between measures of 9/11-related dust exposure and self-reported physician-diagnosed heart disease.[a,b] World Trade Center Health Registry participants aged ≥18 on September 11, 2011 ($n = 39{,}324$), New York, 2003–2008.

	Women				Men			
Exposure	No. with HD[c]	Person-time (years)	AHR	95% CI	No. with HD[c]	Person-time (years)	AHR	95% CI
All enrollees								
9/11 dust cloud exposure								
Intense	141	13,357	1.28	1.02–1.61	243	20,371	1.14	0.97–1.34
Some	48	7247	0.83	0.60–1.14	90	8500	1.00	0.79–1.25
None	171	22,237	Ref		412	37,511	Ref	
Rescue/recovery workers								
Time of arrival								
9/11, on pile	4	292	2.25	0.79–6.40	87	7452	1.39	1.04–1.86
911, other WTC site	19	1298	1.94	1.10–3.42	71	5846	1.21	0.89–1.63
9/12–9/17	39	3404	1.76	1.11–2.77	216	17,420	1.24	0.98–1.56
9/18–6/2002	44	6186	Ref		112	9293	Ref	
Area residents								
Damage to home								
Heavy layer of dust ± damage	12	1543	1.23	0.63–2.42	18	1152	2.05	1.15–3.67
Damage without heavy layer of dust	13	1213	1.69	0.87–3.25	7	841	1.09	0.48–2.48
None	34	6369	Ref		39	4666	Ref	
Area workers								
Damage to workplace								
Heavy layer of dust ± damage	21	1822	1.35	0.85–2.14	31	2075	1.55	1.03–2.31
Damage without heavy layer of dust	31	3178	1.23	0.83–1.82	29	2864	1.12	0.75–1.69
None	128	15,501	Ref		124	13,792	Ref	

Abbreviations: Heart disease (HD); adjusted hazard ratio (AHR); confidence interval (CI).
[a] Heart disease defined as physician-diagnosed angina, heart attack, or other heart problem first reported on the 2006–2008 Wave 2 survey.
[b] Models were adjusted for age, race/ethnicity, education, marital status, smoking, hypertension, and diabetes.
[c] Frequencies may not sum to total due to missing values.

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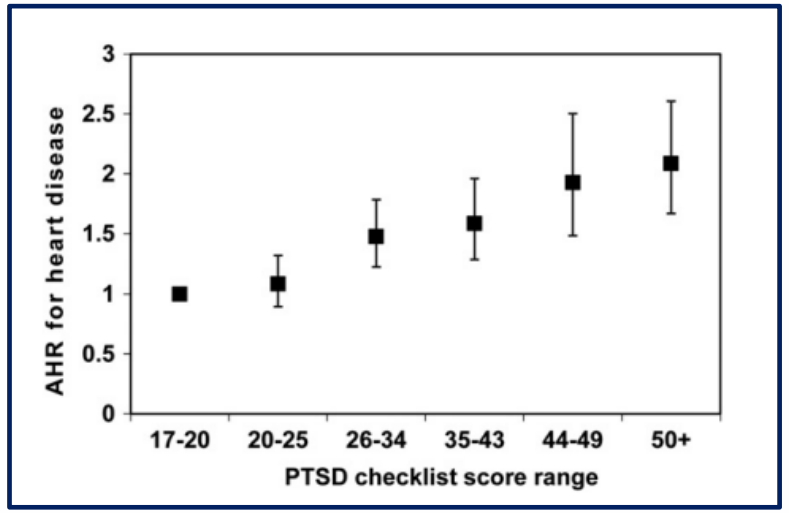
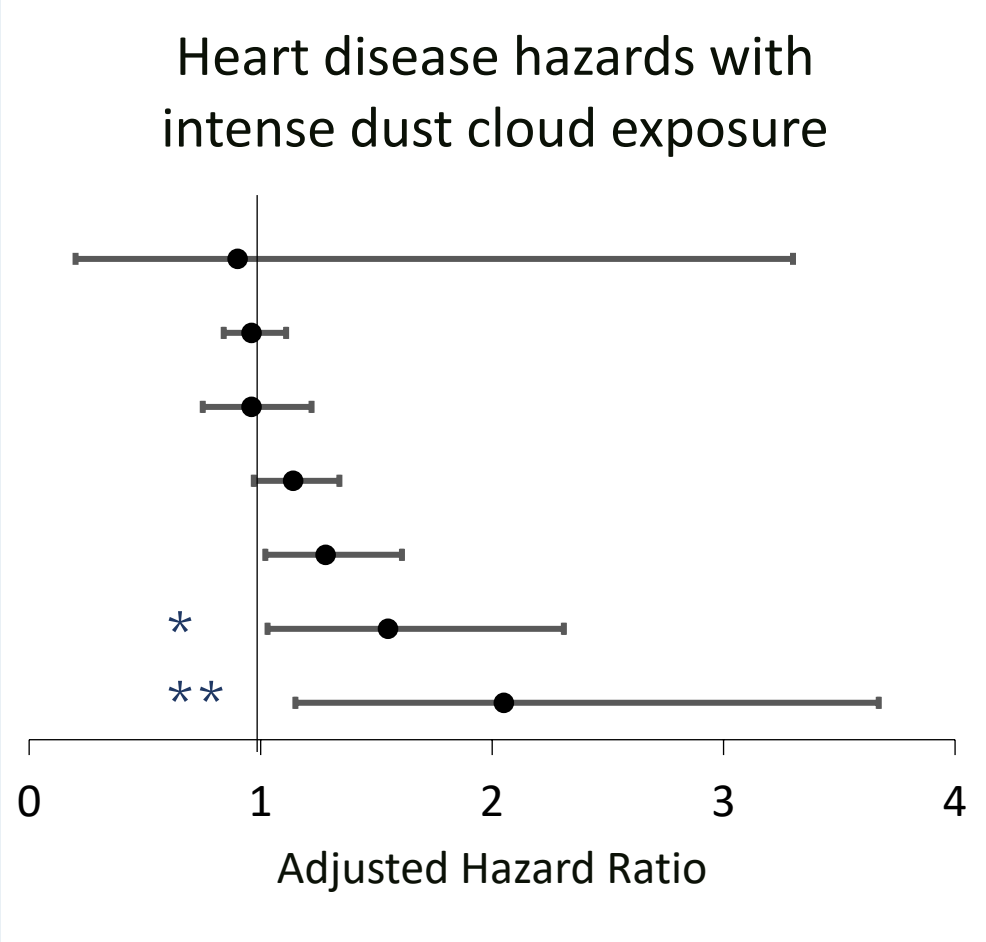
Probable PTSD and Injury were consistently associated with self reported heart disease (Jordan 2011)

Exposure(s) added to model	Women				Men			
	No. with HD[c]	Person-time (years)	AHR	95% CI	No. with HD[c]	Person-time (years)	AHR	95% CI
Model 1								
9/11 dust cloud exposure								
Intense	141	13,357	1.28	1.02–1.61	243	20,371	1.14	0.97–1.34
Some	48	7247	0.83	0.60–1.14	90	8500	1.00	0.79–1.25
None	171	22,237	Ref		412	37,511	Ref	
Model 2								
Injured on 9/11[d]								
Yes	186	16,298	1.46	1.19–1.79	348	26,551	1.33	1.15–1.53
No	195	27,928	Ref		433	42,529	Ref	
Model 3								
PTSD at enrollment[e]								
Yes	107	7317	1.68	1.33–2.12	137	7491	1.62	1.34–1.96
No	260	35,688	Ref		624	60,166	Ref	
Model 4								
9/11 dust cloud exposure								
Intense	136	13,002	1.17	0.92–1.48	238	19,902	1.09	0.93–1.29
Some	47	7078	0.80	0.58–1.11	89	8307	1.00	0.80–1.26
None	165	21,610	Ref		400	36,816	Ref	
PTSD at enrollment[e]								
Yes	101	7062	1.62	1.26–2.07	126	7061	1.56	1.27–1.91
No	247	34,628	Ref		601	57,965	Ref	
Model 5								
Injured on 9/11[d]								
Yes	179	15,750	1.35	1.09–1.68	344	25,964	1.29	1.12–1.50
No	188	27,253	Ref		417	41,693	Ref	
PTSD at enrollment[e]								
Yes	107	7317	1.54	1.21–1.97	137	7491	1.50	1.24–1.83
No	260	35,686	Ref		624	60,166	Ref	



Health

Highly exposed male area residents and workers show strong association with HD



Source and population	Measure
Alper 2017, Passersby	Self Report heart attack/angina
Jordan 2013, Men	Hospitalized for heart disease
Jordan 2013, Women	Hospitalized for heart disease
Jordan 2011, Men	Self report heart disease
Jordan 2011, Women	Self report heart disease
Jordan 2011, Area Worker, Men	Self Report heart disease
Jordan 2011, Area Residents, Men	Self Report heart disease

* = Area workers with Heavy dust coating ± damage at place of work

** = Area residents with Heavy dust coating ± damage at home

PTSD and highly exposed Rescue/Recovery Worker associated with heart disease hospitalization (Jordan 2013)

Table 3. Sex-Specific Associations of 9/11-Related Exposures and PTSD With Heart Disease Hospitalization Among Participants in the World Trade Center Health Registry residing in New York State, 2003–2010

	Women (n=18 551)				Men (n=27 511)			
	Number of Events*	Person-Years	AHR	95% CI	Number of Events*	Person-Years	AHR	95% CI
9/11 Dust cloud exposure								
Yes	178	73 826	0.96	0.75 to 1.22	450	95 219	0.96	0.84 to 1.11
No	118	48 488	Ref.		402	82 794	Ref.	
Injured on 9/11†								
Yes	126	50 418	0.93	0.74 to 1.19	377	75 256	1.11	0.97 to 1.28
No	170	72 544	Ref.		478	103 512	Ref.	
PTSD at enrollment								
Yes	94	26 413	1.32	1.01 to 1.71	146	25 947	1.16	0.97 to 1.40
No	197	94 878	Ref.		698	150 597	Ref.	
Rescue/recovery enrollees	Women (n=3 634)				Men (n=16 137)			
Overall level of exposure‡§								
Low	4	4036	Ref.		16	4468	Ref.	
Intermediate	36	17 616	1.72	0.60 to 4.94	407	80 225	1.63	0.99 to 2.69
High	5	1317	3.29	0.85 to 12.69	82	16 242	1.82	1.06 to 3.13
Nonrescue/recovery enrollees	Women (n=15 045)				Men (n=11 530)			
Overall level of exposure‡								
Low	98	48 223	Ref.		164	41 003	Ref.	
Intermediate	125	40 755	0.94	0.71 to 1.25	140	27 775	0.92	0.72 to 1.16
High	20	8661	0.88	0.54 to 1.43	22	5157	0.94	0.60 to 1.47

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Acute exposure and diagnosed chronic conditions
(Alper et al, 2017)

- Study focused on persons who experienced acute exposure as opposed to chronic exposure
  - Occupants of collapsed and/or damaged buildings
  - Rescue and Recovery workers
  - Passersby on streets on morning of 9/11
  - Office workers who were present on 9/11
  - Residents who were present on 9/11
- Persons older than 64 and persons who reported diagnosed chronic conditions before 2002 (e.g. heart attack, asthma, diabetes) were excluded
- Study sample (n=8701)
  - 7503 area workers
  - 249 R/R workers
  - 131 residents
  - 818 passersby

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In a sample limited to acutely exposed populations there was a strong injury dose response association with angina/heart attacks

[Person-time began at enrollment up to first report of any of the selected diagnosed conditions or Wave 3 interview]

Exposure	Angina/heart attack	Asthma	Other non-neoplastic lung disorders	Diabetes
Injury (ref – None)				
1 type	2.0 (1.1,3.6)	1.3 (0.9,1.8)	0.7(0.5,1.0)	0.9 (0.7,1.4)
2 types	3.1(1.2,7.9)	0.8 (0.4, 1.7)	0.7 (0.4, 1.5)	0.8 (0.4, 1.7)
3+ types	6.8 (2.0, 22.6)	0.8 (0.2, 3.4)	0.3 (0.0, 2.4)	0.8(0.2,3.0)
Dust Cloud				
Intense	0.8 (0.5, 1.3)	1.3 (1.0,1.6)	1.3 (1.0, 1.6)	1.1 (0.9,14)
Some/None	Ref	Ref	Ref	Ref
PTSD at Wave 1				
Yes	0.9 (0.6, 1.6)	1.1 (0.8, 1.5)	1.6 (1.2, 2.1)	0.9 (0.7, 1.3)
No	Ref	Ref	Ref	Ref

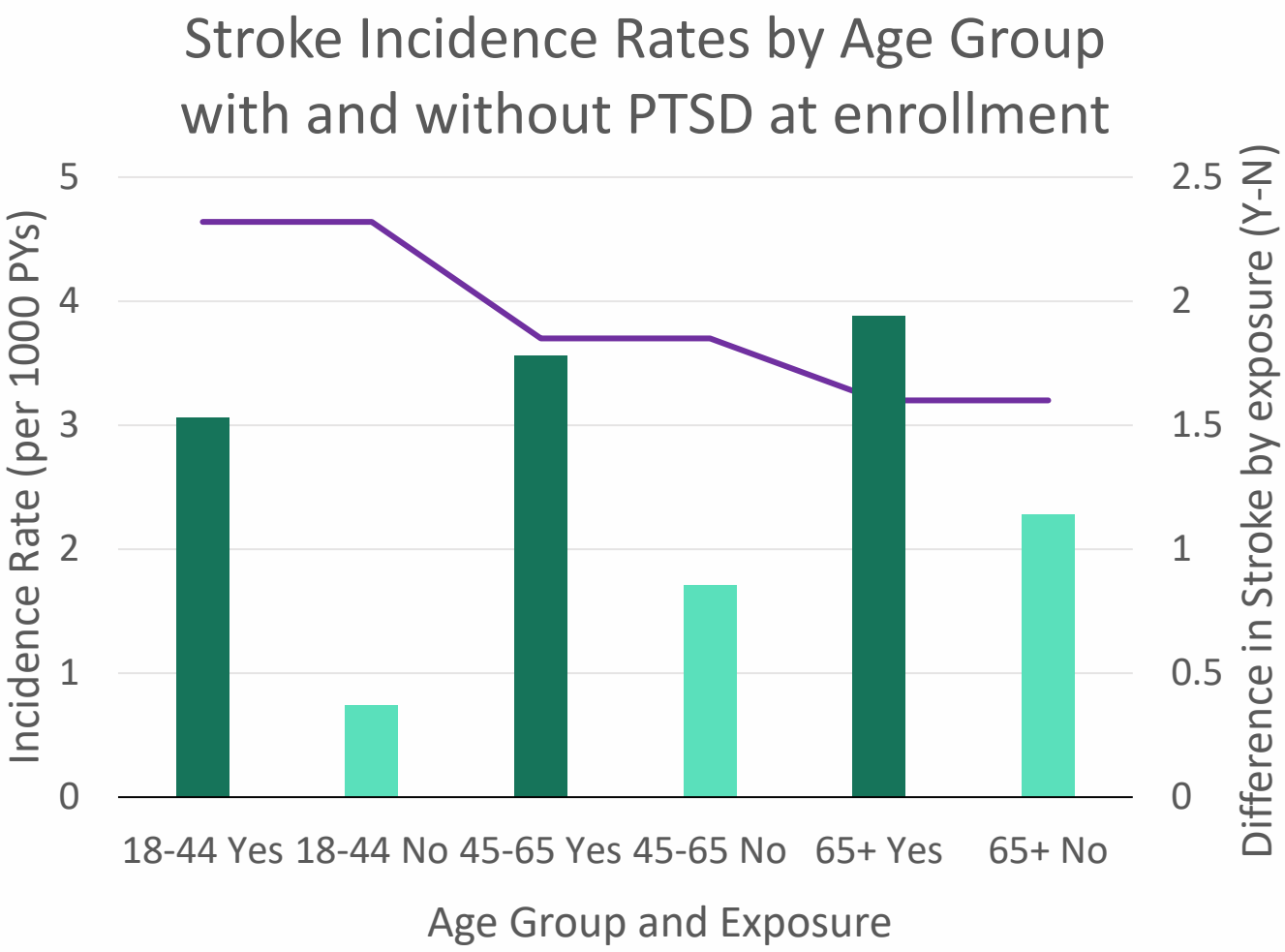
Key Takeaways for 9/11 exposure and heart disease

- There were mixed associations (by gender and sample) for dust cloud exposure and household and workplace dust and heart disease
  - A distinction between acute and chronic dust exposure may be important. Residents and office workers had the highest AHRs for heart disease.
- The associations between PTSD and heart disease were consistent between both self reported and hospitalization for Jordan (2011, 2013) but was not replicated by Alper (2017)
  - Alper limited the sample to acute exposed persons
- 9/11 injury and heart disease was consistently associated for self-report heart disease but not for heart disease hospitalization

Stroke

Stroke self-report and hospitalization publications applied similar methods (Yu et al, 2018, 2021)

- Created groups of completes for participants from Waves 1 to 4
- Survival analysis from 2003/04 to first reported stroke and diagnosis year or 12/31/2016
- Dust cloud defined by Waves 1 and 2
- Selected value of PTSD, smoking, and marital status closest to but preceding when stroke was reported
- Yu, 2021 (hospitalization) conducted multinomial regression on number of hospitalizations for stroke (0, 1, 2)



- Incidence rates of stroke were significantly higher (two to four times) among those with PTSD than those without PTSD in younger age groups **(Yu et al 2018)**
- Stroke incidence between those with and without intense dust exposure among groups 18-44 and 45-46 were also significantly different, though less pronounced than with PTSD

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PTSD and 9/11 dust are associated with self-reported Stroke (Yu 2018)

TABLE 3. Evaluation of PTSD and 9/11-Related Dust Cloud Exposure as Independent Risk Factors for Self-Reported Physician-Diagnosed Stroke

			Model 1: Without Dust Exposure*		Model 2: Without PTSD*		Model 3: Full Model*	
	N With Stroke	Person-Time, Years	AHR	95% CI	AHR	95% CI	AHR	95% CI
Age groups at 9/11								
18–24	6	20,011	0.35	(0.14–0.85)	0.34	(0.14–0.83)	0.35	(0.14–0.84)
25–44	224	209,278	Ref	Ref	Ref			
45–64	436	148,691	2.11	(1.77–2.52)	2.07	(1.73–2.47)	2.12	(1.77–2.52)
65+	87	9,747	6.65	(5.01–8.83)	6.45	(4.89–8.52)	6.74	(5.07–8.94)
Smoking status								
Never	344	204,947		Ref		Ref		Ref
Former	261	129,944	0.96	(0.81–1.14)	0.96	(0.81–1.14)	0.96	(0.81–1.15)
Current	137	37,743	2.04	(1.65–2.54)	2.15	(1.73–2.66)	2.03	(1.64–2.52)
History of hypertension								
Yes	570	167,235	2.48	(2.06–2.98)	2.55	(2.12–3.07)	2.46	(2.05–2.97)
No	172	219,499		Ref		Ref		Ref
History of diabetes								
Yes	253	48,789	2.22	(1.88–2.63)	2.31	(1.96–2.73)	2.22	(1.88–2.62)
No	449	337,150	Ref		Ref		Ref	
PTSD								
Yes	211	59,831	1.69	(1.42–2.02)			1.64	(1.37–1.96)
No	532	323,899	Ref					Ref
9/11 dust cloud exposure								
None/minimal	482	271,552	Ref					Ref
Intense	271	116,174			1.30	(1.10–1.53)	1.20	(1.02–1.42)

World Trade Center Health Registry enrollees aged ≥18 on September 11, 2001, and participants of at least Waves 1 and 2 surveys ($n = 42{,}527$), New York, 2003–2016.
AHR, adjusted hazards ratio; CI, confidence interval; PTSD, posttraumatic stress disorder.
*In addition to variables shown in this table, all models adjusted for other factors, including sex, race/ethnicity, education, marital status, and enrollees' eligibility group.

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PTSD associated with both ischemic and hemorrhagic stroke (Yu, 2021)

Risk Factors for Stroke Hospitalizations by Stroke Subtype

	N = 27,439		N = 27,194	
	Ischemic Stroke or Transient Ischemic Attack (n=348)		Hemorrhagic Stroke (n=103)	
	AHR	95% CI	AHR	95% CI
Posttraumatic Stress Disorder				
Yes	**1.64**	**(1.28, 2.10)**	**1.73**	**(1.10, 2.71)**
No	*Ref*		*Ref*	
Dust Intensity				
Intense	1.20	(0.96, 1.50)	0.87	(0.57, 1.32)
None/Minimal	*Ref*		*Ref*	

AHR = adjusted hazard ratio 95% CI = 95% confidence interval

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PTSD is associated with both single and recurrent stroke hospitalizations; dust cloud is associated with single hospitalization (Yu (2021): Multinomial Logistic Regression Model

Stroke & Recurrent Strokes and their Association with 9/11-related PTSD and Dust Exposure

	0 Strokes (n=28,537)	1 Stroke (n=396)			≥2 Strokes (n=79)		
	N	N	AOR	95% CI	N	AOR	95% CI
Posttraumatic Stress Disorder							
Yes	4,973	103	**1.39**	**(1.09, 1.77)**	26	**1.79**	**(1.09, 2.95)**
No	22,949	284	*Ref*		53	*Ref*	
Dust Intensity							
Intense	9,773	170	**1.33**	**(1.08, 1.65)**	26	0.79	(0.48, 1.29)
None/Minimal	18,763	226	*Ref*		53	*Ref*	

AHR = adjusted hazard ratio 95% CI = 95% confidence interval

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Key take aways for 9/11 exposure and stroke

- Incidence rates for self-reported strokes follow expected patterns (Yu, 2018)
- Dust debris cloud on 9/11 and PTSD independently associated with self-reported strokes (Yu, 2018)
- PTSD predicted both ischemic and hemorrhagic stroke hospitalizations (Yu, 2021)
- Dust debris cloud had marginal association with ischemic strokes but significant association with 1 hospitalization for any stroke (Yu, 2021)
- Other findings (Yu, 2021):
  - Male enrollees had higher odds of two or more strokes (AOR 2.08, 95% CI 1.17 to 3.67)
  - Non-Hispanic Black enrollees also had higher odds of two or more strokes (AOR 2.60, 95% CI 1.48 to 4.58)
  - Education, marital status, and Registry eligibility group were not associated with having either one stroke or ≥2 strokes

Self-report and Administrative (hospitalization records)

- Self-report
  - Self –report easier to collect
  - Assured that answer represents subject
  - No limitation on coverage
  - Recall bias
  - Attrition bias

- Hospitalization
  - Objective and independent of subject
  - Limited coverage
  - Subject to matching errors

"The current findings suggest that misreporting of disease status is non-differential for the exposure measures employed, at least among this cohort, as the point estimates obtained via hospitalization data are slightly attenuated but close to those obtained via self-report. This provides evidence that either data source may be sufficient for research on the association of chronic physical disease with environmental"

Alper et al. Comparison of prevalence and exposure disease associations using self-report and hospitalization data among enrollees of the World Trade Center Health Registry. BMC Medical Research Methodology, 2021

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Strength and limitations for Registry cerebro-cardiovascular studies (heart disease and stroke)

- Strengths
  - Survival analysis methods applied to longitudinal data
  - Both self-report and hospitalized defined outcomes employed
  - Comprehensive inclusion of Registry exposure information and variation in exposure definitions
  - Length of observation period 12 years for two Yu studies
- Limitations
  - Self-report exposure not specific for content and level of environmental dust exposure
  - Definition of self-report outcomes not consistent
    - For instance, Jordan defined heart disease as heart attack, angina, and other heart disease and did not evaluate these separately
  - Length of observation period only five years for two Jorden papers

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Jordan combined several conditions into the Heart Disease definition

- Preliminary re-analysis of Jordan 2011, analysis with separate outcomes

	Heart attack	Angina	Other heart condition
Dust	1.30 (0.99,1.73)	1.1 (0.8,1.5)	0.98(0.84,1.13)
Injury	1.32(1.03,1.7)	1.4(1.1,1.8)	0.91(0.8,1.04)
PTSD	2.29(1.7,3.05)	2.2(1.7,3.09)	1.01(0.86,1.19)

Separate HD outcomes with combined men and women

GERD and Heart Attacks

Gastroesophageal reflux disease (GERD) and heart attack (Brackbill et al, unpublished findings)

- A number of observational studies have reported an association between GERD (clinical endoscopy) and coronary heart disease
- GERD is currently 3rd in number of cases treated by WTC Health Program
- Myocardial infarction (MI-reported as heart attack by self-report) was selected outcome for survival analysis
- Self-reported GERD diagnosis was available from Wave 3 (2011/12) to Wave 5 (2020/21); self reported MI with year of diagnosis was available since Wave 2

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Methods (Brackbill et al.)

- GERD with gastroesophageal symptoms (GERS) and medical intervention defined GERD/GERS
- First reported heart attack with diagnosis defined outcome; enrollees with heart attacks before 2002 were excluded
- Enrollees who reported GERD and no symptoms or no GERD and symptoms were excluded leaving sample of 14,880
- Cases (GERD/GERS) were matched with controls (no GERD/GERS) by age (+/- 1 year) and gender; matched pair controls were assigned case year of diagnosis
- Person-years computed from year of diagnosis for case and matched control up to heart attack year of diagnosis or year of Wave 5 interview

Heart attacks two times more likely among persons with GERD/GERS (preliminary findings)

- 626 MIs (heart attacks)
- Adjusted hazard ratios unadjusted and adjusted for race/ethnic group, 9/11 exposure, BMI, Probable PTSD (Wave 1), ever smoker, binge drinking

Variable	Hazard Ratio	95% CI
GERD/GERS only	2.03	1.66-2.49
GERD/GERS adjusted	1.85	1.46-2.35
Probable PTSD at Wave 1	2.07	1.28-3.36
Ever smoking	1.82	1.25-2.67

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Recommendations for future research

- Revisit exposure definitions with the goal of utilizing all available information to categorize exposure levels especially environmental exposures
  - Seek out environmental data that could be matched to Registry
- Reanalyze cerebro-cardiovascular outcomes using available observational data up 2021 (Wave 5) for both self-report and hospitalization
- Conduct nested case-control studies (consider control external to Registry)
- Conduct matching with Medicare data utilizing specific ICD outcomes for both heart disease and stroke
- Expand research on coronary heart disease to include other 9/11 driven risk factors such as gastro-esophageal disease and PTSD

Acknowledgements

We acknowledge the following for making this research possible:

- World Trade Center Health Registry enrollees who have maintained their commitment to the Registry and contributed their time and energy to completing multiple surveys for over 20 years;

- continued support by the National Institute for Occupational Safety and Health through multiple cooperative agreements;
- New York City Department of Health and Mental Hygiene for providing the infrastructure that supports the Registry;
- and Matthew Di Vitto who helped put this presentation together and all the reviewers in the Registry who contributed suggestions and edits.

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