The Association Between World Trade Center Rescue/Recovery Work and Physician Diagnoses of Obstructive Airway Disease

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The scientific question

- The World Trade Center (WTC) terrorist attack of 9/11/2001(9/11) produced an enormous dust cloud that was associated with both upper and lower respiratory conditions in responders.
- New onset obstructive airway disease (including asthma, chronic bronchitis and COPD/emphysema) continued to be diagnosed in responders even many years after the exposure.
- But conventional wisdom, based on previous research, is that occupational exposures are associated with new diagnoses and symptoms of asthma (and possibly non-asthma obstructive airway disease) for only a short time (weeks, months) after exposure.
- *For how long do we see an exposure-response relationship among WTC responders?*

Study Aims

1. For how long is WTC exposure associated with incident obstructive airway disease ?
2. What is the magnitude of the exposure-response relationship between WTC exposure and incident obstructive airway disease?
3. Is the relationship between WTC exposure and incident obstructive airway disease limited to a single subtype (i.e., asthma)?
4. What is the relationship of physician-diagnosed obstructive airway disease with symptoms self-reported shortly after 9/11/2001.

FDNY Cohort and Exposure

- Male firefighters on active duty on 9/11 with no history of obstructive airway disease who consented for research and answered a smoking questionnaire (N=9,778 included in analysis).
- Exposure intensity based on arrival time at WTC
  - High (morning of 9/11/01) N=1,589 (16.3%)
  - Moderate (afternoon of 9/11/01, or 9/12/01) N=6,992 (71.5%)
  - Low (9/13/01 through 9/24/01) N=1,197 (12.2%)
- ≥ 1 FDNY Bureau of Health Services treatment exam between 9/11 and 9/10/2011.
- Outcome is obstructive airway disease diagnosed by FDNY physician 9/11 - 9/10/2011.
- N=9,778 representing 93.6% of potentially eligible firefighters.

More about the cohort

- Mean age on 9/11= 39.6 years.
- 93.9% Non-Hispanic white.
- 62.8% never smokers.
- 31.3% Retired by 9/10/2011.
- Median 28 treatment visits to FDNY physicians in first ten years after 9/11.
- Mean 97.2 person months follow-up to disease diagnosis or loss to follow-up.

Outcomes

Primary study outcome: Any obstructive airway disease

- 23.4% cumulative incidence of obstructive airway disease by 9/10/2011
- Asthma (2 diagnoses ≥ 30 days apart) 13.2% cumulative incidence
- Chronic Bronchitis (2 diagnoses ≥ 30 days apart in 1 year with at least one follow-up in the next 3 years)
- COPD/Emphysema (2 diagnoses ≥ 30 days apart)
- Chronic Bronchitis and COPD/Emphysema combined in subtype analyses 10.2% cumulative incidence

Statistical methods (I)

We used piecewise exponential survival models.

- We modeled relative rates of disease incidence with respect to exposure intensity.
- We can estimate incidence rate in reference group.
- This is similar to a Cox regression model, but with baseline hazard changing every 3 months rather than with every event.
- Age, smoking history, retirement status, and number of FDNY treatment visits included as possible confounders in all models.
- Analyses censor follow-up as of 9/10/2011.

Statistical Methods (II)

We allow relative rates to change over follow-up.

- Estimate the time(s) of those changes in relative rates from the data using “change point” models using goodness of fit (profile likelihood).
- Estimate the relative rates, with confidence intervals, for entire follow-up period.
- If there is a change point after which relative incidences did not differ significantly from one, that would show that the exposure-response relationship between WTC-exposure and incident OAD was limited to the period prior to the change point.

Profile Likelihood

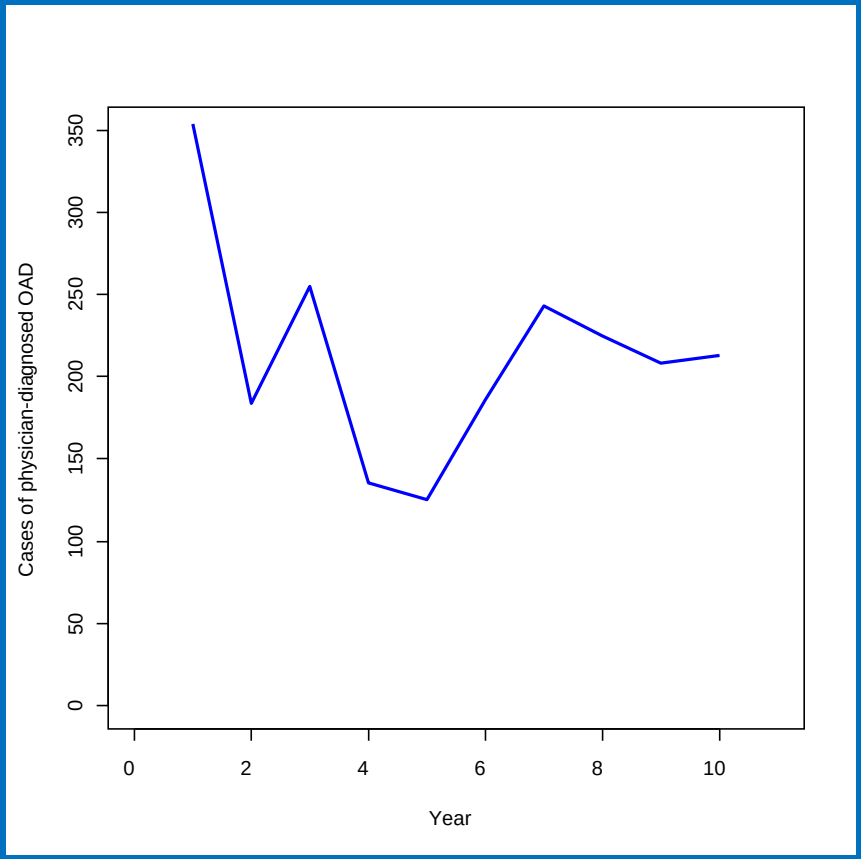
- Basic idea: Try a variety of change points; see which fits best based on likelihood.
- This is the *Profile Likelihood* method which allows rigorous statistical inferences.
- The change point value which has the highest profile likelihood value is the maximum likelihood estimate for the change point.
- Profile likelihood values above a threshold are the interior of a confidence interval.

Medication coverage increased diagnoses

Complete Medication coverage (100% free) began in year six (2007).

By 2009, diagnoses increased to levels of year three (2004).

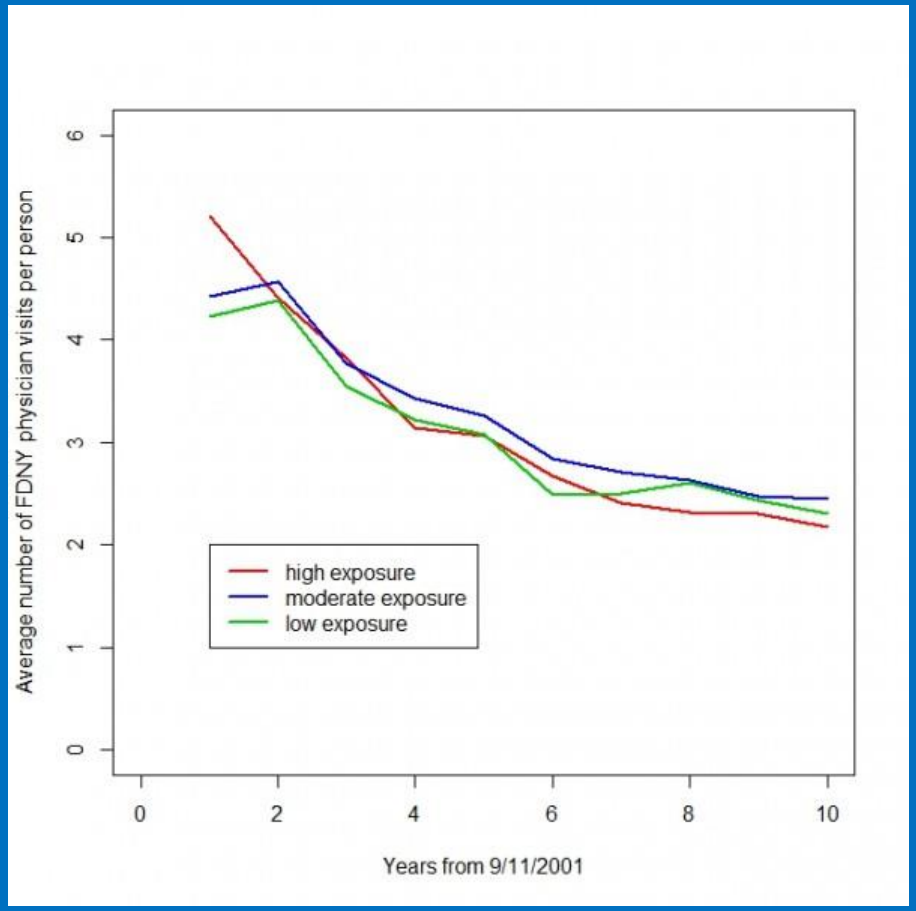
From year 2008 on, incidence of new diagnoses remain above pre-9/11 levels.



Treatment visits similar in all groups

Number of treatment visits declines over time.

More treatment visits in high exposure group ONLY in first year, but likelihood of diagnosis in first year also elevated in high exposure group.



Results for ten year follow-up

Best fitting model had change points at 15 and 84 months post-9/11.

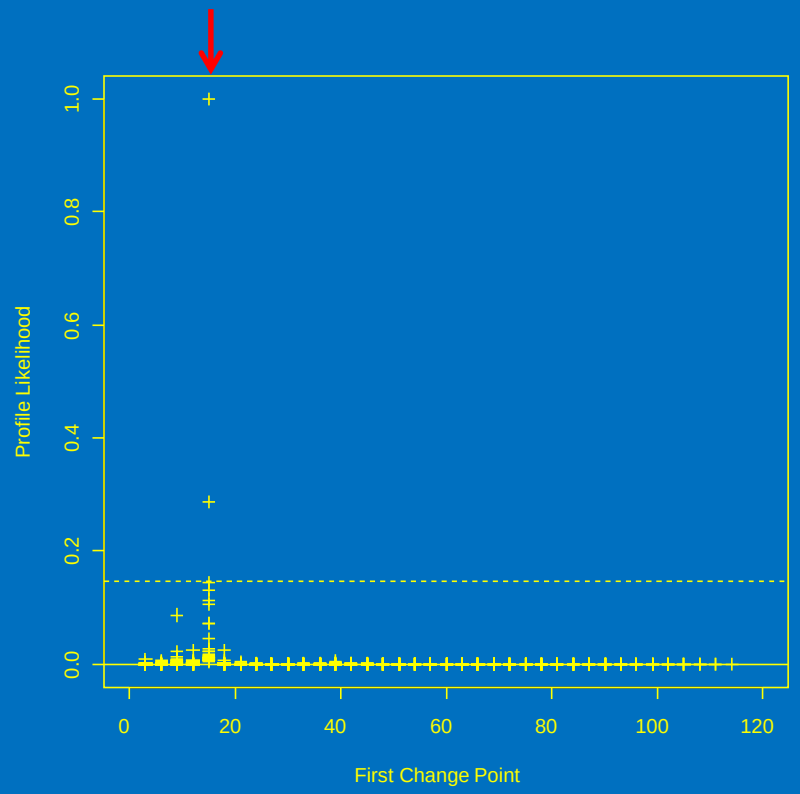
The analysis controls for

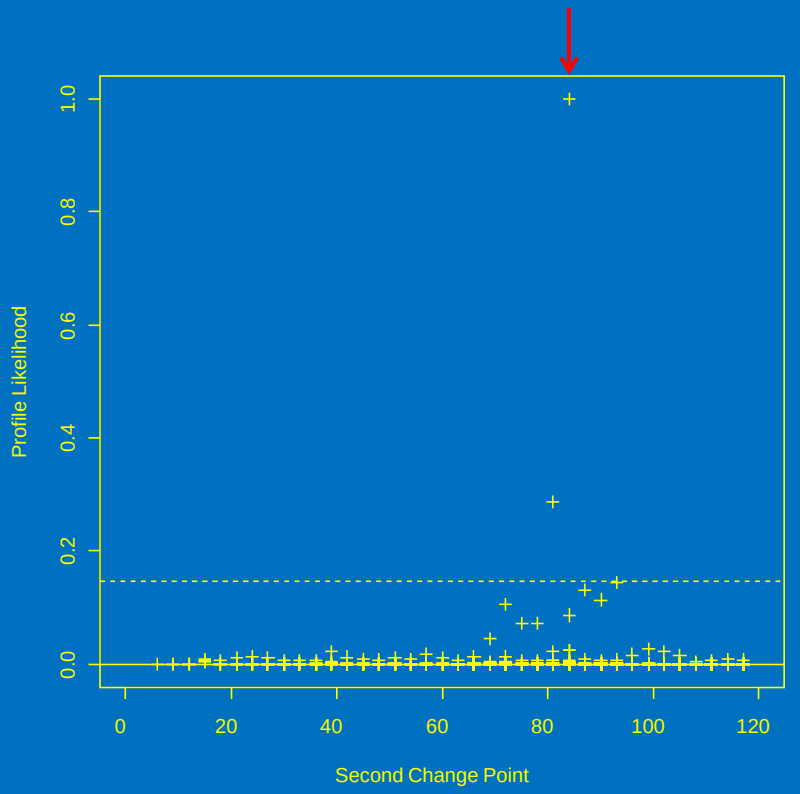
- age on 9/11
- retirement status (time dependent)
- smoking status (ever vs. never)
- seasonality (by quarter).

Trend tests significant ($p<0.0001, p<0.0001$)

	Exposure Contrast	Hazard Ratio (95% CI)
< 15 mos.	High vs. Low	4.02 (2.62,6.16)
	High vs. Mod.	2.11 (1.71,2.61)
	Mod. vs. Low	1.90 (1.26,2.86)
15-84 mos.	High vs. Low	1.90 (1.49,2.44)
	High vs. Mod.	1.20 (1.03,1.39)
	Mod. vs. Low	1.59 (1.28,1.98)
85-120 mos.	High vs. Low	1.20 (0.92,1.56)
	High vs. Mod.	1.17 (0.97,1.42)
	Mod. vs. Low	1.02 (0.82,1.27)

Profile likelihood graphs





Results for ten year follow-up – subtypes

Asthma	Exposure Contrast	Hazard Ratio (95% CI)	Non-Asthma	Exposure Contrast	Hazard Ratio (95% CI)
< 15 mos.	High vs. Low	4.47 (2.48, 8.06)	< 15 mos.	High vs. Low	3.56 (1.91, 6.66)
	High vs. Mod.	2.05 (1.56, 2.70)		High vs. Mod.	2.21 (1.60, 3.07)
	Mod. vs. Low	2.18 (1.24, 3.84)		Mod. vs. Low	1.61 (0.89, 2.92)
15-84 mos.	High vs. Low	2.02 (1.47, 2.77)	15-84 mos.	High vs. Low	1.74 (1.17, 2.59)
	High vs. Mod.	1.28 (1.06, 1.56)		High vs. Mod.	1.06 (0.83, 1.36)
	Mod. vs. Low	1.57 (1.19, 2.08)		Mod. vs. Low	1.64 (1.16, 2.32)
85-120 mos.	High vs. Low	1.36 (0.93,1.99)	85-120 mos.	High vs. Low	1.03 (0.71, 1.51)
	High vs. Mod.	1.21 (0.92,1.58)		High vs. Mod.	1.14 (0.86, 1.51)
	Mod. vs. Low	1.13 (0.82,1.55)		Mod. vs. Low	0.91 (0.67,1.23)

Physician diagnoses related to self-reported symptoms?

Most reported OAD symptoms (cough, wheeze, shortness of breath) prior to physician diagnosis – this was true throughout follow-up.

- 1,559/1,934 of persons who received an OAD diagnosis and answered the symptoms questionnaire in the first 15 months reported symptoms (80.6% sensitivity).

Month of OAD diagnosis	#/N (%) self-reporting OAD symptoms in first 15 months*	#/N self-reporting OAD symptoms in any prior period
1-15	321/351 (91.5%)	–
16-60	477/585 (81.5%)	477/685 (69.6%)
61-84	288/369 (78.1%)	319/432 (73.8%)
85-120	473/629 (75.2%)	554/745 (74.4%)
Never	4,088/6,373 (64.2%)	4,682/7,492 (62.5%)
Entire cohort	5,647/8,307 (68.0%)	(9,778)

*1,471 persons did not complete a medical monitoring questionnaire during the first 15 months and are excluded from this column.

Physician diagnoses related to self-reported symptoms?

- 6,373 persons did not receive a diagnosis during the follow-up period and responded to the medical monitoring questionnaire item for lower respiratory symptoms.
- Of those, 4,088 reported at least one lower respiratory symptom, for a specificity of 35.9%.

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Physician diagnoses related to self-reported symptoms?

The majority of those who reported lower respiratory symptoms shortly after 9/11/2001 did not receive an OAD diagnosis during the study period.

- 1,559 of 5,647 individuals reporting a lower respiratory symptom during the first 15 months received a physician diagnosis of OAD during follow-up, for PPV of 27.6%.

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Conclusions

- *Physician diagnoses of* incident obstructive airway disease are *associated with more intense WTC exposure for seven years post 9/11.*
- *Results are consistent with other modeling approaches.*
- *We cannot determine how much of this represents progressive development of disease compared to delayed diagnosis.*
- *Cannot compare WTC-exposed individuals to unexposed in this cohort; therefore we cannot support or rule out an association of WTC exposure with OAD that is not intensity-related.*

Impact on 9/11 survivors

- These results support current policy to provide health care for these conditions to exposed rescue/recovery workers regardless of the year of diagnosis.
- Most FDNY responders reported symptoms of obstructive airway disease in the first year after 9/11, but these symptoms did NOT necessarily progress to diagnoses of obstructive airway disease.
- We can neither support nor rule out a continued exposure response relationship past seven years. Beyond that time, however, an exposure response relationship does not appear to be associated with arrival time at the WTC site.

Thank you!

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The FDNY members who save lives every day.

And remember the 343 FDNY members who died on 9/11/2001.