World Trade Center (WTC) Health Program

World Trade Center (WTC) Health Program

Research Meeting 2023 NOVEMBER

NYU Langone Murphy Auditorium (Main Auditorium) | 550 1st Ave., New York, NY 10016

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WTC Health Program

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WTC Health Program Research Meeting

NYU Langone Murphy Auditorium (Main Auditorium) 2023

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Agenda

9:00 AM – 10:15 AM WELCOME ANNOUNCEMENTS AND UPDATES–NIOSH/WTCHP

MASTER OF CEREMONIES: MAX LUM

WTCHP RESEARCH PROGRAM UPDATES: TRAVIS KUBALE

HORIZONS IN RESEARCH: WTC ENVIRONMENTAL HEALTH CENTER SURVIVOR PROGRAM – JOAN REIBMAN

PRESENTATIONS

10:15 M – 11:30 AM SESSION 1: THE CAREER FIREFIGHTER HEALTH STUDY

20 MINUTE PRESENTATIONS OF *KEY FINDINGS, IMPACT, RESEARCH GAPS* FOLLOWED BY 15-MINUTE Q/A

10:15 AM — CREATING THE CAREER FIREFIGHTER HEALTH STUDY – DAVID PREZANT, MD

10:35 AM — CURRENT FINDINGS USING THE CFHS CANCER AND MORTALITY DATA – RACHEL ZEIG-OWENS DRPH

10:55 AM — CURRENT FINDINGS USING THE CFHS SURVEY DATA – ALEXANDRA MUELLER, MPH

11:15 AM Question and Answer Session

11:30 AM – 1:00 PM  **LUNCH** 

PRESENTATIONS WILL RESUME AFTER LUNCH *(SEE OTHER SIDE FOR PRESENTERS)*

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WTC Health Program Research Meeting

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Agenda

PRESENTATIONS

1:00 PM – 3:15 PM SESSION 2 (PANEL): WTCHP MENTAL HEALTH RESEARCH

20 MINUTE PRESENTATIONS OF *KEY FINDINGS, IMPACT, RESEARCH GAPS* FOLLOWED BY 35-MINUTE PANEL DISCUSSION

1:00 PM — THE BIDIRECTIONAL RELATIONSHIP BETWEEN POSTTRAUMATIC STRESS SYMPTOMS AND SOCIAL SUPPORT IN A 9/11-EXPOSED COHORT: *A LONGITUDINAL CROSS-LAGGED ANALYSIS* – JAMES CONE, MD, MPH

1:20 PM — PERCEIVED ABILITY TO COPE, SOCIAL SUPPORT, AND PTSD SYMPTOM SEVERITY – MARY KOWALCHYK, MA

1:40—2:00 PM BREAK (20 MINUTES)

2:00 PM — TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION TO REDUCE POST TRAUMATIC STRESS DISORDER (PTSD) SYMPTOMS IN WORLD TRADE CENTER RESPONDERS – REBECCA SCHWARTZ, PHD AND THEODOROS ZANOS, PHD

2:20 PM — UPDATES ON KETAMINE TREATMENT FOR CHRONIC PTSD – ADRIANA FEDER, MD

2:40 PM — Panel Discussion Moderated by – REBECCA ROSEN, PHD

3:15 PM – 3:30 PM WRAP-UP AND ADJOURN —THANK YOU FOR YOUR ATTENDANCE

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World Trade Center (WTC) Health Program

PI: David Prezant, MD

Presentation Title: Creating the Career Firefighter Health Study

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Creating the Career Firefighter Health Study

DAVID PREZANT, MD

Background (FDNY)

- **FDNY** has shown many health outcomes are elevated among WTC-exposed firefighters compared with lower exposed participants and the general population
- However, firefighting in general is also associated with many health outcomes
  - e.g., cancer, mortality, asthma, respiratory symptoms ***(cough, sore throat, dyspnea),*** pulmonary function, acute cardiovascular events, and mental health symptoms
- *Conversely*, actively employed individuals are healthier and have less mortality compared to general population
  - Firefighters may have even better health
    - Required to pass physical fitness test
    - National hiring guidelines often exclude those with pre-existing conditions

FDNY CFD PFD SFFD | Career Firefighter Health Study | WTC Health Program

Background (NISOH)

- **NISOH** assembled a cohort of **29,992** professional firefighters employed any time between **1950-2009** from the San Francisco ***(5,313)***, Chicago ***(15,184),*** and Philadelphia *(9,495)* fire departments to study cancer and mortality. *(Daniels RD et al., Occup Environ Med, 2014)*
- In **2016**, we were funded to use this cohort as a comparison population for **WTC-exposed** firefighters
- Follow-up study now includes **FDNY** firefighters and is called the *Career Firefighter Health Study* to better reflect long-term goals.

Background (NISOH)

- To compare cancer rates in **WTC-exposed** firefighters ***(FDNY)*** and non-**WTC-exposed** firefighters ***(SFFD, CFD, PFD)*** to those of the US general population.
- To establish a subgroup of firefighters for lifelong follow-up via the completion of a health questionnaire, and then
  - Track mental and physical health symptoms and diagnoses among firefighters
  - Compare mental and physical health symptoms and diagnoses in **WTC-exposed** firefighters and **non-WTC-exposed** firefighters.

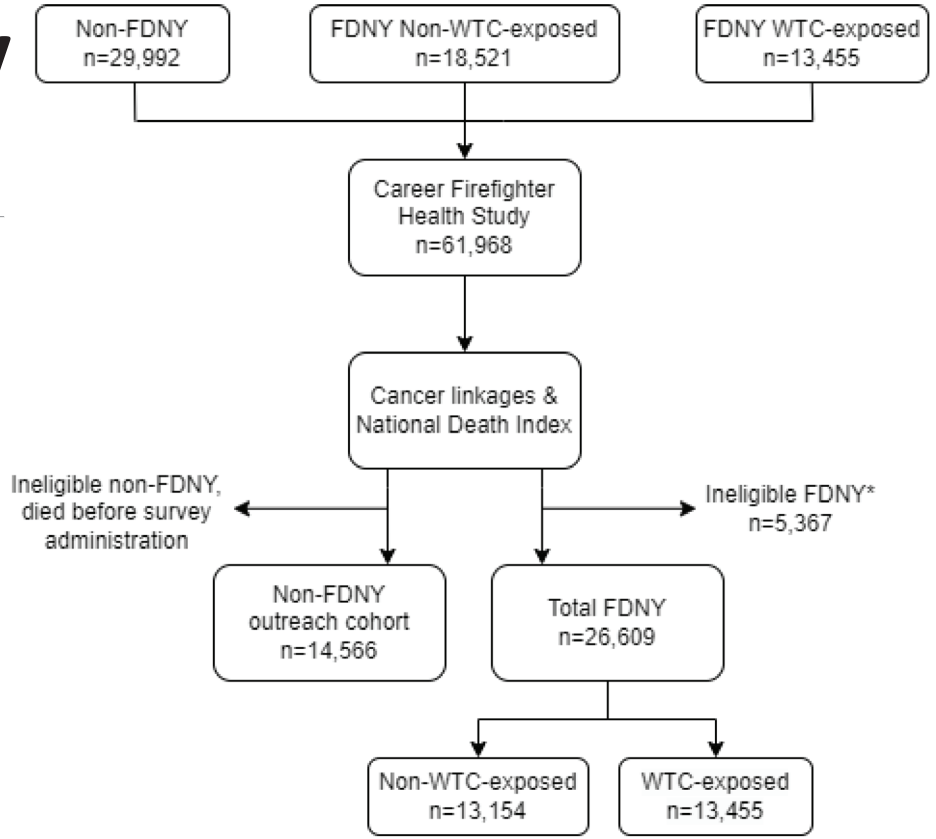
What have we already accomplished:

- We added the **FDNY** firefighters to the original **NIOSH** population
  - **WTC-exposed** (***n=13,833***) and **non-WTC-exposed** ***(currently, n=18,521)***
- Career Firefighter Health Study now totals over **60,000 firefighters**

We have conducted:

- Linkages ***(State cancer registries, National Death Index registry)***
- Web-based survey for health characteristics & self-reported diseases

Linkages and Survey Flowchart



*died before 9/11/01 or retired before 9/11/01 and non-WTC-exposed

Challenges

- State Cancer Registry Linkage Delays
  - It took nearly **3 years** to receive data from all the cancer registries
- Data Use Agreements
  - In **2016**, Philadelphia Fire Department was the only department that required a **DUA**. This process still took over a year to complete.

New NIOSH Funding

- In September 2022, FDNY was funded to maintain & expand the Career Firefighter Health Study cohort.
- Our goals are to:

1. Update the 4-city cohort (FDNY, Chicago, Philadelphia, San Francisco) by adding firefighters hired after 2009:
2. Repeat our linkages with state cancer registries and the National Death Index to identify new cancers
   - We already have cancer & cause of death through 2016 obtained under our earlier grant
3. Add other cities/geographic areas
   - Discussion on-going with Boston, Miami & Miami-Dade, and Indianapolis

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World Trade Center (WTC) Health Program

PI: Rachel Zeig-Owens DrPH

Presentation Title: Current findings using the CFHS Cancer and Mortality data

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Current findings using the CFHS Cancer and Mortality data

RACHEL ZEIG-OWENS, DrPH

Original NIOSH findings *(Daniels RD et al., Occup Environ Med, 2014)*

Table 2 Standardised mortality and incidence ratios in firefighters for select outcomes compared to results from a recent meta-analysis

	Current study results (US population referent)					
	Mortality (1950–2009)†		Cancer incidence (1985–2009)			
			All cancers		First cancer	
Underlying cause (ICD-10 codes)	Obs	SMR (95% CI)	Obs	SIR (95% CI)	Obs	SIR (95% CI)
MN stomach (C16)	110	1.10 (0.91 to 1.33)	93	1.15 (0.93 to 1.40)	72	1.02 (0.80 to 1.28)
MN small intestine (C17)	8	1.66 (0.72 to 3.27)	17	1.15 (0.67 to 1.85)	16	1.43 (0.82 to 2.33)
			166	1.11 (0.95 to 1.30)	140	1.09 (0.91 to 1.28)
MN breast (C50)	8	1.39 (0.60 to 2.73)	26	1.26 (0.82 to 1.85)	24	1.32 (0.84 to 1.96)
MN prostate (C61)	282	1.09 (0.96 to 1.22)	1261	1.03 (0.98 to 1.09)	1176	1.03 (0.97 to 1.09)
MN other male genital (C60, C62-C63)	<5	0.47 (0.13 to 1.20)	17	0.62 (0.36 to 0.99)	17	0.67 (0.39 to 1.07)
MN testes (C62)	<5	0.73 (0.15 to 2.14)	15	0.75 (0.42 to 1.24)	15	0.79 (0.44 to 1.30)
	84	0.99 (0.79 to 1.22)				
MN brain (C47, C70-C72)	73	1.01 (0.79 to 1.27)	51	1.02 (0.76 to 1.34)	48	1.06 (0.78 to 1.41)
NHL (C46.3, C82-C85, C88.0, C88.3, C91.4, C96)§	123	1.17 (0.97 to 1.40)	170	0.99 (0.85 to 1.15)	145	0.99 (0.83 to 1.16)
Leukaemia (C91.0-C91.3, C91.5-C91.9, C92-C95)	122	1.10 (0.91 to 1.31)	100	0.94 (0.77 to 1.15)	85	0.93 (0.74 to 1.15)
Multiple myeloma (C88.7, C88.9, C90)	42	0.89 (0.64 to 1.20)	36	0.72 (0.50 to 0.99)	33	0.75 (0.52 to 1.06)
Other cancers:¶						

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CFHS cancer linkages

- Linked with **10** state cancer registries based on areas where the firefighters lived/retired to
  - Arizona, California, Florida, Illinois, Indiana, Michigan, New Jersey, Oregon, Pennsylvania, and Washington
  - Data from the original NIOSH study could not be used because of DUAs with states
  - *Once we add new fire departments, future linkages will include additional states and/or the Virtual Pooled Registry*
- Cancer data are complete through **2016**
- All **29,992** firefighters were included in the linkages
  - Population includes firefighters hired between **1950** and **2009**
  - To date, cancer analyses have focused on firefighters active on **9/11/2001 (~9,000)** to be comparable to **WTC-exposed** FDNY firefighters

Population Characteristics

19,599** Firefighters employed on **9/11/2001

	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001	Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*
Total N	10,786	8,813
Age on 9/11, mean ± SD	40.4±7.5	43.9±9.2
Race/ethnicity, N (%)		
Non-Hispanic White	10,121 (93.8%)	6,117 (69.4%)
Non-Hispanic Black	282 (2.6%)	1,589 (18.0%)
Hispanic	353 (3.3%)	736 (8.3%)
Other[a]	30 (0.3%)	371 (4.2%)
Smoking status, N (%)		
Current	373 (3.5%)[b]	189 (6.6%)[c]
Former	3,233 (30.2%)[b]	1,056 (37.0%)[c]
Never	7,117 (66.4%)[b]	1,611 (56.4%)[c]
Deceased by 12/31/16, N (%)	261 (2.4%)	605 (6.9%)

Note:

Throughout this presentation, CFHS includes only males due to low numbers of females. Next phase should enable their inclusion.

a Includes Asian and Native American race categories;

b N=10,723 who self-reported smoking status;

c N=2,856 who completed Career Firefighter Health Study survey

* Firefighters from **San Francisco**, **Chicago**, & **Philadelphia**

Career Firefighter Health Study Cancer Results

Firefighters' vs US Standardized Incidence Ratios (SIRs)

	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001		Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*	
Site	SIR	95% CI	SIR	95% CI
All cancer sites	1.15	(1.08-1.23)	1.05	(0.98-1.12)
Prostate	1.70	(1.53-1.88)	1.22	(1.11-1.35)
Lung	0.53	(0.39-0.72)	0.71	(0.57-0.89)
Kidney	0.93	(0.67-1.28)	1.19	(0.90-1.56)
Non-Hodgkin Lymphoma	1.39	(1.06-1.83)	1.04	(0.77-1.41)
Melanoma (skin)	1.59	(1.30-1.96)	1.39	(1.07-1.79)
Thyroid	2.37	(1.78-3.17)	1.01	(0.61-1.67)

Career Firefighter Health Study WTC Health Program

Refs: Webber et al OEM 2021
Daniels RD et al., Occup Environ Med, 2014

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Career Firefighter Health Study Cancer Results

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Thyroid	**2.37**	**(1.78-3.17)**	1.01	(0.61-1.67)

Cancer Risk was elevated for:

- All cancer sites ***(WTC)***
- Prostate cancer ***(Both cohorts)***
- Non-Hodgkin Lymphoma ***(WTC)***
- Melanoma ***(Both cohorts)***
- Thyroid Cancer ***(WTC)***

Refs: Webber et al OEM 2021
Daniels RD et al., Occup Environ Med, 2014

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Career Firefighter Health Study Cancer Results

Firefighters' vs US Standardized Incidence Ratios (SIRs)

	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001		Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*	
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Kidney	0.93	(0.67-1.28)	1.19	(0.90-1.56)
Non-Hodgkin Lymphoma	1.39	(1.06-1.83)	1.04	(0.77-1.41)
Melanoma (skin)	1.59	(1.30-1.96)	1.39	(1.07-1.79)
Thyroid	2.37	(1.78-3.17)	1.01	(0.61-1.67)

Cancer Risk was reduced for:

- Lung Cancer (Both cohorts)

Refs: Webber et al OEM 2021
Daniels RD et al., Occup Environ Med, 2014

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Career Firefighter Health Study Cancer Results

Firefighters' vs US Standardized Incidence Ratios (SIRs)

	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001		Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*		Original NIOSH findings (1985-2009)	
Site	SIR	95% CI	SIR	95% CI	SIR	95% CI
All cancer sites	1.15	(1.08-1.23)	1.05	(0.98-1.12)	1.09	(1.06 -1.12)
Prostate	1.70	(1.53-1.88)	1.22	(1.11-1.35)	1.03	(0.98-1.09)
Lung	0.53	(0.39-0.72)	0.71	(0.57-0.89)	1.12	(1.04-1.21)
Kidney	0.93	(0.67-1.28)	1.19	(0.90-1.56)	1.27	(1.09-1.48)
Non-Hodgkin Lymphoma	1.39	(1.06-1.83)	1.04	(0.77-1.41)	0.99	(0.85-1.15)
Melanoma (skin)	1.59	(1.30-1.96)	1.39	(1.07-1.79)	0.87	(0.73-1.03)
Thyroid	2.37	(1.78-3.17)	1.01	(0.61-1.67)	0.87	(0.56-1.28)

Original Cohort was older and may have had different exposures due to changes in PPE and health behaviors

Career Firefighter Health Study WTC Health Program

Refs: Webber et al OEM 2021
Daniels RD et al., Occup Environ Med, 2014

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Career Firefighter Health Study Cancer Results

WTC vs. **Non-WTC**

- We compared incidence rates in **FDNY WTC**-exposed male firefighters to incidence rates to the non-**WTC**-exposed male firefighters ***(CFD, PFD, SFFD)***

		FDNY WTC-exposed vs non-FDNY, non-WTC-exposed firefighters
		Webber et al, 2021 *Data through 2016*
RR (95% CI)	**All cancers**	1.13 (1.02-1.25)
	Thyroid	2.53 (1.37-4.70)
	Prostate	1.39 (1.19-1.63)
	Lung	0.87 (0.57-1.33)
	Skin Melanoma	1.12 (0.80-1.57)

Ref: Webber et al OEM 2021

CFHS Mortality Linkage

- We linked with the **National Death Index** to obtain date of death and cause of death
  - As with the **cancer** linkages, we could not use data from the original **NIOSH** study
- Analyses were also restricted to firefighters active on **9/11/2001**

Career Firefighter Health Study Mortality Results

Firefighters' vs US Standardized Mortality Ratios (SMRs)

Cause of death	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001		Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*	
	SMR	95% CI	SMR	95% CI
All	0.30	0.26-0.34	0.60	0.55-0.65
All cancers	0.40	0.32-0.49	0.73	0.64-0.84
Heart diseases	0.27	0.20-0.35	0.51	0.42-0.60
Other diseases of the circulatory system	0.18	0.08-0.35	0.38	0.24-0.56
Diseases of the respiratory system	0.31	0.17-0.51	0.57	0.40-0.79
Diseases of the digestive system	0.13	0.06-0.26	0.42	0.27-0.62
Fire in building	5.79	2.64-10.99	4.56	1.83-9.39
Intentional self-harm (suicide)	0.36	0.21-0.58	1.01	0.68-1.43

Both **WTC-exposed** and **non-exposed** firefighter had **lower** than expected all-cause mortality compared with **US** rates.

Refs: Singh et al OEM 2023
Pinkerton L et al Occup Environ Med. 2020

Career Firefighter Health Study Mortality Results

Firefighters' vs US Standardized Mortality Ratios (SMRs)

Cause of death	Male WTC-exposed FDNY firefighters actively employed on 9/11/2001		Male non-FDNY, non-WTC-exposed firefighters actively employed on 9/11/2001*		Original NIOSH findings (1950-2016)	
	SMR	95% CI	SMR	95% CI	SMR	95% CI
All	0.30	0.26-0.34	0.60	0.55-0.65	0.97	0.95-0.98
All cancers	0.40	0.32-0.49	0.73	0.64-0.84	1.12	1.08-1.16
Heart diseases	0.27	0.20-0.35	0.51	0.42-0.60		
Other diseases of the circulatory system	0.18	0.08-0.35	0.38	0.24-0.56		
Diseases of the respiratory system	0.31	0.17-0.51	0.57	0.40-0.79		
Diseases of the digestive system	0.13	0.06-0.26	0.42	0.27-0.62		
Fire in building	5.79	2.64-10.99	4.56	1.83-9.39		
Intentional self-harm (suicide)	0.36	0.21-0.58	1.01	0.68-1.43		

Original Cohort was older and may have had different exposures due to changes in PPE and health behaviors

Refs: Singh et al OEM 2023
Pinkerton L et al Occup Environ Med. 2020

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Career Firefighter Health Study Mortality Results

WTC vs. **Non-WTC**

- All-cause and cause-specific mortality were lower in WTC-exposed compared with non-WTC-exposed firefighters.

Adjusted relative rates (RR) of deaths in male WTC-exposed FDNY firefighters vs. male non-WTC-exposed non-FDNY firefighters, 9/11/2001-12/31/2016	
Cause of death (NIOSH major category)	Adj. RR (95% CI)[a]
All deaths	0.54 (0.49-0.59)
All cancers	0.72 (0.65-0.79)
Diseases of the heart (16)	0.61 (0.55-0.67)
Other diseases of the circulatory system (17)	0.74 (0.66-0.84)
Diseases of the respiratory system (18)	0.69 (0.62-0.77)
Diseases of the digestive system (19)	0.54 (0.48-0.60)
Intentional self-harm (suicide) (27; 116)	0.44 (0.39-0.50)

[a]***Regression models adjusted for age on 9/11/2001 and race/ethnicity;***

Ref: Singh et al OEM 2023

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Impact to the members

- While the **WTC-exposed** firefighters have a greater incidence of cancer compared with non-exposed firefighters, their risk of mortality is lower.
  - This could be because of the care the **WTC-exposed** firefighters receive as part of the **WTCHP**
  - *Currently funded to investigate this among responders diagnosed with cancer*

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World Trade Center (WTC) Health Program

PI: Alexandra Mueller, MPH

Presentation Title: Current Findings Using the CFHS Survey Data

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Current findings using the CFHS survey data

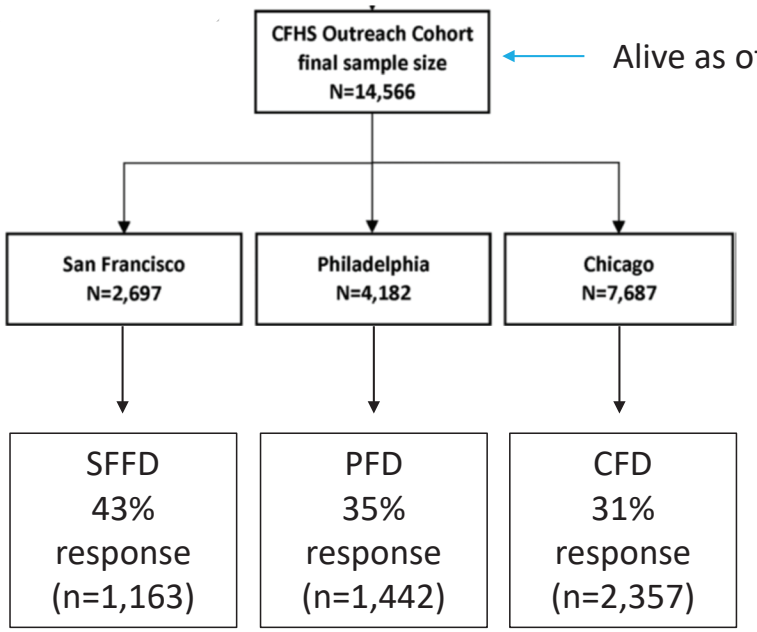
ALEXANDRA MUELLER, MPH

CFHS Survey

- FDNY administers health questionnaires at members' annual medical monitoring exams
- CFHS survey was designed to be nearly identical and provide insight on self-reported health status and conditions
- Questions/health topics:
  - Lower & upper respiratory symptoms/conditions/medications
  - Sleep
  - Gastrointestinal conditions
  - Cancer diagnoses & prevention
  - Musculoskeletal conditions
  - Cardiovascular conditions
  - Vascular & neurological symptoms/conditions
  - Smoking/alcohol use
  - Depression, PTSD, and cognitive function screening
  - Endocrine conditions

FDNY CFD PFD SFFD Career Firefighter Health Study WTC Health Program

CFHS Survey
Non-FDNY Firefighters



Total response 34% (n=4,962)

Zeig-Owens et al. *Am J Ind Med*. 2021.

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CFHS Survey Studies to date

- Mental Health Outcomes
- Obstructive Airway Disease
- Cardiovascular Disease

Mental Health

- Objective: to evaluate subjective cognitive concerns, PTSD symptoms, and depressive symptoms by fire department

	WTC-Exposed FDNY*	Chicago FD*	Philadelphia FD*	San Francisco FD*
Median number of CFI Cognitive Concerns	0	1	2	1
Probable PTSD[a] (%)	671 (8%)	64 (5%)	68 (9%)	28 (4%)
Probable Depression[b] (%)	1,408 (17%)	182 (15%)	168 (22%)	110 (17%)

*Actively employed on 9/11/2001, and answered the mental health questions
[a]score ≥44 on PCL-S (PTSD screening questionnaire)
[b]score ≥16 on CES-D (depression screening questionnaire)

Mueller et al *Am J Ind Med*. 2021.

Mental Health

Summary

- WTC exposure associated with fewer subjective cognitive concerns
  - Variability between fire departments limited ability to evaluate the association of WTC exposure and PTSD/depression
- Across departments, older age associated with more cognitive concerns, but fewer PTSD and depressive symptoms

Obstructive Airway Disease

- Objective: to estimate the association between WTC exposure and OAD in career firefighters and a US general population
- Outcomes: self-reported obstructive airway diseases
  - Asthma
  - COPD/emphysema/bronchitis (“COPD”)
  - Any OAD (at least one of the above conditions)

Mueller et al *Am J Ind Med*. 2023.

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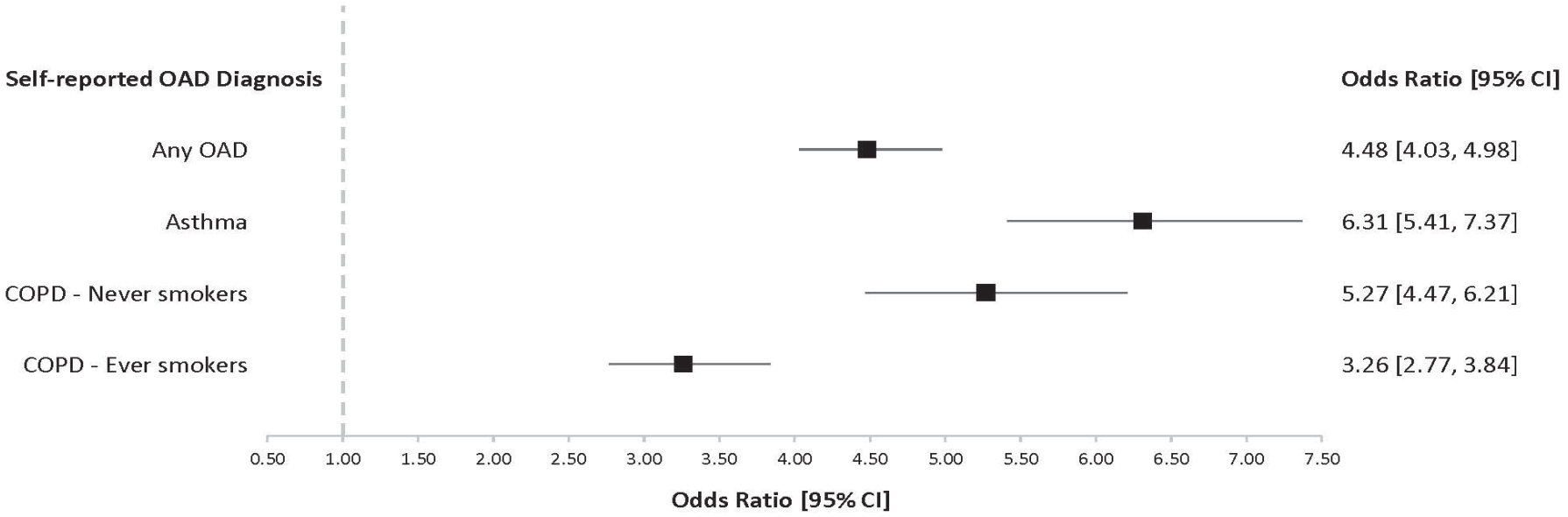
Figure 1: Estimated odds ratios from a logistic regression[1] of self-reported OAD diagnoses in WTC-exposed[2] vs. non-WTC-exposed[3] firefighters



[1]Controlling for age, race, smoking status, and having a last medical visit within 2 years

[2]WTC-exposed firefighters from the New York City fire department

[3]Non-WTC-exposed firefighters from Chicago, Philadelphia, and San Francisco fire departments

Abbreviations: OAD: Obstructive airway disease; WTC: World Trade Center; COPD: Chronic obstructive pulmonary disease; 95% CI: 95% confidence interval

Obstructive Airway Disease

Summary

- All firefighters had higher rates than US population (NHIS).
- WTC-exposed firefighters had higher rates than non-exposed firefighters
- Compared with the US population, non-WTC-exposed firefighters were less likely to report asthma, but more likely to report COPD.

Cardiovascular Disease

- Objective: to assess the effect of WTC exposure on cardiovascular disease (CVD) in career firefighters cross-sectionally
- Outcomes: self-reported cardiovascular diseases
  - Coronary artery disease (CAD) – includes myocardial infarction, angina, and coronary artery disease
  - Stroke – includes stroke/cerebrovascular accident and transient ischemic attack
  - Stroke/CAD – includes reporting either or both of the above conditions

Self-reported cardiovascular disease in career firefighters with and without World Trade Center exposure. *JOEM*. Under review.

10

US General Population Comparison

- For an additional external comparison, used a US general population survey
- National Health Interview Survey 2019
  - Cross-sectional interview conducted in 2019 of the US noninstitutionalized civilian population

Cardiovascular Disease – Firefighters Only

Estimated odds ratios (95% CI) for self-reported CVD diagnoses by exposure status

	Stroke/CAD[1]	Stroke[2]	CAD[3]
WTC-exposed	1.23 (1.06, 1.43)	1.03 (0.79, 1.35)	1.25 (1.06, 1.47)
Non-exposed	ref	ref	ref

Estimated odds ratios (95% CI) for self-reported CVD diagnoses by exposure level

	Stroke/CAD[1]	Stroke[2]	CAD[3]
High exposure	1.45 (1.18, 1.79)	1.18 (0.80, 1.75)	1.48 (1.18, 1.86)
Moderate exposure	1.31 (1.11, 1.54)	1.07 (0.79, 1.44)	1.32 (1.10, 1.57)
Low exposure	1.00 (0.83, 1.21)	0.90 (0.64, 1.27)	1.03 (0.84, 1.26)
Non-exposed	ref	ref	ref
P for trend	P<0.0001	P=0.33	P<0.0001

[1]Includes any report of stroke or CAD
[2]Includes diagnoses of stroke/CVA or TIA
[3]Inclused diagnoses of CAD, MI, or angina

Age, race, and BMI were included in the model (complete case analysis, n=12,516)

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Cardiovascular Disease – Firefighters & US Population

Estimated odds ratios (95% CI) for self-reported CVD diagnoses in all firefighters compared with the US population by exposure status

	Stroke/CAD[1]	Stroke[2]	CAD[3]
WTC-exposed	0.81 (0.73, 0.90)	0.62 (0.51, 0.74)	0.86 (0.77, 0.97)
Non-exposed	0.71 (0.62, 0.82)	0.66 (0.51, 0.84)	0.74 (0.64, 0.87)
US Population	ref	ref	ref

Estimated odds ratios (95% CI) for self-reported CVD diagnoses in all firefighters compared with the US population by exposure level

	Stroke/CAD[1]	Stroke[2]	CAD[3]
High exposure	0.96 (0.80, 1.14)	0.68 (0.48, 0.95)	1.02 (0.84, 1.24)
Moderate exposure	0.86 (0.76, 0.98)	0.62 (0.49, 0.78)	0.91 (0.79, 1.04)
Low exposure	0.67 (0.58, 0.79)	0.54 (0.40, 0.72)	0.72 (0.61, 0.86)
US Population	ref	ref	ref
P for trend	P<0.0001	P<0.0001	P<0.0001

[1]Includes any report of stroke or CAD
[2]Includes diagnoses of stroke/CVA or TIA
[3]Inclused diagnoses of CAD, MI, or angina

Age, race, and BMI were included in the model (complete case analysis, n=12,516)

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Validated Cardiovascular Disease

- Self-report can be a significant limitation
- Using medical record diagnoses, we evaluated the agreement between self-reported diagnoses and confirmed diagnoses.
- The agreement was similar to both WTC and non-WTC published estimates for each condition, suggesting that self-report bias would be non-differential

Cardiovascular Disease

Summary

- Increasing WTC exposure was positively associated with two CVD outcomes comparing WTC-exposed firefighters to non-WTC-exposed firefighters
- Compared with the NHIS population, all firefighters had lower odds of all three CVD outcomes (strong healthy worker effect for CVD)
- These results show a consistent message to prior findings within FDNY WTC-exposed firefighters
  - Cohen et al. 2019 (JAMA Open) used medical record-validated diagnoses to examine long-term CVD risk
  - Findings suggest a significant association between greater WTC exposure and long-term CVD risk

Impact
How the CFHS serves WTC-exposed members

- Improves understanding of the extent to which WTC exposure is associated with various health conditions by controlling for the firefighting-occupation confounder
- Important to have this comparison group, since general population comparisons shown to be biased by healthy worker effect
  - E.g. underestimated association between WTC exposure and asthma
    - True WTC and asthma association was *higher* when controlling for the firefighter occupation because non-WTC-exposed firefighters had lower odds of asthma than the general population.

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Future research

- More years of follow-up with future cancer and death linkages
- Additional firefighters (depts and those hired after 2009)
- Follow-up survey

Acknowledgments

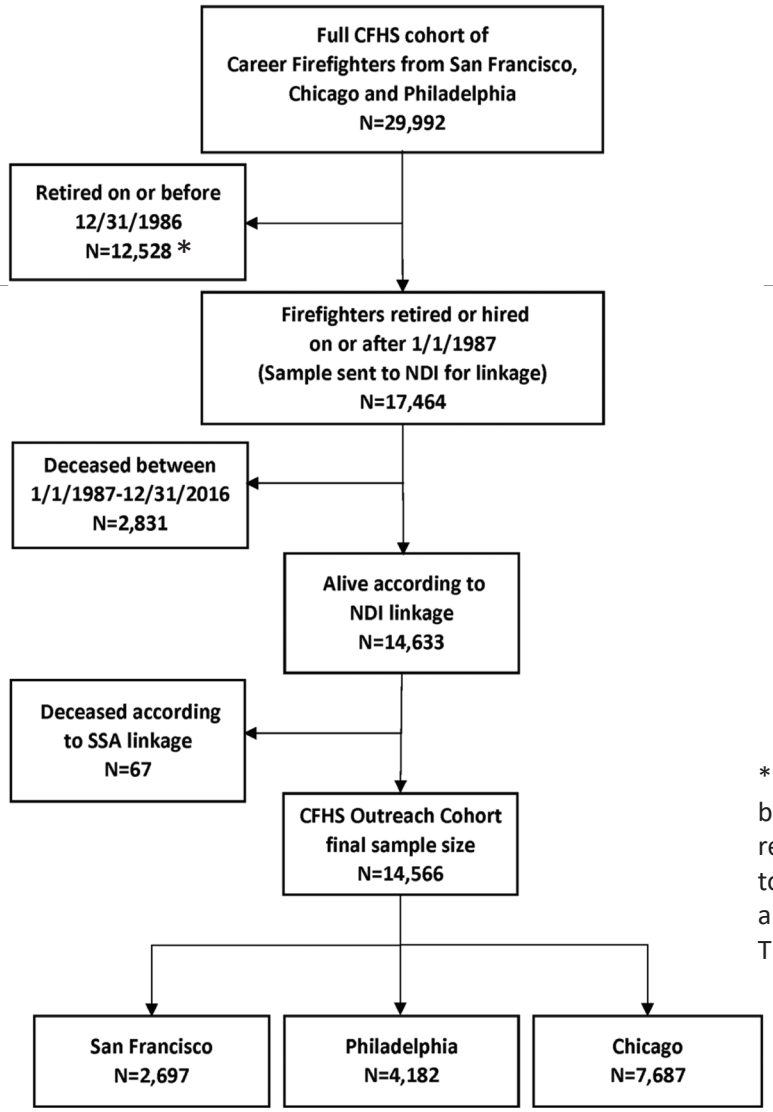
Thank you to the study participants, participating cities/fire departments, and the FDNY WTC Health Program study team.

Extra Slide


FIRE DEPARTMENT
CITY OF
NEW YORK


FDNY
CFD
PFD
SFFD
Career Firefighter
Health Study
WTC Health Program

Flow chart for identifying CFHS Outreach Cohort for the survey.



* FDNY's electronic database begins in ~1987 so firefighters who retired before then were not sent to NDI as they would not be analyzed in comparison to FDNY. This also reduced expenses.

Zeig-Owens et al *Am J Ind Med*. 2021.

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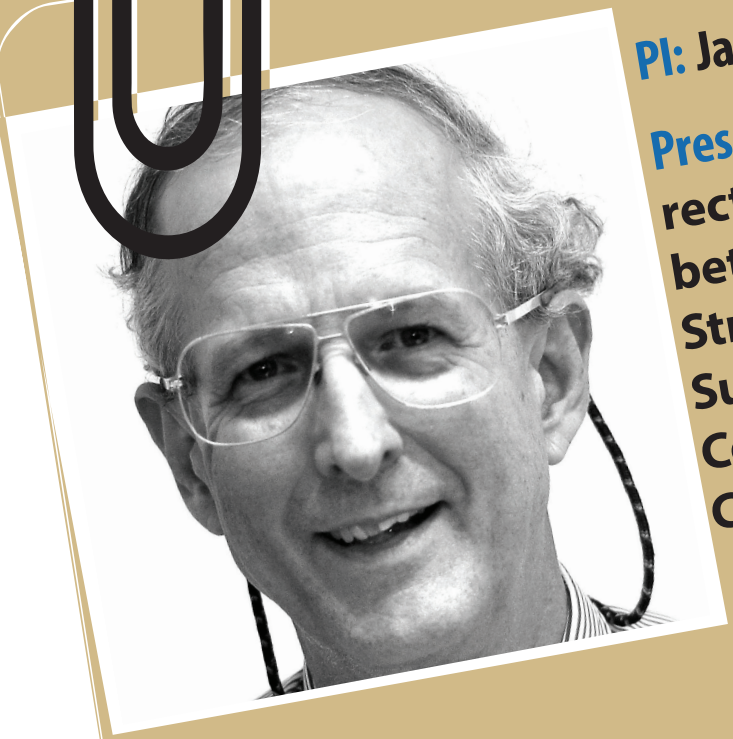
World Trade Center (WTC) Health Program



PI: James Cone, MD, MPH

Presentation Title: The Bidirectional Relationship between Posttraumatic Stress Symptoms and Social Support in a 9/11-Exposed Cohort: A Longitudinal Cross-Lagged Analysis

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Bidirectional Relationship between Posttraumatic Stress Symptoms and Social Support in a 9/11-Exposed Cohort:

A Longitudinal Cross-Lagged Analysis

Presented by James Cone, ***MD, MPH Medical Director, WTCHR***

Introduction

- Following the **September 11, 2001**, attacks on the **World Trade Center**, the prevalence of **PTSD** has varied from ***3.8%*** to ***29.6%*** depending on the population and time period.
- A growing body of literature has focused on social context as a possible protective factor against the development of or worsening of ***9/11*** **PTSD**.

Liu SY, Li J, Leon LF, Schwarzer R, Cone J. The Bidirectional Relationship between Posttraumatic Stress Symptoms and Social Support in a 9/11-Exposed Cohort: A Longitudinal Cross-Lagged Analysis. Int. J. Environ. Res. Public Health **2022**, 19, 2604. https://doi.org/10.3390/ijerph19052604

PTSD and Social Support

- Previous research shows conflicting results about the relationship between **PTSD** and social support.

- This study analyzes the time-varying relationship between **PTSD** symptoms and social support over **14** years among **WTC Health Registry** enrollees.

- **GOAL:** Is there a cross-lagged effect between **PTSD** and social support after controlling for prior levels of both variables?

Social Support

- **Emotional support**: Have someone in your life who shows verbal or nonverbal care towards you

- **Tangible support**: Have someone in your life who gives you concrete, direct assistance

Methods

- Cross-lagged structural equation modeling
- Lavaan package in **R**
- Sub-analyses stratified by enrollee group ***(rescue/recovery workers vs. community members)*** and by type of perceived social support ***(emotional vs. tangible)***.

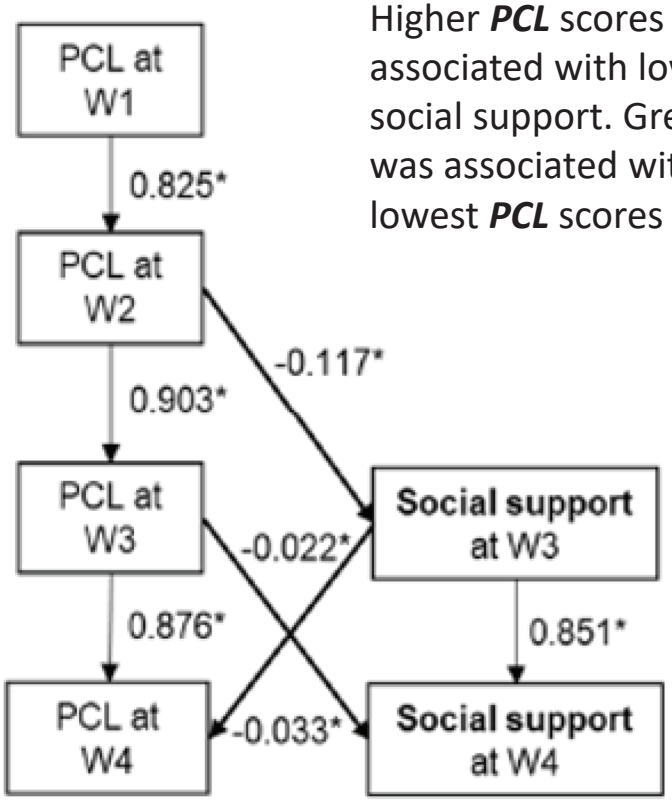
Study Population

Inclusion: **71,426** exposed enrollees in the **WTCHR**, of whom **27,959** participated in all three follow-up surveys, **W2**-**W4**.
Exclusion: Incomplete data on social support ***(n=1661)*** and PCL ***(n=2948),*** **pre-9/11** diagnosed **PTSD** ***(n=185).***

Participants in all three follow-up surveys more likely to be male, non-Latino White, and to have higher educational attainment.

Participants were also slightly older at **W1** ***(mean age 45.6 years (SD: 10.8)*** vs. ***43.5 (12.8))*** and had lower mean PCL scores than non-participants ***(29.6 (SD: 12.4)*** **vs.** ***31.5***

Results

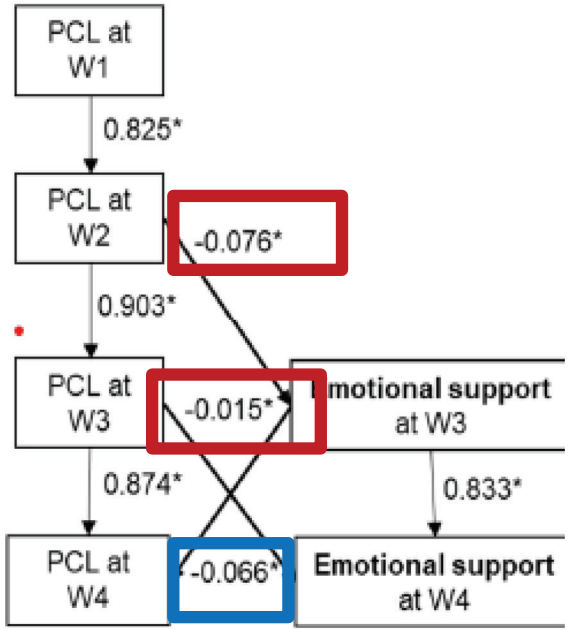


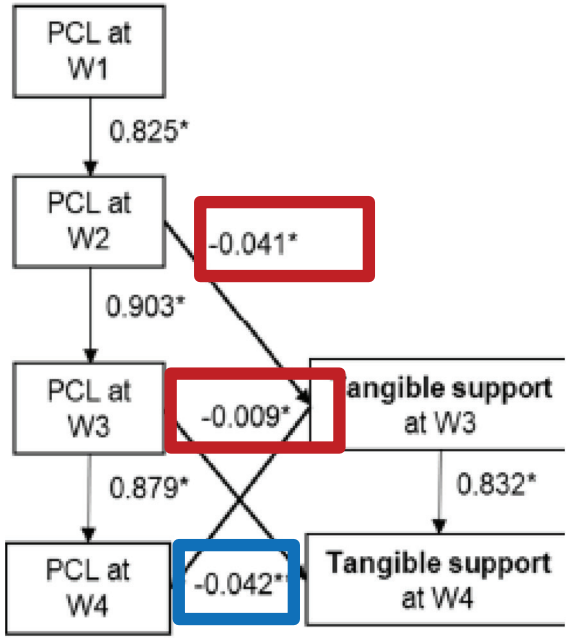
Higher ***PCL*** scores for ***PTSD*** was associated with lower subsequent social support. Greater social support was associated with subsequent lowest ***PCL*** scores for ***PTSD***.

Cross-lagged models for PTSD and social support through four waves in the full sample, WTCHR, 2003–2016 (n = 23,165)

Results (Larger Effects)

Larger effect estimates for ***PCL*** scores of ***PTSD*** to subsequent reported support were found for Emotional Support compared to Tangible Support.

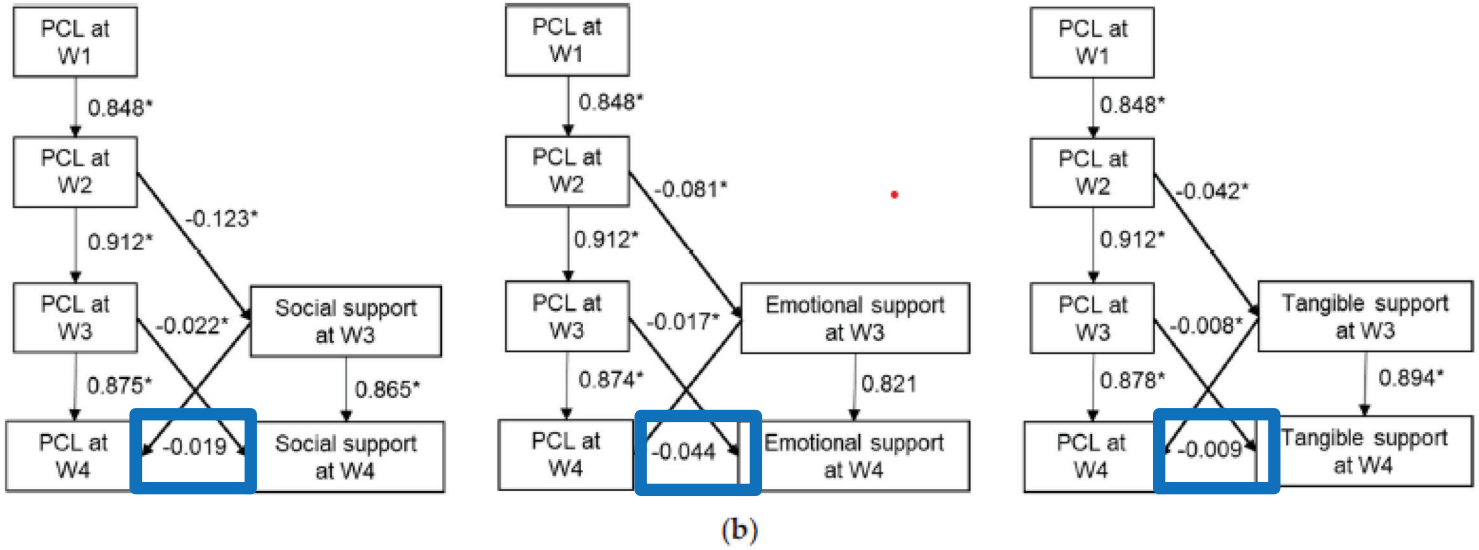




Cross-lagged models for PTSD and social support through four waves in the full sample, with Emotional and Tangible Support WTCHR, 2003–2016 (n = 23,165)

Results

Similar patterns where PCL scores of PTSD was associated with decreased subsequent support found in rescue/recovery workers.
NO statistically significant association between W3 reported support and W4 PCL scores of PTSD for rescue/recovery workers.



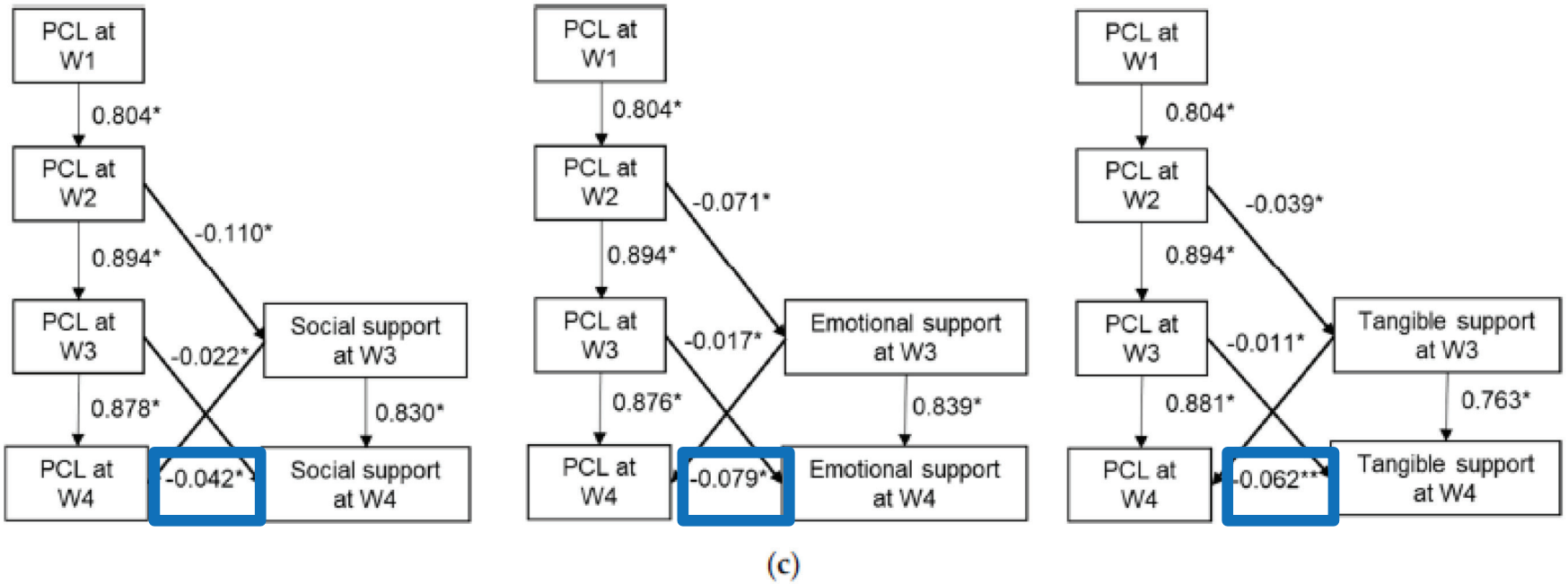
(b)

Rescue/recovery workers, WTCHR, 2003–2016 ***(n = 11,137)***

Results

Similar patterns where PCL scores of PTSD was associated with decreased subsequent support found in rescue/recovery workers.

Statistically significant association between W3 reported support and W4 PCL scores of PTSD among community member's subsample.



Cross-lagged models for PTSD and social support through four waves among community members, WTCHR, 2003–2016 (n = 12,028)

Discussion

- Previous waves' ***PTSD*** symptom scores were highly associated with ***PTSD*** symptoms measured in subsequent waves.

- Same temporal pattern for social support.

- Increase in ***PTSD*** symptom scores associated with subsequent lower social support.

- Social support buffered ***PTSD*** symptoms over time, especially among community members.

Discussion (continued on next page)

- Greater effects of ***PTSD*** on emotional support than tangible support

- Greater effects in community members than ***rescue/recovery*** workers.

Discussion (continued from previous page)

- Both the social erosion and social causation processes may be simultaneously occurring.
- Erosion model supported by our finding of an inverse association between **PTSD** symptoms and subsequent social support.
- Social causation model supported by our finding of an inverse association between social support at **W3** and **PTSD** symptoms at **W4**.

Impact

- Clinicians should consider the role of social support in **PTSD** treatment.

Future Research Needs

- Better understanding of the role different types of social support play in **PTSD** over time.

- Better understanding of whether effects differ according to severity of **PTSD**.

Acknowledgements

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- Enrollees of the World Trade Center Health Registry.
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Questions?

- Thanks!

PI: Mary Kowalchyk, MA

Presentation Title: Perceived Ability to cope, Social Support, and PTSD Symptom Severity

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Icahn School of Medicine at Mount Sinai

Perceived Ability to Cope, Social Support, and PTSD Symptom Severity

Presenter: **Mary Kowalchyk, MA**

Funding: **CDC-NIOH grant U01 OH 010729 (MPIs Adriana Feder, MD, and Robert H. Pietrzak, PhD, MPH)**

Disclosures

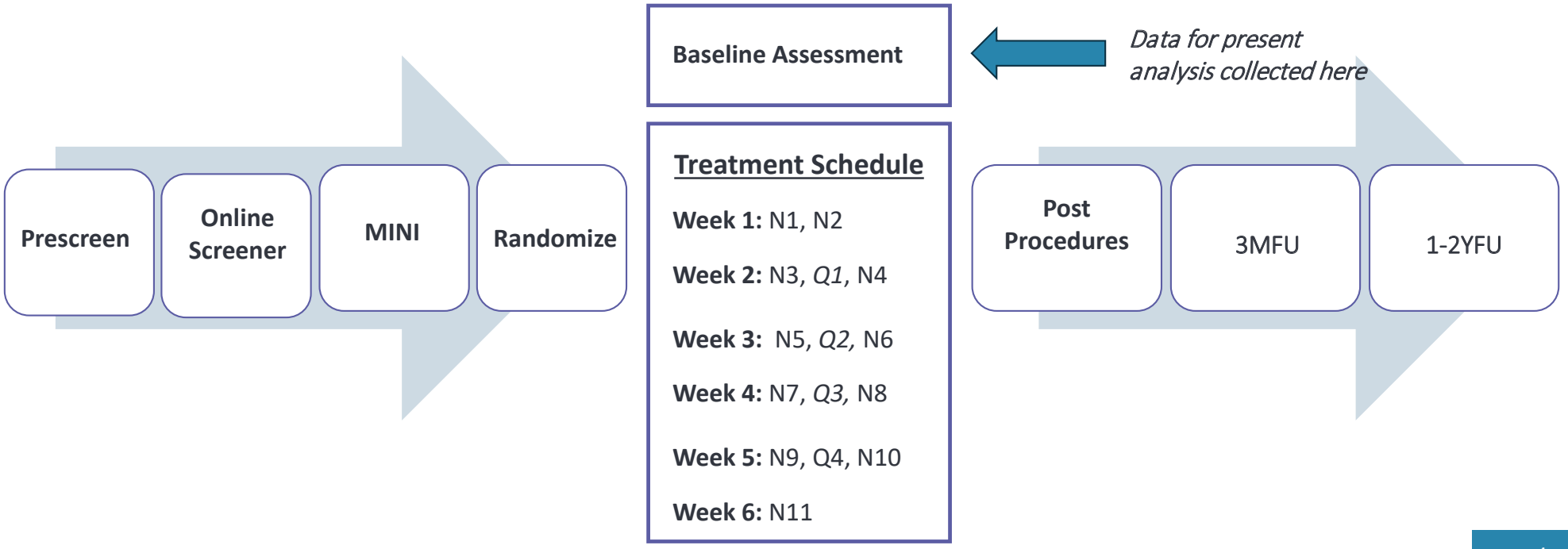
Nothing to disclose

Internet-based psychotherapies for PTSD symptoms in WTC responders and survivors

https://images.app.goo.gl/BbQYVPdLUmAj6iGe7

- A clinical trial comparing two different forms of online writing therapy designed for WTC responders and survivors
- **Two treatment arms**
    1. Integrative Testimonial Therapy (ITT) – designed to help the patient integrate the trauma into their own biography through trauma exposure writing narratives
    2. Modified Present-Centered Therapy (MPCT) – active control condition; designed to help the patient develop problem solving skills and solutions to present day issues they may be experiencing (i.e. family problems, work struggles, etc.)
- Each treatment is designed to last for 6 weeks and involves 11 writing narratives. Patients are instructed to complete 2 narratives per week, each lasting 45 minutes, following therapist written instructions and receiving written feedback.

Online Therapy Study Flow



Study Battery at Baseline

- General Self-Efficacy Scale
- Purpose in Life Scale – Short Form
- MOS Cognitive functioning (past week)
- PCL-5 (past week)
- PTGI
- GAD-7 (last weeks)
- BDI-II : Question 22 is the adapted item from the S-HTS
- Questions about medications, alcohol and drugs
- Trauma History Screen **Used as a control variable*
- MOS Social Support Survey
- SF-8 (past week)
- Endicott QOL (past week)
- Endicott work productivity (for those currently working) (past week)
- Future Self-Continuity Measure
- Centrality of Event Scale
- Perceived Ability to Cope with Trauma (PACT) Scale
- Sentence Completion for Events in the Future Test (SCEFT)
- The Relationships Questionnaire (RQ)

Perceived Ability to Cope with Trauma (PACT) Scale

- Bonanno et al., 2011
- 20-item self-report questionnaire designed to assess one's perceived ability to utilize either **trauma-focused coping** strategies or **forward-focused coping** strategies following a traumatic event. This scale also assesses one's **coping flexibility.**
  - Two subscales for each coping type:
    1. **Trauma-focused coping subscale:** measures one's ability to face feelings and cognitions relating to a traumatic event
    2. **Forward-focused coping subscale:** measures one's ability to maintain goals and plans following a traumatic event
    - Higher scores on these subscales indicated greater perceived ability to engage in these coping strategies.
  - Coping flexibility score
    - Measures one's ability to engage in both forward-focused coping and trauma-focused coping strategies following a traumatic event.
    - Calculated by: (forward-focused + trauma-focused) - |forward-focused – trauma-focused|
    - A higher flexibility score indicates greater perceived ability to engage in both trauma- and forward-focused coping strategies.

Other Variables of Interest

- **Social Support**
  - The Medical Outcomes Study – Social Support Survey ***(MOS-SSS; Sherbourne & Stewart, 1991)***
    - Abbreviated 5-item version of the MOS-SSS was used. These questions were self-report on a 5-point Likert scale with the average of the items measuring social support.
- **Posttraumatic Stress Disorder (PTSD)**
  - PTSD Checklist for DSM-5 ***(PCL-5; Weathers, et al., 2013)***
    - 20-item self-report rating scale corresponding to the DSM-5 symptom criteria for PTSD.
- **Trauma History**
  - Trauma History Screen ***(THS; Carlson et al., 2011)***
    - Used to assess exposure to 14 different lifetime traumatic events
    - We also included the NHRVS to assess exposure to life-threatening illness or injury
    - Summation of potentially traumatic events endorsed, ranging form 0-15, was used as index for lifetime traumatic burden

Existing Literature

PTSD Prevalence in WTC Responders and Survivors following 9/11

- 19% in 9/11 survivors
- 9.3% of police responders have full PTSD *(17.5% have subthreshold PTSD)*
- 21.9% of nontraditional responders have full PTSD (24.1% have subthreshold PTSD)

Perceived Ability to Cope with Trauma

- Greater perceived coping flexibility was related to lower depressive and PTSD-severity symptoms in trauma-exposed Korean adults (Park et al., 2015)
- Combat veterans with PTSD had lower PACT scores than those without PTSD and showed relationships between the trauma- and forward-focused PACT scores and indices of psychological difficulties (Bartholomew et al., 2017).

Social Support & PTSD

- Social support has been shown to be a significant factor in mitigating PTSD symptoms in multiple trauma populations, including WTC responders and survivors.

PACT & Social Support

- While these factors have been investigated independently in relation to PTSD, literature is lacking in the combined relationship between these factors and PTSD.

Sample Characteristics

n = 100	n or mean	% or SD
Age	54.2	9.8
Male sex	60	60%
Race-Ethnicity		
White	62	62%
African American	10	10%
Hispanic	17	17%
Asian	2	2%
Other/Unknown	9	9%
Education		
Some High School/High School Graduate	7	7%
Some College	34	34%
College Graduate	36	36%
Graduate School	23	23%
Marital Status		
Single	13	13%
Married/Partnered	73	73%
Widowed/Divorced/Separated	14	14%
WTC Participant Type		
Traditional Responder (e.g., Police Officer)	46	46%
Non-traditional Responder (e.g., Construction Worker)	24	24%
Survivor	30	30%
Number of lifetime traumas	4.7	2.8
Total PCL-5 score	27.7	13.4
Met for current depressive episode on MINI	23	23%
Met for generalized anxiety disorder on MINI	17	17%
Forward-focused coping score	4.4	1.1
Trauma-focused coping score	4.4	1.2
Coping Flexibility score	70.7	19.1
Perceived social support score	3.2	1.0
History of mental health treatment	76	76%
Current Psychotropic Medication Use	21	21%

Analyses & Results

Results of linear regression analysis predicting severity of PTSD symptoms

	β	t	p
Age*	0.19	2.09	0.039
Lifetime traumas	0.08	0.87	0.39
Lifetime MH treatment	-0.13	1.38	0.17
Trauma-focused coping	-0.02	0.15	0.88
Forward-focused coping	0.13	0.83	0.41
Coping flexibility	-0.01	0.15	0.88
Social support	-0.05	0.26	0.79
Trauma-focused coping x Social support	-0.11	0.64	0.52
Forward-focused coping x Social support***	-0.35	3.81	<.001
Coping flexibility x Social support	0.03	0.28	0.78

Significant association: *p<0.05; ***p<0.001.

- Bivariate correlations were conducted to examine associations between perceived ability to cope with trauma, perceived social support, and PTSD symptom severity. A multivariable linear regression analysis was then conducted to identify main and interactive effects of perceived coping ability and social support in predicting PTSD symptom severity.

- Controlling for participant age, life-time trauma exposure, and mental health treatment history (sex and responder type were not correlated with PTSD severity), higher forward-focused coping (r = -0.24) and perceived social support (r = -0.32) were associated with lower PTSD symptoms severity; trauma-focused coping (r= -0.14) and flexibility (r= -0.17) were not significantly associated with PTSD symptom severity (p's>0.09).

Analyses & Results

- Perceived social support was found to significantly moderated the relationship between forward-focused coping and overall PTSD symptom severity (β= -0.36), as shown in the figure.
- Greater engagement in forward-focused coping was associated with lower PTSD symptom severity among participants who reported higher levels of perceived social support.

Moderating Effect of Social Support on Forward-Focused Coping and Overall PTSD Symptom Severity

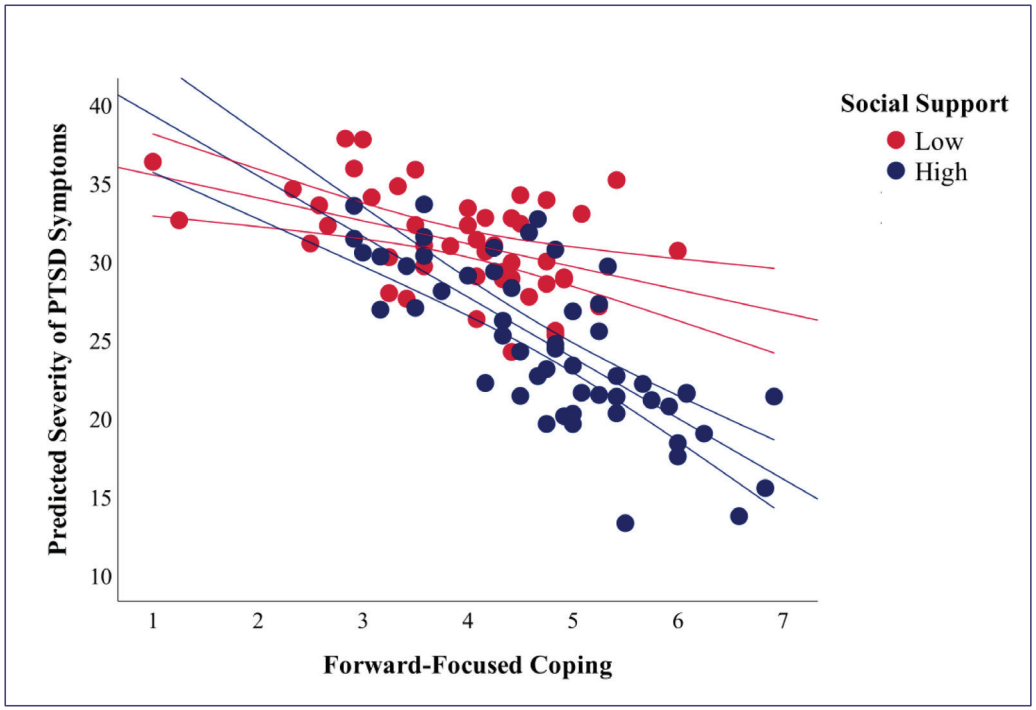


Figure shows the moderating effect of social support (indicated by the red and blue dots) on forward-focused coping (forward-focused subscale scores on the x-axis) and overall PTSD symptom severity (PCL-5 scores on the y-axis).

Conclusions

- It is clear from the results that social support plays a crucial role in moderating PTSD symptom severity. Without social support, forward-focused coping strategies would not be significantly related to over PTSD severity.

- It is important for us to understand what this relationship means. Are those who engage in forward-focused coping strategies more likely to elicit social support? OR do those who elicit social support feel more capable of looking towards the future to move past a traumatic event?

Future Directions

- From a clinical perspective, these findings should be studied more closely in a controlled manner to determine their effectiveness in treating PTSD. However, these findings preliminarily suggest that PTSD treatment modalities should aim at enhancing forward-focused coping strategies and social support to effectively reduced PTSD symptom severity.

- For future research directions, there are several options that could be explored. For instance, clinical research could investigate the implications of social support building strategies in those with greater perceived forward-focused coping on PTSD symptom severity. From a computational approach, researchers could utilize predictive modeling to further conceptualize the relationship between perceived coping strategies and efficacy of treatment modalities to inform clinical decision making.

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Thank you!

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World Trade Center (WTC) Health Program

PI: Rebecca Schwartz, PhD and Theodoros Zanos, PhD

Presentation Title: Transcutaneous Auricular Vagus Nerve Stimulation to Reduce Post Traumatic Stress Disorder (PTSD) Symptoms in World Trade Center Responders

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Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) to Reduce Post Traumatic Stress Disorder (PTSD) Symptoms in World Trade Center (WTC) Responders

Rebecca Schwartz, PhD
Theodoros Zanos, PhD

Funding for the study provided by U01 with CDC/NIOSH

Background

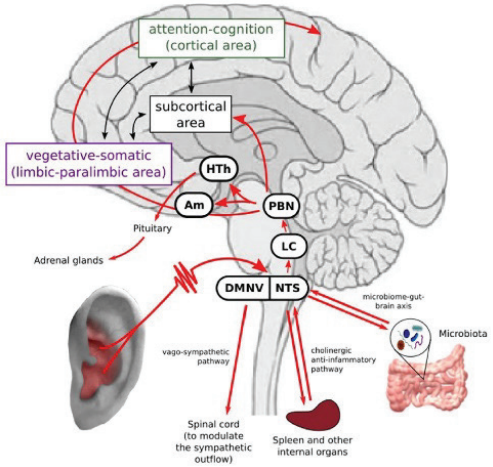
- Approximately 40,000 to 60,000 first responders provided emergency services at Ground Zero
- PTSD remains the most prevalent MH diagnosis
- While many EBTs exist for PTSD (e.g. PE, CPT, EMDR), high dropout rates (30%) are observed across treatments for PTSD; 18% among active treatments in clinical trials for PTSD
  - Reasons include stigma, clinician availability and tedious treatment sessions
- In 2017, only 40% of responders and 20% FDNY responders who are certified for MH treatment received any form of MH care at the WTCHP
- Need to develop additional treatment for those already engaged in MH care to reduce PTSD symptoms

Transcutaneous Vagus Nerve Stimulation (taVNS) as a Viable Option to Address PTSD Symptoms

- taVNS supplies electrical signals to the cymba conchae region of the auricle, a region innervated exclusively by the auricular branch of the vagus nerve.
- It shows promise in treating PTSD including:
  - down-regulation of the inflammatory reflex through adjustment of the microbiome-brain-gut axis
  - suppression of inflammation
  - modulation of the activity of mood-related brain centers
  - impacts on sympathetic tone and hyperarousal
  - enhancement of consolidation of extinction memories
  - rapid reduction of anxiety and PTSD-associated symptoms

taVNS has shown promising results in those with:

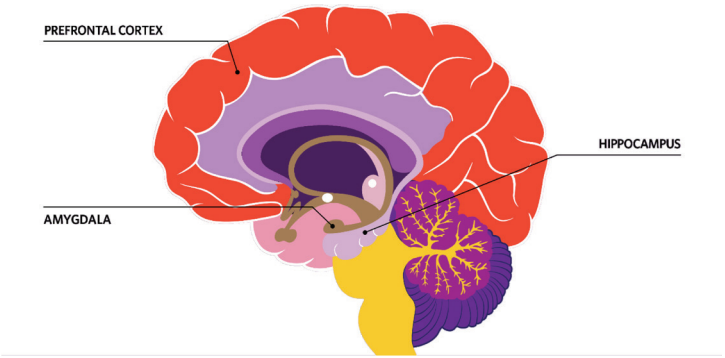
- refractory epilepsy
- patients with inflammatory conditions
- pre-diabetes
- tinnitus
- depression
- oromotor dysfunction
- rheumatoid arthritis
- stroke



Transcutaneous Vagus Nerve Stimulation (taVNS) as a Viable Option to Address PTSD Symptoms.

- PSTD symptomology:
  - intrusive thoughts or memories of the event
  - difficulties with emotional and psychological regulation
  - becoming easily startled
  - avoiding situations which are connected to the trauma
  - emotional numbness
  - detachment from others

- It can potentially benefit treatment of PTSD due to its projections to brain areas like the amygdala and hippocampus, by downregulating activity in these areas which are known to be related to stress responses and hyperarousal.



The innovation of this work involves applying the latest advances in non-invasive bioelectronic medicine technology to a population with PTSD.

taVNS Device

The taVNS device is Nesos MAUI PROTECT System– a wearable, external stimulator that generates electrical pulses transcutaneously delivered to the auricular branch of the vagus nerve through the ear canal.

Earpieces

The earbuds are designed to transcutaneously-deliver electrical stimulation to the external ear. Each earbud is manufactured using ear molds unique to each user's ears.

Stimulator

Delivers charge-balanced, current-controlled, biphasic, square waves to electrodes (in the earbuds) in contact with the skin of the user's ear.

Smartphone/App

The APP allows the user to turn stimulation ON/OFF, monitor sessions, and notify the user of poor electrode/skin contact.

Data Dashboard

The data dashboard allows the study staff to track compliance days and percentages for all participants.

Aim 1

Objectives

- To conduct a formative phase needs assessment in order to understand responders' perceptions of mental health needs and barriers/facilitators to engagement in mental health care
- To conduct a formative phase evaluation in order to ensure that the taVNS intervention and the pilot study methodology are feasible, relevant and acceptable for use with 9/11 WTC responders with PTSD using a focus group

Eligibility Criteria

- WTCHP responder who agreed to be contacted to participate in research
- Diagnosed as having PTSD, as per the WTCHP certification criteria as indicated by the WTC GRDC
- Elevated symptoms of PTSD, as per the PCL-S; score of >44 during an annual monitoring visit between 2018—2020

Participant Recruitment

- Investigators received a list of those eligible for recruitment based on the three inclusion criteria from the Queens WTCHP
- List was randomized using the RAND syntax in Excel
- A research coordinator contacted those on the list by phone and email until 10 people were recruited.
- Recruited participants provided informed consent in October 2021

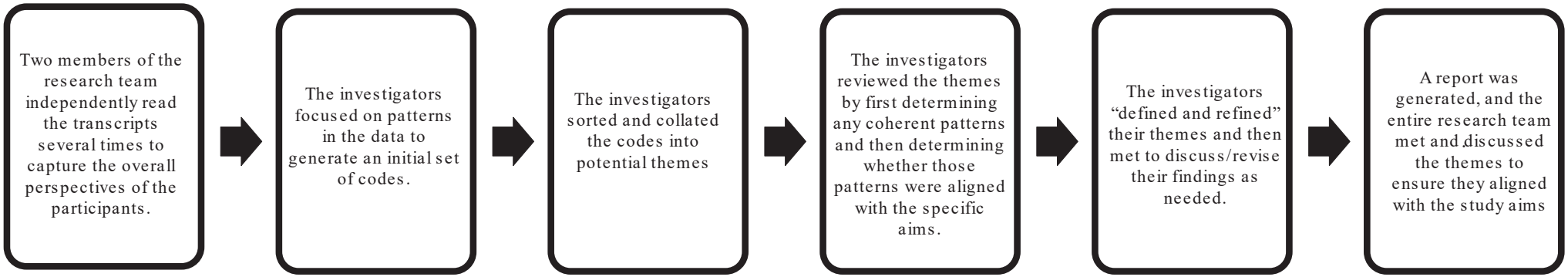
Focus Group Procedure

- Facilitated by one member of the research team with a secondary co-facilitator and a note-taker
- A semi-structured focus group discussion guide was utilized, composed of open-ended questions that were informed by the research focus and aims, and guided by previous research.
- Sample questions include:
    - Can you please describe what you see as WTC responders' greatest needs currently as they related to mental health?
    - Please describe factors that might be barriers for a responder to engage in mental health care.
    - What factors might make it easier for responders to engage in mental health care?
- Participants were then shown a demonstration of the taVNS device and usage of the Nesos System and asked to give feedback about the device and study methodology.

Qualitative Analysis

The focus group discussion was audio-recorded and professionally transcribed verbatim.

An inductive thematic analysis was used to analyze the transcribed focus group discussion.



Results

- n = 6
- 3 male ; 3 female
- Age Range: 51 - 77 years old

Theme 1: Mental Health needs; barriers/facilitators to engaging in mental health care

- Subthemes:
  - Mental health difficulties continue to be prevalent (comorbidities; employers not taking MH seriously)
  - Systemic challenges to getting access to treatment for PTSD and other mental health problems (stigma, retaliation; lack of access)
  - Suggestions to overcome barriers to mental health treatment (e.g. traditional talk therapy → holistic approaches like acupuncture or yoga/meditation ; transportation vouchers)

Theme 2: Device Feedback

- Subthemes:
  - Initial reactions (enthusiasm for the novelty, convenience and transportability of device)
  - Concerns about interactions with other illnesses or comorbidities (effect on seizures and tinnitus; investigators reviewed exclusion criteria)
  - Questions on peripherals of device (mobile connectivity and Wi-Fi; accurate setup)

Theme 3: Feedback on Research Methodology

- Subthemes:
  - Adjustments to or clarification of screening process (undergo additional PTSD screening despite current diagnosis; who has access to info)
  - Confidentiality concerns (device usage tracking; privacy concerns)
  - Difficulties with questionnaires (repeated survey measures; survey fatigue)
  - Challenges to participation (time constraints; veracity on surveys &usage)
  - Recommendations for increasing participation (upfront about compensation; reduce notification fatigue; emphasize portability)

Quotes

"I don't even ride a train because of anxiety. I get -- I get fear...I start sweating. I can't board the train."

"And as -- as time goes by, it gets -- it gets worse. It doesn't get any better. My problem didn't start for a few years after, and then when it -- when it started, the -- the sounds and -- and it was so horrible and so loud, and I hear the ... from that and it gets louder and louder and I have to get up. I can't sleep."

"There is a stigma with mental health in general, but there's a stigma at least from my standpoint in the law enforcement."

"One other thing is I think that they don't have enough things available for us to do besides give us drugs and talk therapy."

Quotes (continued)

"… So, I think that's a big barrier is when you have to go to somebody's office, and you have to travel and you have to get off the work, you have to -- like I could do it on a lunch break, I can, you know, you can really do it anywhere and that's huge, huge."

Manuscript submitted to IJERPH's Special Issue "To Mark the 20th Anniversary of 9/11: Long-Term Health Effects" based on findings from the focus group

International Journal of *Environmental Research and Public Health*

MDPI

Article

Understanding Mental Health Needs and Gathering Feedback on Transcutaneous Auricular Vagus Nerve Stimulation as a Potential PTSD Treatment among 9/11 Responders Living with PTSD Symptoms 20 Years Later: A Qualitative Approach

Rebecca M. Schwartz [1,2,3,4], Pooja Shaam [1,2,3,*], Myia S. Williams [2,4,5], Molly McCann-Pineo [1,2,4], Laura Ryniker [1,2,3], Shubham Debnath [6] and Theodoros P. Zanos [2,4,6]

Schwartz, R. M., Shaam, P., Williams, M. S., McCann-Pineo, M., Ryniker, L., Debnath, S., & Zanos, T. P. (2022). Understanding Mental Health Needs and Gathering Feedback on Transcutaneous Auricular Vagus Nerve Stimulation as a Potential PTSD Treatment among 9/11 Responders Living with PTSD Symptoms 20 Years Later: A Qualitative Approach. International journal of environmental research and public health, 19(8), 4847. https://doi.org/10.3390/ijerph19084847

Aim 2

Objectives

- To conduct a randomized, double-blind placebo controlled parallel-design pilot study with 30 WTC responders affiliated with the WTCHP who have PTSD to determine whether the taVNS intervention and efficacy study methodology are feasible and acceptable for use with this population.

Eligibility Criteria

- WTCHP responder who agreed to be contacted to participate in research
- having PTSD as per DSM criteria indicated by the GRDC
- having elevated PTSD symptoms, indicated by a PCL-S score > 44 during an annual monitoring visit between 2018-2020
- having a score of 33 or greater on the PCL-5 to determine current symptomatology
- meeting diagnostic indication of PTSD using a Clinician-Administered PTSD Scale (CAPS), which is a clinical interview assessment

Participant Recruitment

- Identify and randomize eligible participants
- Contact eligible participants on the list by phone and/or email.
- Participants complete the CAPS interview and PCL-5 questionnaire to determine eligibility for RCT.
- Recruit, consent, enroll and randomize 30 participants
  - Staggered appointments for enrolled participants at FIMR for device fitting
  - Baseline visit
  - 8 weeks post baseline visit

Assessments and Measures

Biological Assessments

- Electroencephalogram (EEG)
- Electrocardiogram (ECG)
- Beat-to-beat blood pressure (Human Non-invasive Blood Pressure)
- Galvanic skin response (GSR)
- Pupil Dilation
- Facial & Neck Electromyography (EMG electrodes)
- Respiratory rate
- Skin Temperature
- Blood Draw (TNF α, Interleukin (IL), C Reactive Protein (CRP), cortisol, and alpha amylase)

*Autonomic battery tests will also be conducted

Mental Health Measures

- PTSD Symptom Score (Baseline & 8-week follow-up)
  - PCL-5 (range = 0-80)
- Anxiety Symptom Score (Baseline & 8-week follow-up)
  - GAD-7 (range = 0-21)
- Depression Symptom Score (Baseline & 8-week follow-up)
  - PHQ-9 (range = 0-27)
- Sleep Score (Baseline & 8-week follow-up)
  - Pittsburg Sleep Quality Index (range = 0-21)
- taVNS Satisfaction and Usefulness Questionnaire (8-week follow-up only)

*incl. demographic information, occupation and

Study Endpoints

Feasibility	Acceptability	Mental Health and Biologic Endpoints
Feasibility will be evaluated as: • rates of recruitment (per month) • adherence to the taVNS intervention • 8-week retention • duration and completion rate of study assessments Ability to recruit 75% of eligible participants who were approached and adherence to the intervention and retention rates of 70% each	Acceptability will be evaluated by assessing: • the time to completion of questionnaires • percentage of missing data from questionnaires • the time to completion of the biological data and blood draw • the rate of refusal of biologic measurements and blood draw • score on the taVNS Satisfaction and Usefulness Questionnaire	Measured at the baseline and 8-week follow-up time point Baseline visit: • MH surveys, blood draw, biological measures (10 minutes before therapy), and then the first therapy 8 Week Follow-up: • MH surveys, final therapy, blood draw, and then biological measures (approx. 10 minutes after therapy) Assess measurement quality, amount of missingness/non-response, length of measurement collection, and costs

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World Trade Center (WTC) Health Program

PI: Adriana Feder, MD

Presentation Title: Updates on Ketamine Treatment for Chronic PTSD

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Icahn School of Medicine at Mount Sinai

Updates on Ketamine Treatment for Chronic PTSD

Adriana Feder, MD

Professor of Psychiatry

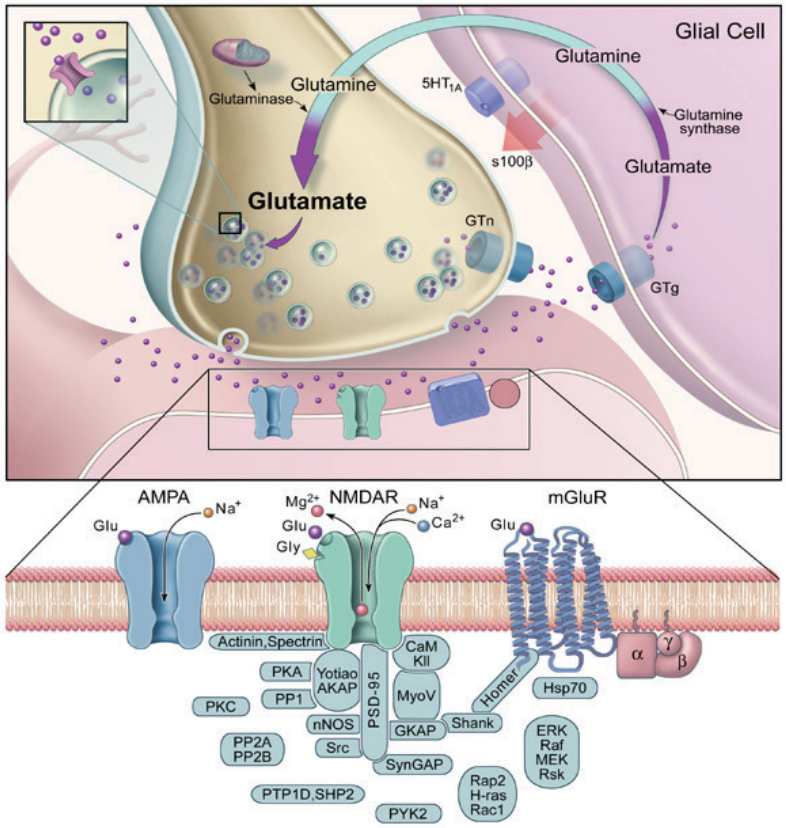
Director, Trauma and Resilience Program

Co-Director, Ehrenkranz Laboratory for the Study of Human Resilience, Depression and Anxiety Center

Disclosure:

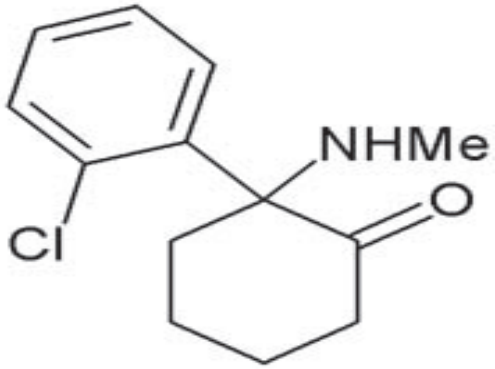
I am named co-inventor with Dennis Charney on an issued patent in the **United States** and several issued patents outside of the United States, filed by the **Icahn School of Medicine at Mount Sinai** for the use of ketamine as therapy for ***posttraumatic stress disorder***; this intellectual property has not been licensed.

Ketamine Pharmacology and **NMDA** Glutamate Receptor



Receptor Subunit Types

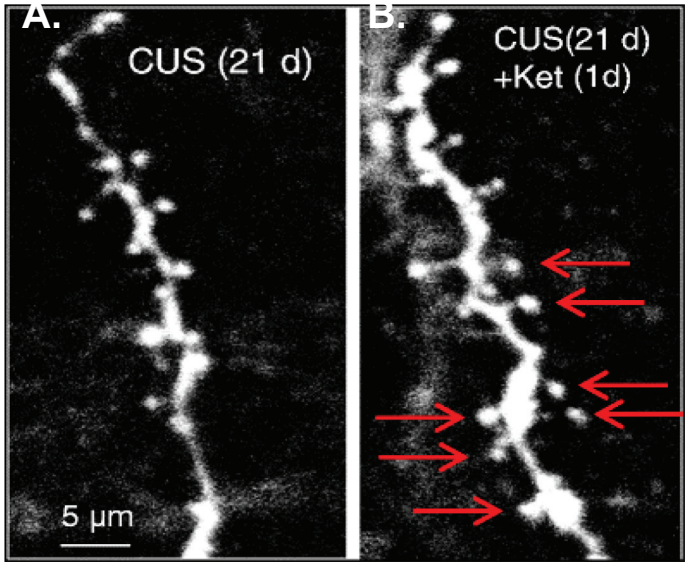
Ionotropic			Metabotropic		
NMDA	AMPA	Kainate	Group I	Group II	Group III
NR1 NR2 A-B-C-D NR3 A-B	GluR 1 GluR 2 GluR 3 GluR 4	GluR 5 GluR 6 GluR 7 KA 1 KA 2	mGlu 1 a-b-c-d mGlu 5 a-b	mGlu 2 mGlu 3	mGlu 4 a-b mGlu 6 mGlu 7 a-b mGlu 8 a-b



- Non-competitive high-affinity NMDA receptor antagonist
- **IV ketamine:** Demonstrated antidepressant efficacy in patients with TRD; rapid response
- Repeated IV infusions are necessary to maintain improvement
- Esketamine ***(Spravato),*** its S-enantiomer, is **FDA**-approved for intranasal administration as adjunct to oral antidepressant for **TRD** and for **MDD** with acute suicidal ideation or behavior

Animal Model of Chronic Stress

Rapid Reversal of Synaptic Atrophy by Ketamine

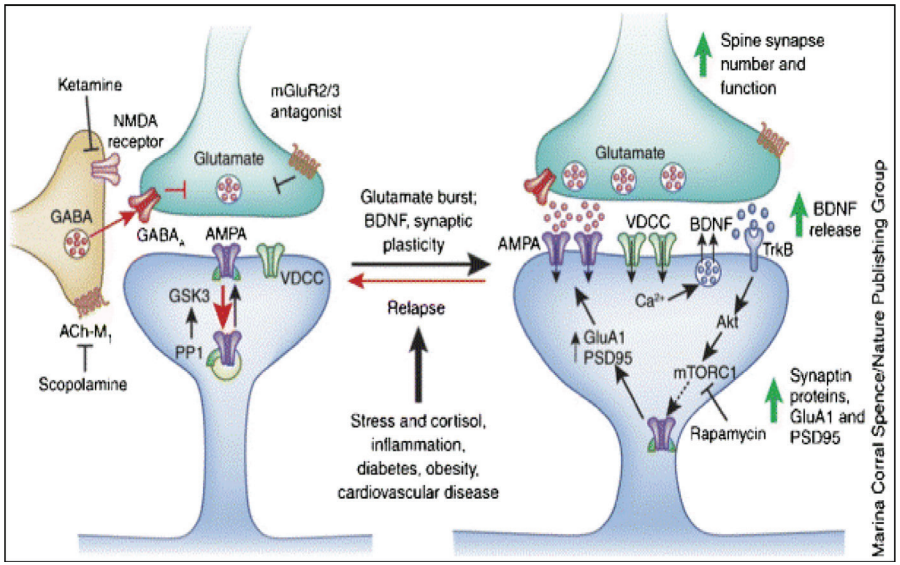


A. Low numbers of dendritic spines present in the dendrites of layer V pyramidal neurons after 21 days of chronic uncontrollable stress (CUS).

B. Reversal following a single dose of ketamine 1 day later.

Ketamine [N-methyl-D-aspartate (NMDA)-type glutamate receptor antagonist] → burst of glutamate → stimulates AMPA receptors → activation of intracellular pathways → increased protein synthesis → synapse maturation and formation

Reversal of abnormal connectivity patterns in key brain regions.

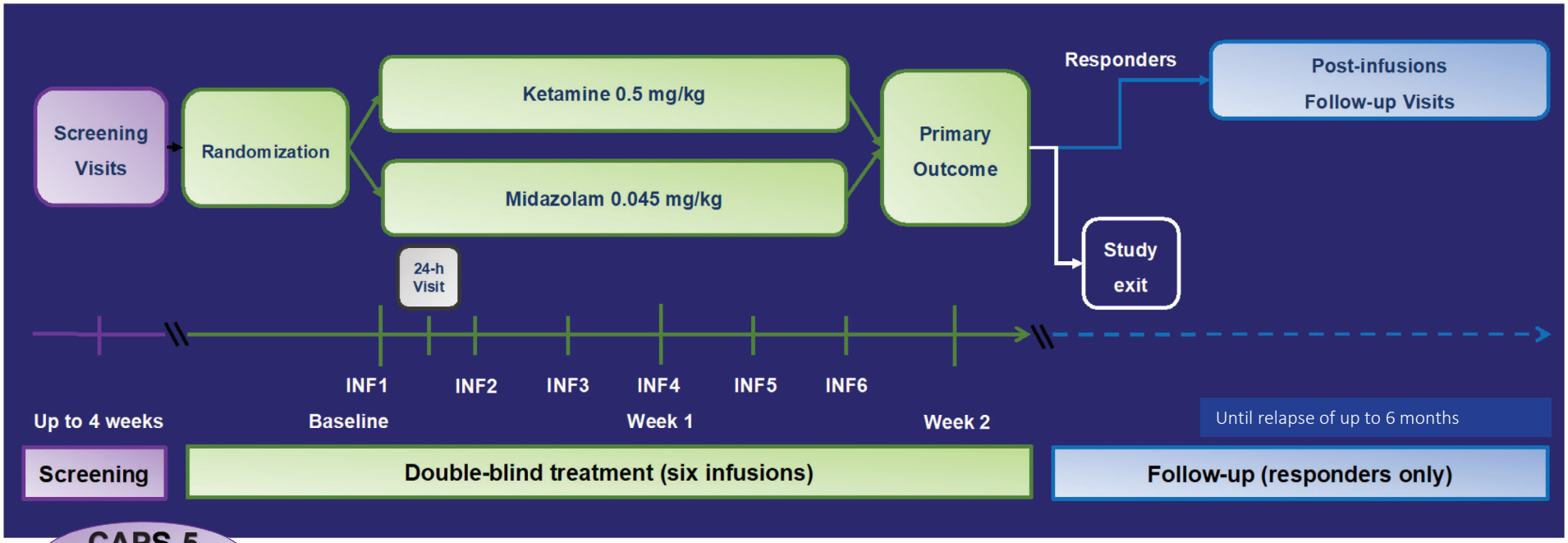


Li et al 2011
Krystal el al 2017

Ketamine for Chronic PTSD

- First proof-of-concept **RCT** of single IV ketamine infusion ***(compared to IV midazolam infusion)*** in patients with chronic **PTSD** (n=41, civilians, 54% male) (Feder et al 1014)
- First **RCT** of repeated IV ketamine infusions (compared to repeated IV midazolam) in patients with chronic **PTSD** **(n=30, civilians, 77% female)** (Feder et al 2021)
  - Total **6** infusions, **3** times a week over **2** consecutive weeks
  - Rapid and robust PTSD symptom improvement in the ketamine group **(67% ketamine responders vs. 20% midazolam responders)**
  - Among ketamine responders, median time to loss of response was **4** weeks following course of infusions
- Open-label clinical trial of repeated IV ketamine infusions in pts with co-morbid **PTSD** and **TRD** () (Albott et al 2018)
  - Total **6** infusions, **n=15, veterans, 67% male**3 times a week over 2 consecutive weeks
  - Rapid improvement in **PTSD** and depression symptoms; median time to relapse among **PTSD** remitters was **41** days
- **RCT** of repeated IV ketamine infusions (compared to repeated IV saline) in veterans and active-duty military personnel with antidepressant-resistant **PTSD** **(n=178, military, 77% male)** (Abdallah et al 2022)
  - Total **8** infusions, **2** times a week over **4** consecutive weeks
  - **PTSD** symptoms (**PCL-5**) were significantly reduced over time but did not differ between treatment groups; significant antidepressant effect from ketamine.

Randomized Controlled Trial of Repeated-Dose Intravenous Ketamine for PTSD Study Flow Chart



CAPS-5
PM=30

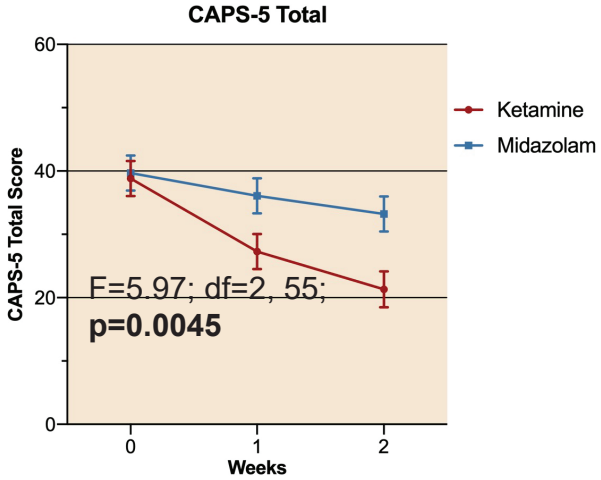
CAPS-5 severity scoring range

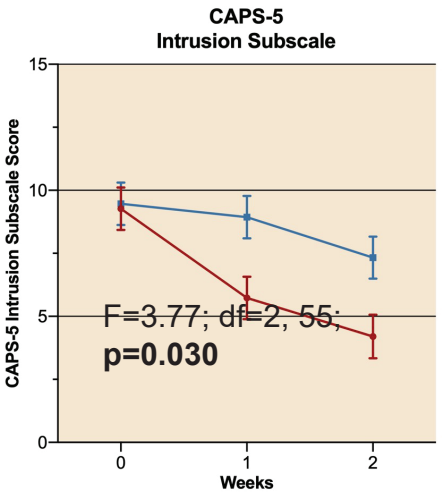
0-10	asymptomatic/few symptoms
11-22	mild PTSD/subthreshold
23-34	moderate PTSD
35-46	severe PTSD
47+	extreme PTSD

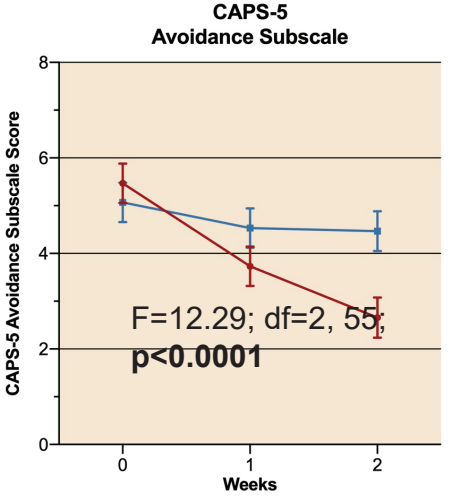
Mean age = **39 years, 77% female**
Mean **CAPS-5 score** at **screening= 41**
Mean **PTSD** duration= **15** years
Primary trauma:
- **43%** sexual assault/molestation
- **27%** physical assault/abuse

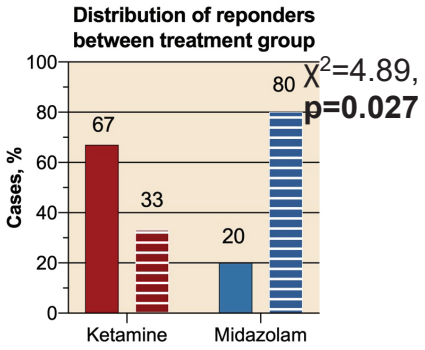
Feder et al 2021

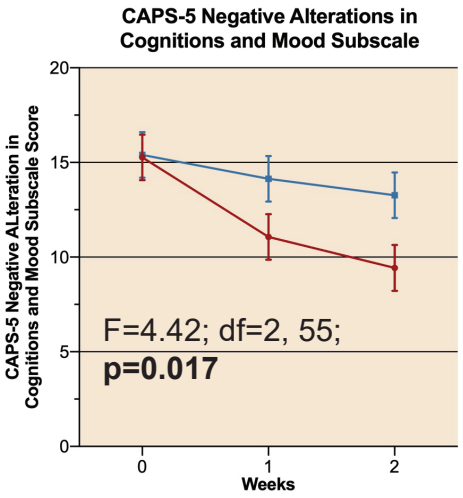
Effect of Treatment with Ketamine Compared to Midazolam on PTSD Severity in Patients with Chronic PTSD

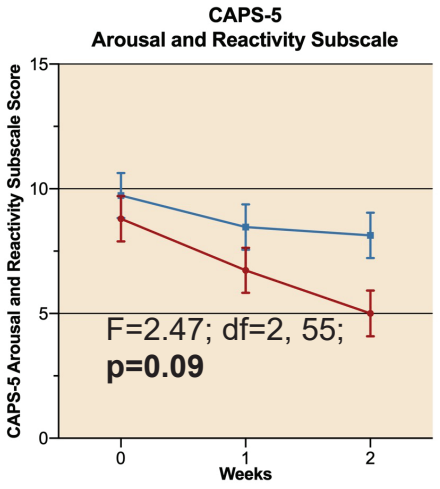












Feder et al 2021

Selected quotes from ketamine responders Obtained as part of clinical assessment

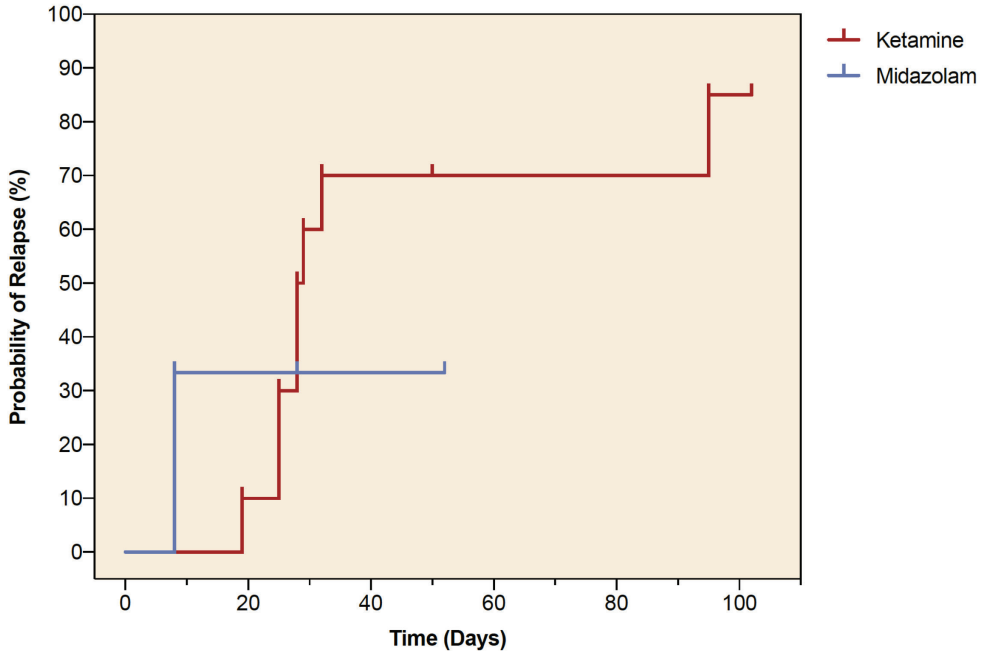
"I don't feel my life is going to end anymore, it made it impossible to plan a future. I want a life now too." *[After interacting with someone who had been harassing her]: "One huge thing I noticed that is different. Before I would have panicked. He's been very aggressive, I don't feel panicky or afraid."*

"I feel like a normal person. I seem like a normal person. My brain doesn't [any longer] let me envision or picture a thought of suicide". [Now, when she thinks about her past trauma], "it doesn't make me feel weighed down" "I have to dig out the memory as if from an attic". "Before, talking about it used to make me feel a terrible feeling."

[Feeling] "like I have energy and want to do things again. I felt safe and able to confront feelings [about the trauma] without problems. I could just feel it, and figure out what happened and why it happened."
[Reported that during infusions, she felt] "like I made peace, I could go past it, I could, can let it go. [It's been a] gradual acceptance. I haven't felt this safe in a long time."

Feder et al 2021, Am J Psychiatry

Risk of Relapse Among Responders to Repeated Ketamine and Midazolam Infusions in Posttraumatic Stress Disorder

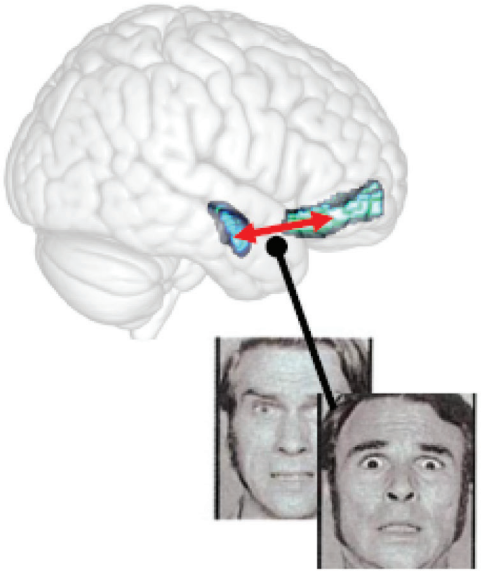


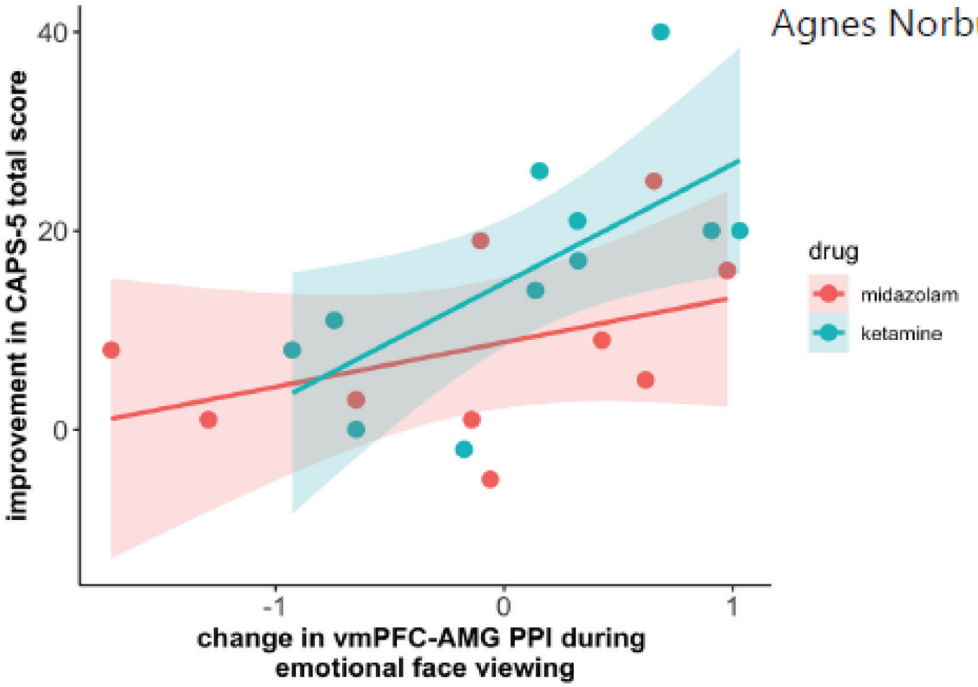
- Among ketamine responders, median time to relapse was 27.5 days from the primary outcome assessment day;
- 25th and 75th percentiles were 23 and 32 days;
- Two participants had not relapsed by their last assessment (50 and 102 days after the primary outcome assessment)

Feder et al 2021

Correlates of PTSD symptom improvement: interaction with drug

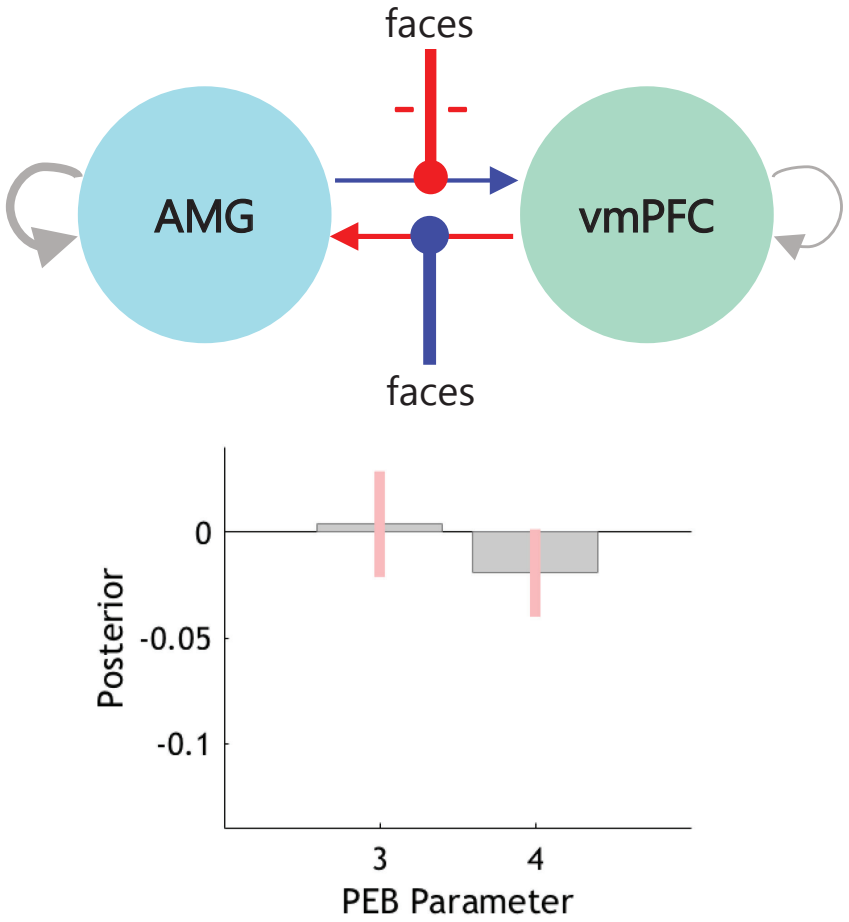
Agnes Norbury, PhD



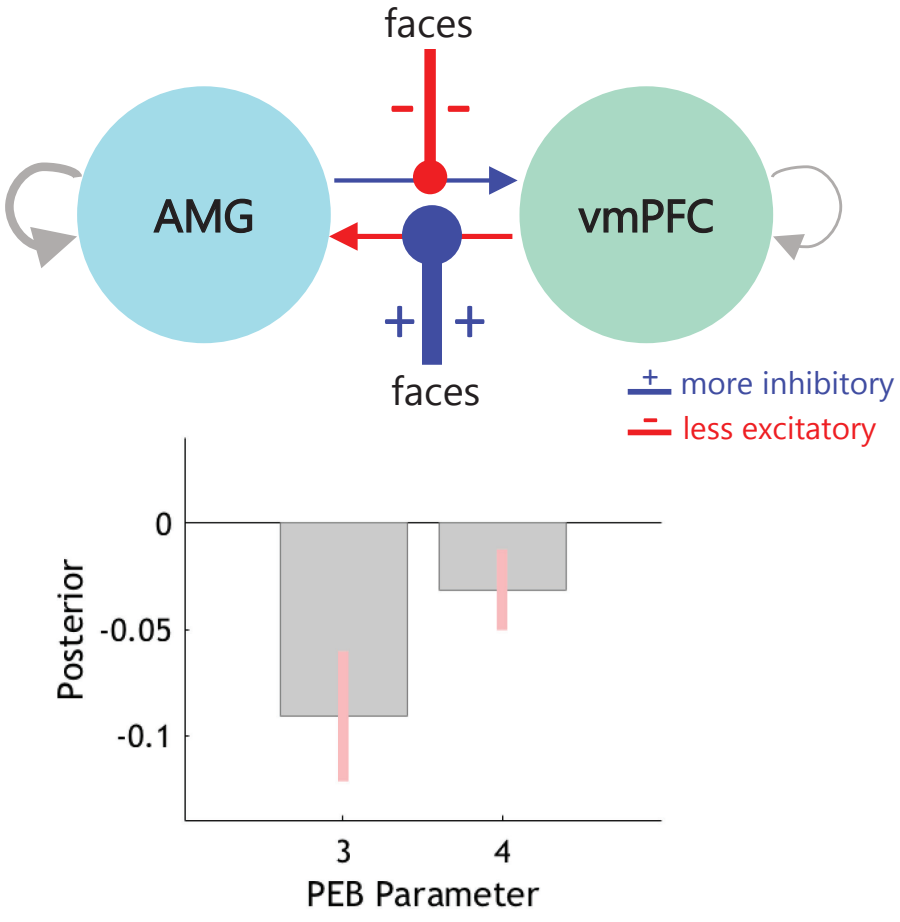


An interaction between drug and face-related increase in vmPFC-AMG connectivity was retained in the winning model, suggesting that **the association is stronger in individuals who received ketamine**.

MIDAZOLAM
pre-post infusion*CAPS-5 change interaction
on emotional faces modulation of connectivity



KETAMINE
pre-post infusion*CAPS-5 change interaction
on emotional faces modulation of connectivity

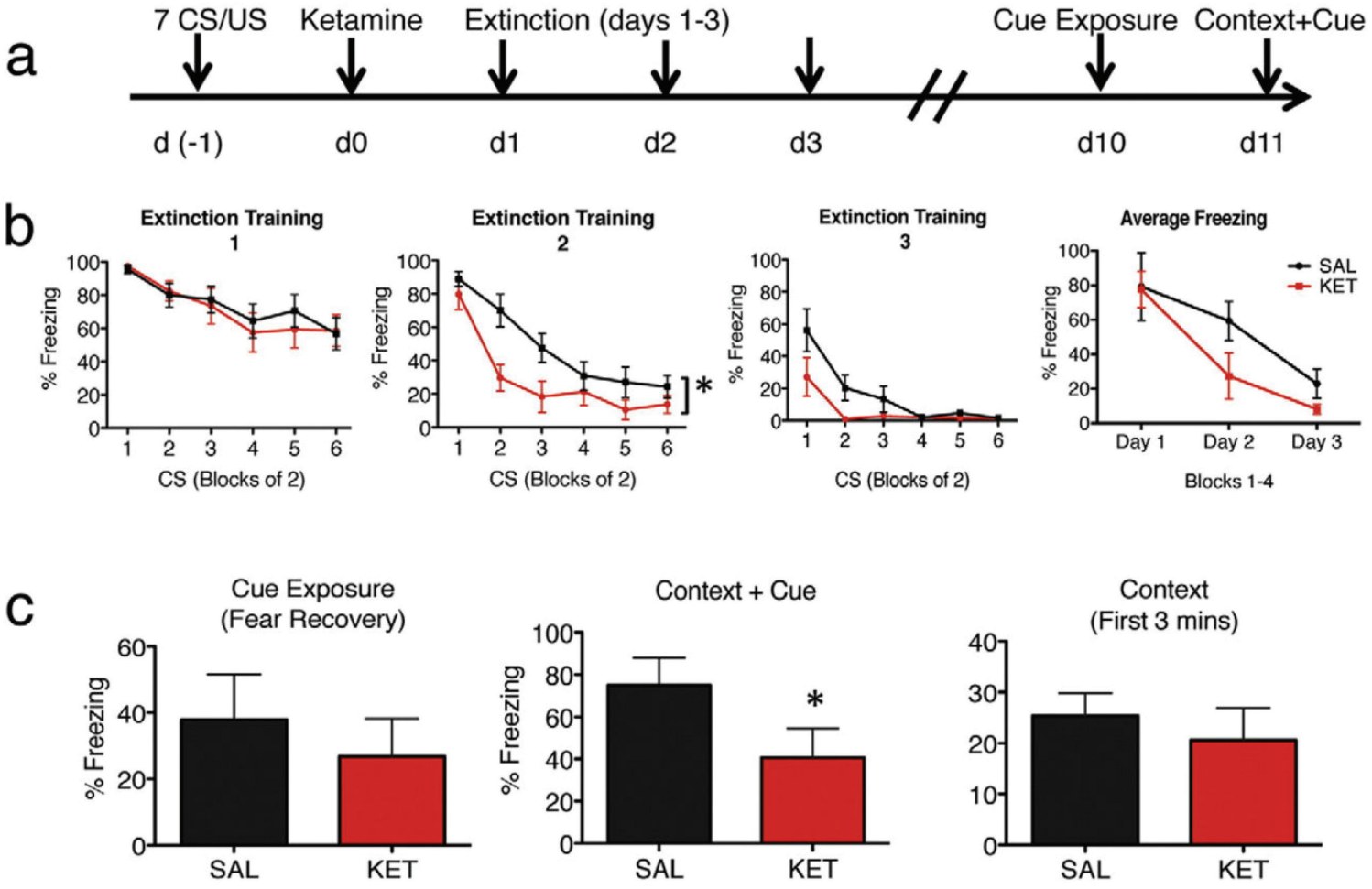


- In both groups, association between greater symptom improvement and less face-related excitation of the vmPFC by the AMG (*Pp*=0.94,1.0).
- However, the relationship between PTSD symptom improvement and greater top-down inhibition of the AMG by the vmPFC was only evident in the ketamine group

Adding Trauma-focused Psychotherapy to Ketamine Treatment for Chronic PTSD

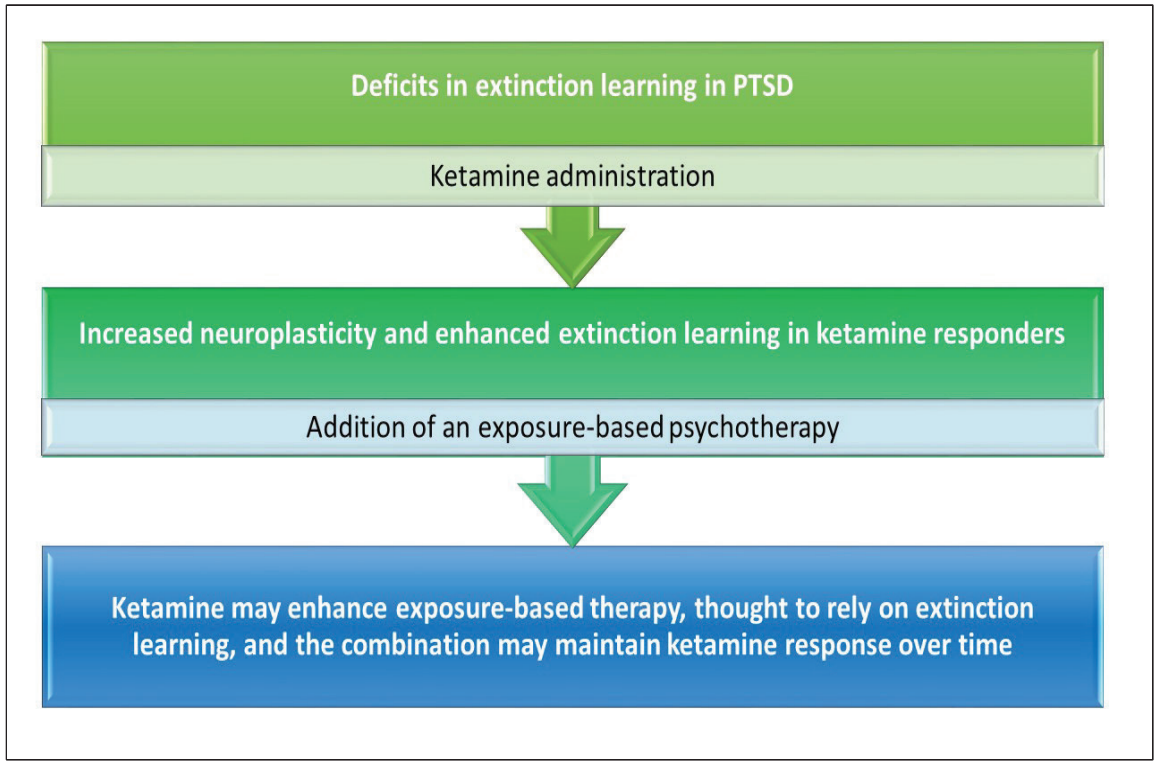
An Open-label Pilot Study

Ketamine accelerates fear extinction via mTOR signaling



Girgenti et al... Duman 2017

- **Ketamine** is thought to open a window of increased neuroplasticity in the brain
- **Adding** an exposure-based therapy to ketamine treatment for **PTSD**: Potential synergistic effect ***TIMING???***



Choice of Trauma-focused Therapy
Written Exposure Therapy *(WET)*

- Brief, evidence-based, tolerable and efficient, very low dropout rates
- **Extinction learning** is thought to underlie exposure-based therapies
- Total 5 sessions:
  - Treatment rationale, psychoeducation
  - Pts write repeatedly about details of trauma linked to their symptoms
    - Particular attention to felt emotions and meaning of the traumatic event

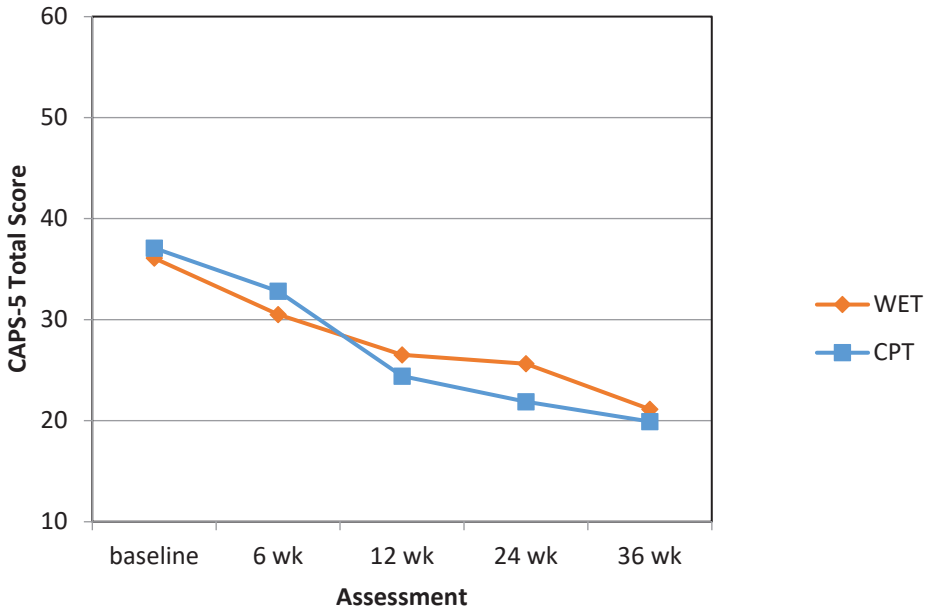
To date, three non-inferiority **RCTs** in **PTSD:**

- Sloan et al 2018: WET non-inferior to CPT
(n=126, 74% civilians)

- Sloan et al 2022: WET non-inferior to CPT
(n=169, active duty military service members)

- Sloan et al 2023: WET non-inferior to PE (n= 178, veterans)

Fig. 2: Non-inferiority RCT



Sloan et al 2018

Standard Written Exposure Therapy Instructions

- Session 1: Write about your trauma from the beginning (how it happened, who was involved, what you saw/heard/smelled) + details, thoughts, feelings during trauma (and immediately after) as you remember it now
- Session 2: Trauma – continue where you left off or write about entire trauma again as you look back upon it now + details (setting, people involved, saw/heard/felt), thoughts, feelings
- Session 3: Trauma – write about trauma again or pick "worst" part (most upsetting/stressful) + begin to write about how trauma changed your life (the way you view life, meaning of life, how you relate to others) + thoughts, feelings
- Session 4: Trauma – pick "worst" part (most upsetting/stressful) + how trauma has changed your life (the way you view life, meaning of life, how you relate to others) + thoughts, feelings
- Session 5: Thoughts and feelings related to trauma and how trauma changed your life + how trauma is related to your current life and future + thoughts, feelings

Adding Trauma-focused Psychotherapy to Ketamine Treatment for Chronic PTSD Study Design - Flowchart

Preliminary Outcomes

Participants

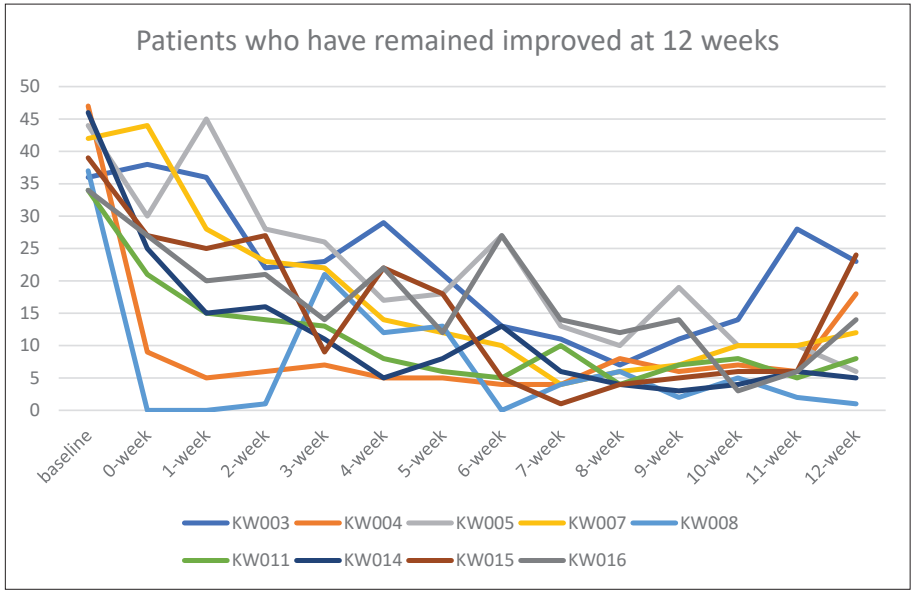
- **N=13** women
- Age: **38.3 (7.5)** years **(range 24-53 years)**
- Chronic **PTSD** stemming from childhood or adulthood trauma

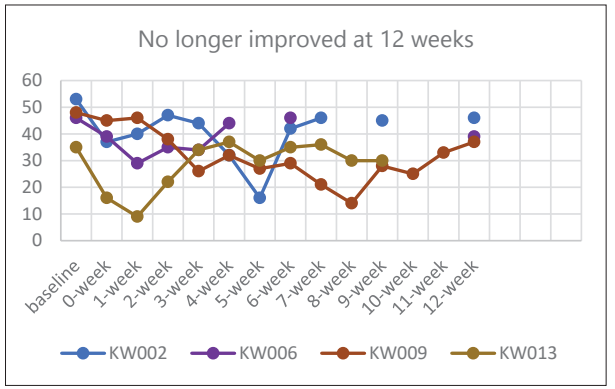
Results

- Large magnitude improvement in **PTSD** symptoms from baseline **[CAPS-5 score= 41.6 (6.2)]** to **12 weeks [CAPS-5 score= 20.7 (14.8)]**, Cohen's D=**1.6 (95% CI= 1.0 – 2.2, p<0.001)**

- 1 week after completion of the combined treatment, **10 (77%)** pts were treatment responders **(≥ 30% improvement)**

- At **12 weeks, 9 (69%)** maintained treatment response, and **6 (46%)** no longer met **DSM-5** diagnostic criteria for **PTSD**





Summary and Future Directions

- Repeated ketamine infusions are associated with rapid and robust improvement in PTSD symptoms in patients with chronic PTSD

***** How to maintain PTSD symptom improvement in the long term?*****

- Ketamine induces window of increased neuroplasticity, thought to normalize/improve fear circuitry function
  - Ketamine might enhance efficacy of exposure-based psychotherapy
  - Pilot trial of ketamine infusions + written exposure therapy ***(administered on different days)***
- Larger randomized controlled trial is needed
  - Including WTC-affected individuals with chronic **PTSD**
- Mechanistic neuroimaging study examining changes in fear circuitry function

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