

# **Apnea, Insomnia, and Cognition in Veterans with Gulf War Illness**

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screen for Obstructive Sleep Apnea (OSA)

**S**nore loudly

**T**ired, fatigued, or sleepy during daytime

**O**bserved apnea; gasping during sleep

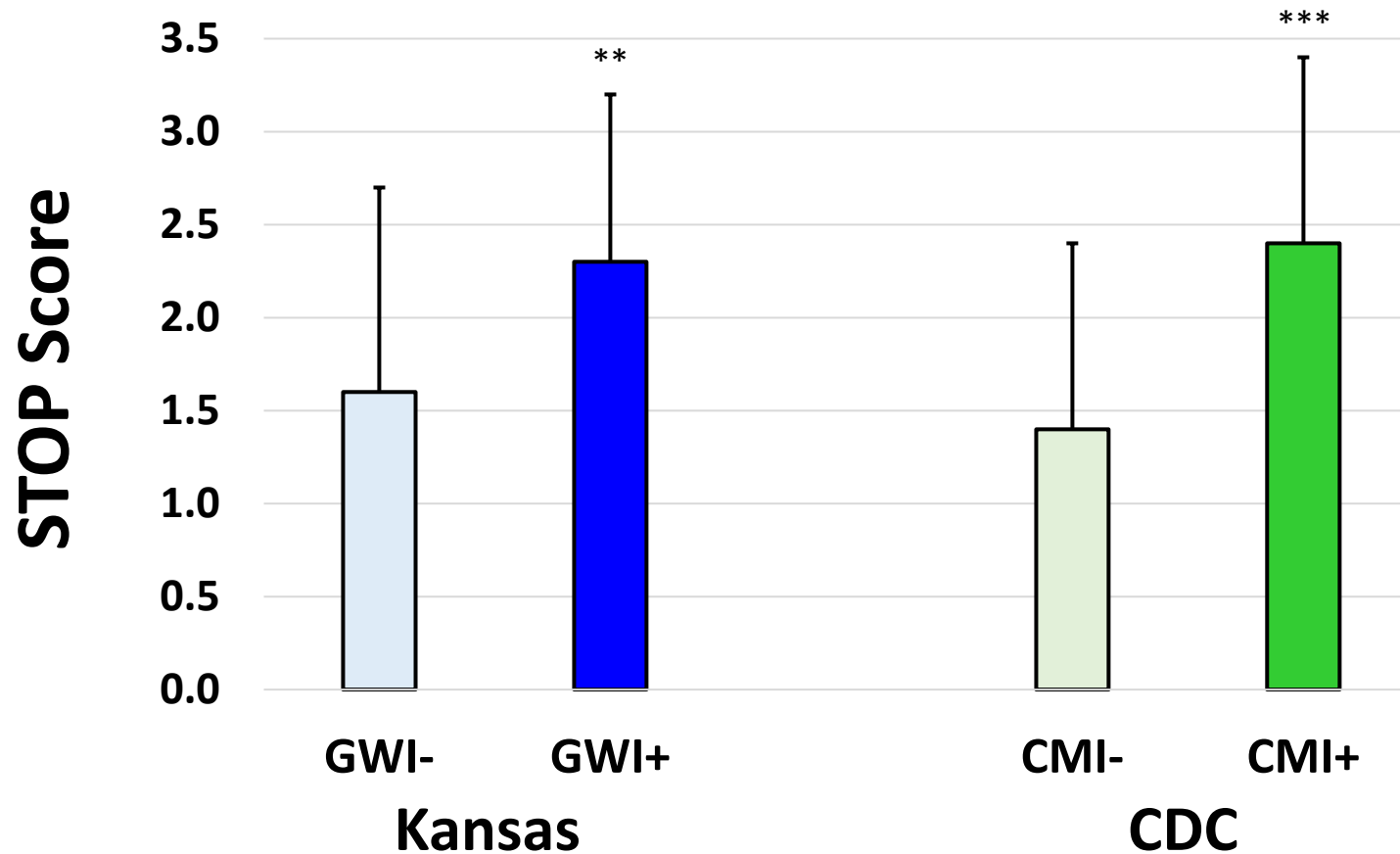
**P**ressure (high blood pressure)



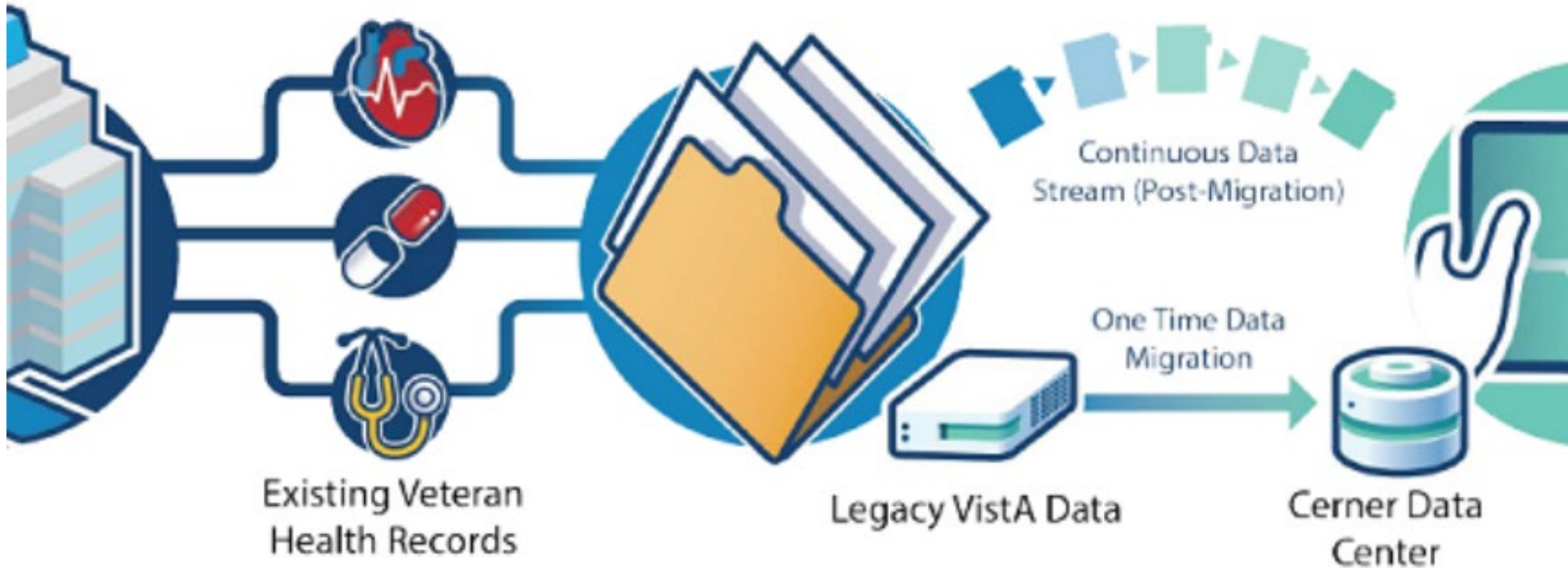
# Insomnia Severity, Subjective Sleep Quality, and Risk for Obstructive Sleep Apnea in Veterans With Gulf War Illness

Linda L. Chao, PhD\*†‡; Linda R. Abadjian, PhD\*; Iva L. Esparza, BA\*; Rosemary Reeb, BS\*†

MILITARY MEDICINE, 181, 9:1127, 2016



# VHA's electronic health records (EHR)



Slides removed because it is unpublished data.

## **The Association of Ambient Air Pollution with Sleep Apnea: The Multi-Ethnic Study of Atherosclerosis**

Martha E. Billings<sup>1</sup>, Diane Gold<sup>2,3</sup>, Adam Szpiro<sup>4</sup>, Carrie P. Aaron<sup>5</sup>, Neal Jorgensen<sup>4</sup>, Amanda Gasset<sup>6,7</sup>, Peter J. Leary<sup>1</sup>, Joel D. Kaufman<sup>6,7</sup>, and Susan R. Redline<sup>2\*</sup>

Individuals with higher exposures to NO<sub>2</sub> and PM<sub>2.5</sub> had a greater odds of sleep apnea.



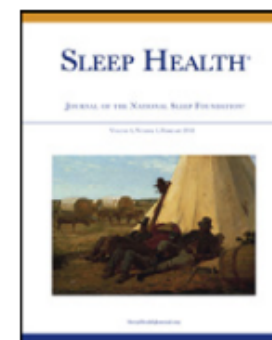
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Contents lists available at ScienceDirect

# Sleep Health

Journal of the National Sleep Foundation

journal homepage: [sleephealthjournal.org](http://sleephealthjournal.org)



## Sleep apnea and pesticide exposure in a study of US farmers<sup>☆</sup>



Brittney O. Baumert, MPH<sup>a</sup>, Megan Ulmer Carnes, PhD<sup>a</sup>, Jane A. Hoppin, ScD<sup>b</sup>, Chandra L. Jackson, PhD<sup>a</sup>, Dale P. Sandler, PhD<sup>a</sup>, Laura Beane Freeman, PhD<sup>c</sup>, Paul K. Henneberger, ScD<sup>d</sup>, David M. Umbach, PhD<sup>e</sup>, Srishti Shrestha, PhD<sup>a</sup>, Stuart Long, BS<sup>f</sup>, Stephanie J. London, MD, DrPH<sup>a,\*</sup>

# Factors that increase OSA risks:

- Male sex
- **Advancing age**




International Journal of  
*Environmental Research  
and Public Health*



*Article*

## **Rates of Chronic Medical Conditions in 1991 Gulf War Veterans Compared to the General Population**

Clara G. Zundel <sup>1,2</sup>, Maxine H. Krengel <sup>1,3</sup>, Timothy Heeren <sup>4</sup>, Megan K. Yee <sup>1</sup>,  
Claudia M. Grasso <sup>1</sup>, Patricia A. Janulewicz Lloyd <sup>5</sup>, Steven S. Coughlin <sup>6</sup> and  
Kimberly Sullivan <sup>5,\*</sup> 



# Factors that increase OSA risks:

- Male sex
- Advancing age
- **Hormonal changes**

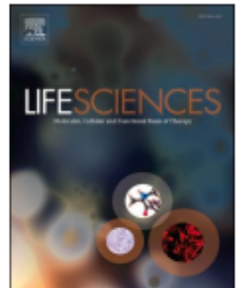
Life Sciences 328 (2023) 121908



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Life Sciences

journal homepage: [www.elsevier.com/locate/lifescie](http://www.elsevier.com/locate/lifescie)



## Hormonal changes in veterans with Gulf War Illness

Gursimrat Bhatti <sup>a,b</sup>, Audri Villalon <sup>a,b</sup>, Ruosha Li <sup>c</sup>, Mohamed Elammari <sup>a,b</sup>, Alexandra Price <sup>b</sup>,  
Lea Steele <sup>b</sup>, Jose M. Garcia <sup>d</sup>, Marco Marcelli <sup>a</sup>, Ricardo Jorge <sup>a,b,\*</sup>



# Factors that increase OSA risks:

- Male sex
- Advancing age
- Hormonal changes
- **Obesity**

*The Open Epidemiology Journal, 2011, 4, 140-146*

Open Access

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**Selected Health Conditions Among Overweight, Obese, and Non-Obese Veterans of the 1991 Gulf War: Results from a Survey Conducted in 2003-2005**


Steven S. Coughlin<sup>\*</sup>, Han K. Kang and Clare M. Mahan

Slides removed because it is unpublished data.



*Review*

# **Comorbid Insomnia and Obstructive Sleep Apnea (COMISA): Current Concepts of Patient Management**

Beatrice Ragnoli <sup>1</sup>, Patrizia Pochetti <sup>1</sup>, Alberto Raie <sup>1</sup> and Mario Malerba <sup>1,2,\*</sup> 

- **6%-84%** patients with **sleep apnea** have **co-occurring insomnia**.
- **7%-69%** patients with **insomnia** have **co-occurring OSA**.

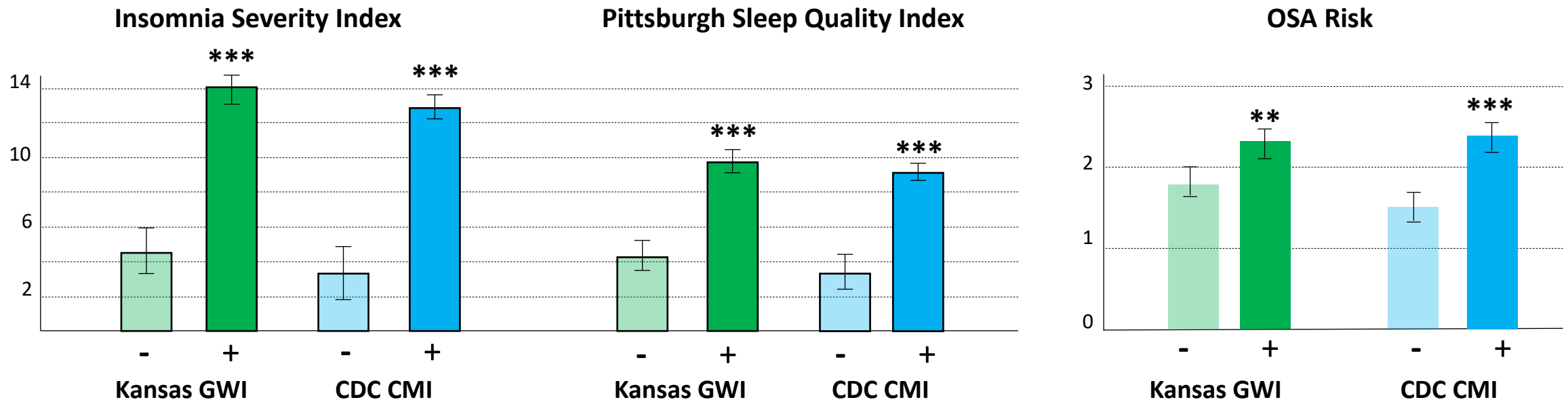
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# Insomnia Severity, Subjective Sleep Quality, and Risk for Obstructive Sleep Apnea in Veterans With Gulf War Illness

*Linda L. Chao, PhD\*†‡; Linda R. Abadjian, PhD\*; Iva L. Esparza, BA\*; Rosemary Reeb, BS\*†*

MILITARY MEDICINE, 181, 9:1127, 2016



## ASSOCIATIONS BETWEEN SLEEP QUALITY AND BRAIN VOLUME IN GULF WAR VETERANS

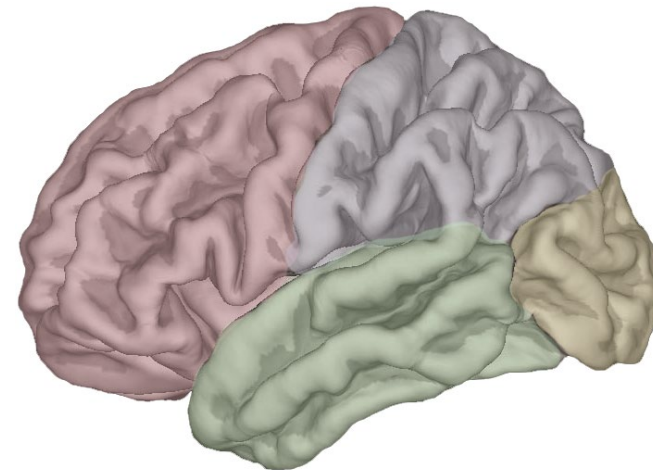
<http://dx.doi.org/10.5665/sleep.3472>

# Associations between Subjective Sleep Quality and Brain Volume in Gulf War Veterans

Linda L. Chao, PhD<sup>1,2,3</sup>; Brian S. Mohlenhoff, MD<sup>2,3</sup>; Michael W. Weiner, MD<sup>1,2,3</sup>; Thomas C. Neylan, MD<sup>2,4</sup>

*Departments of <sup>1</sup>Radiology and Biomedical Imaging and <sup>2</sup>Psychiatry, University of California, San Francisco, CA; <sup>3</sup>Center for Imaging of Neurodegenerative Diseases and <sup>4</sup>Mental Health Service, Department of Veterans Affairs Medical Center, San Francisco, CA*

- Sleep quality was inversely related to total gray matter and frontal lobe gray matter volume



**ASSOCIATIONS BETWEEN SLEEP QUALITY AND BRAIN VOLUME IN GULF WAR VETERANS**

<http://dx.doi.org/10.5665/sleep.3472>

# Associations between Subjective Sleep Quality and Brain Volume in Gulf War Veterans

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Region	Intercept	PSQI	Age	ICV	GWI	Adult trauma	Psych Med	Lifetime CAPS	Current CAPS	HAM-D
Total gray matter	127722 (24220)	<b>-1080 (494)</b>	-1288 (192)	0.255 (0.013)	7938 (4430)	5735 (5665)	-6127 (5054)	-28 (142)	6 (164)	287 (438)
Frontal Lobe	57132 (11317)	<b>-567 (231)</b>	-540 (90)	0.087 (0.006)	1690 (2070)	-8 (2647)	-2828 (2376)	38 (67)	-23 (77)	239 (205)
Parietal Lobe	32733 (8394)	-237 (171)	-343 (37)	0.073 (0.004)	2881 (1535)	1307 (1964)	-304 (1762)	-5 (49)	-12 (57)	20 (152)
Temporal Lobe	25180 (7110)	-148 (145)	-261 (56)	0.059 (0.004)	2908 (1300)	3225 (1663)	-752 (1493)	-41 (42)	9 (48)	31 (129)
Occipital Lobe	8858 (5179)	-86 (106)	-128 (41)	0.028 (0.003)	581 (947)	999 (1211)	-2110 (1087)	-17 (30)	21 (35)	-3 (94)



# Poor sleep quality/insomnia has been linked with:

- **brain atrophy** (Sexton et al., 2014; Koo et al., 2017; Altena et al., 2010; Li et al., 2018; Winkleman et al. 2013; Joo et al., 2014; Grau-Rivera et al., 2020).
- **higher risk of late-life dementia** (Potvin et al., 2012; Sindi et al., 2018; Lim et al., 2013).
- **$\beta$ -amyloid and tau accumulation in the brain** (Ju et al., 2015; Holth et al., 2019).
- **Impaired cognition, particularly executive function** (Grau-Rivera et al., 2020).

## OSA has been linked with:

- **brain atrophy and decreased white matter integrity** (Cross et al., 2018; Macey et al., 2008; Kumar et al., 2012; Joo et al., 2014).
- **cognitive deficits in multiple domains** (Bucks et al. 2013; Leng et al., 2017).
- **increased risk for and earlier progression to Mild Cognitive Impairment (MCI) and dementia** (Yaffe et al., 2011; Osoris et al., 2015).


# Mild Cognitive Impairment (MCI)

- Clinical syndrome defined as cognitive decline greater than that expected for the person's age but does not impact activities of daily life.
- Transition between normal aging and dementia.
- Increased risk for dementia.



*Article*

# The Prevalence of Mild Cognitive Impairment in a Convenience Sample of 202 Gulf War Veterans

Linda L. Chao <sup>1,2,3</sup> 

- 12% of GW Veteran sample (median age 52 years) had MCI according to actuarial neuropsychological criteria.

# Practice guideline update summary: Mild cognitive impairment

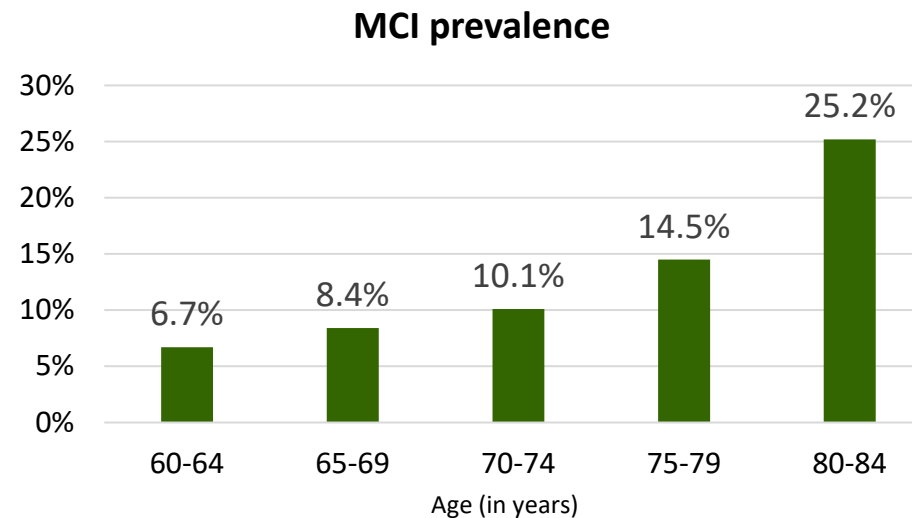
Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Ronald C. Petersen, MD, PhD, Oscar Lopez, MD, Melissa J. Armstrong, MD, MSc, Thomas S.D. Getchius, MD, MPH, David Gloss, MD, MPH&TM, Gary S. Gronseth, MD, Daniel Marson, JD, PhD, Tamara Pringsheim, MD, Gregory S. Day, MD, MSc, Mark Sager, MD, James Stevens, MD, and Alexander Rae-Grant, MD

## Correspondence

American Academy of  
Neurology  
guidelines@aan.com

*Neurology*<sup>®</sup> 2018;90:126-135. doi:10.1212/WNL.0000000000004826



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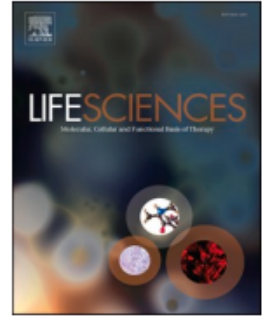


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## Cognitive behavioral therapy for insomnia in veterans with gulf war illness: Results from a randomized controlled trial

Linda L. Chao<sup>a,b,\*</sup>, Jennifer C. Kanady<sup>c</sup>, Nicole Crocker<sup>a</sup>, Laura D. Straus<sup>a,b,d</sup>, Jennifer Hlavin<sup>a</sup>,  
Thomas J. Metzler<sup>a,b,d</sup>, Shira Maguen<sup>a,b,d</sup>, Thomas C. Neylan<sup>a,b,d</sup>

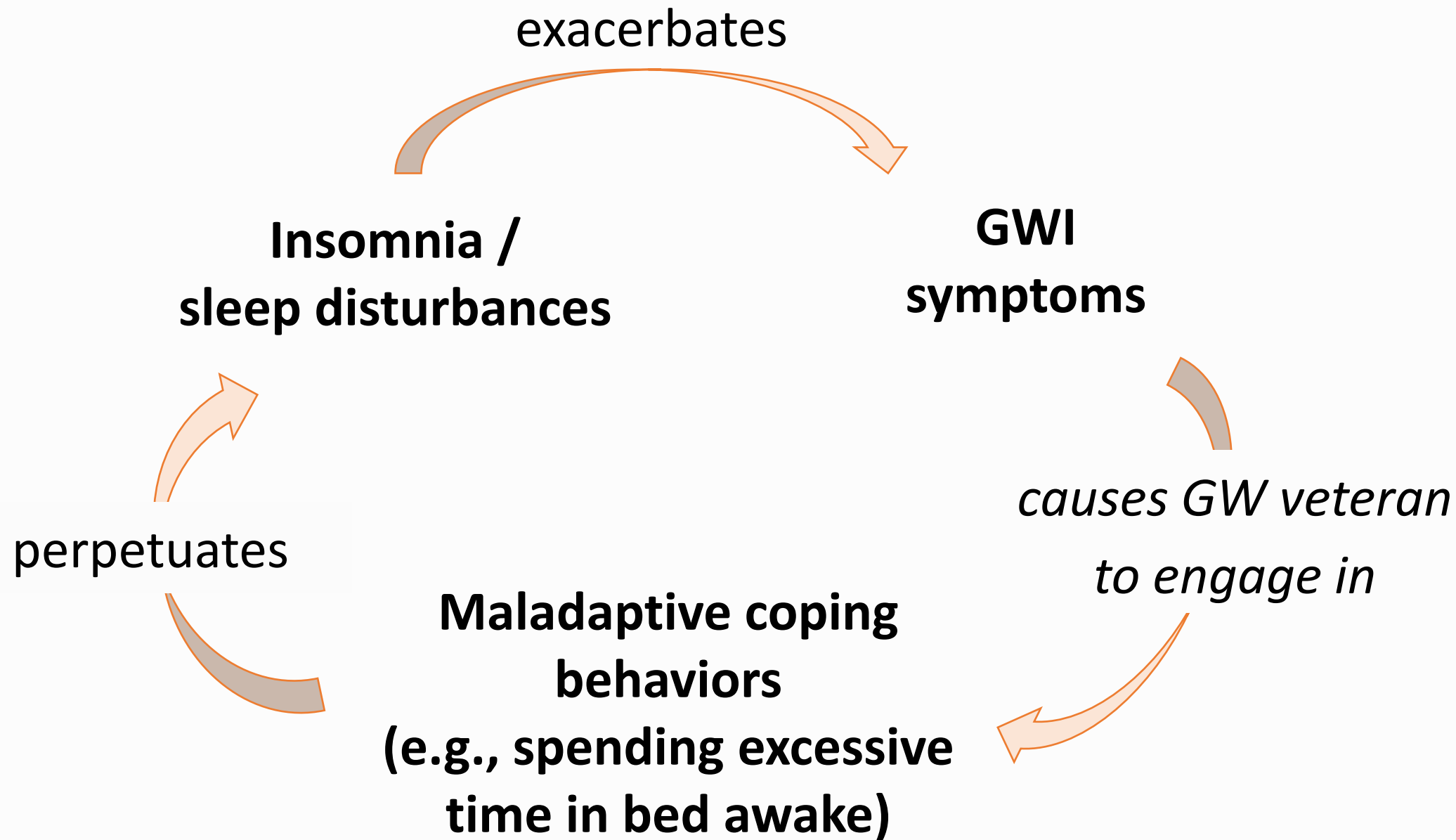
<sup>a</sup> San Francisco Veterans Affairs Health Care System, San Francisco, CA 94121, USA

<sup>b</sup> University of California, San Francisco, CA 94143, USA

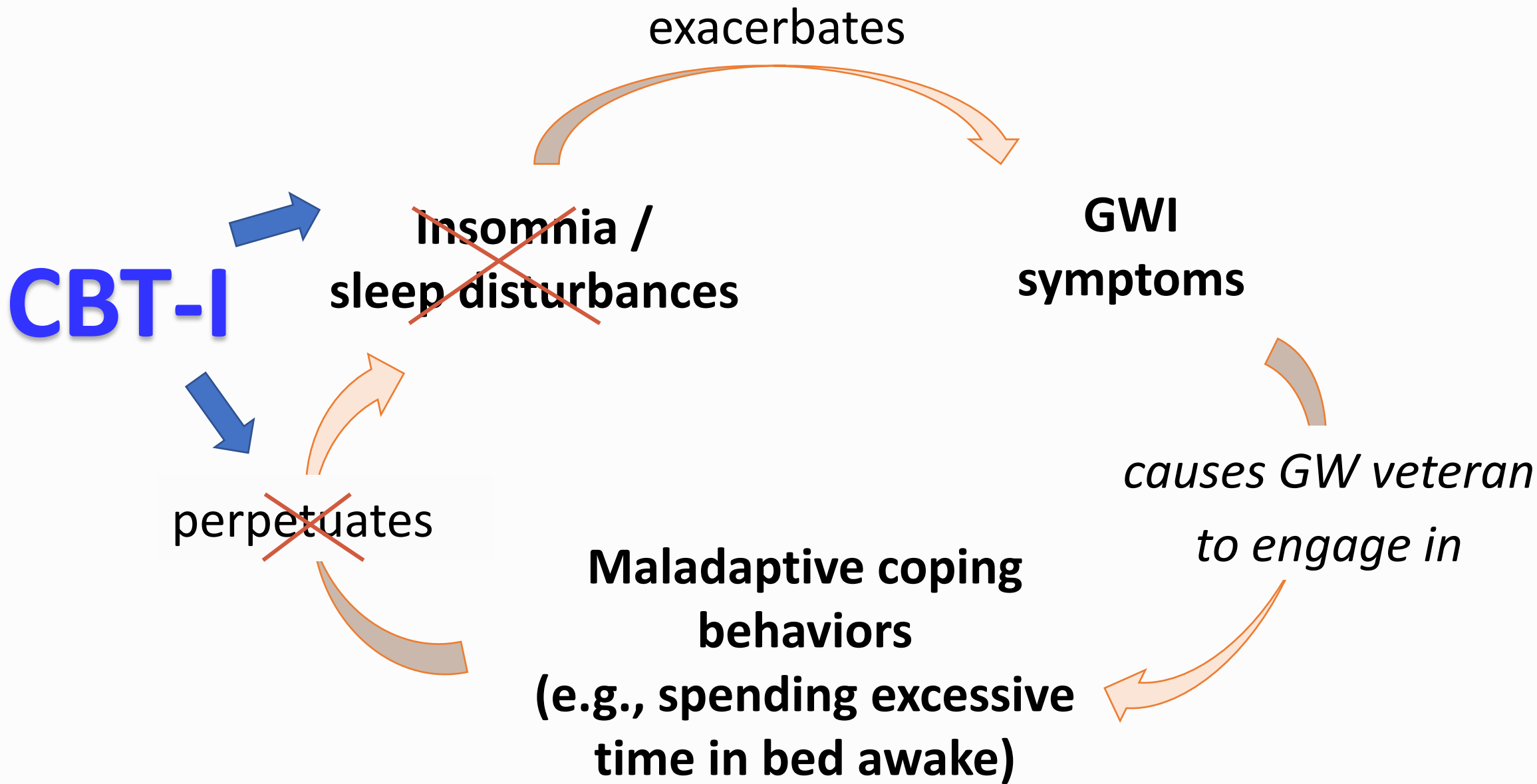
<sup>c</sup> Big Health, Sleepio, San Francisco, CA 94108, USA

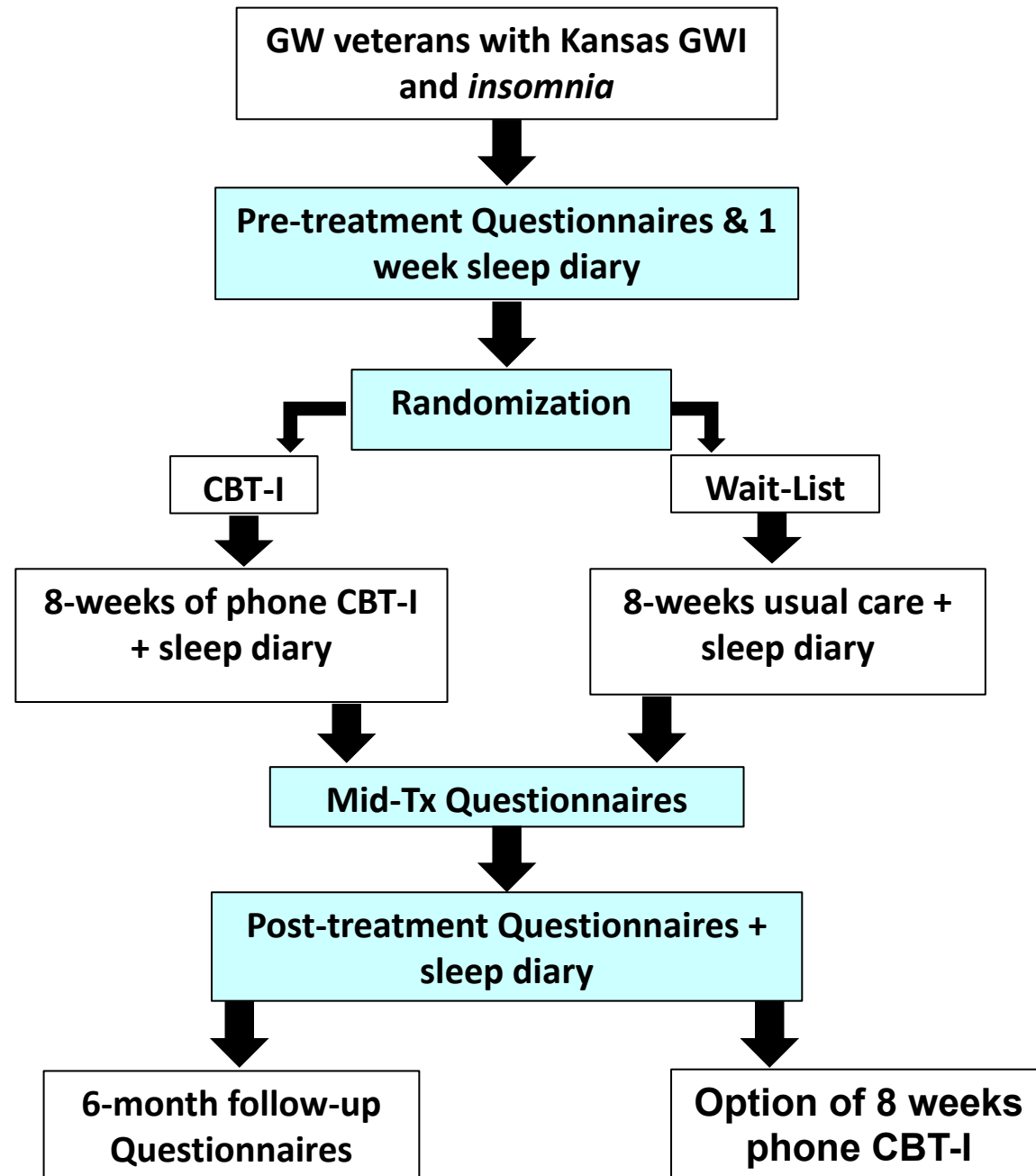
<sup>d</sup> Sierra Pacific Mental Illness Research, Education, and Clinical Center, San Francisco, CA 94121, USA

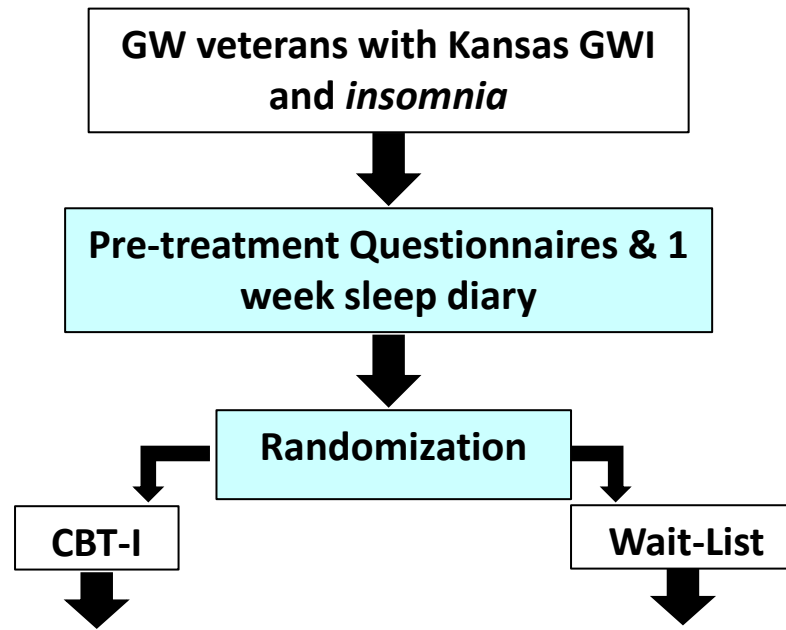








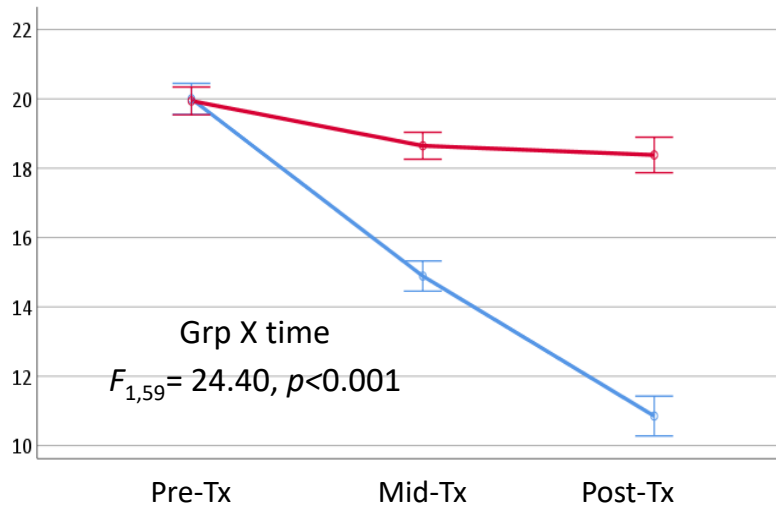




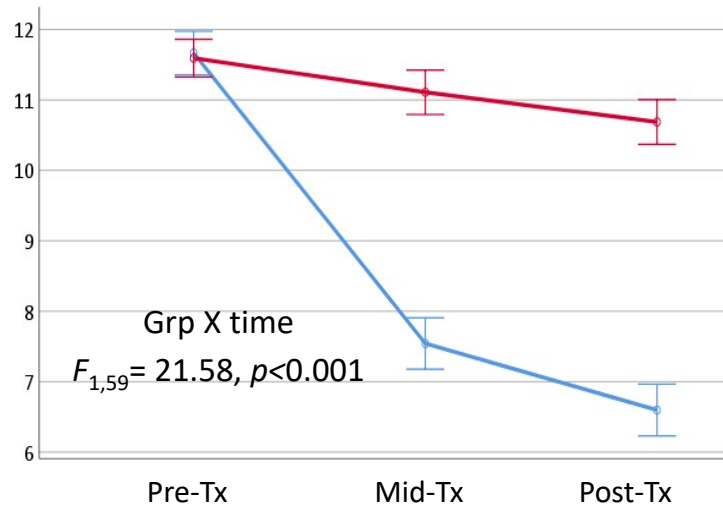
	CBT-I	Wait-List
N	29	35
No. Female (%)	8 (28%)	7 (20%)
Age, years	51.8 ± 11.4	54.5 ± 6.1
Education, years	14.9 ± 3.5	15.7 ± 4.8
No. Caucasian (%)	18 (62%)	27 (77%)
No. current PTSD (%)	4 (11%)	8 (28%)
No. current MDD (%)	2 (6%)	4 (14%)
Baseline ISI	20 ± 5.5	20 ± 3.8
Baseline GWI severity	69.4 ± 16.7	66.0 ± 14.6

# Insomnia severity, subjective sleep quality, and GWI symptoms improved after CBT-I

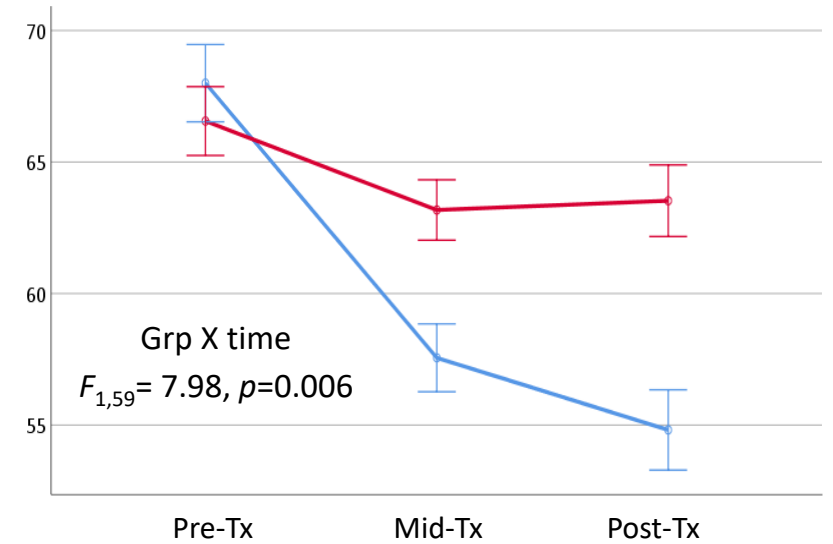
### Insomnia Severity Index (ISI)



### Subjective Sleep Quality (PSQI)



### GWI Severity Index

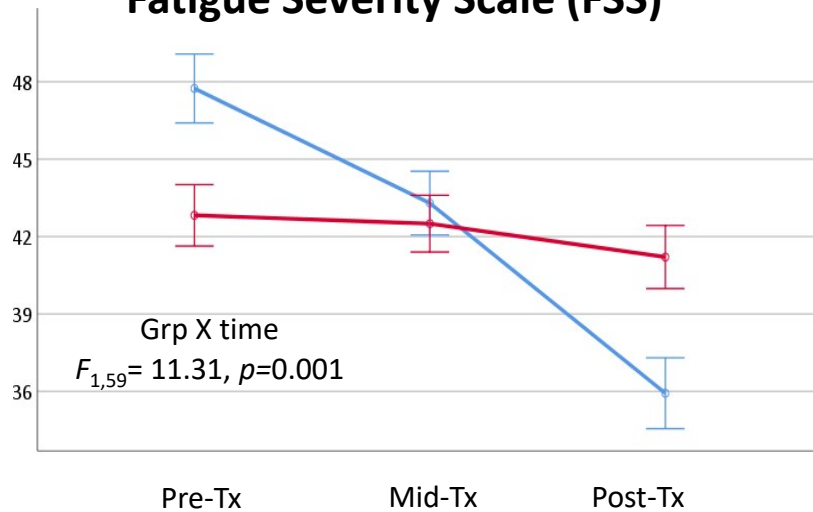


— Wait List  
— CBT-I

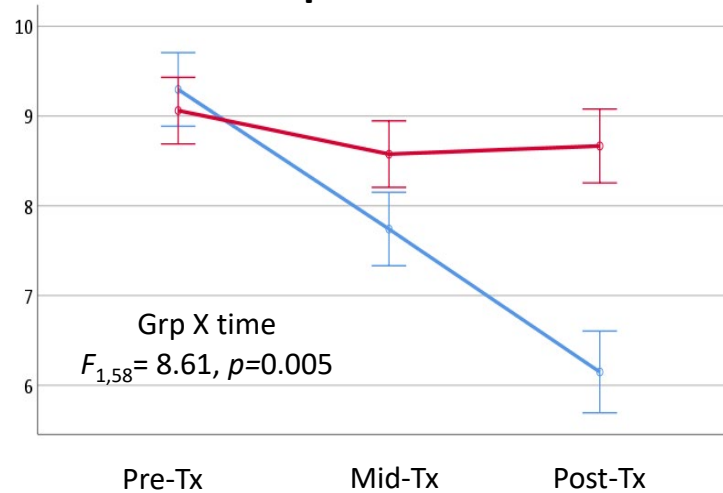
# Fatigue, depression and anxiety decreased after CBT-I

## Hospital Anxiety and Depression Scale (HADS)

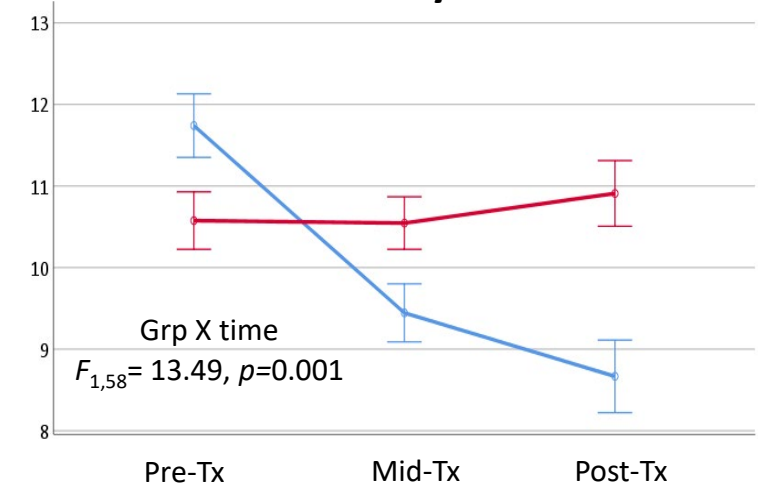
### Fatigue Severity Scale (FSS)



### Depression



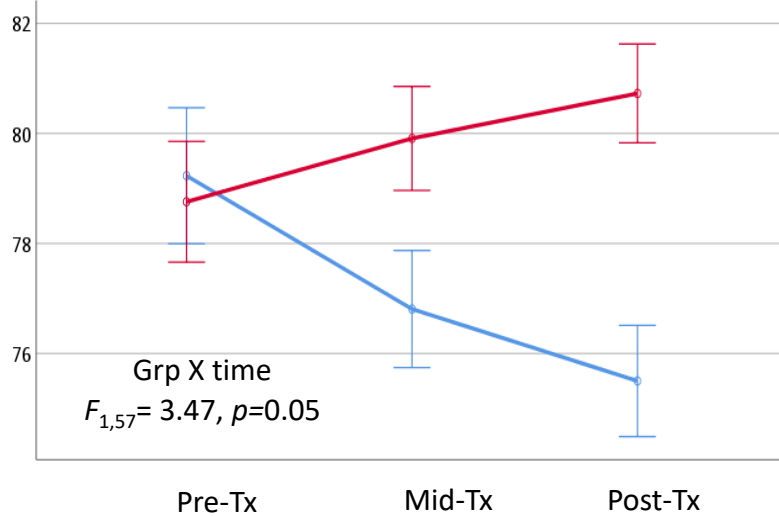
### Anxiety



— Wait List  
— CBT-I

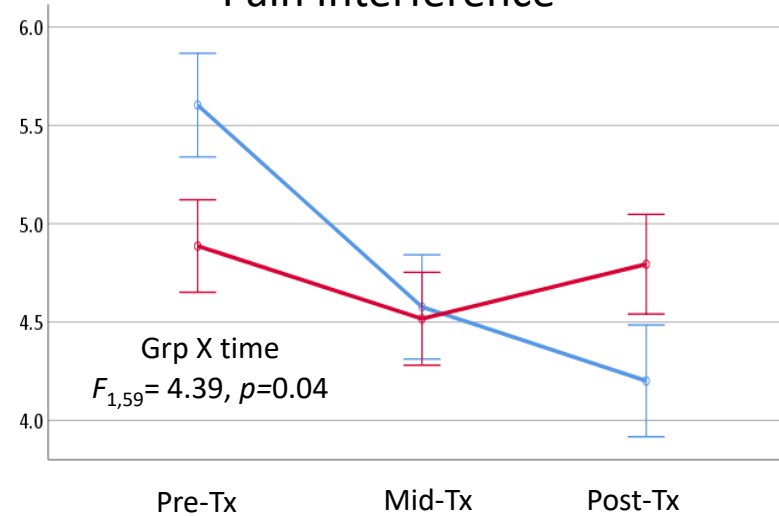
# Cognition and Pain Interference Improved after CBT-I

## Multiple Ability Self-Report Questionnaire (MASQ - cognition)

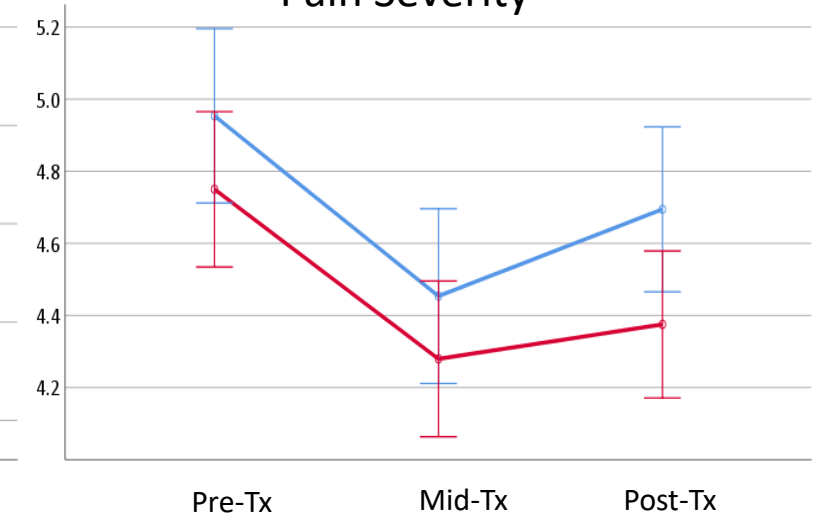


## Brief Pain Inventory (BPI)

### Pain Interference

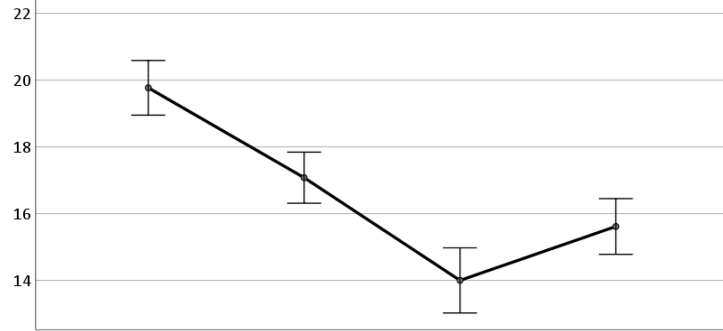


### Pain Severity

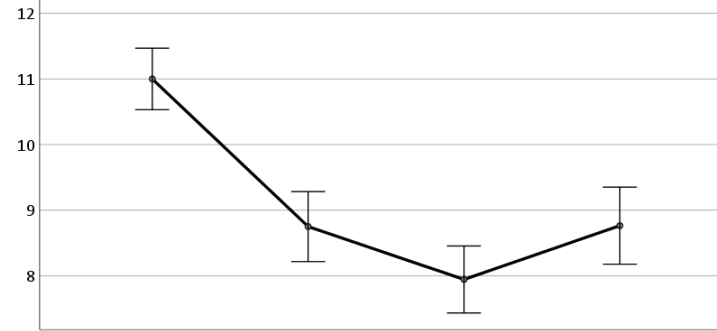


— Wait List  
— CBT-I

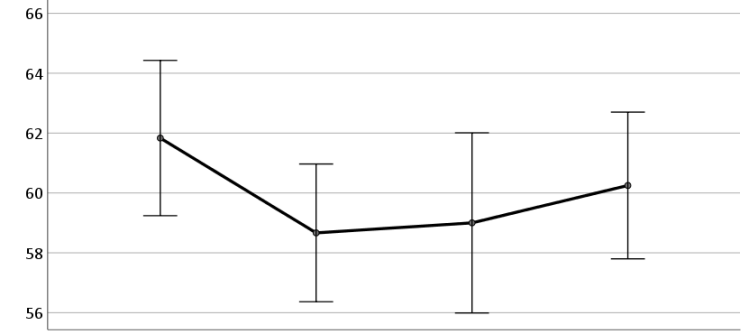
### Insomnia Severity (ISI)



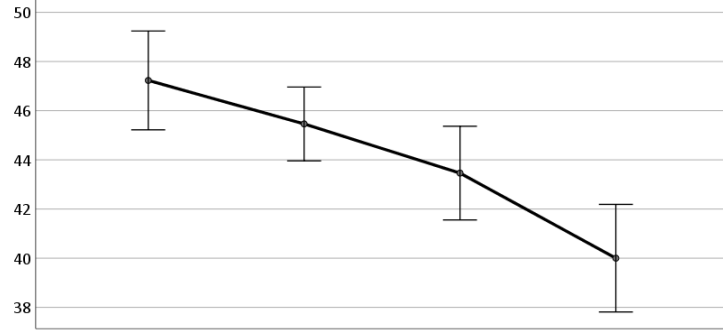
### Subjective Sleep Quality (PSQI)



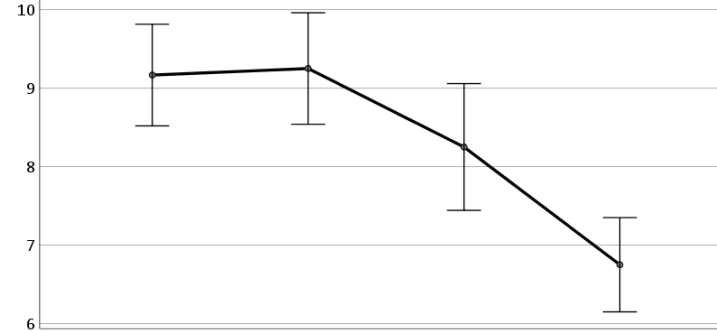
### GWJ Severity



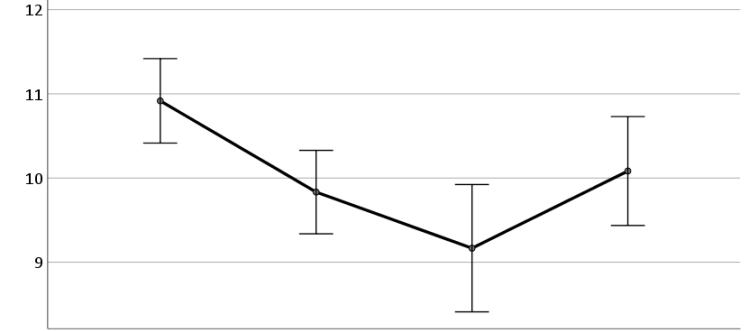
### Fatigue (FSS)



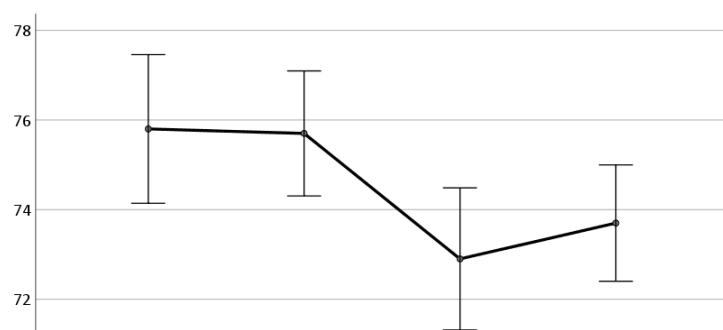
### Depression (HADS-D)



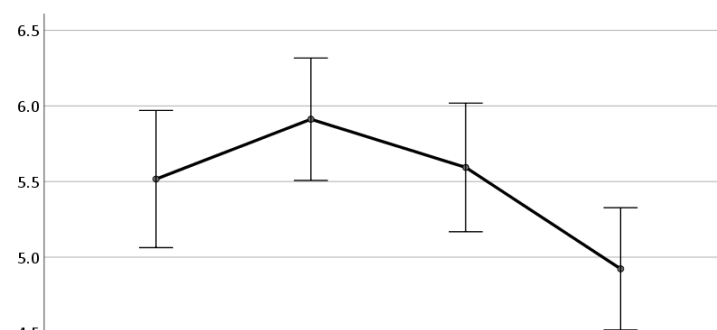
### Anxiety (HADS-A)



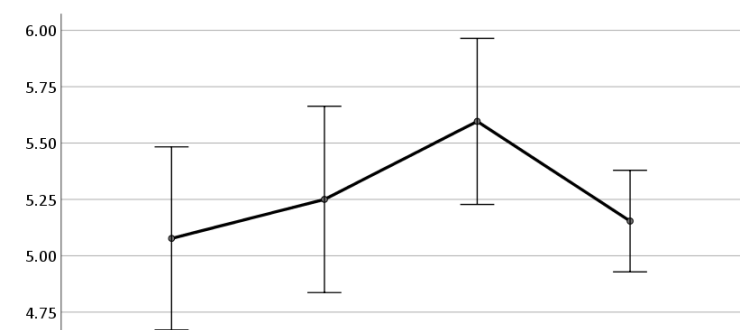
### Cognitive Abilities (MASQ)



### Pain Interference (BPI)



### Pain Severity (BPI)



Pre-Tx

Mid-Tx

Post-Tx

6-month

Pre-Tx

Mid-Tx

Post-Tx

6-month

Pre-Tx

Mid-Tx

Post-Tx

6-month

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