Adapting and implementing sleep and circadian treatment for mental illness and for community mental health settings

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Plan

- Treatment development to implementation science
- Disorder-focused (bipolar disorder) to transdiagnostic (severe mental illness, broadly defined)
- Use of the process of clinical science
- Change of context: university clinic to community mental health
- Sleep tips and tricks

Bipolar Disorder

- Typically alternate between episodes of mania (or hypomania) and depression (APA, 2000)
- The lifetime prevalence of Bipolar I, II, NOS is 2.6% and 6.5%, respectively (Merikangas et al., 2011)
- Each episode lasts between 2 and 7 months
- High rates of suicide (Isometa, 1993)
- Ranked in the top 10 leading causes of disability worldwide (World Health Organization, 2001)
- Sleep symptoms are prominent correlates of episodes and inadequate recovery (Harvey, 2008; Plante & Winkelman, 2008; Wehr, 1990)

Is Sleep Disturbance Epiphenomenal?

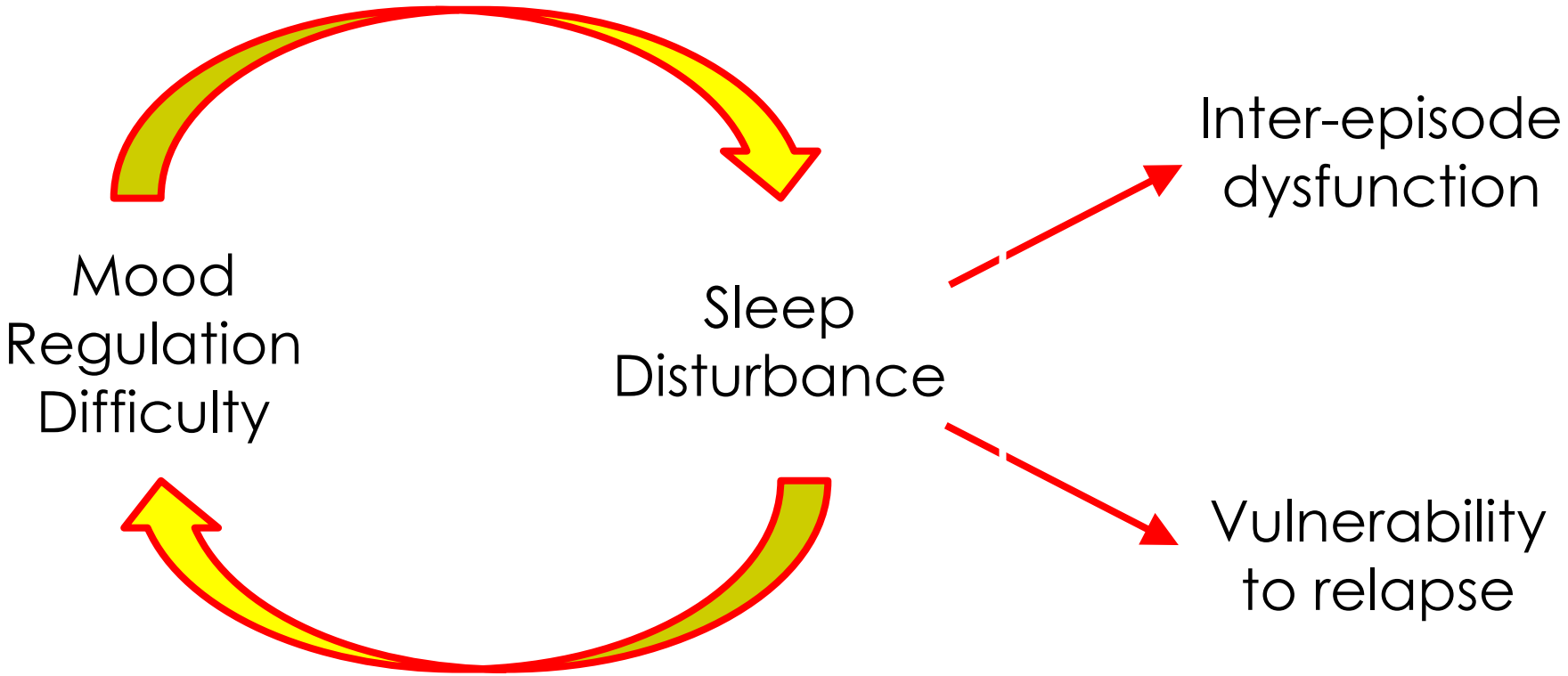
Goodwin & Jamison (1990; 2007), Ehlers, Frank & Kupfer (1988), Wehr (1979; 1985)

Sleep disturbance is the most common prodrome of mania and the sixth most common prodrome of depression (Jackson *et al.*, 2003)

Sleep loss is highly correlated with daily manic symptoms (Barbini *et al.*, 1996) and negative affect (Talbot *et al.*, 2012; Gershon *et al.*, 2012)

Induced sleep deprivation triggers hypomania or mania in a proportion of patients (Colombo *et al.*, 1999)

Bi-Directional Escalating Vicious Cycle



Step-BD

- N = 2,024 patients diagnosed with bipolar disorder
- Variability in sleep/wake times across one week:
  - 2.78 hours (SD = 3.02)

Dr. June Gruber

Gruber, J., Harvey, AG., Wang, PW., Brooks, JO., Thase, ME., Sachs, GS., Ketter, TA. *J Affect Disord* 114:41-49, 2008.

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Step-BD

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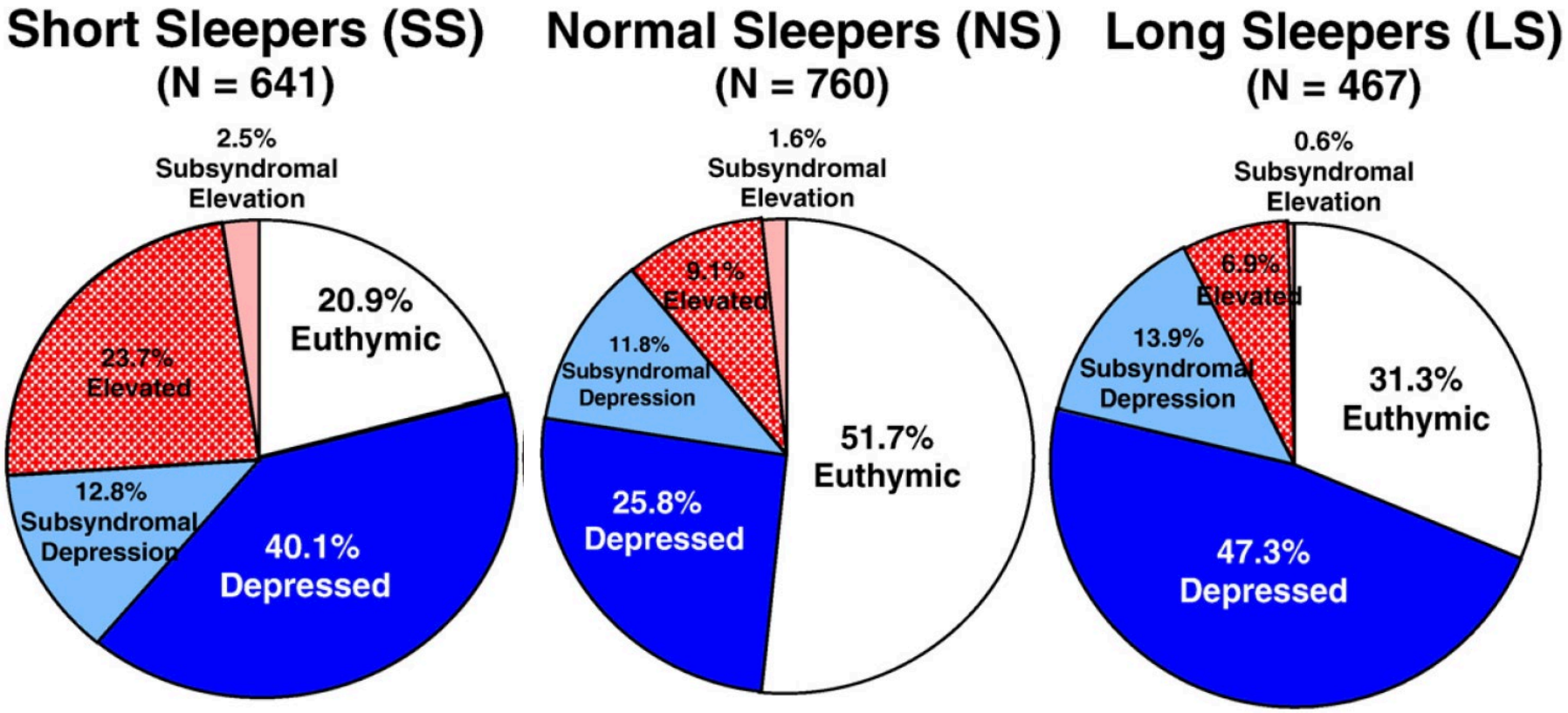
Gruber et al. *J Affect Disord* 114:41-49, 2008.

- Variability in sleep is associated with more past and current depressive episodes
  - sleep efficiency (r=0.50, p<.05)
  - total wake time (r=0.56, p<.005)
  - sleep onset latency (r=0.70, p<.05)

Dr. Polina Eidelman

Eidelman, P. J et al. *BT & Exp Psyc* 41: 145-149, 2010.

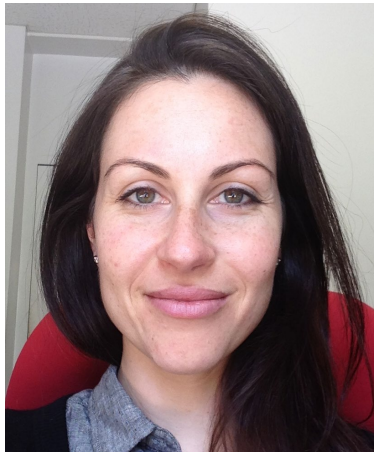
Step-BD



Gruber J, et al. *J Affect Disord* 114:41-19, 2008.

Hypersomnia in Inter-Episode Bipolar Disorder

- Rate = 25%



Dr. Kate Kaplan

- Total Sleep Time (TST) or Time In Bed (TIB) ?
  - 4% TST > 9 hrs
  - 53% TIB > 9 hrs
  - TIB (av *r*=0.55) more highly correlated with all other measures of hypersomnia than TST (av *r*=0.38)

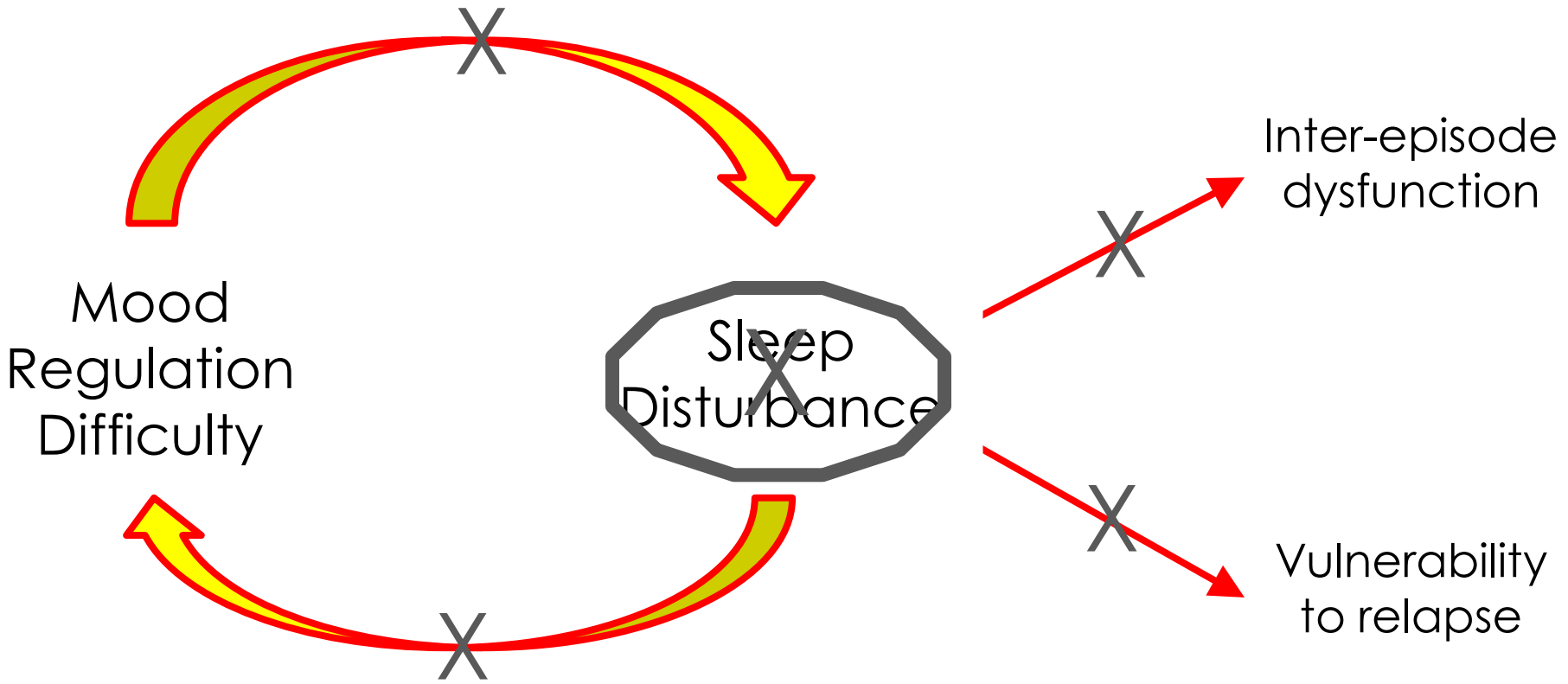
Kaplan et al. (2011). *J Affective Disorders*.

More complex than we expected

- Insomnia
- Hypersomnia (?TIB problem)
- Short sleepers
- Irregular bed and wake times
- And more!

R34 to adapt CBT-I for bipolar disorder …
Recruited patients with bipolar disorder & insomnia
Did not exclude hypersomnia or delayed sleep phase

A *Modifiable* Pathway?

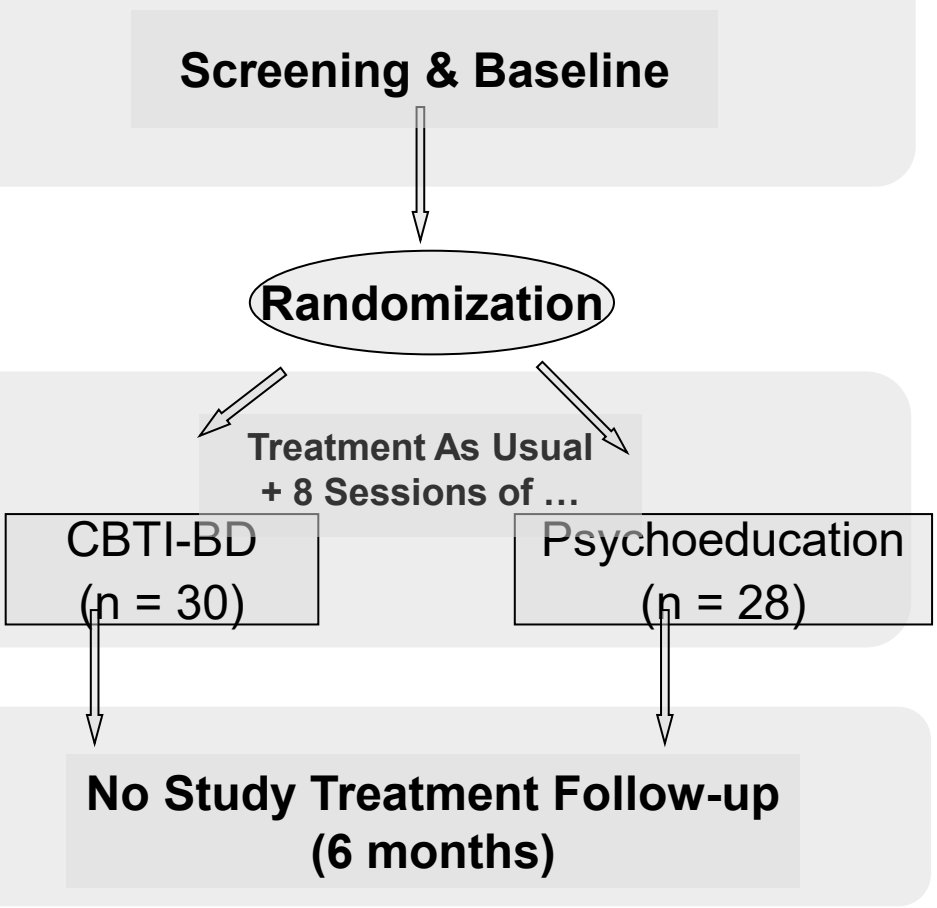


Inter-episode, Bipolar 1 Disorder + Insomnia

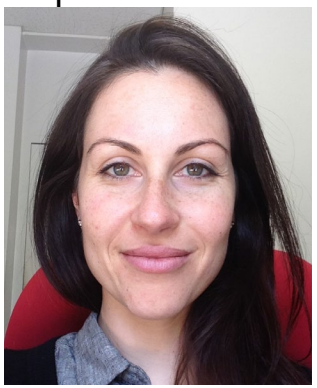
Dr. Dan Buysse

Dr. Adriane Soehner

NIMH R34



Included hypersomnia & delayed sleep phase

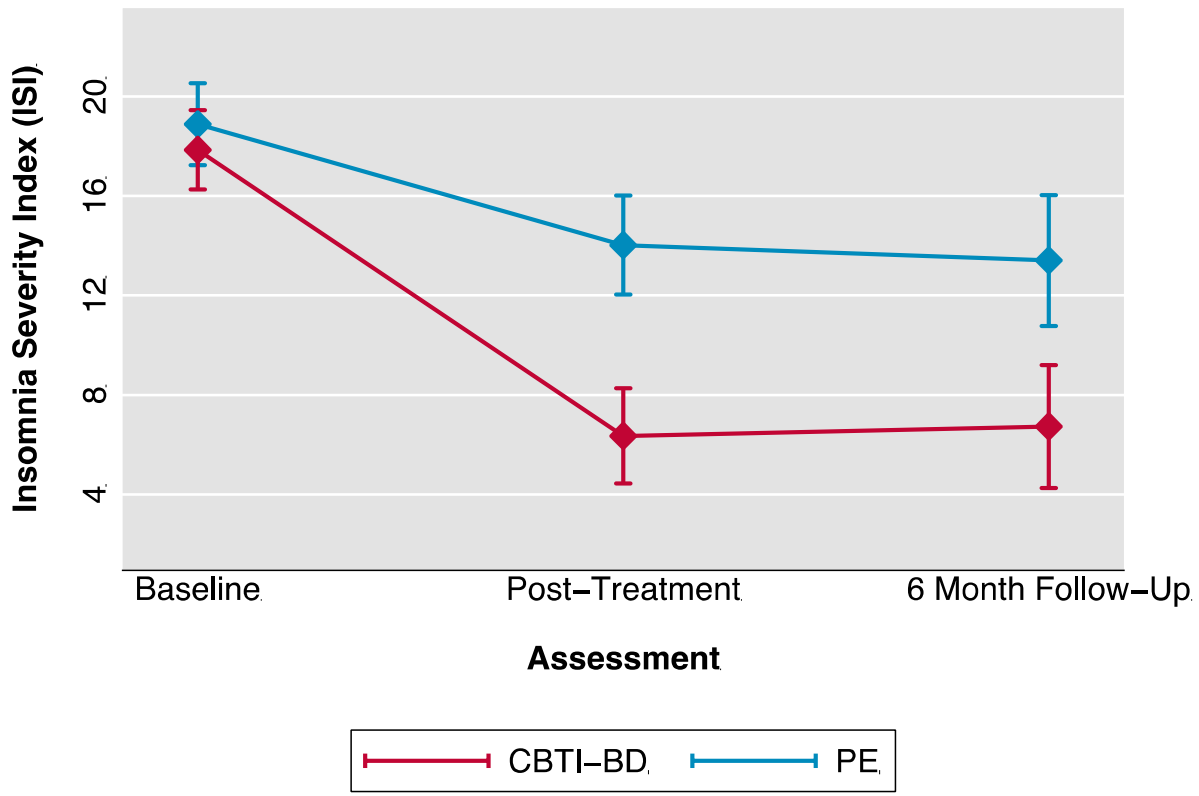


Dr. Kate Kaplan

Kerrie Hein

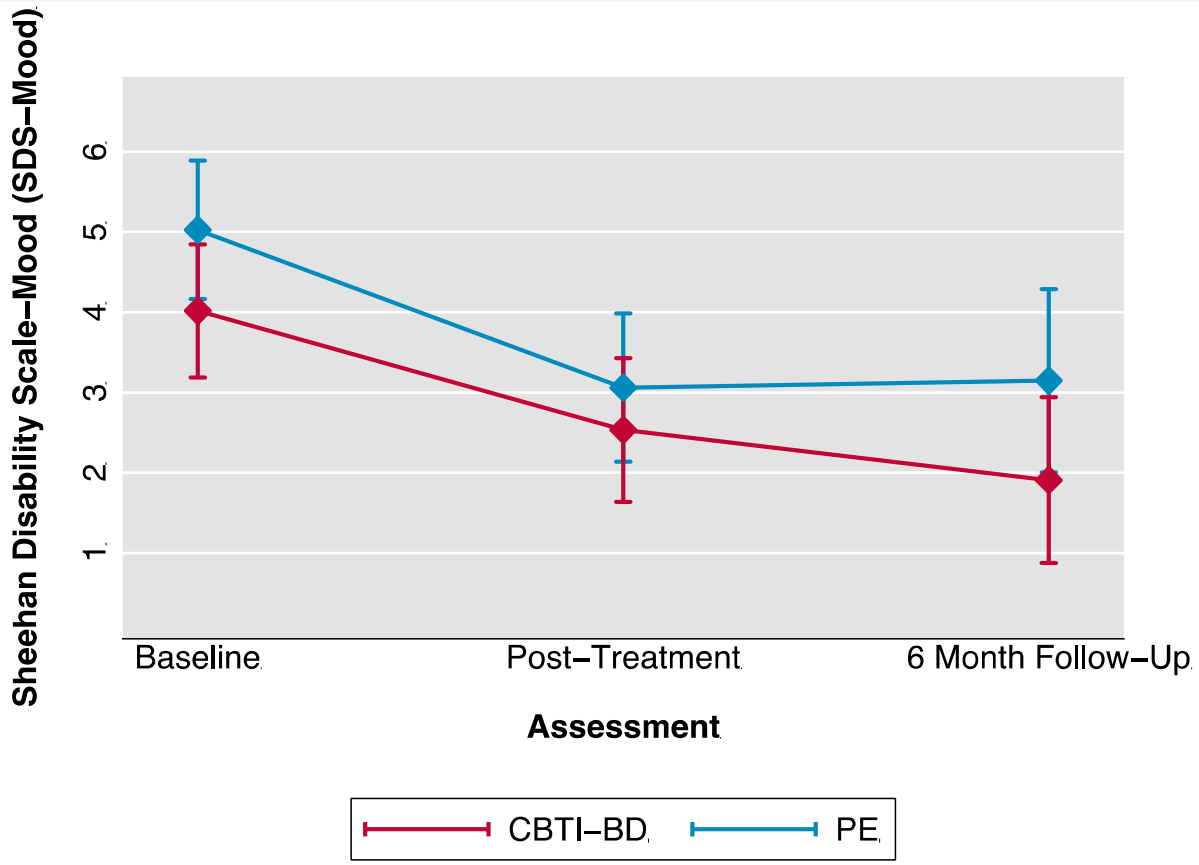
Harvey AG, Soehner AM, Kaplan K., Hein K., Lee J., Kanady J., Li D., Rabe-Hesketh S, Ketter TA, Neylan TC, Buysse DJ, . *JCCP*. 2015.

Insomnia Severity Index



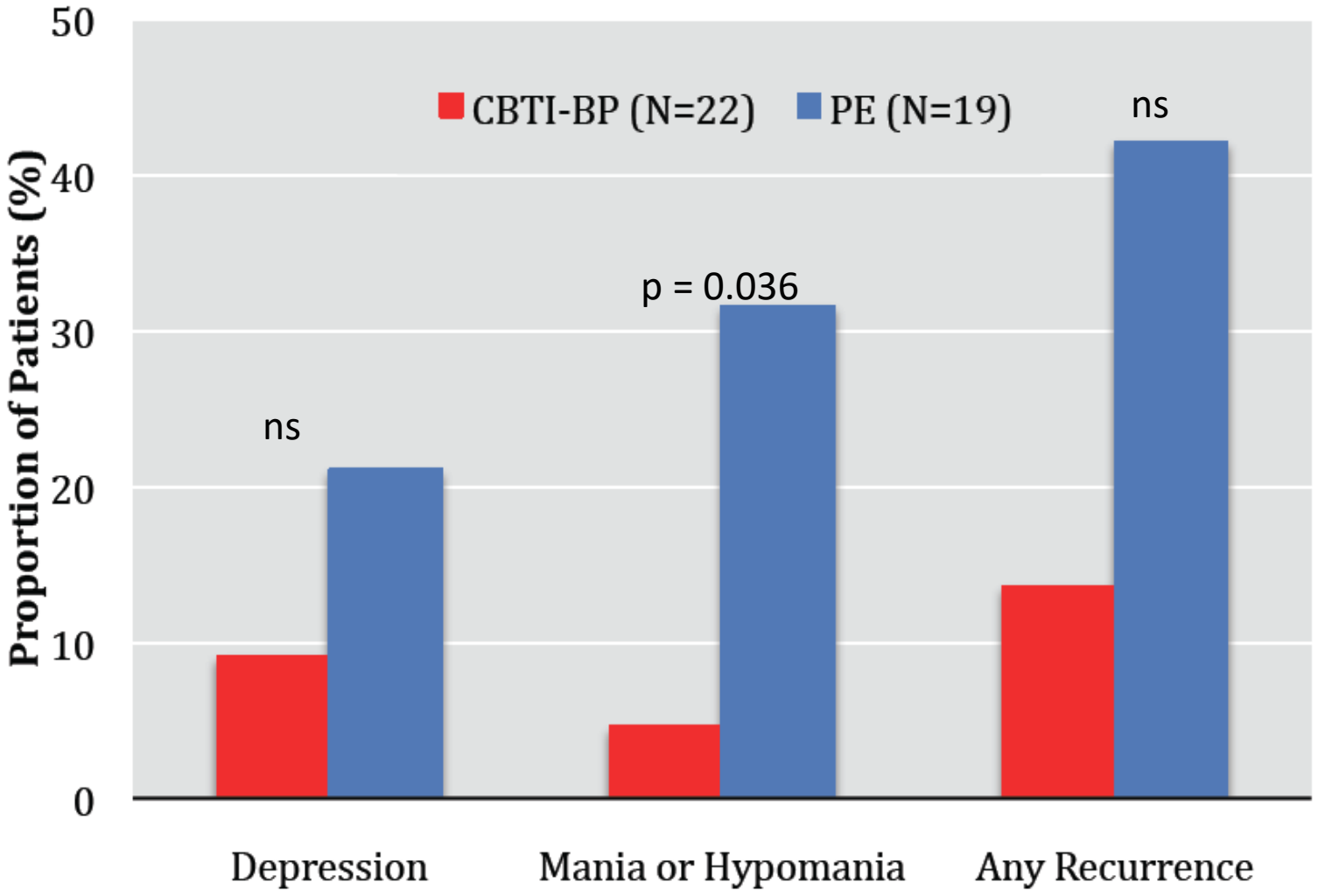
Time X Condition Pre-Post β=-6.64, p<0.001
Time X Condition Pre-Follow-up β=-5.64, p<0.01
Standard error is depicted

Sheehan Disability Scale - Mood

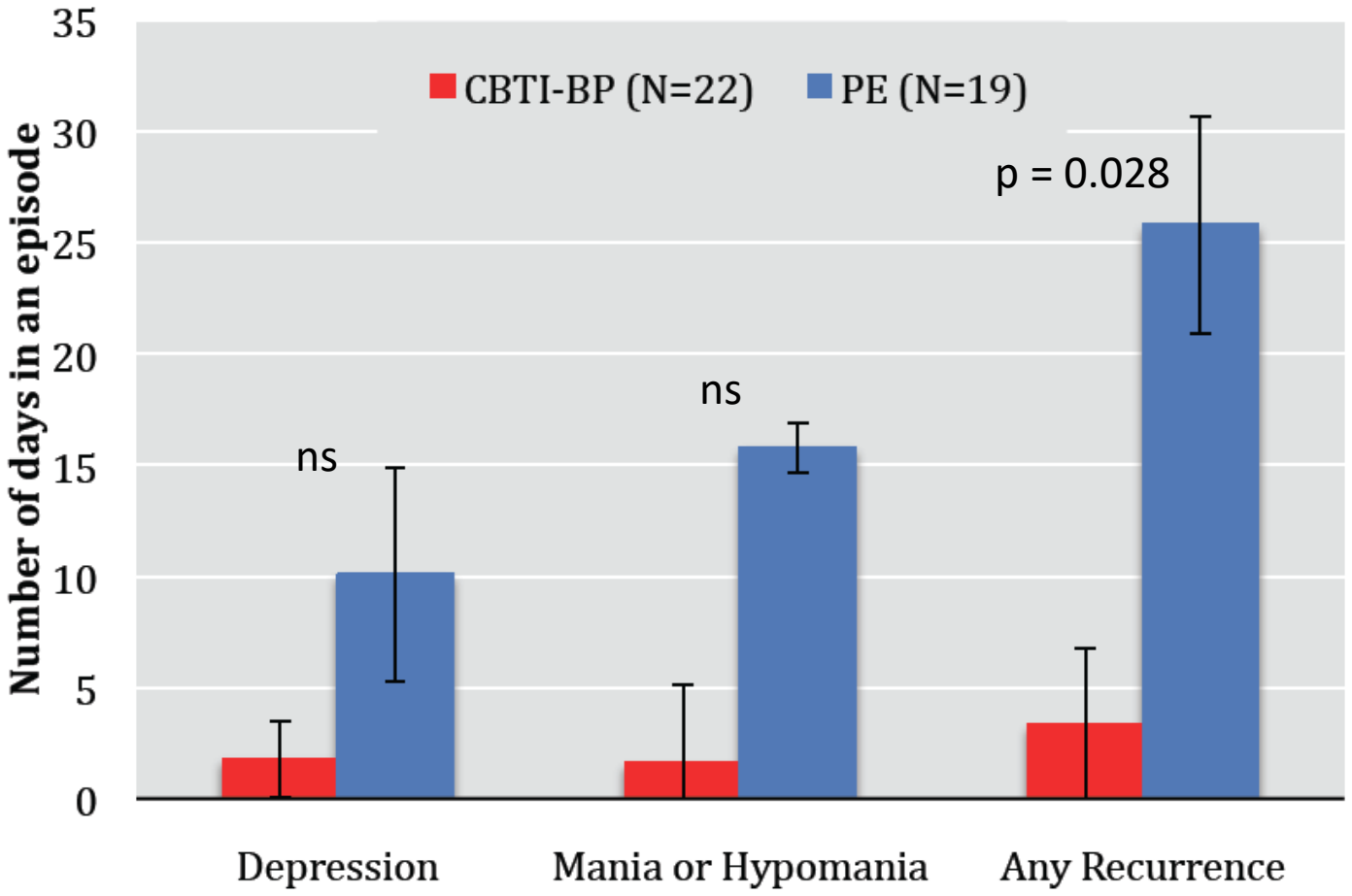


Time Pre-Post β=-1.97, p<0.001
Time Pre-Follow-up β=-1.88, p<0.01
Standard error is depicted

Relapse: 6 Month Follow-up



Days Spent in Episodes: 6 Mth Follow-up



Standard errors depicted

Convergence

Sleep intervention improves sleep and symptoms of comorbid mental disorder

- Bipolar disorder (Harvey et al., 2015; R34MH080958)
- Depression: Youth (Clarke et al., 2015; R34MH082034)
- Schizophrenia (Myers et al., 2011)
- Depression: Adults (Manber et al., 2008)
- PTSD (Germain et al., 2009)
- And others including meta-analyses (e.g., Geiger-Brown et al., 2015)

Disorder-focused (on insomnia) but real life sleep and circadian problems are not so easily categorized (clinical or subclinical features of hypersomnia, delayed phase, irregular sleep & wake times)

How do we deal with the complexity?

- Do we continue to develop multiple disorder-focused treatments?

'Too many empirically supported treatments problem' (p. 68) (Weisz, Ng & Bearman, 2014)

Burden on clinicians, who must learn multiple disorder-focused protocols, with common theoretical underpinnings

Current Direction

Could one treatment be devised that is helpful ...

- Across the various sleep and circadian disturbances
- Across mental illnesses (?physical health)
- Across (some phases of) development (?)

Advantageous for dissemination: Substantial cost advantage to training providers in one treatment that covers multiple problems (McHugh & Barlow, 2010)

Transdiagnostic Intervention for Sleep and Circadian Dysfunction (TranS-C)
(Harvey & Buysse, 2017, Guilford Press)

Dr. Dan Buysse

Sources for TranS-C

Sleep and Circadian Basic Science

Sleep Health Framework (Buysse, 2014)

Transdiagnostic Intervention for Sleep and Circadian Dysfunction (TranS-C)

Cognitive Behavior Therapy for Insomnia (CBT-I)

- Stimulus control and sleep restriction
- Cognitive therapy

Chronotherapy

- Light exposure
- Regular sleep schedules

Interpersonal and Social Rhythms Therapy (IPSRT)

- Stabilize bedtime, wake time, meal times, socializing, exercise, etc.

de Bruin et al., 2014; Schlarb et al. 2010; Gradisar et al., 2011; Pain & Gradisar, 2011; Morin et al., 2006; Frank, Swartz, & Kupfer, 2000; Frank et al., 2005; Wirz-Justice et al., 2009

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What is this complexity doing …

- Insomnia
- Hypersomnia (or Too much time in bed)
- Delayed phase
- Irregular bed and wake times
- And other complexities

Implications for the Biological Orchestra of Clocks: Desynchony!

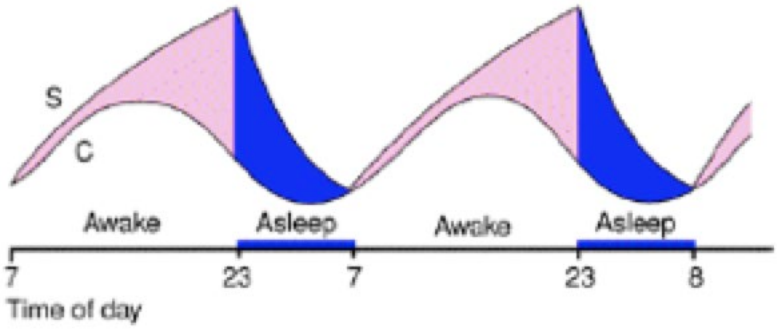
- There are clocks in every cell in the body
  - Central clock: Suprachiasmatic nucleus (SCN) controls the circadian system and is responsive to light and dark
  - Clocks in the muscle, liver and lung synchronize to a variety of stimuli at their own rates but interact with all the other clocks

- Double desynchonization can occur:
  - between internal (SCN) and external time
  - between different clocks and organs in the body itself

Logan & McClung, 2018; Wirz-Justice, 2003; 2006

Sleep System vs. Circadian System

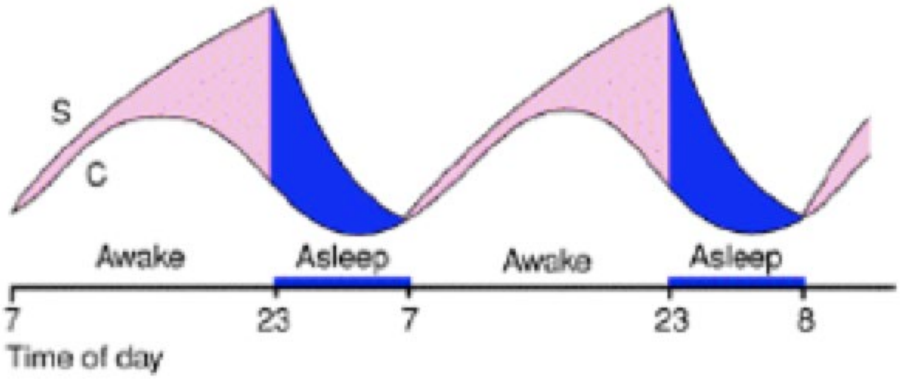
- *Separate systems*
- They interact



- We do not know the specific contribution of the two systems to the sleep problems experienced by people with a mental illness

Borbely, 1982

Open System



Exogenous Inputs
Modifiable

Social rhythms

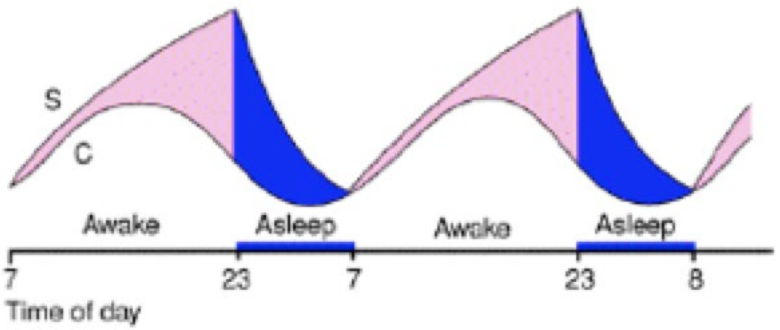
Sleep deprivation

Light

Arousal

Temperature

Stress/
Emotions



Meal times

Locomotor activity

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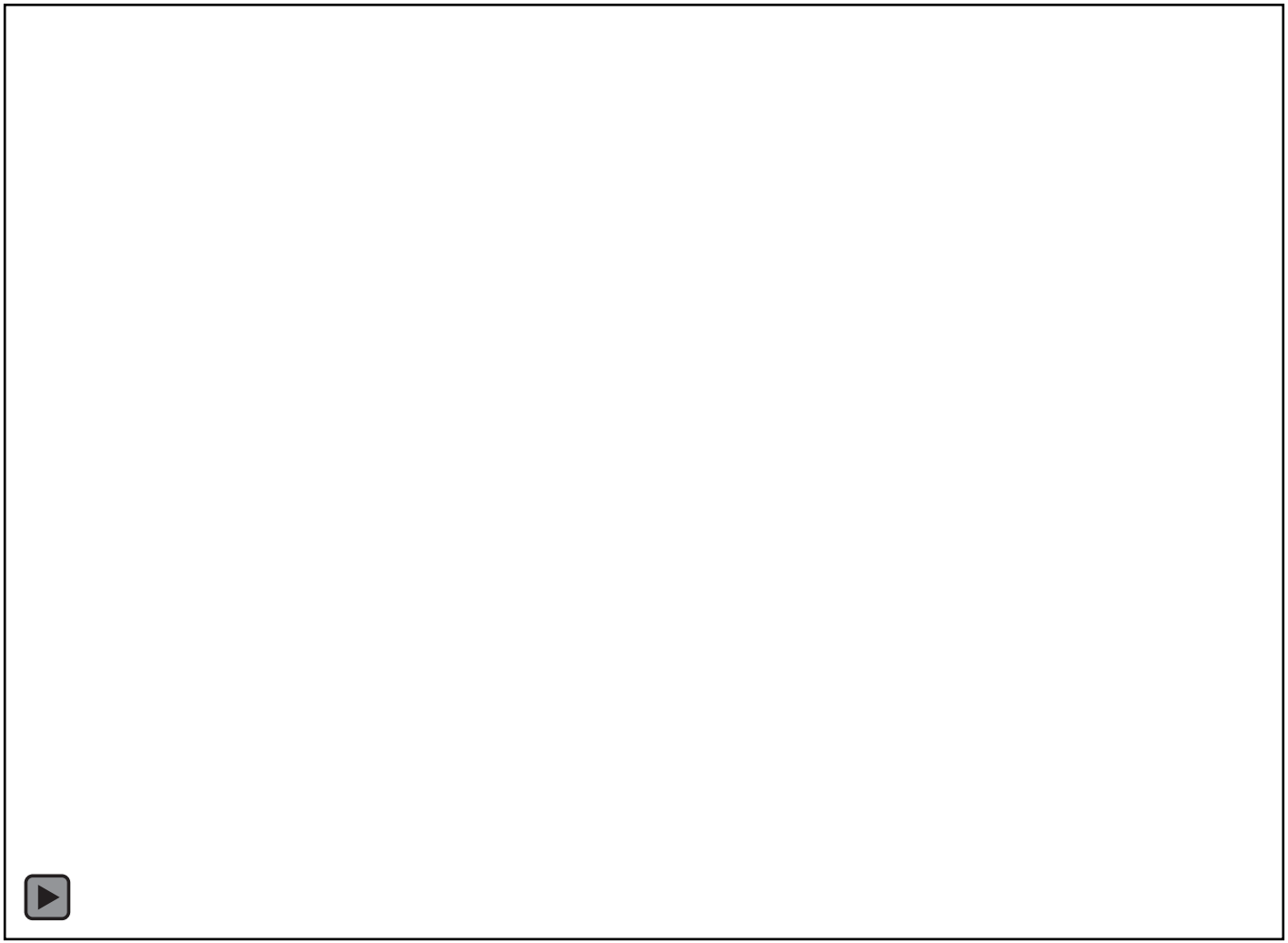
Glimpse of CBT-I

- Go to bed only when sleepy
- Awaken at the same time every morning
- Use the bed mainly for sleeping – no reading, watching TV, or eating in bed
  - Maladaptive conditioning or learned association between *wakefulness* and the bedroom

Bootzin RR, Epstein DR. *Stimulus Control*. In: Lichstein KL, Morin CM, eds. Treatment of late-life insomnia. Thousand Oaks, Calif: Sage; 2000:167-184.



Why don't we just use CBT-I?

- TranS-C incorporates CBT-I
- And addresses a broader range of sleep and circadian dysfunctions common to mental illness
  - Chronotherapy approaches and rise-up routines for delayed phase
  - CPAP adherence approaches for OSA
  - Negotiating sleep in a complex environment
- A notable proportion of SMI patients exhibit sleep efficiency >85% or their sleep efficiency is corrected by regularizing bed and wake times (Kaplan & Harvey, 2013, AJP)
- Safety: stimulus control and sleep restriction can involve partial sleep deprivation and SMI relapse (Columbo et al., 1999)

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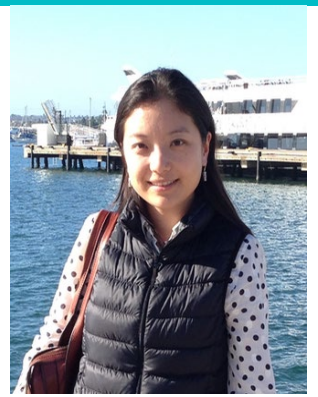
TranS-C: A modular treatment

Cross-Cutting Modules				Common Transdiagnostic Sleep-Circadian Problems	Treatment Module
Case Formulation	Education	Behavior Change & Motivation	Goal Setting	Establishing regular sleep-wake times	Core Module 1
				Learning a wind-down routine	Core Module 1
				Learning a wake-up routine	Core Module 1
				Improving daytime functioning	Core Module 2
				Correcting unhelpful sleep-related beliefs	Core Module 3
				Improving sleep efficiency	Optional Module 1
				Reducing time in bed	Optional Module 2
				Dealing with delayed or advanced phase	Optional Module 3
				Reducing sleep-related worry/vigilance	Optional Module 4
				Promoting compliance with CPAP/exposure therapy for claustrophobic reactions to CPAP	Optional Module 5
				Negotiating sleep in a complicated environment	Optional Module 6
				Reducing nightmares	Optional Module 7
				Maintenance of behavior change	Core Module 4

Change of context



Dr. Lulu Dong

- Representativeness of the samples
  - In a highly diverse location
  - 50%+ with graduate level degrees
  - Difficulty recruiting ethnic and racial minority group members

- Who is not comfortable attending a university clinic for treatment?
- What are the barriers for those people?

Community Mental Health Centers

- "Unique national asset"
- 1960's "War on Poverty" to eliminate health disparities
- SMI (serious mental illness)
- Serves 29 million Americans. No one is turned away: 40% uninsured, 36% Medicaid, 63%+ racial or ethnic minority, 91% low-income (200% Federal poverty level or below)
- Publicly funded providers
- Seriously under-resourced
- Providers carry a heavy, complex and comorbid caseload
- Providers may not receive training or supervision in EBTs

(Aarons et al., 2012; Adashi et al. 2010; Bruns et al., 2015; Chin et al., 2010; Drake et al., 2001; Garland et al., 2010; Lefkowitz et al., 2005; Rodríguez et al., 2014; Prosner, 2005; Weissman et al., 2006)

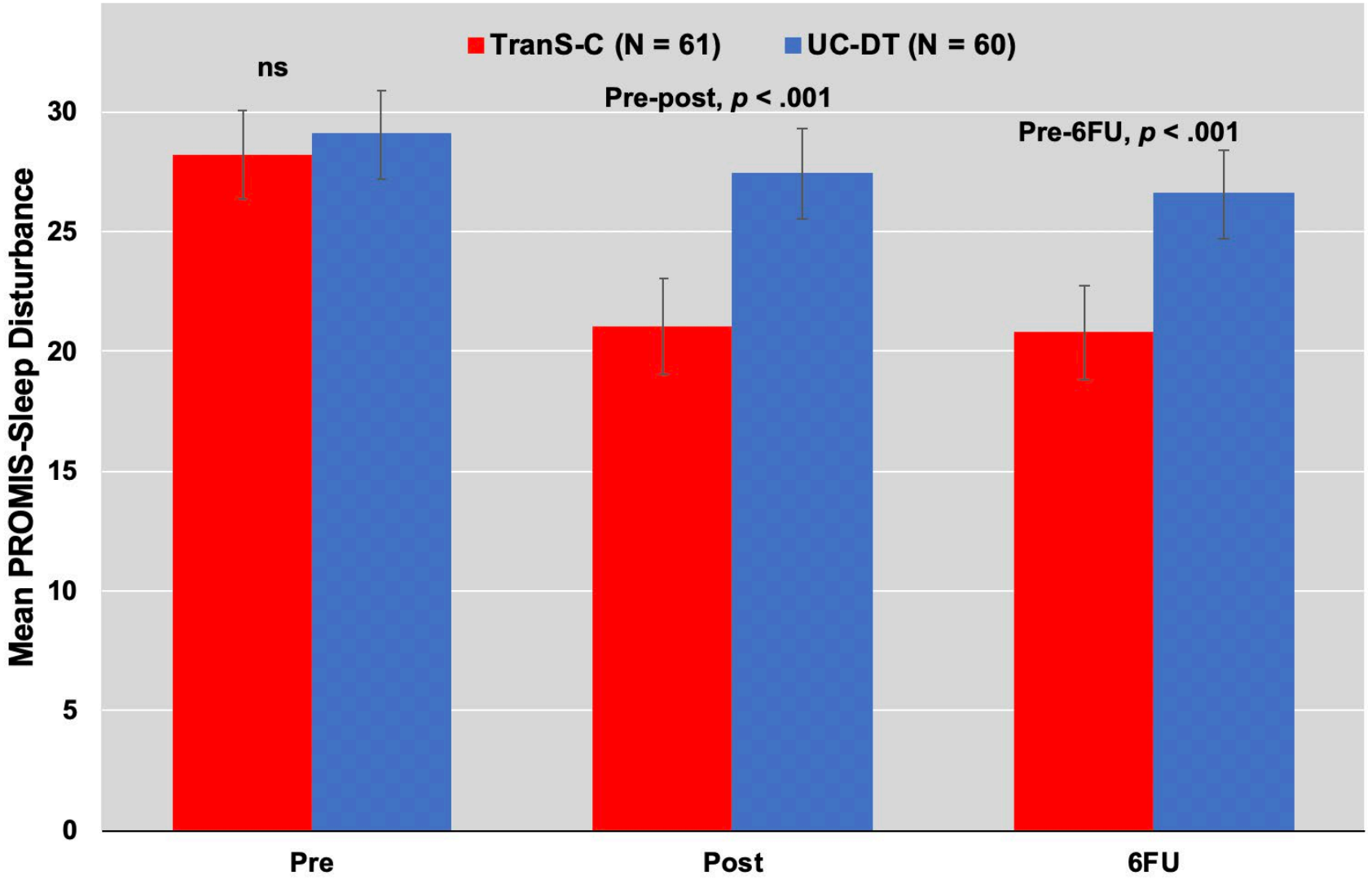
Snapshot of patient demographics (n=121)

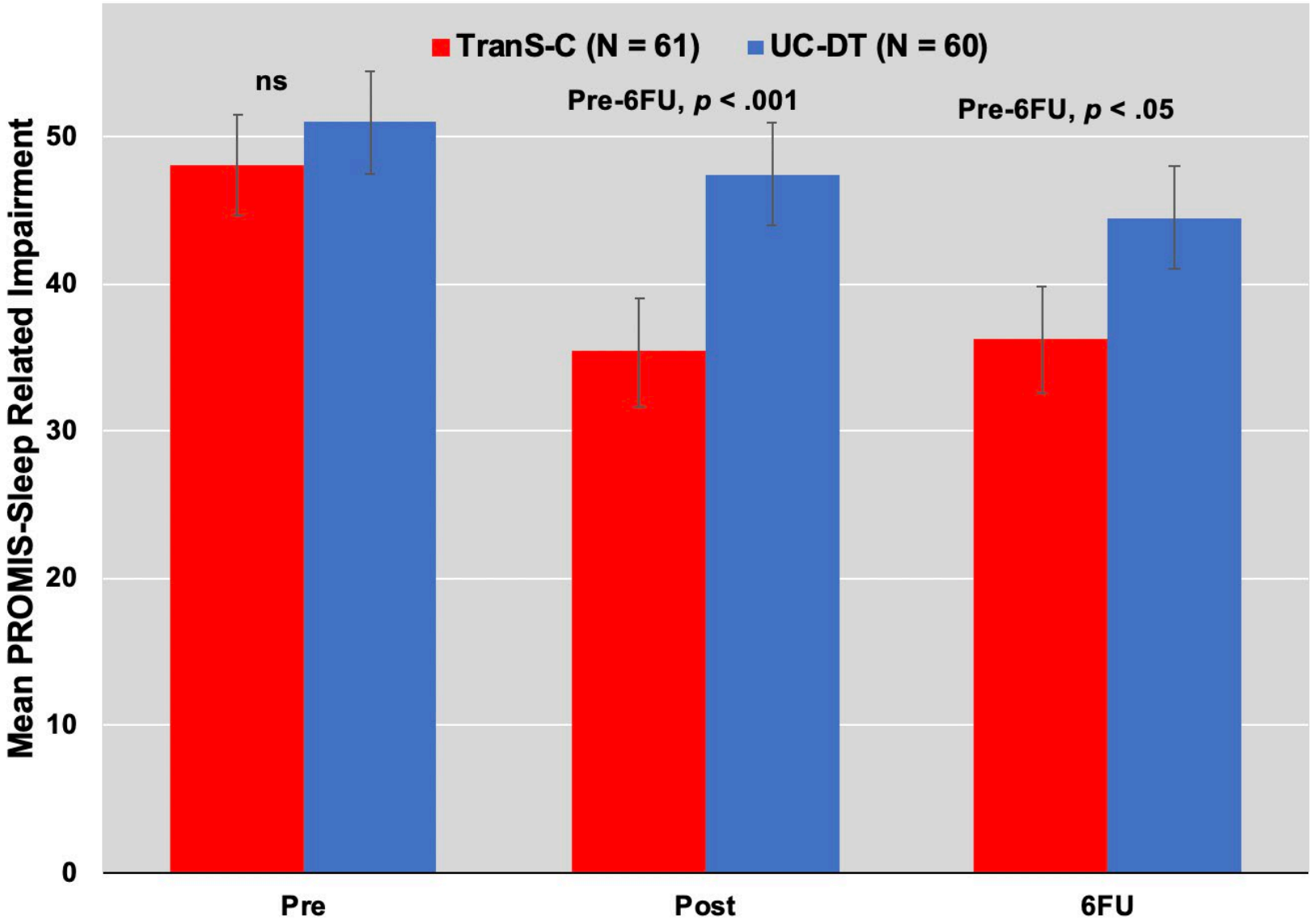
- Av personal income $12,751 per yr
- 68% single
- 2% attended graduate school
- 80% not currently employed
- 55% living in a supported living environment
- 43% African American / Black

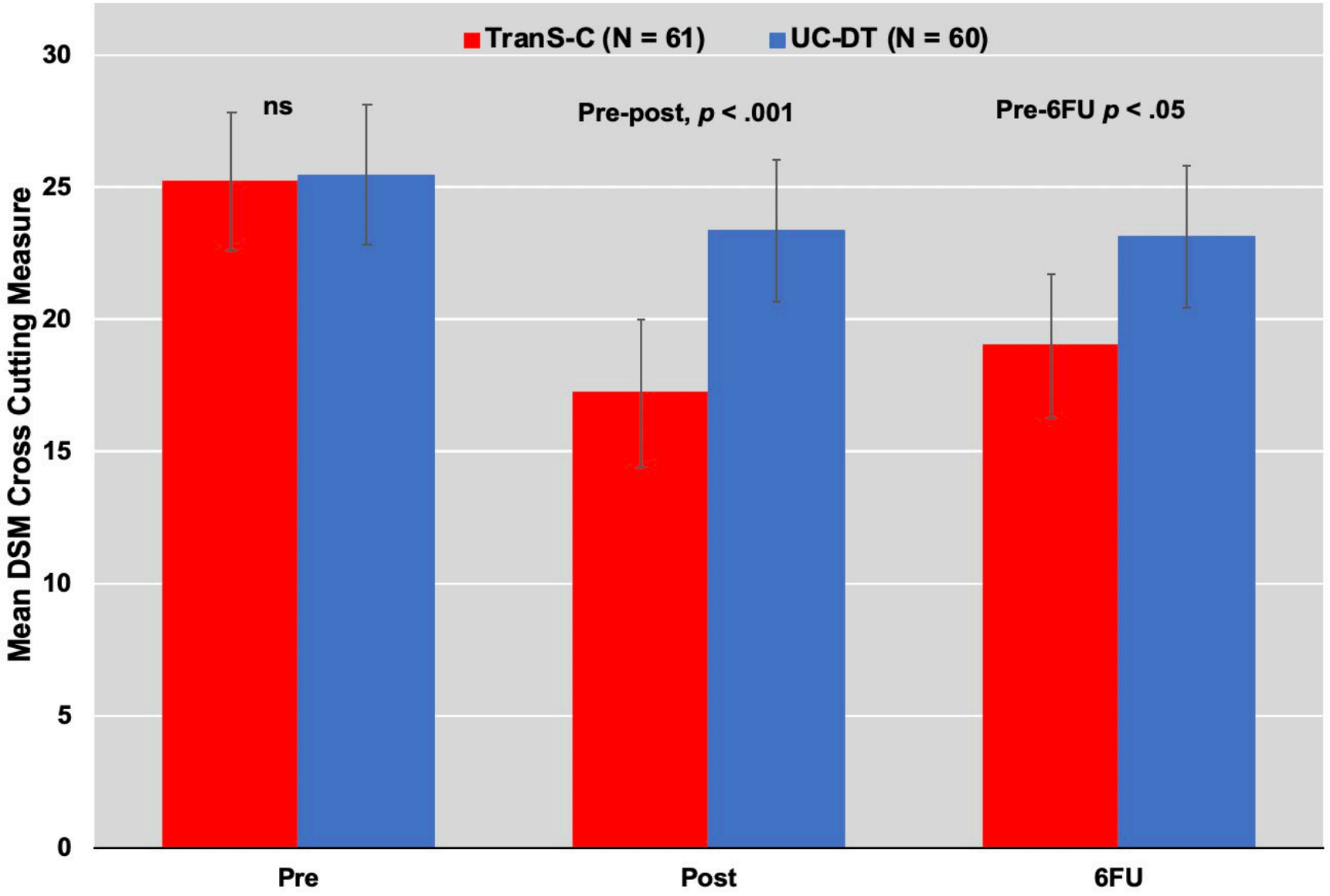
SMI diagnosis
50% Schizophrenia spectrum disorder
18% Bipolar disorder
32% MDD
(anxiety disorders & substance use often comorbid)

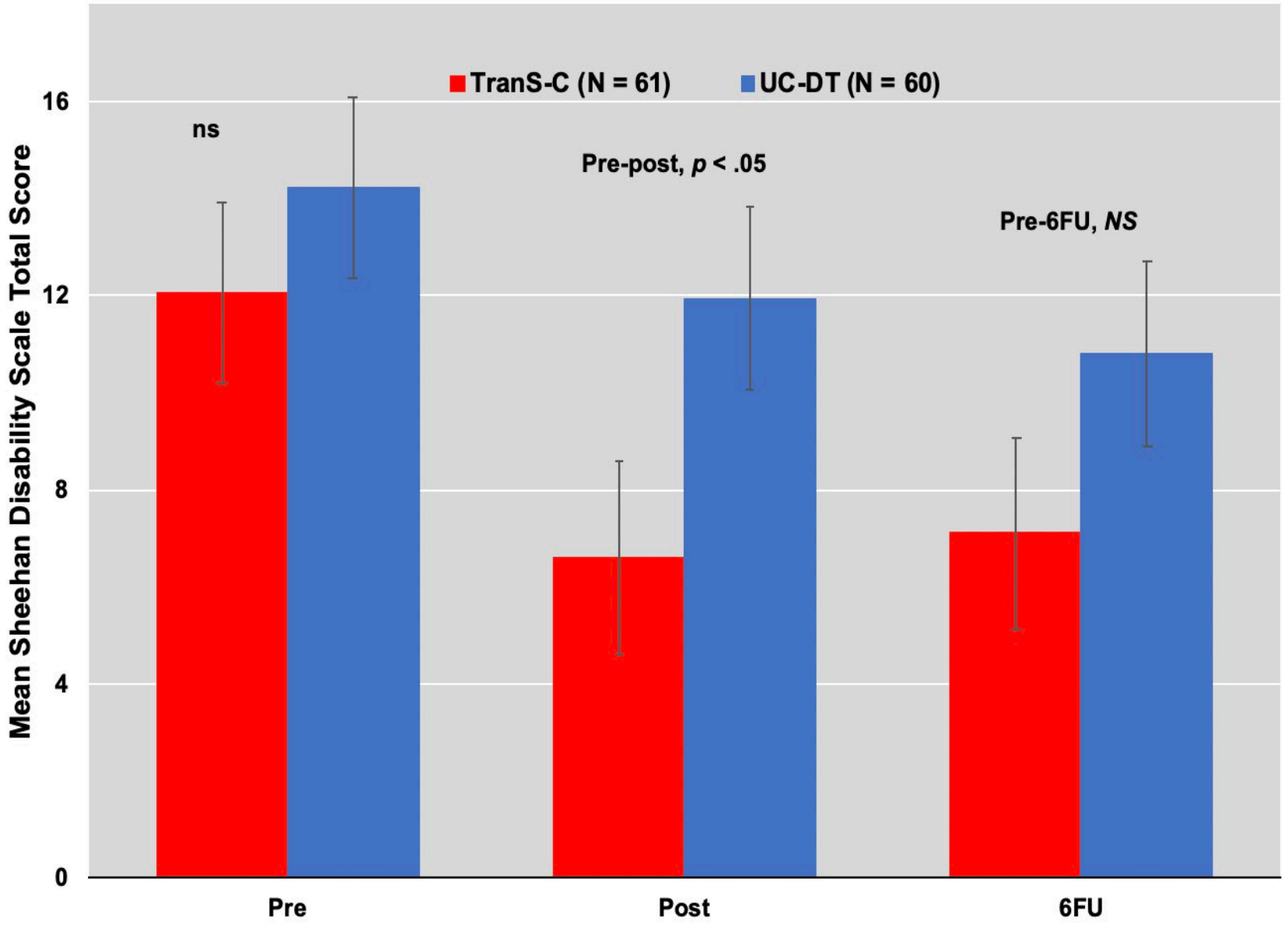
Alameda County, CA

UC Berkeley providers delivering the treatment in CMHCs


TranS-C (N = 61)
UC-DT (N = 60)
ns
Pre-post, p < .001
Pre-6FU, p < .001
Mean PROMIS-Sleep Disturbance
30
25
20
15
10
5
0
Pre
Post
6FU


TranS-C (N = 61)
UC-DT (N = 60)
ns
Pre-6FU, p < .001
Pre-6FU, p < .05
Mean PROMIS-Sleep Related Impairment
0
10
20
30
40
50
Pre
Post
6FU


TranS-C (N = 61)
UC-DT (N = 60)
ns
Pre-post, p < .001
Pre-6FU p < .05
Mean DSM Cross Cutting Measure
30
25
20
15
10
5
0
Pre
Post
6FU


TranS-C (N = 61)
UC-DT (N = 60)
ns
Pre-post, p < .05
Pre-6FU, NS
Mean Sheehan Disability Scale Total Score
16
12
8
4
0
Pre
Post
6FU

Secondary Outcomes

TranS-C, relative to usual care, *reduction* on:
Psychotic Symptom Rating Scales (PSYRATS)

Total Wake Time
Wake Time Variability
Earlier Bedtime
Improvement on:
Sleep Efficiency

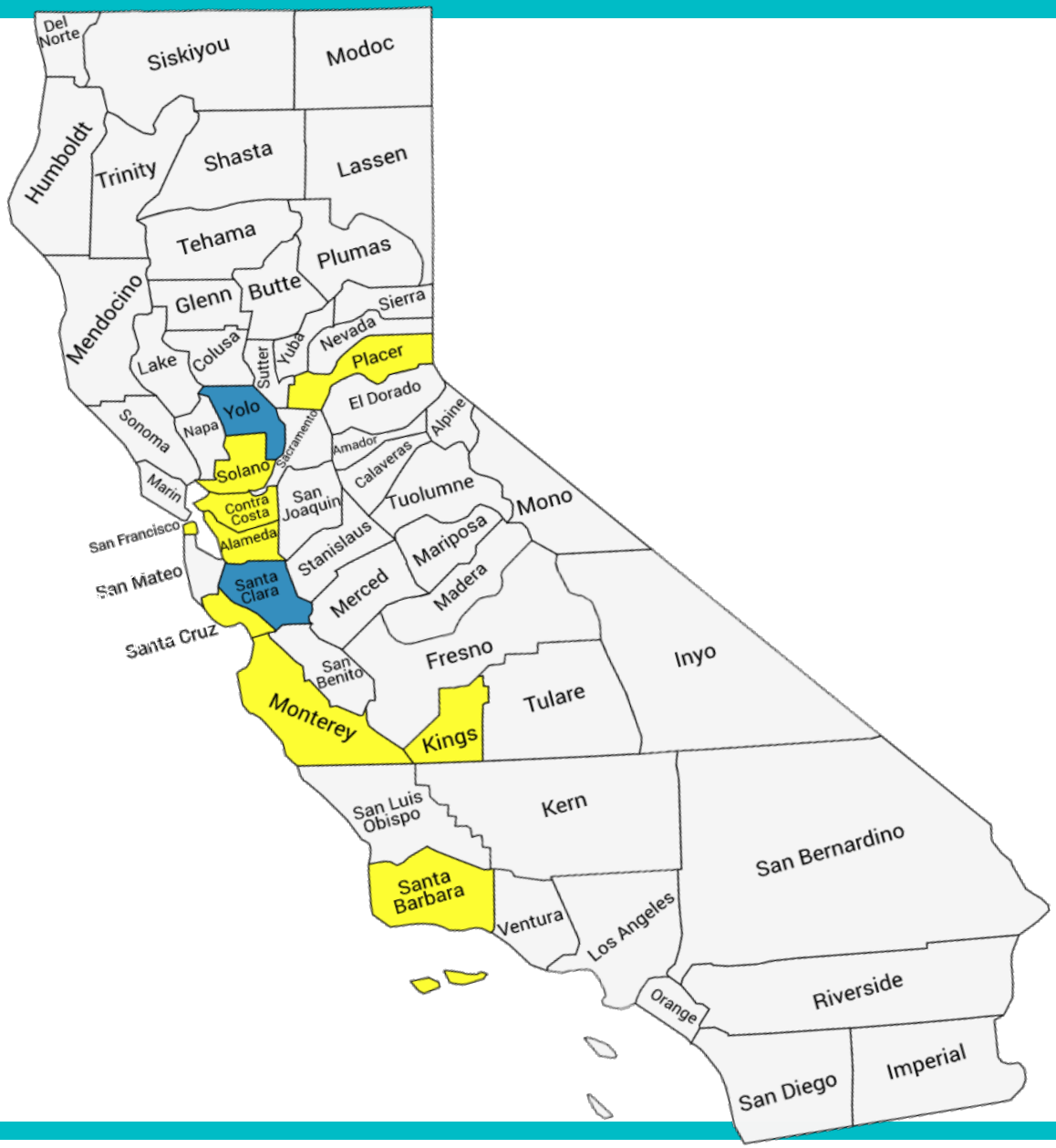
} 7-day sleep diary

Sleep Health Composite (Buysse, 2014; Dong et al., 2019)

New Project

CMHCs we are working with

FQHCs we are working with



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New Project

- Funded by NIMH
- Patients n = 624; CMHC Providers n = 104
- Does TranS-C improve sleep and mental health and reduce substance use?
- Implementation science questions:
  - Can TranS-C can be effectively delivered by providers within CMHCs?
  - The implementation process (facilitation: Kirchner and PARIHS)
  - Supervision and fidelity
  - Training e.g., train-the-trainer

May I offer some sleep tips and tricks?

Look for 8+ tweaks to your sleep

Cut out checking the clock (bright light & arousal)

Cut down on caffeine & alcohol

Regular bedtimes

Regular waketimes (most important)

Accept that poor night's of sleep will happen

Consider timeframe

'Romantic' lighting before bedtime

Rid bedroom of all light pollution

Ensure bedroom is very dark so the summer morning light doesn't wake you

Cont ..

Be aware of liquid intake before bedtime

Increase exercise

Perception of sleep: we often get more sleep then we think

Watch for vicious 'racing mind' cycles

'I'm never going to get back to sleep'
'I won't cope tomorrow'
'I will get sick'
Vs.
'It's so nice to be comfy here'
'I feel so warm and calm'

Summary

- Disorder focused – Transdiagnostic
- TranS-C: Behavior change approach
  - Generated from sleep and circadian science
  - Generated from existing evidence-based treatments
  - Simple, short … disseminable
  - Promising initial results for sleep & the comorbid mental illness
- Advantages for dissemination, particularly in under resourced settings (e.g., CMHCs)
- Challenge ahead: Scaling of sleep treatment within many other contexts and populations …

Eunice Kennedy Shriver National Institute of Child Health and Human Development
Health research throughout the lifespan

National Institute on Drug Abuse
Advancing Addiction Science

National Institute of Mental Health

Our community partners

R01, Implementation
Dr. Lulu Dong
Dr. Dan Buysee
Emma Agnew
Marlen Diaz
Krista Fisher
Shayna Howlett

R34, Bipolar Disorder
Dr. Dan Buysee
Dr. Adriane Soehner
Kerrie Hein
Dr. Kate Kaplan
Dr. Jen Kanady

R01, TranS-C
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Kerrie Hein
Stephanie Yu
Isaac Mirzadegan
Alice Mullin
Armando Martinez
Caitlin Eggleston
Niki Gumport
Dr. Mike Dolsen
Cece Armstrong
Eve Fine

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Dr. Lulu Dong
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Dr. Gullion
Dr. Dickerson
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