



University of California
San Francisco

Mood Disorders

Andrew D. Krystal, MD, MS

Director, Clinical and Translational Sleep Research Laboratory

Director, Dolby Family Center for Mood Disorders

Ray and Dagmar Dolby Distinguished Professor

Vice-Chair for Research

Department of Psychiatry and Behavioral Sciences

UCSF

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Professor Emeritus, Duke University

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OVERVIEW

- Introduction: The Relationship of Insomnia and major depression
- Correlations suggest insomnia and depression appear to have a bi-directional relationship. Correlation vs Causation?
- Evidence that insomnia plays a causative role in major depression and suicidality

90% with MDD Have Sleep Problem: DSM-IV Major Depression

- 2-week period of depressed mood or loss of interest
- Clinically significant distress or impairment of functioning
- Symptoms not due to substance abuse or medical condition
- 4 or more of the following symptoms:
 - Insomnia/hypersomnia
 - Weight loss/decreased appetite
 - Psychomotor agitation/retardation
 - Fatigue/loss of energy
 - Worthlessness and guilt
 - Diminished concentration/indecisiveness

Insomnia in MDD: Symptom or Co-Morbid Condition?

- ~70% with MDD have insomnia;
~20% report daytime sleepiness
- Is insomnia/hypersomnia best thought of as symptom or condition that is co-morbid with MDD?

Sleep and MDD

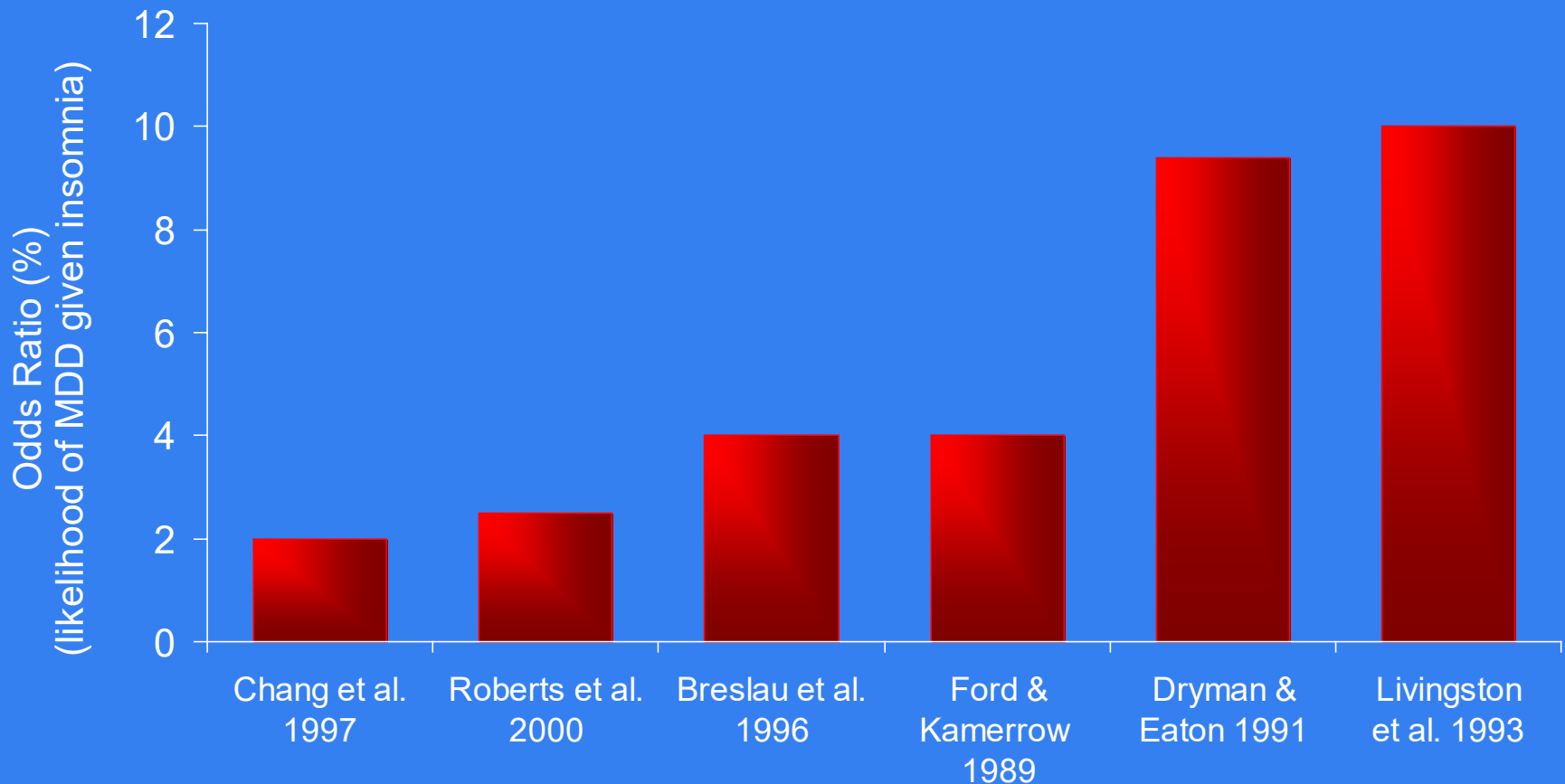
- Traditional View: Insomnia is among MDD symptoms so does not require specific treatment; Treating the MDD should address the insomnia
- Evidence suggests: Insomnia impacts depression; The relationship is bi-directional; Insomnia specific treatment is indicated.



Evidence for Bidirectionality, Insomnia Independence

- Insomnia increases the risk of future depression
- Insomnia decreases antidepressant response
- Insomnia is independent risk factor for suicidality, attempts and completed suicide in MDD pts
- Insomnia is the most frequent residual symptom in antidepressant responders
- Residual insomnia increases relapse risk

>Six Studies Show That Insomnia Is a Risk Factor for Major Depressive Disorder (MDD) Correlation or Causation?



Insomnia Is a Risk-Factor for Suicidality in Depressed Patients

Correlation or Causation?

- >40 studies indicate that insomnia is associated with suicidality after controlling for depression severity and other factors
 - It is one of the most robust predictors of ideation, attempts, and completed suicides
 - Better predictor than self-reported ideation, intent to self-harm, or plan
 - Relative risk of suicide death up to 2.4

Evidence that Treating Insomnia Decreases Risk of MDD Emergence

- 3 Recent studies all suggest that treating insomnia with CBT for insomnia in non-depressed individuals decreases subsequent MDD emergence

Treating Insomnia During Pregnancy Prevents Post-Partum Depression

- 208 pregnant women with insomnia were randomized to digital Cognitive Behavioral Therapy for Insomnia (CBT-I) or standard care.
- The proportion of participants with major depression at 3 months postpartum was significantly higher among standard care (18%) than dCBT-I (0%) participants ($p = 0.006$)



Jenn
Felder,
UCSF



Aric
Prather,
UCSF

Treating Insomnia Decreases Depression Severity 1 Year Later

- Insomnia patients were randomized to dCBT-I (n = 358) or sleep education control (n = 300).
- dCBT-I was associated with significantly decreased MDD severity 1 year later. Mediated by increased resilience (measured in terms of ability to recover from stress).

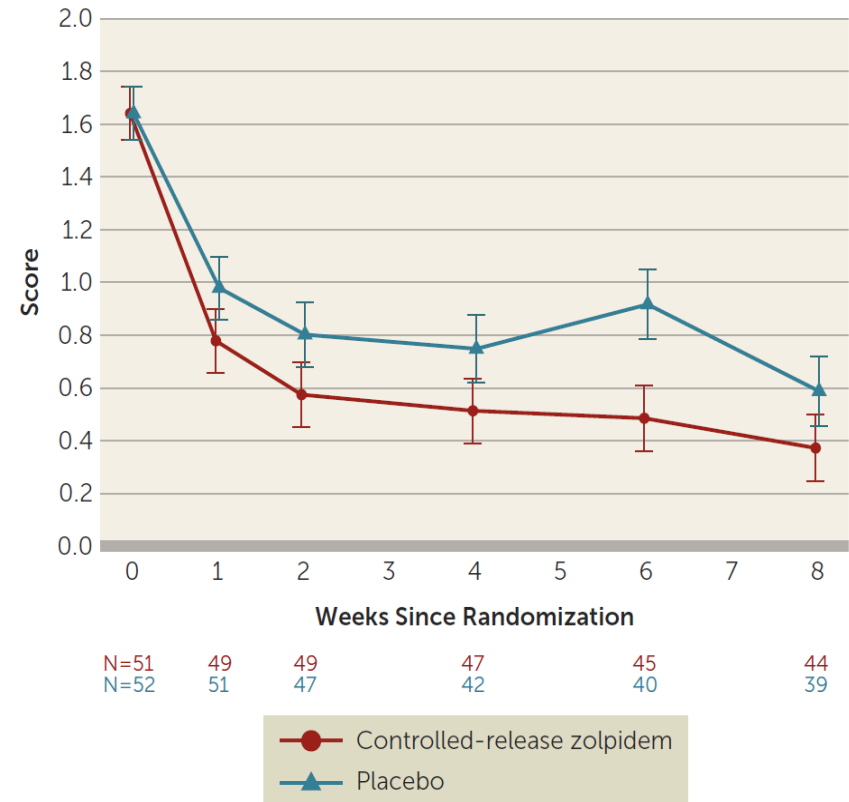
Treating Insomnia Decreases Depression Severity 1 Year Later

- 291 adults 60 years or older with insomnia disorder were randomized to in-person CBT-I (n = 156) or Sleep Education Therapy (SET) (n = 135) and followed for 24 months
- Incident or recurrent major depression occurred in 19 participants (12.2%) in the CBT-I group and in 35 participants (25.9%) in the SET group, with an overall benefit (hazard ratio, 0.51; 95%, CI 0.29-0.88; P = .02) consistent across subgroups.

Treatment of Insomnia Improves Suicidality in Depressed Patients

- Randomized trial of zolpidem CR + fluoxetine vs placebo + fluoxetine in 103 depressed patients with suicidal ideation
 - Insomnia therapy significantly decreased suicidal ideation vs placebo ($p < 0.04$)
 - Insomnia appears to have a causal link to suicidality and could be a treatment target

FIGURE 4. Least squares mean scores for suicidal ideation on the Columbia–Suicide Severity Rating Scale for participants in the Reducing Suicidal Ideation Through Insomnia Treatment study^a



^a Error bars indicate standard errors.

CONCLUSIONS

- Based on correlations, insomnia and depression appear to have a bi-directional relationship.
- This role is causative with respect to the emergence of major depression and suicidality in depressed patients
- Work is needed to understand mechanisms
 - Overlapping circuitry modulating mood and sleep.
 - Preliminary evidence that intracranial stimulation that improves depression alters sleep/wake acutely
 - Genes regulating sleep need also modulate resilience - a mediator of CBTI mitigation of depression emergence

We Don't All Sleep The Same Way But We All Need to Do It

Andrew Krystal
Lauren Asarnow
Katherine Scangos
Eddie Chang

Louis Ptacek
Liza Ashbrook
Joline Fan

Ying-Hui Fu
Aric Prather
Jenn Felder

