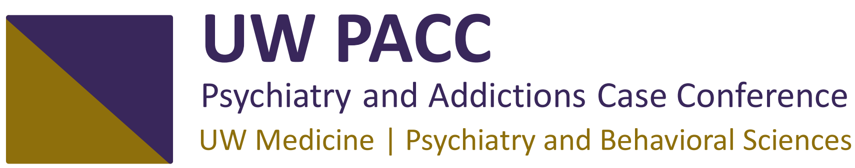


# TAPERING SLEEP MEDICATIONS

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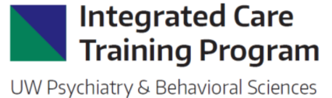

# DISCLOSURES

We have no conflicts of interest to report.

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# OBJECTIVES

- The learner will know about trends in the prescription of sleep aids for insomnia
- The learner will be able to articulate concerns about use of sleep aids.
- The learner will know how to address challenges in sleep aids discontinuation and help patients discontinue use of sleep aids.

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# QUESTIONS TO CONSIDER

- What are the trends in the prescribing of hypnotics for insomnia?
- Why should we care if patients use sleep aids?
- What are the challenges in discontinuing sleep aids?
- How can we best help patients eliminate use of sleep aids?

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# CHALLENGES IN INSOMNIA TREATMENT

- Clinical guidelines recommend cognitive behavioral therapy for insomnia (CBT-I) as the first-line treatment for insomnia, and that medications should only be considered if CBT-I is ineffective or unavailable
- Recommendations are also to use medications for short-term treatment - most sleep aids have only been tested over 4 weeks
- However, sleep medications are frequently prescribed and continued for years to decades without reevaluation

Schutte-Rodin et al, J Clin Sleep Med, 2008; Sateia et al, J Clin Sleep Med, 2017

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# TREATING INSOMNIA: THE PRESCRIBER DILEMMA

- Cognitive Behavior Therapy for Insomnia recommended as first line of treatment
- Access to, and dissemination of, evidence-based psychological interventions remains inadequate
- Sedative-hypnotics are *relatively* fast and effective

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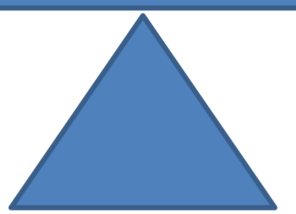
# THE PRESCRIBER DILEMMA: "ASK YOUR DOCTOR."

Patient autonomy (choice, advocacy)
Patient satisfaction
Drug vending machine?

Do no harm
Beneficence
Withholder of goodies?



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# COMMONLY USED SLEEP AIDS

- Benzodiazepines (BZDs)
- Benzodiazepine receptor agonists (BzRAs)
- First-generation antihistamines
- Sedating antidepressants
- Melatonin receptor agonists
- Orexin receptor antagonists
- Antipsychotics
- Alcohol
- Cannabis

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# SLEEPLESSNESS-RELATED TRENDS OF INSOMNIA COMPLAINT, INSOMNIA DIAGNOSIS, BDZ AND BZRA PRESCRIPTION AS A RESULT OF PHYSICIAN OFFICE VISITS, 1993-2007

Sleeplessness complaints
Insomnia diagnoses
BDZ prescriptions
NBSH prescriptions

Millions of Visits

BzRA prescriptions

Sleeplessness complaints, insomnia diagnoses, BDZ prescriptions

Moloney et al, 2011

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# ANNUAL NUMBER OF OFFICE VISITS ACCOMPANIED BY A PRESCRIPTION FOR SLEEP MEDICATIONS, NATIONAL AMBULATORY MEDICAL CARE SURVEY, 1999-2010

Millions

0 5 10 15 20 25

1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010

Benzodiazepines

Nonbenzodiazepines

Benzodiazepine receptor agonists

Any sleep medication

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# HOUSEHOLD EXPOSURE TO PHARMACEUTICAL TV ADVERTISEMENTS FOR SLEEP DISORDERS AS PERCENT OF TOTAL EXPOSURE TO ALL DRUG ADVERTISEMENTS

14
12
10
8
6
4
2
0

2003 2004 2005 2006 2007 2008 2009 2010 2011

Kornfield et al 2015

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# BENZODIAZEPINE RECEPTOR AGONISTS (BZRAS), OR “Z DRUGS”

- Include zolpiclone, eszopiclone, zolpidem, zaleplon
- Started appearing in the mid-eighties
- Traditional benzodiazepines associated with high risk of dependence, daytime drowsiness, tolerance, rebound insomnia, impaired performance, amnesia
- Do not appreciably change sleep architecture

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# BZRA PROBLEMS

- Reports of abuse and dependence emerged in the 90's - - high doses
- Reports of increased hip fracture risk in the geriatric population
- Reports of "sleep driving"
- Sleepwalking/night eating (black box warning)
- Next-day grogginess
- Dementia risk with long-term usage reported

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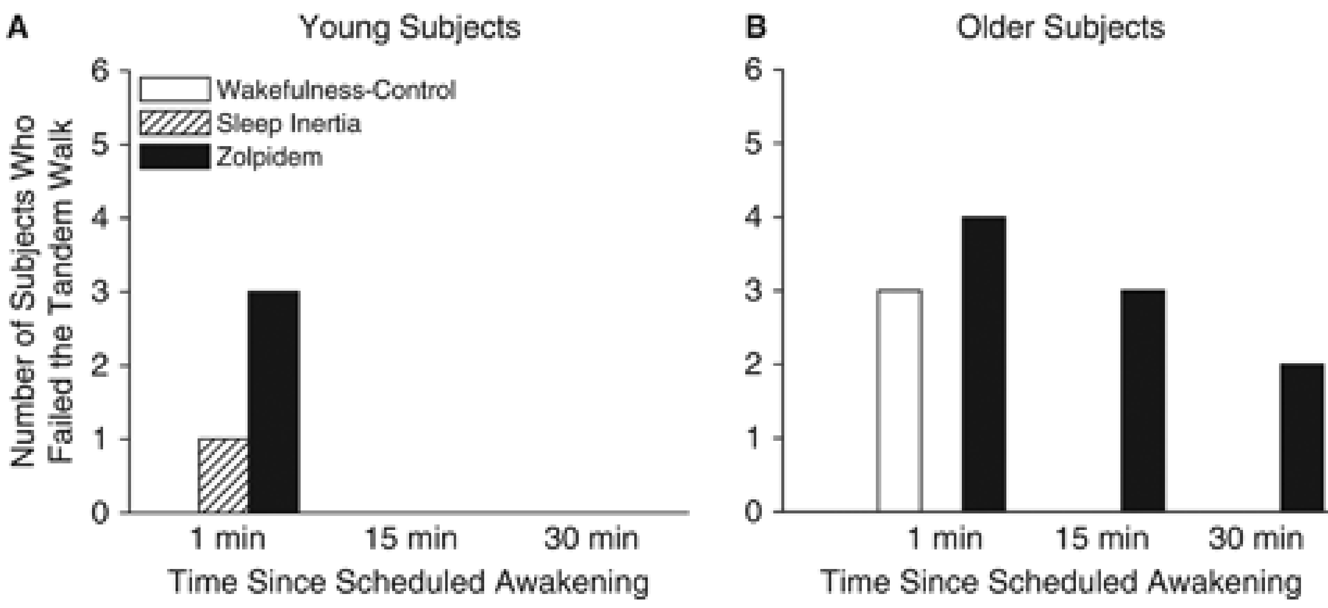
Influence of Zolpidem and Sleep Inertia on Balance and Cognition During Nighttime Awakening: A Randomized Placebo-Controlled Trial




**Frey et al, 2011. Wiley.**

Journal of the American Geriatrics Society, Volume: 59, Issue: 1, Pages: 73-81, First published: 13 January 2011, DOI: (10.1111/j.1532-5415.2010.03229.x)

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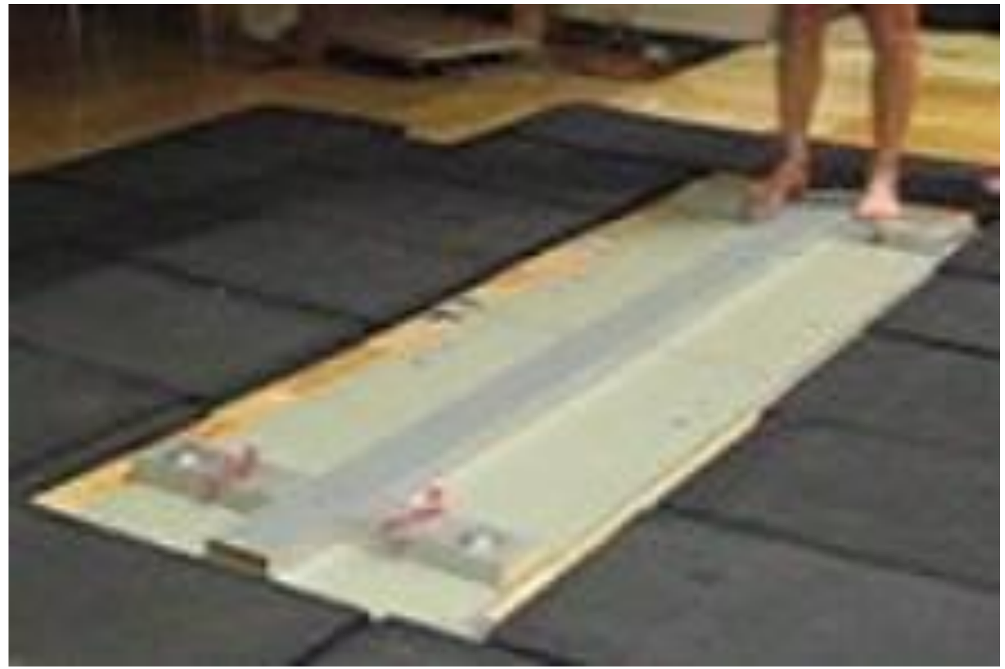
# BALANCE BEAM TEST



Frey et al, 2011. Wiley.

Journal of the American Geriatrics Society, Volume: 59, Issue: 1, Pages: 73-81, First published: 13 January 2011, DOI: (10.1111/j.1532-5415.2010.03229.x)

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# CASE EXAMPLE:
# MR. RETIRED EMPTY NESTER

- 65 yo man, retired x3 yrs
- Zolpidem XR 12.5 mg qhs (6.25 + 6.25)
- Variable morning oob times (TIB 10-12 hrs)
- 4-6 standard drinks most nights
- Prolonged SOL, multiple awake after sleep onset, multiple sleep locations within house
- PHQ-9 = 11; GAD-7 = 2; ISI = 16

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# APPROACHING THE TOPIC WITH A PATIENT

- First, ensure you have the right diagnosis - why is the patient on this medication?
- Do they have chronic insomnia? Or were they started on a medication for sleep problems without a full sleep evaluation?

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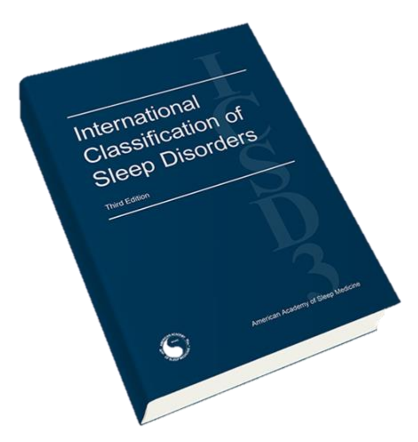
# DIAGNOSTIC CRITERIA FOR CHRONIC INSOMNIA DISORDER




- One or more of the following:
  - *Difficulty initiating sleep*
  - *Difficult maintaining sleep*
  - *Waking up earlier than desired*
- AND one or more related problems like fatigue, impaired performance, mood problems, or dissatisfaction about sleep
- Cannot be explained by lack of opportunity to sleep or a poor sleep environment
- Has occurred at least 3 times/week for at least 3 months
- Not better explained by another **sleep** disorder

*International Classification of Sleep Disorders, 3rd Edition, 2014*

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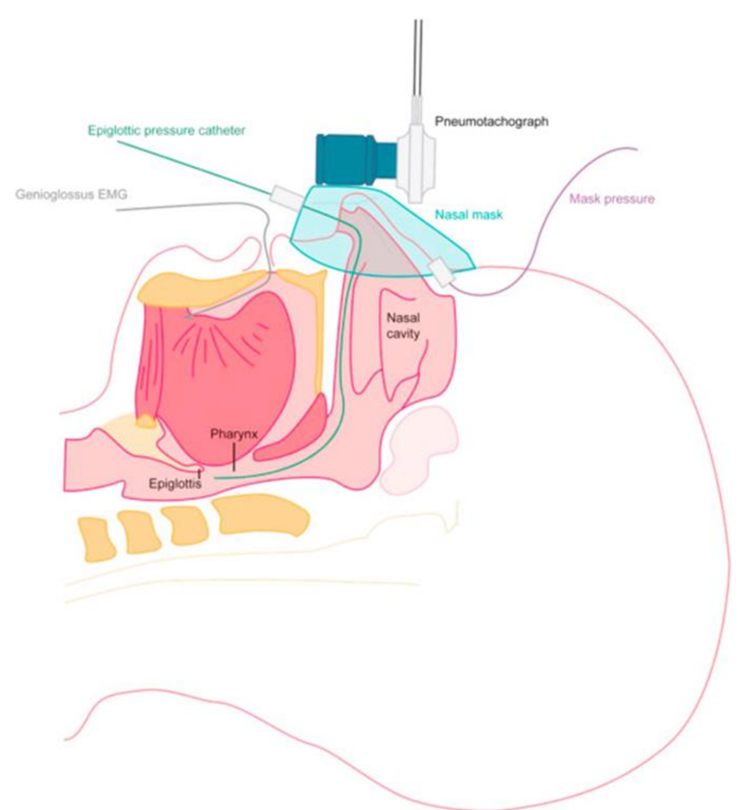
# RULING OUT OTHER SLEEP DISORDERS

- Comorbid insomnia with obstructive sleep apnea (COMISA) is very common
  - 35% of insomnia patients meet OSA criteria
  - 38% of OSA patients meet insomnia criteria
- How do hypnotic medications impact OSA and oxygen saturation? This may depend on the OSA phenotype (low versus high arousal threshold)




Zhang et al, Sleep Med Rev, 2019; Sweetman et al, Brain Sci, 2019; Carter & Eckert, Sleep Med Rev, 2021

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# RULING OUT OTHER SLEEP DISORDERS, CONTINUED

- Circadian rhythm disorders
  - Delayed sleep-wake phase disorder: the extreme night owl
  - Advanced sleep-wake phase disorder: the extreme morning lark
- Restless legs syndrome
- Nightmares

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# MR. RETIRED EMPTY NESTER - POLYSOMNOGRAM

STAGING

Wake
N1
N2
N3
REM

11:23 PM 12:20 AM 1:18 AM 2:15 AM 3:12 AM 4:10 AM 5:07 AM 6:05 AM

RESPIRATORY

50
0

11:23 PM 12:13 AM 1:03 AM 1:53 AM 2:43 AM 3:33 AM 4:23 AM 5:13 AM 6:03 AM

AHI: 1a = 28.8, 1b = 10.7 events per hour; $O_2$ nadir = 72%

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# KEYS TO ADDRESSING INSOMNIA DURING GRADUAL DOSE REDUCTION OF HYPNOTICS

- Take a curious and collaborative stance with patients
- Ask – Tell – Ask
- Tell: Provide detailed explanations and rationale
- Acknowledge change will be difficult and respect decisions to not change
- Offset withdrawal effects by increasing sleep drive

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# DISCUSSING HISTORY OF TREATMENT

- Find out:
  - Prior treatments
    - Prescribed sedative-hypnotics and sedating medications
    - Over-the-counter aids
    - Substances (such as alcohol and cannabis)
    - Sleep hygiene
    - CBT-I
  - Current treatments (including all categories above)
- What has worked? What hasn't worked?

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# EDUCATION

- Self-help booklet – 18% vs 5% reduction in BZD Rx (Bashir)
- Letter encouraging BZD reduction – cessation 14-27% (Voshaar, Gorgels)

| | Option 1' Gradual tapering alone | Option 2' Gradual tapering with CBT-I |
|---|---|---|
| 3 months | Of 100 people, 27 can stop taking sleeping pills after 3 months since starting gradual tapering alone. | Of 100 people, 48 can stop taking sleeping pills after 3 months since starting gradual tapering with CBT-I. |
| 12 months | Of 100 people, 30 can stop taking sleeping pills after 12 months since starting gradual tapering alone. | Of 100 people, 49 can stop taking sleeping pills after 12 months since starting gradual tapering with CBT-I. |

Bashir et al, Br J Gen Pract, 1994; Voshaar et al, Br J Psychiatry, 2003; Gorgels et al, Drug Alcohol Depend, 2005; Image: Aoki et al, Neuropsychopharmacol Rep. 2022

# CLARIFY THE PATIENT'S GOALS

Patient on a sleep aid

Discontinue

Taper + CBT-I

Taper – CBT-I

Continue

Revisit

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# STRATEGIES FOR TAPERING

- Tapering strategies vary widely – no consensus
- Frequently described approach is a **dose reduction of 25% every 1-2 weeks until complete discontinuation** (Hopkins, Murphy, Voshaar, Gorgels, Morin, Mishimi, Aoki)
  - Discontinuation rates: 24-61%, withdrawal symptoms reported
- Longer tapers:
  - 25% dose reduction every 2-4 weeks – 80% discontinued, 64% BZD-free at 12 months (Lopez-Peig)
  - 10-25% reduction every 2-3 weeks – 40% abstinence rate at 36 months (Vicens)
- Allowing patient to control the rate of taper – some rapidly discontinue, while others preferred a longer taper (Rahu)

Hopkins et al, J R Coll Gen Pract, 1982; Murphy & Tyrer, Br J Psychiatry, 1991; Voshaar et al, Br J Psychiatry, 2003; Gorgels et al, Drug Alcohol Depend, 2005; Morin et al, Am J Psychiatry, 2004; Mishimi et al, JIHO, 2014; Aoki et al, Neuropsychopharmacol Rep, 2022; Lopez-Peig et al, BMC Res Notes, 2012; Rahu & Meagher, Ir J Psychol Med, 2005; Vicens et al, BMC Res Notes, 2012

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# STRATEGIES FOR TAPERING, CONTINUED

- Switching from short-acting to long-acting BZD before starting a taper (Vicens)
- Switching from a BZD to a BzRA as a bridge to discontinuation (Pat-Horenczyk)
- Not as tested: switching a BzRA to another hypnotic

Pat-Horenczyk et al, Psychopharmacology, 1998

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# STRATEGIES FOR TAPERING, CONTINUED

Psychological therapies

- Sleep hygiene – insufficient evidence to recommend
- Relaxation therapy
- Stimulus control therapy
- Sleep restriction therapy
- Cognitive behavioral therapy for insomnia (CBT-I): the gold standard for chronic insomnia treatment
  - A systematic review and meta-analysis in 2019 found that CBT-I with gradual tapering is more effective than gradual tapering alone of BZDs/BZRAs (Takaesu)

Hintze & Edinger, 2020; Takaesu, Sleep Med Rev, 2019

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# SESSION 1 INSTRUCTIONS: MR. EMPTY NESTER

- Start keeping Sleep Log
- Maintain zolpidem XR at 6.25 mg/qhs
- Refrain from alcohol use
- Sleep hygiene/Stimulus control
- TIB restriction midnight – 9 am

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# MR. EMPTY NESTER'S RESULTS:

| | Time in Bed (min) | Total Sleep Time (min) | Sleep Efficiency |
|---|---|---|---|
| Week 2 | 447 | 261 | 58% |
| Week 3 | 429 | 349 | 81% |
| Week 4 | 483 | 402 | 83% |

- Discontinued zolpidem by end of first week
- Stayed out of bed longer than necessary during awakenings, prior to Week 2
- Significant stressor prior to Week 4
- Starting to use CPAP just prior to Week 4

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# DISCONTINUING MULTIPLE SLEEP AIDS/MEDICATIONS

- Sometimes (fairly often), patients will take multiple medications and/or over-the-counter sleep aids
- When determining the order of discontinuation, consider:
  - comorbidities
  - side effect profiles
  - effectiveness
  - age

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