Insomnia: Help me make it though the night…

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Learning Objectives

- List 4 potential causes of chronic insomnia
- List 4 drugs that can worsen or cause insomnia
- Be familiar with ‘proper’ sleep hygiene techniques
- List the goals of therapy for insomnia
- Describe the short and long term benefits and risks associated with benzodiazepines
- Be familiar with the benefits and risks associated with the use of zopiclone and other medications used for treating chronic insomnia

Case 1. Ms. Jitters

- ID: 31 year old female with difficulty falling asleep (takes over 60 min) for the last month. She complains of daytime fatigue and takes naps
- PMHx:
  - Generalized Anxiety Disorder x 2 years
  - Asthma x 15 yrs
- Meds: Takes fluoxetine 40 mg daily x 1 year which is helpful for reducing GAD symptoms by about 60%
- Salbutamol and betamethasone inhalers – helpful in controlling asthma

How would you treat Ms. Jitters?

Case 2: Mr. Ian Somnia

- ID: 63 year old with fatigue, difficulty sleeping, poor concentration for 6 weeks
- HPI: otherwise healthy, no sleep apnea, no psychiatric conditions, etc.
- Social: occasional ethanol and caffeine; married; retired engineer
- Medications: occasional ibuprofen for pain, nicotine 14 mg patch (been on a patch x 7 wks)
- Physical exam and labs unremarkable

How would you treat Ian?

What is Insomnia?

- Difficulty falling asleep, maintaining sleep, or not feeling rested in spite of sufficient opportunity to sleep
- Most common sleep complaint
- Common reason to seek advise from a health care professional
- Can be transient or persistent

DSM IV Diagnostic Criteria for Primary Insomnia

- Difficulty initiating or maintaining sleep, or having nonrestorative sleep for at least a month
- Causes distress or impairment in social, occupational or other important areas of functioning
- Not related to medical disorder or other sleep disorder
- Not the result of substances

Classification of Insomnia

Primary:

Psychophysiological

Secondary:

Psychiatric, Medical, Substance Use

Categories

Transient	⇨	2-3 days
Short-term	⇨	< 3 weeks
Long-term	⇨	> 3 weeks

Goals of Therapy

1) Promote sound and restorative sleep
2) Minimize external (stress, noise, environment) and internal (anxiety, mood, pain) factors
3) Reduce daytime impairment (fatigue, poor concentration) and complications of lack of sleep
4) Improve the effectiveness of behavioural interventions in managing patients with primary, chronic insomnia

Treatment of Insomnia

Step 1: Get a good history, consider a sleep diary, look for potential underlying causes

Step 2: Nonpharmacological therapy

Step 3: Pharmacological options

What information do you need for both these cases?

Sleep History

- Time data
  - Napping, bed time, lights, how long to fall asleep, how many times awoken, longest awake period, time out of bed, hours of sleep
- Questions about the sleep period
  - Physical symptoms preventing sleep (pain), mental or emotional symptoms (worry, anxiety), what awakens during the night (snoring, gasping for air, nightmares), symptoms when you wake up (headache, confusion, sleepiness)
- Questions for the patient's bed partner
  - Snoring, gasping, breathing; leg twitching, jerking, kicking; alcohol, nicotine, caffeine, other drugs; change in mood or emotional state

Sleep History Questionnaire

Name: _____ Date: _____

Birthdate: _____ Age: _____ Occupation: _____

Sex: _____Height: _____ Weight: _____ Weight Last Year: _____

Referring Doctor: _____ Family Doctor: _____

Describe your sleep problem: _____

_____

What results do you expect: _____

_____

A. MEDICATION SURVEY

Please list all PRESCRIPTION and NON-PRESCRIPTION medications you're curr

MEDICATION	REASON TAKEN	

ALLERGIES: _____

B. PLEASE LIST ALL PAST OR PRESENT *MEDICAL CONDITIONS* OR *SU*

C. SLEEP PATTERN

1. Circle the days of the week you work:

   Monday Tuesday Wednesday Thursday Friday Saturday Sunday

2. *ON WORKDAYS*
   a. What time do you go to bed: _____
   b. What time do you get out of bed: _____
3. *ON WEEKENDS & HOLIDAYS*
   a. What time do you go to bed: _____
   b. What time do you get out of bed: _____
4. How long does it take for you to fall asleep? _____
5. How many times a night do you awaken? _____
   a. How long do the awakenings last? _____
   b. List any symptoms associated with the awakenings: _____

   _____
6. *SLEEP TIME*
   a. How many hours do you usually sleep? _____
   (do not include hours spent in bed awake)
   b. How many hours does it take to make you feel rested? _____
   c. How many daytime naps do you take per week? _____
7. *SLEEP QUALITY*
   a. Do you feel unrefreshed and still sleepy upon awakening? **YES** **NO**
   b. How long does it take to fully awaken in the morning? _____
8. In the daytime, are you chronically sleepy, fatigued or tired? **YES** **NO**
9. Grade your tendency to ***FALL ASLEEP*** during the following situations:
   (0=would never sleep, 1=slight chance of sleeping, 2=moderate chance of sleeping, 3=high chance of sleeping)

	0	1	2	3
a. Sitting and reading				
b. Watching TV				
c. Sitting inactive in a public place (e.g. theater or meeting)				
d. As a passenger in a car for an hour without a break				
e. Lying down to rest in the afternoon				
f. Sitting and talking to someone				
g. Sitting quietly after lunch without alcohol				
h. In a car, while stopped for a few minutes				

http://www.sjo.org/documents/1/sleephistoryquestionnaire.pdf

D. SLEEP AND BREATHING

1. Do you snore?
2. Is your snoring broken by hesitations, gasps and snorts?
3. Are the hesitations long enough to frighten your sleep pa
4. Has your snoring driven your bed partner from the bedro
5. Do you awaken with a dry mouth?
6. Do you awaken with headaches?

E. INSOMNIA

1. Do you have trouble falling or staying asleep?
2. Do you worry about being able to fall asleep on time?
3. Do you feel sleepy prior to getting into bed?
4. Does your mind race with thoughts when lying awake?
5. Do daytime worries keep you awake at night?
6. Does pain disturb your sleep?
7. Does heat, cold, hunger or thirst disturb your sleep?
8. Is your insomnia the primary reason your life is in disarr
9. Do you rely on a sleeping medication?
10. Do you watch TV, read, or work in bed?
11. Do you frequently travel across 2 or more time zones?

F. SLEEP DISTURBANCES

1. Do you experience unpleasant leg sensations at bedtime?
2. Do you kick or jerk your legs and/or arms during sleep?
3. Do you have sweats or awaken from sleep feeling flushe
4. Do you awaken with a bitter or acid taste?
5. Do you frequently have nightmares or vivid dreams?
6. Do you grind your teeth or have bitten your cheek during
7. Have you ever walked or talked in your sleep?
8. Have you ever been unable to move for a few moments a
9. Have you ever seen or felt things from your dreams *after*
10. Have you ever experienced weakness when laughing or s
11. Have you ever had unusual movements or behaviors dur

    Describe: _____

G. PERSONAL HABITS

1. Do you use tobacco now or have you in the *past*?
   a. If yes, how many per day and for how many years?
   b. If yes, what time of day is your last use? _____
2. Do you drink alcohol?
   a. If yes, how many drinks? _____ per day / per w
   b. If yes, what time of day is your last drink? _____
3. How many caffeinated beverages do you drink per day?
   a. If yes, what time of day is your last drink? _____

H. FAMILY HISTORY

	AGE	MEDICAL CONDITIONS
Father:	_____	_____
Mother:	_____	_____
Sibling 1:	_____	_____
Sibling 2:	_____	_____
Sibling 3:	_____	_____

(continue below if necessary)

1. List any relatives who have sleep problems or snore?

_____ _____

_____ _____

I. PERSONAL HISTORY (Check any and all that apply)

☐ skipped heart beats	☐ heart failure	☐ heart attack	☐ heart murmur
☐ high blood pressure	☐ thyroid problems	☐ diabetes	☐ stroke
☐ epilepsy	☐ headaches	☐ emphysema	☐ sinusitis
☐ nasal congestion	☐ deviated nasal septum	☐ enlarged tonsils	☐ allergies
☐ asthma	☐ glaucoma	☐ depression/anxiety	☐ Bipolar disorder

J. BED PARTNER QUESTIONNAIRE (Please have your bed partner check any and all that apply)

☐ Light snoring	☐ Sleep walking	☐ Leg or body twitching
☐ Heavy snoring	☐ Sleep talking	☐ Leg jerking
☐ Pauses in breathing	☐ Bed-wetting	☐ Daytime sleepiness
☐ Snorting	☐ Head rocking/banging	☐ Daytime confusion
☐ Teeth grinding	☐ A shaking fit	☐ Depression/anxiety

1. Provide additional detail regarding any of the above. Please describe the activity, the time it occurs, and how often it occurs.

_____

_____

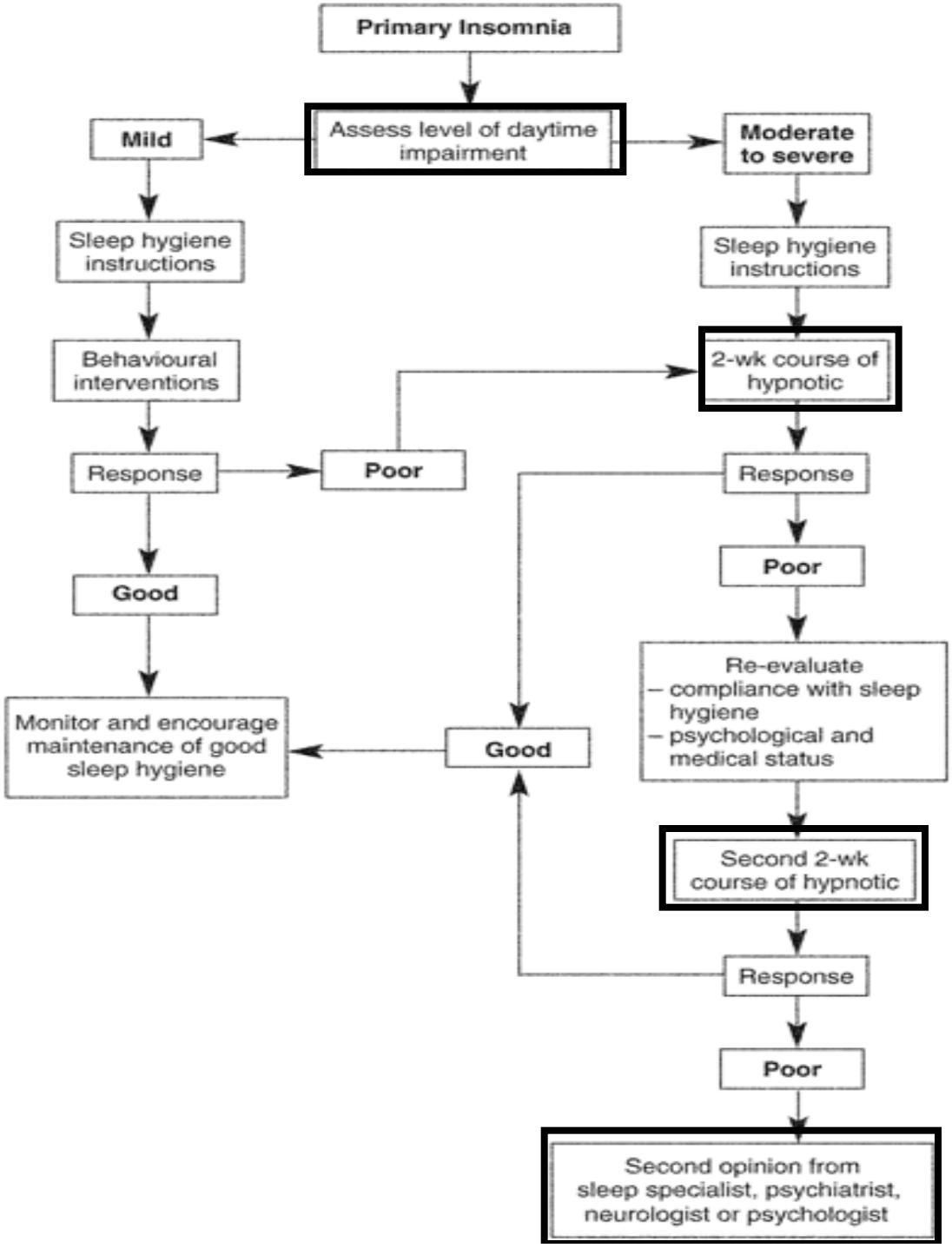
_____

K. ADDITIONAL INFORMATION

_____

Medications that can Cause or Worsen Insomnia

- Antidepressants
  - bupropion, fluoxetine, SNRIs, MAOIs, TCAs
- Antihypertensives
  - beta blockers, methyldopa
- Nicotine
- Sympathomimetic Amines
  - amphetamines, methylphenidate, caffeine, cocaine, decongestants, appetite suppressants, bronchodilators (e.g., salbutamol),
- Miscellaneous
  - corticosteroids, anticonvulsants (e.g., phenytoin, valproic acid), levodopa, quinidine, hormones (e.g., thyroid supplements, estrogen)



Ther. Choices 5th Edn

Nonpharmacological Options

- Proper sleep hygiene *(see slide in handout)*
- Relaxation exercises and tapes
- Stimulus control
- Sleep restriction
- Sleep diary *(see sample in handout)*
- Increase aerobic exercise earlier in the day (~45 minutes and should induce sweating)
- Cognitive behavioural therapy for insomnia (CBTi)

National Sleep Foundation Sleep Diary

Fill out days 1-4 below and days 5-7 on page 2	COMPLETE IN MORNING							COMPLETE AT END OF DAY				
	I went to bed last night at:	I got out of bed this morning at:	Last night, I fell asleep in:	I woke up during the night: *(Record number of times)*	When I woke up for the day, I felt: *(Check one)*	Last night I slept a total of: *(Record number of hours.)*	My sleep was disturbed by: *(List any mental, emotional, physical or environmental factors that affected your sleep: e.g. stress, snoring, physical discomfort, temperature)*	I consumed caffeinated drinks in the: *(e.g. coffee, tea, cola)*	I exercised at least 20 minutes in the:	Approximately 2-3 hours before going to bed, I consumed:	Medication(s) I took during the day: *(List name of medication/drug(s))*	About 1 hour before going to sleep, I did the following activity: *(List activity: e.g. watch TV, work, read)*
DAY 1 DAY_____ DATE_____	____PM/AM	____PM/AM	___Minutes	____Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____Hours	_____ _____ _____ _____ _____	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not applicable	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not applicable	☐ Alcohol ☐ A heavy meal ☐ Not applicable	_____ _____ _____ _____ _____	_____ _____ _____ _____ _____
DAY 2 DAY_____ DATE_____	____PM/AM	____PM/AM	___Minutes	____Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____Hours	_____ _____ _____ _____ _____	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not applicable	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not applicable	☐ Alcohol ☐ A heavy meal ☐ Not applicable	_____ _____ _____ _____ _____	_____ _____ _____ _____ _____
DAY 3 DAY_____ DATE_____	____PM/AM	____PM/AM	___Minutes	____Times	☐ Refreshed ☐ Somewhat refreshed ☐ Fatigued	____Hours	_____ _____ _____ _____	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not	☐ Morning ☐ Afternoon ☐ Within several hours before going to bed ☐ Not	☐ Alcohol ☐ A heavy meal ☐ Not	_____ _____ _____ _____	_____ _____ _____ _____

Sleep Hygiene

1. Keep a regular sleep/wake schedule 7 days a week
2. Limit daily “in-bed” time to average sleep time prior to the sleep disturbance
3. Avoid sleeping in or daytime naps
4. Stop offending medications/substances (caffeine, nicotine, alcohol, stimulants)
5. Avoid evening stimulation
6. Try a warm, 20 minute bath near bedtime
7. Eat regularly during the day and avoid large meals near bedtime
8. Use bedroom only for sleep and intimacy – not for TV or something that keeps you too alert

Pharmacological Options

- Antihistamines
- Benzodiazepines
- Zopiclone
- Eszopiclone*
- Zaleplon*/Indiplon*
- Zolpidem*
- Antidepressants (e.g., trazodone, doxapin)
- Alcohol?
- Melatonin
- Ramelteon* (melatonin receptor agonist)
- Chloral Hydrate
- Antipsychotics
- L-Tryptophan
- Herbs (valerian, chamomile)

*Not available in Canada

6 Basic Principles

- Use lowest effective dose
- Intermittent dosing (PRN) – e.g., <4/week
- Short term treatment (2-4 weeks) depending on presentation
- Need for medication tapering if longer term
- Select and monitor medications by assessing daytime functioning and adverse effects
- Patient plays an active role in treatment

Benzodiazepines

- Effective in promoting sleep onset and maintaining sleep
- Consider half-life and metabolites
  - Particularly for the elderly
    - Increased risk of higher cortical impairment
      - Confusion and falls
    - Reduced Phase I metabolism
    - Reduced GFR and hepatic blood flow
    - “LOT” – lorazepam, oxazepam, temazepam

Benzodiazepines

- Bind to gamma sub-unit of GABA-A receptor, resulting in an increase in GABA-A receptor activity

Improve insomnia by:

- Reducing REM sleep
- Decreasing sleep latency
- Decrease nocturnal awakenings
- Tolerance develops with repeated administration

Problems with Benzodiazepines

- Short-term
  - Adverse effects
  - Carry-over effects
  - Cognition
  - Anterograde amnesia
- Long-term
  - Tolerance
  - Withdrawal
  - Rebound
  - Dependence

Adverse Effects of BDZs

- Daytime drowsiness/tiredness
- Cognitive impairment
- Rebound insomnia (even after 2 wks)
- Anterograde amnesia
- Incoordination and falls
- Paradoxical effects
- Respiratory depression
- Dependence/tolerance
- Sleep walking?

Physical Dependence vs. Abuse

- Physical Dependence:
  - Down regulation of benzodiazepine receptor sensitivity
  - Need to continue to use a drug to relieve or avoid physical withdrawal symptoms
- Abuse
  - Recreational use
  - Continued use despite negative consequences
  - Dose escalation
  - Loss of control over use

Zopiclone

- Acts at the benzodiazepine receptor
  - Not a benzodiazepine
- Compared to benzodiazepines, zopiclone appears to have less or no:
  - Rebound insomnia
  - Tolerance and dependence
  - Amnesic effects
  - Morning hang-over (short half life)

Zopiclone Pharmacokinetics

- Absorption: Elderly: 75% to 94%
- Protein binding: ~45%
- Metabolism: Extensively hepatic
- $T_{1/2}$: 5 hours; Elderly: 7 hours; Hepatic impairment: 11.9 hours
- Time to peak, serum: <2 hours; Hepatic impairment: 3.5 hours
- Excretion: Urine (75%); feces (16%)

Zopiclone

- Drug interactions:
  - CNS depressants
  - CYP2C9 and CYP3A4 drugs (inducers and inhibitors)
- Adverse effects: bitter taste, dry mouth, headache, somnolence
- Serious AEs: suicidal ideation, aggression, worsening of depression
- Eszopiclone (Lunesta) available in the US

Zolpidem (Ambien or Sublinox)*

- Non-benzodiazepine, binds to the omega -1 (BZ-1) receptor subtype of the GABA-A receptor complex.
- Rapid onset of action; sleep onset/duration
- $T_{1/2}$: 2.5 - 3 h
- 5 – 10 mg Sublingual (sublinox), 6.25 mg CR (Ambien) before bedtime
- Common SE: nausea, dizziness, drowsiness, rebound insomnia
- Serious SE: suicidal ideation, worsening of depression, aggressive behaviour
- Contraindications: severe hepatic impairment, respiratory insufficiency

*Not currently sold in Canada

Trazodone

- Limited data in primary insomnia (only 2 studies)
- Lack of objective efficacy measures
- Short duration of trials (longest is 6 weeks)
- Consideration for side effects (sedation, dizziness, orthostasis, psychomotor impairment, priapism, etc.)

Mendelson WB. A review of the evidence for the efficacy and safety of trazodone in insomnia. J Clin Psychiatry. 2005 Apr;66(4):469-76.

Trazodone vs. zolpidem

- 14 day, placebo controlled, primary insomnia
- Subjective sleep latency and duration showed significant improvement with both trazodone and zolpidem vs. placebo
- Effect was greater with zolpidem

Silber MH. Clinical practice. Chronic insomnia. N Engl J Med. 2005 Aug 25;353(8):803-10.

Doxepin

- Limited data in elderly primary insomnia
- Dose = 1-3 mg!
- 12 week RCT, DB, Dox 1 mg (n = 77) or Dox 3 mg (n = 82), or placebo (n = 81)
- Outcomes: Polysomnography (PSG), patient and clinician ratings, CGI at nights 1, 29, and 85

Results:

- DXP 3 mg > placebo for all measures and 1mg > placebo for some outcomes

Krystal AD et al. Efficacy and safety of doxepin 1 mg and 3 mg in a 12-week sleep laboratory and outpatient trial of elderly subjects with chronic primary insomnia. *SLEEP* 2010;33(11):1553-1561.

Antipsychotics

- Not FDA approved for insomnia
- When used, doses are usually lower than those for treating psychosis
- Can be helpful, but associated with weight gain, increased risk for diabetes, high blood pressure, restless leg syndrome, muscle spasm or Parkinson-like symptoms
- Quetiapine and ziprasidone have been studied in clinical trials and were shown to increase total sleep time as well as sleep efficiency

Adil's Comparison of First Line Drugs in Canada for Insomnia

Drug	Night-time Dose (mg)	Half-life (hours)	Metabolites	Comments
Lorazepam	Initial 0.5 Maximum 1	10 to 20	Inactive metabolite	No "hangover" effects; may cause more rebound insomnia on withdrawal than temazepam or oxazepam; may cause amnesia with higher doses
Oxazepam	Initial 15 Maximum 30	5 to 10	Inactive metabolite	Slowly absorbed – delayed onset of action; take 60-90 minutes before retiring; no "hangover" effects
Temazepam	Initial 7.5 Maximum 30	10 to 12	Inactive metabolite	Short duration of action limits morning sedation. Does not accumulate.
Triazolam	Initial 0.125 Maximum 0.25	2 to 3	Inactive metabolite	Anterograde amnesia (esp. with ↑ dose, concomitant alcohol); other dose-related side effects (rebound insomnia, daytime anxiety) have limited its use. Absence of "hangover" effects is major advantage.
Zopiclone	Initial 3.75 Maximum 7.5	5 to 10	N-Desmethyl (has activity) N-Oxide (has weak activity)	Does not accumulate; free of cognitive effects; major adverse effect is bitter/metallic taste; may cause less rebound on withdrawal; minimal additive effects with low doses of alcohol

SPECIAL ARTICLE

Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults

Sharon Schutte-Rodin, M.D.[1]; Lauren Broch, Ph.D.[2]; Daniel Buysse, M.D.[3]; Cynthia Dorsey, Ph.D.[4]; Michael Sateia, M.D.[5]

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Insomnia is the most prevalent sleep disorder in the general population, and is commonly encountered in medical practices. Insomnia is defined as the subjective perception of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep, and that results in some form of daytime impairment.[1] Insomnia may present with a variety of specific complaints and etiologies, making the evaluation and management of chronic insomnia demanding on a clinician's time. The purpose of this clinical guideline is to provide clinicians with a practical framework for the assessment and disease management of chronic adult insomnia, using existing evidence-based insomnia practice parameters where available, and consensus-based recommendations to bridge areas where such parameters do not exist. Unless otherwise stated, "insomnia" refers to chronic insomnia, which is present for at least a month, as opposed to acute or transient insomnia, which may last days to weeks.

Citation: Schutte-Rodin S; Broch L; Buysse D; Dorsey C; Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med 2008*;4(5):487-504.

SUMMARY RECOMMENDATIONS

General:

- Insomnia is an important public health problem that requires accurate diagnosis and effective treatment. **(Standard)**
- An insomnia diagnosis requires associated daytime dysfunction in addition to appropriate insomnia symptomatology. **(ICSD-2 definition)**

Evaluation:

- Insomnia is primarily diagnosed by clinical evaluation through a thorough sleep history and detailed medical, substance, and psychiatric history. **(Standard)**
  - The sleep history should cover specific insomnia complaints, pre-sleep conditions, sleep-wake patterns, other sleep-related symptoms, and daytime consequences. **(Consensus)**
  - The history helps to establish the type and evolution of insomnia, perpetuating factors, and identification of comorbid medical, substance, and/or psychiatric conditions. **(Consensus)**
- Instruments which are helpful in the evaluation and differential diagnosis of insomnia include self-administered questionnaires, at-home sleep logs, symptom checklists, psychological screening tests, and bed partner interviews. **(Guideline)**
  - At minimum, the patient should complete: (1) A general medical/psychiatric questionnaire to identify comorbid disorders (2) The Epworth Sleepiness Scale or other sleepiness assessment to identify sleepy patients and comorbid disorders of sleepiness (3) A two-week sleep log to identify general patterns of sleep-wake times and day-to-day variability. **(Consensus)**
  - Sleep diary data should be collected prior to and during the course of active treatment and in the case of relapse or reevaluation in the long-term. **(Consensus)**
  - Additional assessment instruments that may aid in the baseline evaluation and outcomes follow-up of patients with chronic insomnia include measures of subjective sleep quality, psychological assessment scales, daytime function, quality of life, and dysfunctional beliefs and attitudes. **(Consensus)**
- Physical and mental status examination may provide important information regarding comorbid conditions and differential diagnosis. **(Standard)**
- Polysomnography and daytime multiple sleep latency testing (MSLT) are not indicated in the routine evaluation of chronic insomnia, including insomnia due to psychiatric or neuropsychiatric disorders. **(Standard)**
  - Polysomnography is indicated when there is reasonable clinical suspicion of breathing (sleep apnea) or movement disorders, when initial diagnosis is uncertain, treatment fails (behavioral or pharmacologic), or precipitous arousals occur with violent or injurious behavior. **(Guideline)**

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Table 12—Pharmaceutical Therapy Options

Drug	Dosage Form	Recommended Dosage	Indications/Specific Comments
Benzodiazepine Receptor Agonistic Modulators (Schedule IV Controlled Substances)			
Non-benzodiazepines			
cyclopyrrolones			
eszopiclone	1, 2, 3 mg tablets	2-3 mg hs 1 mg hs in elderly or debilitated; max 2 mg 1 mg hs in severe hepatic impairment; max 2 mg	✧ Primarily used for sleep-onset and maintenance insomnia; ✧ Intermediate-acting; ✧ No short-term usage restriction
imidazopyridines			
zolpidem	5, 10 mg tablets	10 mg hs; max 10 mg 5 mg hs in elderly, debilitated, or hepatic impairment	✧ Primarily used for sleep-onset insomnia ✧ Short-to intermediate-acting
zolpidem (controlled release)	6.25, 12.5 mg tablets	12.5 mg hs 6.25 mg hs in elderly, debilitated, or hepatic impairment	✧ Primarily used for sleep-onset and maintenance insomnia; ✧ Controlled release; swallow whole, not divided, crushed or chewed
pyrazolopyrimidines			
zaleplon	5, 10 mg capsules	10 mg hs; max 20 mg 5 mg hs in elderly, debilitated, mild to moderate hepatic impairment, or concomitant cimetidine	✧ Primarily used for sleep onset insomnia ✧ Maintenance insomnia as long as 4 hours is available for further sleep ✧ Short-acting
Benzodiazepines			
estazolam	1, 2 mg tablets	1-2 mg hs 0.5 mg hs in elderly or debilitated	✧ Short- to intermediate-acting
temazepam	7.5, 15, 30 mg capsules	15-30 mg hs 7.5 mg hs in elderly or debilitated	✧ Short- to intermediate-acting
triazolam	0.125, 0.25 mg tablets	0.25 mg hs; max 0.5 mg 0.125 mg hs in elderly or debilitated; max 0.25 mg	✧ Short-acting
flurazepam	15, 30 mg capsules	15-30 mg hs 15 mg hs in elderly or debilitated	✧ Long-acting ✧ Risk of residual daytime drowsiness
Melatonin Receptor Agonists (Non-Scheduled)			
ramelteon	8 mg tablet	8 mg hs	✧ Primarily used for sleep-onset insomnia

First-line Pharmacotherapy: Highest level of evidence supporting efficacy and safety

Agents	Recommended Dose	Comments
Zopiclone	3.75-7.5 mg	• Short half-life provides lower risk of morning hang-over effect • Metallic after-taste most common adverse reaction
Temazepam	15-30 mg	• Intermediate half-life carries a low-moderate risk of morning hang-over effect

Second-line Pharmacotherapy: Moderate level of formal evidence. Extent of current use and favorable tolerability support use as second-line agents

Agents	Recommended Dose	Comments
Trazodone	25-50 mg	• Shorter half-life carries lower risk of morning hang-over effect

Variable Evidence

Agents	Recommended Dose	Comments
L'Tryptophan	500 mg-2 gm	• Evidence supporting efficacy is variable and insufficient. May be requested by individual patients looking for a "natural source" agent. Taken 60 minutes before bedtime
Melatonin	0.3-5 mg	
Valerian	400-900 mg	

Other Non-Prescription Products

Agents	Usual Dose	Comments
Diphenhydramine - Benadryl® - Sleep Eze - Simply Sleep - Nytol® - Unisom®	25-50 mg hs	Potential for serious side effects arising from anticholinergic properties (especially in elderly); residual daytime sleepiness, diminished cognitive function, dry mouth, blurred vision, constipation, urinary retention, etc. These products are not intended for long term use and tolerance to sedative effects likely develops rapidly (3 days) Gravol not approved in Canada as a sleep aid
Dimenhydrinate - Gravol	25-50 mg hs	
Doxylamine - Unisom 2	25-50 mg hs	

Toward Optimized Practice Program. Guideline for adult primary insomnia. 2010 Feb

Not Recommended

The following agents are not recommended for the management of conditioned insomnia except in cases where the agent is being used specifically to mange a co-morbidity such as depression.

Agents	Comments
Antidepressants - mirtazapine, fluvoxamine, tricyclics	Relative lack of evidence
Amitriptyline	Relative lack of evidence and significant adverse effects (such as weight gain)
Antihistamines - chlorpheniramine	Relative lack of evidence or excessive risk of daytime sedation, psychomotor impairment and anticholinergic toxicity
Antipsychotics (Conventional or 1st-Generation) - chlorpromazine, methotrimeprazine, loxapine	Relative lack of evidence and unacceptable risk of anticholinergic and neurological toxicity
Antipsychotics (Atypical or 2nd-Generation) - risperidone, olanzapine, quetiapine	Relative lack of evidence and unacceptable cost and risk of metabolic toxicity
Benzodiazepines (Intermediate and Long-Acting) - diazepam, clonazepam, flurazepam, lorazepam, nitrazepam, alprazolam, oxazepam Benzodiazepines (Short-Acting) - triazolam	Excessive risk of daytime sedation and psychomotor impairment No longer recommended due to unacceptable risk of memory disturbances, abnormal thinking and psychotic behaviors

Toward Optimized Practice Program. Guideline for adult primary insomnia. 2010 Feb

Selected References

1. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med. 2008 Oct 15;4(5):487-504. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2576317/pdf/jcsm.4.5.487.pdf
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QUESTIONS???