

Understanding Insomnia: From Pathophysiology to Diagnosis

Insomnia is one of the most commonly reported sleep disorders in clinical practice worldwide.¹ It is a multifactorial condition, influenced by biological vulnerability, psychological processes, environmental factors, and learned behaviors.² A clear understanding of how insomnia develops and how it is assessed allows healthcare providers to identify meaningful intervention points and plan individualized management strategies.

Mechanism of Insomnia Development

Insomnia arises from the interaction of pre-existing vulnerability, triggering events, and behaviors that maintain sleep disturbance over time.³ The Spielman 3P Model—Predisposing, Precipitating, and Perpetuating factors—is a widely used framework for describing the development and maintenance of insomnia.⁴ Figure 1 illustrates how these factors contribute across different phases of the disorder.

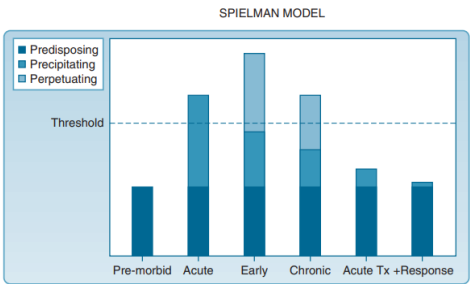


Figure 1. The Spielman 3P Model of Insomnia Development. This diagram illustrates the contribution of Predisposing, Precipitating, and Perpetuating factors across the natural history of insomnia.

Diagram explanation:

- **Pre-morbid:** Baseline vulnerability (predisposing factors) exists before insomnia onset.
- **Acute:** A precipitating event triggers initial sleep disruption.
- **Early:** Both predisposing and precipitating factors drive early insomnia, with perpetuating behaviors beginning to appear.
- **Chronic:** Perpetuating factors dominate, maintaining insomnia beyond the initial trigger.
- **Acute Treatment & Response:** Effective treatment reduces perpetuating behaviors, lowering the combined 3P contribution below the clinical threshold.

The 3P model highlights how insomnia develops over time: predisposing factors create vulnerability, precipitating factors trigger sleep disruption, and perpetuating factors maintain it. Understanding each component clarifies why some sleep difficulties become chronic and guides targeted interventions.

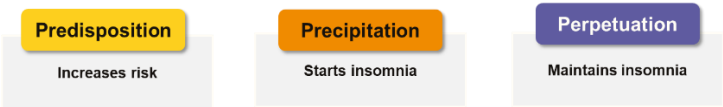


Figure 2. Core Components of the 3P Model.

Predisposing Factors

Predisposing factors are long-term characteristics that increase susceptibility to insomnia. These factors are typically present before symptom onset and lower the threshold for sleep disruption:

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- **Biological:** Trait hyperarousal, including chronically elevated cortisol, increased metabolic rate, heightened startle response, or slow physiologic recovery after arousal.⁵
- **Psychological:** Cognitive tendencies such as excessive worry or repetitive, intrusive thinking (rumination).⁶
- **Social:** Persistent sleep/wake schedule conflicts, e.g., differing schedules with a bed partner or external demands such as childcare.

Predisposing factors do not cause insomnia on their own but increase sensitivity to sleep-disrupting events.

Precipitating Factors

Precipitating factors are acute events that trigger insomnia in a vulnerable individual. Common precipitating factors include:^{2,4}

- Medical illness
- Psychiatric illness
- Significant psychosocial stressors (e.g., bereavement, occupational stress)

Once a precipitating event occurs, acute sleep disturbance often begins.

Perpetuating Factors

Perpetuating factors are behaviors and cognitive strategies adopted in response to sleep loss that inadvertently maintain insomnia, even after the initial trigger resolves.³ Two primary patterns are recognized:

- **Staying in bed while awake:** Spending extended periods awake in bed weakens the association between the bed and sleep, conditioning arousal within the sleep environment. This mechanism is a core target of stimulus control therapy.⁷
- **Extension of sleep opportunity:** Going to bed earlier, waking later, or both to “catch up” on sleep. This behavior often creates a mismatch between actual sleep ability and allotted sleep time, increasing nocturnal wakefulness. This principle underpins sleep restriction therapy, as emphasized in the Spielman model.⁴

Clinical Assessment of Insomnia

Insomnia is primarily a clinical diagnosis, supported by validated subjective and objective measures that quantify symptom severity, characterize sleep patterns, and guide treatment planning.¹

A. Insomnia Severity Index (ISI)

The ISI is a 7-item questionnaire assessing insomnia symptoms over the previous two weeks.⁸

- Strong internal consistency (Cronbach’s $\alpha \approx 0.90$)
- Cutoff ≥ 10 identifies clinically significant insomnia (sensitivity 86.1%, specificity 87.7%)⁹
- Severity categories:
 - 0–7: No clinically significant insomnia.
 - 8–14: Mild insomnia.
 - 15–21: Moderate insomnia.
 - 22–28: Severe insomnia.

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Name: _____ Date: _____

1. Please rate the current (i.e., last 2 weeks) **SEVERITY** of your insomnia problem(s).

	None	Mild	Moderate	Severe	Very
Difficulty falling asleep:	0	1	2	3	4
Difficulty staying asleep:	0	1	2	3	4
Problem waking up too early:	0	1	2	3	4

2. How **SATISFIED** are you with your current sleep pattern?

	Very Satisfied	1	2	3	Very Dissatisfied
	0	1	2	3	4

3. To what extent do you consider your sleep problem to **INTERFERE** with your daily functioning (e.g., daytime fatigue, ability to function at work/daily chores, concentration, memory, mood, etc.)

	Not at all	A Little	Somewhat	Much	Very Much
Interfering	0	1	2	3	4

4. How **NOTICEABLE** to others do you think your sleeping problem is in terms of impairing the quality of your life?

	Not at all	Rarely	Somewhat	Much	Very Much
Noticeable	0	1	2	3	4

5. How **WORRIED**/distressed are you about your current sleep problem?

	Not at all	A Little	Somewhat	Much	Very Much
	0	1	2	3	4

Guidelines for Scoring/Interpretation:

Add scores for all seven items (1+1+1+1+2+3+4+5) = _____

Total score ranges from 0-28

0-7 = No clinically significant insomnia

8-14 = Subthreshold insomnia

15-21 = Clinical insomnia (moderate severity)

22-28 = Clinical insomnia (severe)

Figure 3. Insomnia Severity Index Form.

The ISI is widely used for baseline assessment and treatment follow-up.

B. Pittsburgh Sleep Quality Index (PSQI)

The PSQI evaluates sleep quality across a one-month period through 19 items covering sleep duration, latency, efficiency, and disturbances.¹⁰

- Demonstrates strong reliability (Cronbach's $\alpha \approx 0.83$).
- A global score > 5 indicates poor sleep quality.
- Provides a broad view of sleep patterns, making it useful in patients with comorbid medical or psychiatric conditions.

Appendix. Pittsburgh Sleep Quality Index (PSQI)

Name: _____ ID #: _____ Date: _____ Age: _____

Instructions:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME: _____

2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?

NUMBER OF MINUTES: _____

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME: _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT: _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

(a) Cannot get to sleep within 30 minutes

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

Figure 4. PSQI. This figure shows a cropped excerpt of the Pittsburgh Sleep Quality Index (PSQI) for illustrative purposes only. To view or reproduce the full questionnaire, please refer to the original publication.¹⁰

The PSQI complements symptoms-based measures and provides a broader view of sleep patterns.

C. Polysomnography (PSG)

Polysomnography (PSG) is an objective tool measuring sleep continuity, architecture (REM and non-REM), arousals, and other physiologic parameters.¹

While insomnia is often diagnosed clinically, PSG is used to:

- Objectively confirm disrupted sleep patterns.
- Characterize sleep architecture abnormalities (e.g., reduced sleep efficiency, altered REM/non-REM ratios, increased nocturnal awakenings).
- Evaluate atypical or treatment-resistant insomnia.

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- Support differentiation from other sleep disorders.^{11,12,13}

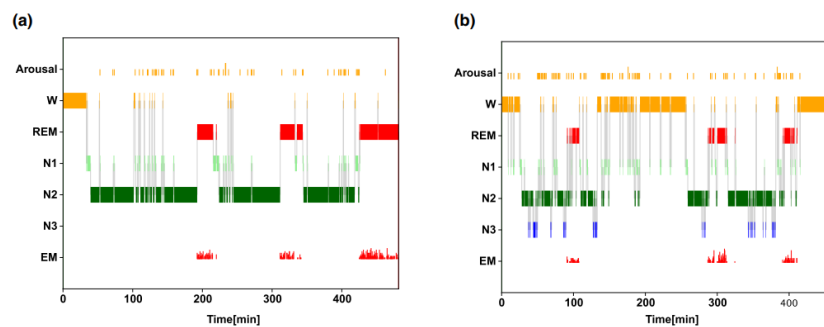


Figure 5. Polysomnographic Patterns in Insomnia: Normal (a) vs. Disturbed Sleep Continuity (b).¹⁴

Diagram Explanation:

(a) illustrates insomnia disorder without objective sleep continuity disturbance, showing generally preserved sleep efficiency despite subjective complaints. Minor findings such as slightly prolonged sleep onset or reduced N3 sleep may appear but are non-specific.

(b) illustrates insomnia disorder with objective sleep continuity disturbance, characterized by increased wake time after sleep onset and reduced total sleep time and sleep efficiency. These patterns highlight the variability of PSG findings in insomnia and the frequent mismatch between subjective and objective sleep reports.

PSG provides complementary physiologic insight, particularly when subjective measures are insufficient to fully characterize the patient's sleep disturbance.

Summary

Insomnia develops through the interaction of predisposing vulnerabilities, precipitating stressors, and perpetuating behaviors. Clinical assessment combines structured patient interviews with validated instruments such as the ISI and PSQI. Objective measures, including PSG, may further characterize sleep continuity and architecture, supporting a comprehensive understanding of insomnia in selected patients and clinical contexts. Together, these approaches create a structured framework for diagnosis and management, enabling healthcare providers to deliver targeted, evidence-based interventions.

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Optimizing Insomnia Therapy

Overview

Effective insomnia management involves accurate diagnosis, identifying comorbidities, selecting appropriate non-pharmacologic and pharmacologic interventions, and ensuring safe use of hypnotics. Lemborexant, a dual orexin receptor antagonist (DORA), provides an alternative to benzodiazepines (BZDs) and Z-drugs with demonstrated efficacy, long-term safety, low withdrawal potential, and preserved sleep architecture.^{1,2}

Indication

Lemborexant (DAYVIGO™) is indicated for the treatment of insomnia characterized by difficulty falling asleep and/or staying asleep.³

The recommended dose is 5 mg nightly, taken immediately before bedtime with at least 7 hours available for sleep. Avoid taking with or immediately after meals, as this may delay onset.³

Precautions

Patients Requiring Caution

Use with increased vigilance in patients with:³

- Mild to moderate hepatic impairment (max 5 mg)
- Severe renal impairment
- Organic brain disorders
- Moderate–severe respiratory impairment (non-OSA/COPD)
- Moderate–severe OSA or COPD (long-term safety not established)

Important Safety Notes

Residual next-day impairment may occur (somnolence, reduced attention, slowed reflexes). Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms may rarely occur. Complex sleep behaviors (e.g., sleepwalking, sleep-driving) require immediate discontinuation.³

Monitor for worsening depression or suicidal ideation³

Contraindications

Lemborexant should not be used in patients with:³

- Narcolepsy
- Known hypersensitivity to lemborexant
- Severe hepatic impairment
- Concomitant use with strong or moderate CYP3A inhibitors/inducers

Drug Interactions

CYP3A-Mediated Interactions

Lemborexant is mainly metabolized by CYP3A.³

Drug Category	Interaction	Recommendation
Strong/moderate CYP3A inhibitors (e.g., itraconazole)	Markedly increased lemborexant exposure	Contraindicated
Strong/moderate CYP3A inducers (e.g., rifampicin, phenytoin)	Greatly decreased exposure and efficacy	Contraindicated
Weak CYP3A inhibitors	Increased exposure	Max dose 5 mg once nightly

Other Interactions

- CYP2B6 substrates (bupropion, methadone): DAYVIGO™ may decreased their effect; consider dose adjustment.
- CNS depressants (benzodiazepines, opioids, antipsychotics, alcohol): additive CNS depression; dosage adjustment may be needed.
- Alcohol significantly increased lemborexant exposure (Cmax +35% / AUC +70%) and impairs cognition; avoid use.

Common Side Effects

Across 884 subjects, adverse events occurred in 28.2%, most commonly:³

- Somnolence (10.7%)
- Headache (4.2%)
- Malaise (3.1%)

Less frequent effects include dizziness, sleep paralysis, abnormal dreams/nightmares, hallucinations, nausea, dry mouth, abdominal pain, palpitations, parasomnias, and disturbance in attention.³

Long-term trials (up to 12 months) show maintained safety, minimal withdrawal, and no rebound insomnia.^{2,4}

Switching From Benzodiazepines to Lemborexant

Switching from BZDs to lemborexant is appropriate when patients experience insufficient benefit, BZD-related risks (falls, dependence, cognitive impairment), or require safer long-term therapy.^{5,6}

Lemborexant shows minimal withdrawal (T-BWSQ scores <3), no rebound insomnia, and stable 12-month efficacy.^{2,4}

Recommended Switching Methods

1. Direct Switch

Best for: low doses, short use (<2–4 weeks), low dependence risk

How:

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- Stop BZD
- Start Lemborexant 5 mg the same night

Evidence:

Direct switching was well-tolerated in psychiatric populations with no major withdrawal⁵

2. Add-On Then Taper (Preferred Method)

Best for: long-term use, medium to high doses, older adults, anxiety-prone patients

How:

- Start Lemborexant 5 mg at bedtime
- Maintain current BZD dose for 3–7 nights
- Begin taper 10–25% per week
- Discontinue BZD once minimal dose reached

Evidence:

Stabilizing sleep with LEM first reduces rebound insomnia and improves taper success (SLIM study; Japanese Expert Consensus).^{5,7}

3. Taper First then Start Lemborexant (“Taper & Wait”)

Best for: high BZD doses, short-acting BZD (alprazolam), or strong withdrawal history

How:

- Gradually taper BZD to low dose
- Stop BZD for 1–2 nights
- Initiate Lemborexant 5 mg

Evidence:

Consistent with ASAM benzodiazepine tapering guidelines and Petunjuk Teknis.^{8,9}

BZD Tapering Principles

- Reduce 5–25% every 1–2 weeks; slower for high doses or long-term use
- Consider switching to a long-acting BZD (diazepam) for smoother taper
- Avoid abrupt cessation (risk of seizures, severe withdrawal)
- Educate patients on temporary rebound insomnia
- Monitor for anxiety, agitation, palpitations, severe insomnia⁹

Why Lemborexant Is a Suitable Switch Target (Evidence)

Multiple trials & systematic reviews report:^{1,2,4,5}

- Improved sleep onset & maintenance vs placebo and zolpidem
- Stable long-term efficacy up to 12 months
- Minimal withdrawal and no rebound

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- Preserved sleep architecture (Increased NREM & REM)
- Better safety in older adults: balance, cognition, driving performance
- Low misuse potential vs BZD/Z-drug classes

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