

BIOME GUIDE PROTOCOL

Sleep & Circadian Health Protocol

Evidence-based prebiotic, probiotic, and dietary strategies
to support deep sleep, circadian rhythm, and nighttime recovery

Covers: Insomnia | Poor Sleep Quality | Stress-Related Sleep Loss | Circadian Rhythm Support

Based on 16 systematic reviews, meta-analyses, and RCTs from PubMed | March 2026

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What This Protocol Addresses

Sleep is not a passive process. It is one of the most biologically active periods of your day, a time when your brain consolidates memories, your immune system rebuilds, your hormones recalibrate, and your gut microbiome performs critical maintenance. Yet roughly one in three adults fails to get the recommended seven or more hours of quality sleep each night, and chronic sleep disruption is now linked to increased risk of obesity, cardiovascular disease, depression, and cognitive decline.

This protocol targets the **gut-sleep axis**, the bidirectional communication network between your intestinal microbiome and the brain systems that regulate sleep architecture, circadian rhythms, and stress recovery. Research now shows that gut microbes directly influence sleep through at least five distinct biological pathways, and that poor sleep, in turn, disrupts the gut ecosystem, creating a vicious cycle that is difficult to break with sleep hygiene alone.

Five Pathways from Your Gut to Better Sleep

Pathway	How It Works	What Goes Wrong
Serotonin / Melatonin	~95% of serotonin is made in the gut. Serotonin converts to melatonin, the master sleep hormone.	Dysbiosis reduces tryptophan availability, cutting serotonin and melatonin production at the source.
HPA Axis (Cortisol)	The hypothalamic-pituitary-adrenal axis governs your stress response and cortisol rhythm.	Poor sleep raises cortisol, which damages gut barrier integrity and feeds dysbiosis. Dysbiosis keeps cortisol elevated.
Vagus Nerve	The vagus nerve carries signals from gut microbes directly to brain sleep centers.	Reduced vagal tone (from dysbiosis) weakens the gut-brain communication needed for normal sleep architecture.
GABA Production	Certain Lactobacillus and Bifidobacterium species produce GABA, the primary inhibitory neurotransmitter.	Depletion of GABA-producing bacteria reduces the calming signals needed for sleep onset and maintenance.
Inflammation (LPS)	A healthy gut barrier prevents bacterial toxins (LPS) from entering the bloodstream.	Leaky gut allows LPS translocation, triggering IL-6 and TNF-alpha, which fragment sleep and reduce slow-wave sleep.

The vicious cycle: Poor sleep causes gut dysbiosis. Gut dysbiosis causes poor sleep. Breaking this cycle requires intervening at the gut level, not just practicing better sleep hygiene. That is why microbiome-targeted strategies can succeed where conventional sleep advice falls short.

Sources: Matenchuk et al. (2020) Sleep Medicine Reviews, DOI: 10.1016/j.smrv.2020.101340; Sen et al. (2021) Trends in Molecular Medicine, DOI: 10.1016/j.molmed.2021.07.004; Galland (2014) J Med Food, DOI: 10.1089/jmf.2014.7000

The Sleep Microbiome Fingerprint

Research comparing the gut microbiota of good sleepers versus poor sleepers reveals a consistent pattern. Certain beneficial bacteria are depleted in people with insomnia and poor sleep quality, while pro-inflammatory or metabolically disruptive species become overrepresented. Understanding this microbial fingerprint is the foundation for targeted intervention.

What Is Depleted in Poor Sleepers

Bacterium	Role in Sleep	How to Restore It
Lactobacillus spp.	GABA production, vagal nerve signaling, serotonin support	Targeted probiotics (L. gasseri CP2305), fermented foods, GOS prebiotic
Bifidobacterium spp.	Tryptophan metabolism, SCFA production, immune regulation	Targeted probiotics (B. breve, B. longum strains), GOS + inulin/FOS
F. prausnitzii	Top butyrate producer; anti-inflammatory; supports gut barrier	Inulin/FOS prebiotics, resistant starch, Mediterranean diet
Bacteroides spp.	Associated with better sleep efficiency in observational studies	Diverse plant fiber intake (30+ plant foods per week)
Lachnospira	Correlated with sleep quality; SCFA-producing commensal	Whole grains, legumes, prebiotic fiber variety

What Is Elevated in Poor Sleepers

Bacterium	Problem
Blautia	Associated with poor sleep quality and increased inflammation
Ruminococcus	Elevated in insomnia patients; linked to gut barrier disruption
Desulfovibrio	Produces hydrogen sulfide; pro-inflammatory; disrupts sleep architecture

Sources: Kang et al. (2021) Clin Res Hepatol Gastroenterol, DOI: 10.1016/j.clinre.2021.101834; Feng et al. (2023) Biomed Pharmacother, DOI: 10.1016/j.biopha.2023.114344

Probiotic Strains for Sleep

Not all probiotics improve sleep. Generic meta-analyses of mixed probiotic formulations show inconsistent results (Gil-Hernandez et al., 2023, P=0.31). However, **strain-specific evidence** tells a very different story. The following strains have each demonstrated significant sleep improvements in well-designed randomized controlled trials. This is precisely why BiomeGuide recommends specific, named strains rather than generic probiotic products.

Lead Strain: Lactobacillus gasseri CP2305

Why CP2305 Is Our Top Pick for Sleep

This is a **para-psychobiotic**: a heat-inactivated (non-living) strain that works through immunomodulatory cell wall components rather than live colonization. This means it is shelf-stable, requires no refrigeration, and its effects are consistent regardless of your existing gut environment. It is the single most-studied probiotic for sleep outcomes, with both individual RCTs and a dedicated meta-analysis confirming its benefits.

Study	Design	Key Results
Nishida et al. (2019)	RCT, n=74, 24 weeks, double-blind	PSQI improved (p<0.05); EEG: shortened sleep latency, increased delta power in first cycle (p<0.05); reduced cortisol marker
Chu et al. (2023) Meta-analysis	7 studies, 6 in MA	PSQI global score: -0.77 (95% CI: -1.37 to -0.16, P=0.01); significant improvements in sleep quality component

Delta power in the first sleep cycle is one of the most meaningful objective sleep markers. It reflects the depth and restorative quality of your initial slow-wave sleep period, which is when the majority of growth hormone release, tissue repair, and memory consolidation occurs. CP2305 is one of the only probiotics to demonstrate improvement on this EEG measure.

Sources: Nishida et al. (2019) Nutrients, DOI: 10.3390/nu11081859; Chu et al. (2023) Clin Nutr, DOI: 10.1016/j.clnu.2023.06.019

Supporting Strains: Choose by Your Primary Complaint

Strain	Best For	Evidence	Key Numbers
B. breve CCFM1025	Stress-related insomnia	RCT, n=40, 4 weeks (Lan 2023)	PSQI 11.6 to 7.75 (p=0.0007); salivary cortisol reduced (p=0.002)
B. longum 1714	General sleep quality + daytime energy	RCT, n=89, 8 weeks (Patterson 2024)	PSQI sleep quality improved (p<0.05); energy/vitality improved at 8 weeks
B. breve 207-1	GABA-deficient sleep disruption	RCT, n=120, 28 days (Li 2024)	PSQI decreased; serum GABA increased; HPA hormones suppressed
L. plantarum JYLP-326	Anxiety-driven insomnia	RCT, n=60, 3 weeks (Zhu 2023)	Anxiety, depression, and insomnia scores all improved; gut microbiota partly restored

Which Strain Should You Choose?

Start with CP2305 (the para-psychobiotic). It has the broadest evidence and works for most types of sleep disruption. Then consider adding one supporting strain based on your primary pattern:

If your main issue is stress-driven insomnia (racing mind, high cortisol): add **B. breve CCFM1025**

If you want better daytime energy alongside sleep: add **B. longum 1714**

If anxiety is the root cause of your sleep problems: add **L. plantarum JYLP-326**

If you feel you lack natural calm (low GABA): add **B. breve 207-1**

Sources: Lan et al. (2023) *Nutrients*, DOI: 10.3390/nu15214700; Patterson et al. (2024) *Sci Rep*, DOI: 10.1038/s41598-024-53810-w; Li et al. (2024) *Eur J Nutr*, DOI: 10.1007/s00394-024-03447-2; Zhu et al. (2023) *Front Immunol*, DOI: 10.3389/fimmu.2023.1158137; Gil-Hernandez et al. (2023) *Nutr Rev*, DOI: 10.1093/nutrit/nuad027

Prebiotics That Support Sleep

Prebiotics feed the beneficial bacteria that produce sleep-supporting metabolites: GABA, serotonin, butyrate, and other short-chain fatty acids. By selectively nourishing the depleted taxa identified in the sleep microbiome fingerprint, prebiotics create a sustainable foundation for long-term sleep improvement that outlasts the probiotic supplementation period.

Prebiotic	Dose	Target Bacteria	Sleep Mechanism
GOS (galacto-oligo saccharides)	5g/day	Bifidobacterium, Lactobacillus	Direct NREM sleep improvement and REM rebound after stress in controlled studies
Inulin / FOS	5g/day	Bifidobacterium, F. prausnitzii	Butyrate production; anti-inflammatory; supports tryptophan metabolism
PHGG (partially hydrolyzed guar gum)	5g/day	Bifidobacterium, Lactobacillus	Gentle SCFA production; well-tolerated; gut barrier support

GOS: The Lead Prebiotic for Sleep

Galacto-oligosaccharides have the most direct sleep evidence of any prebiotic. Animal studies by Thompson et al. (2017) showed that a GOS-containing prebiotic diet improved NREM (non-REM) sleep and enhanced REM sleep rebound after stress exposure. This matters because REM sleep is critical for emotional processing and stress recovery. Participants on the prebiotic diet also maintained healthy gut microbial diversity even after stress, while controls showed dysbiosis.

Practical tip: Start with GOS alone for the first 2 weeks. Add inulin/FOS in week 3. This staged approach minimizes bloating and allows your microbiome to adapt gradually.

Source: Thompson et al. (2017) Front Behav Neurosci, DOI: 10.3389/fnbeh.2016.00240

Targeted Supplements

The following supplements have strong RCT evidence for improving sleep and work synergistically with the probiotic and prebiotic strategies above. Each one has a clear mechanism connecting it to both sleep regulation and gut health.

Magnesium (Glycinate or L-Threonate)

Magnesium is a cofactor in serotonin synthesis and supports GABA receptor function. A meta-analysis of 3 RCTs (n=151) found that magnesium supplementation reduced sleep onset latency by 17.36 minutes (p=0.0006) and trended toward increasing total sleep time by 16 minutes. A 2024 RCT specifically testing Magnesium L-Threonate (MgT), a brain-bioavailable form that crosses the blood-brain barrier, found significant improvements in deep sleep score and REM sleep score measured by Oura ring, plus improvements in daytime energy, mood, and mental alertness.

Form	Dose	Advantage
Magnesium Glycinate	200-400 mg elemental Mg before bed	Well-absorbed, calming (glycine also supports sleep), gentle on stomach
Magnesium L-Threonate (MgT)	1g MgT daily (144 mg elemental Mg)	Crosses BBB; improved deep + REM sleep in RCT; best for cognitive benefits

Sources: Mah & Pitre (2021) BMC Complement Med Ther, DOI: 10.1186/s12906-021-03297-z; Hausenblas et al. (2024) Sleep Med X, DOI: 10.1016/j.sleepx.2024.100121

L-Theanine (200-450 mg/day)

L-Theanine is a non-protein amino acid found naturally in tea leaves. It promotes relaxation without sedation by increasing alpha brain wave activity, boosting GABA, serotonin, and dopamine. It crosses the blood-brain barrier within 30 minutes of ingestion.

An RCT by Hidese et al. (2019) found that 200 mg/day of L-theanine for 4 weeks significantly reduced PSQI scores (p=0.013), with improvements in sleep latency, sleep disturbance, and sleep medication use (all p<0.05). A 2025 systematic review of 13 trials (n=550) concluded that 200-450 mg/day is safe and effective for supporting healthy sleep, with benefits on both objective and subjective outcomes.

L-Theanine practical tips: Take 200 mg about 30-60 minutes before bed. Can be taken alongside magnesium. Especially useful for people whose sleep problems involve a "racing mind" or difficulty "switching off." Unlike prescription sleep medications, L-theanine does not cause morning grogginess or dependency.

Sources: Hidese et al. (2019) Nutrients, DOI: 10.3390/nu11102362; Cotter et al. (2025) Nutr Neurosci, DOI: 10.1080/1028415X.2025.2556925

5-HTP: The Dual-Action Sleep Supplement

Why 5-HTP Is the Ideal BiomeGuide Supplement for Sleep

5-Hydroxytryptophan (5-HTP) crosses the blood-brain barrier and converts directly to serotonin, which then converts to melatonin. But the 2024 RCT by Sutanto et al. revealed something remarkable: 5-HTP simultaneously improved gut microbiota diversity and increased the abundance of SCFA-producing bacteria. This dual action on both the brain and the gut makes 5-HTP the supplement that most directly bridges the gut-sleep axis.

The RCT enrolled 30 older adults (age 66 +/- 3 years) in a 12-week trial of 100 mg 5-HTP daily. Poor sleepers (PSQI > 5) showed significant improvement in global sleep score ($p=0.005$). Serum serotonin increased. Gut microbiota diversity improved, and SCFA-producing bacteria became more abundant. The effect was most pronounced in those who started with poor sleep quality.

Important: 5-HTP safety considerations

Do NOT combine 5-HTP with SSRIs, SNRIs, MAOIs, or triptans. The combination can cause serotonin syndrome, a potentially dangerous condition. If you are taking any antidepressant or migraine medication, consult your doctor before using 5-HTP. Start at 50 mg and increase to 100 mg after one week if tolerated.

Source: Sutanto et al. (2024) Clin Nutr, DOI: 10.1016/j.clnu.2024.01.010

Vitamin D3 (Conditional)

Vitamin D deficiency is associated with poor sleep quality in multiple observational studies, and vitamin D receptors exist in brain regions controlling sleep. Low vitamin D is also linked to reduced *Bifidobacterium* and *Lactobacillus* in the gut. If your serum 25(OH)D is below 30 ng/mL, supplementation (1,000-2,000 IU daily) is recommended as part of this protocol. Take with a fat-containing meal in the morning (not evening, as it may interfere with melatonin timing).

The Protocol: Two Phases

Phase 1: Calm and Restore (Weeks 1-4)

The first phase focuses on lowering cortisol, repairing the gut barrier, and establishing the neurotransmitter production pathways needed for healthy sleep. Think of this as building the foundation before optimizing.

Category	What to Take	When	Notes
Probiotic	L. gasseri CP2305 (heat-inactivated)	Daily with breakfast	Para-psychobiotic; no refrigeration needed
Prebiotic	GOS 5g/day	With evening meal	Start at 2.5g; increase to 5g by week 2
Magnesium	Glycinate 200-400 mg or MgT 1g	30-60 min before bed	Choose glycinate for calm; MgT for deep sleep + cognition
L-Theanine	200 mg	30-60 min before bed	Can combine with magnesium; no dependency risk
Vitamin D3	1,000-2,000 IU (if deficient)	Morning with fat-containing meal	Test 25(OH)D first; target > 30 ng/mL

Phase 2: Optimize and Sustain (Weeks 5-12)

Once the foundation is in place, Phase 2 diversifies your gut ecosystem for long-term sleep resilience and optimizes the serotonin-melatonin pathway.

Category	What to Add or Adjust	Notes
Second Probiotic	B. breve CCFM1025 (stress-insomnia) OR B. longum 1714 (general quality)	Choose based on your primary complaint; see strain selection guide
5-HTP	50-100 mg before bed (optional, especially age 55+)	NOT with SSRIs/SNRIs/MAOIs. Start at 50 mg.
Expand Prebiotics	Add inulin/FOS 5g/day alongside GOS	Supports F. prausnitzii and butyrate production
Fermented Foods	1-2 servings daily (kefir, sauerkraut, kimchi)	Stanford study: 6+ servings/week increased microbiome diversity

Source: Ito et al. (2024) Clin Nutr ESPEN, DOI: 10.1016/j.clnesp.2024.07.006

Dietary Framework for Sleep

What you eat, when you eat it, and which foods you avoid in the evening hours all have measurable effects on sleep quality. The following framework optimizes both your gut microbiome and your body's natural sleep-promoting chemistry.

Sleep-Supporting Foods

Category	Foods	Why It Helps
Tryptophan-rich	Turkey, chicken, eggs, dairy, tofu, nuts/seeds, oats	Provides raw material for serotonin and melatonin synthesis
Prebiotic-rich	Garlic, onions, leeks, asparagus, bananas, oats, legumes	Feeds Bifidobacterium and Lactobacillus; supports SCFA production
Polyphenol-rich	Berries, cherries (tart), dark chocolate, green tea	Feeds Akkermansia and butyrate producers; tart cherries contain melatonin
Omega-3 rich	Salmon, sardines, mackerel, walnuts, flaxseeds	Anti-inflammatory; associated with better sleep quality
Kiwifruit	2 kiwifruits 1 hour before bed	High serotonin and folate content; RCT evidence for improved sleep onset and duration

What to Avoid

Substance	Cutoff	Why
Caffeine	None after 2:00 PM	Blocks adenosine (sleep pressure signal); half-life 5-6 hours
Alcohol	Minimize; none within 3 hours of bed	Fragments sleep architecture despite initial sedation; reduces REM sleep; disrupts gut barrier
Large/heavy meals	None within 2-3 hours of bed	Late heavy meals delay sleep onset and reduce sleep quality
High-sugar foods at night	Avoid in the evening	Blood sugar spikes and crashes disrupt sleep continuity

Sleep Support Smoothie (Evening)

Blend: 1 cup kefir (probiotic + tryptophan) + 1 banana (prebiotic + tryptophan) + 1 tbsp almond butter (magnesium + tryptophan) + 1 tbsp ground flaxseed (omega-3) + 1 tsp raw honey (prebiotic) + pinch of cinnamon

Enjoy 1-2 hours before bed. This provides tryptophan, prebiotic fiber, probiotics, magnesium, and omega-3s in a single glass.

Tracking Your Progress

To know whether this protocol is working, you need to track both subjective sleep experience and, ideally, objective sleep markers. Here is what to monitor and when to expect changes.

Metric	How to Track	Target	Timeline
PSQI Score	Online questionnaire (free)	Score 5 or below (good sleeper)	Check at baseline, week 4, week 8, week 12
Sleep Latency	Sleep diary or wearable	Under 20 minutes	Improvements often by week 2-4
Sleep Efficiency	Wearable (Oura, Whoop, Apple Watch)	85% or above	Gradual improvement weeks 4-8
Deep Sleep	Wearable device	60-90+ minutes per night	Often the last metric to improve (weeks 6-12)
Morning Energy	Daily 1-10 rating	Consistent 7+ rating	Often the first improvement noticed (weeks 2-4)
GI Symptoms	Daily diary	Stable or improving	Monitor especially during prebiotic introduction

Advanced Testing (Optional)

Lab tests that can help personalize this protocol:

25(OH)D (Vitamin D): If below 30 ng/mL, add Vitamin D3 supplementation.

Cortisol (4-point salivary): Reveals whether your cortisol rhythm is inverted (high at night). If so, prioritize CCFM1025 and stress-reduction.

Serum magnesium / RBC magnesium: Serum is standard but insensitive; RBC magnesium is more informative for intracellular status.

Gut microbiome test: Companies like Ombre, Viome, or Thryve can reveal whether your Lactobacillus and Bifidobacterium levels are depleted.

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Medical Disclaimer

This protocol is for educational purposes only and does not constitute medical advice. It is not intended to diagnose, treat, cure, or prevent any disease. Always consult a qualified healthcare professional before starting any new supplement regimen, especially if you are pregnant, nursing, taking medications (particularly SSRIs, SNRIs, MAOIs, or sleep medications), or have a pre-existing medical condition. The information presented here is based on published peer-reviewed research but individual results may vary.

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