Insufficient and Disrupted Sleep in Metabolic Disease: A Critical Review of Insulin Resistance.

Abstract

Sleep duration, continuity, and circadian timing may influence insulin action, but insulin resistance, dysglycemia, and incident diabetes are distinct outcomes.

To assess causal and observational evidence linking sleep to adult insulin resistance and evaluate the metabolic effects of sleep-directed interventions.

This targeted narrative review prioritizes adult human experiments, prospective cohorts, randomized trials, and evidence syntheses. Web-accessible bibliographic records and primary sources were searched on 7 October 2026, with targeted verification of selected intervention findings on 8 October 2026.

Controlled sleep restriction and circadian misalignment can impair insulin action. Evidence for habitual long sleep, insomnia, and irregular schedules is predominantly observational. Autonomic changes, altered lipid availability, and energy balance provide plausible pathways; detailed molecular mechanisms remain partly preclinical. Sleep-extension trials yield inconsistent metabolic results. In a small trial of adults with overweight or obesity and insulin resistance, sleep increased but multiorgan insulin sensitivity did not improve detectably. Insomnia treatment improves sleep symptoms, whereas glycemic benefits remain uncertain. Continuous positive airway pressure (CPAP) produces a small pooled glycated hemoglobin (HbA1c) reduction in type 2 diabetes, with substantial heterogeneity and an association between HbA1c response and nightly CPAP use.

Assess sleep health, diagnose and treat clinically significant sleep disorders, and maintain established metabolic treatment. Neither improvement in sleep nor a glycemic change alone establishes reversal of insulin resistance or prevention of diabetes.

Keywords: sleep restriction; circadian misalignment; insulin resistance; type 2 diabetes; obstructive sleep apnea; sleep extension

Introduction & Background

Insulin resistance denotes a reduced biological response to insulin, including impaired stimulation of glucose disposal and inadequate suppression of hepatic glucose production or adipose lipolysis. It may be accompanied by compensatory hyperinsulinemia while glucose remains normal. Hyperglycemia develops when insulin secretion and other regulatory mechanisms no longer adequately compensate; neither a raised fasting insulin concentration nor an abnormal sleep pattern alone establishes diabetes. Sleep-related studies therefore require careful separation of insulin action, glucose tolerance, and disease incidence.

Prospective syntheses associate short and long sleep, as well as difficulties initiating or maintaining sleep, with subsequent type 2 diabetes [1,2]. Experimental work beginning with controlled sleep-debt protocols provides complementary evidence that sleep loss can directly alter glucose regulation [3,4]. However, the inference that restoring sleep necessarily reverses established insulin resistance is stronger than the intervention evidence currently permits.

The 2026 American Diabetes Association (ADA) Standards of Care recommend assessment of sleep health in people with prediabetes, diabetes, or elevated diabetes risk [5]. The guiding question is whether sleep duration, continuity, architecture, and circadian timing affect insulin action in adults, and whether treating these exposures produces measurable metabolic benefit. Glycemic outcomes and incident diabetes are considered separately from insulin-sensitivity outcomes.

Literature search and selection

This targeted critical narrative review used web-accessible PubMed/MEDLINE records, PubMed Central material, and original journal or professional-society pages. The initial search was dated 7 October 2026. The initial verbatim search strings and screening counts were not retained; consequently, this search cannot be reproduced in full. Direct comprehensive searches of Cochrane Library, Scopus, and Web of Science were not performed.

Selection prioritized adult human experiments, randomized interventions, prospective cohorts, relevant systematic reviews, and measurement or practice guidance. Foundational reports were retained alongside recent publications; preclinical studies provide explicitly identified mechanistic context. Selection was relevance-based rather than protocol-driven. No pooled analysis or formal risk-of-bias grading was performed, and comprehensive coverage is not claimed. Incomplete full-text access and narrative selection introduce potential selection and interpretation bias.

On 8 October 2026, targeted web searches located PubMed records and accessible primary reports concerning sleep extension, cognitive behavioral therapy for insomnia, and continuous positive airway pressure.

Physiological foundations

Sleep emerges from interaction between homeostatic pressure accumulated during wakefulness and circadian regulation of sleep propensity. The two-process framework explains why adequate duration and appropriate timing are related but distinct aspects of sleep health [6]. Non-rapid eye movement (NREM) sleep includes lighter stages and slow-wave sleep, whereas rapid eye movement (REM) sleep has different neurophysiological and autonomic characteristics. Consequently, equal sleep durations need not represent equivalent sleep architecture or continuity. Consensus guidance recommends at least seven hours of regular nightly sleep for healthy adults, with individual needs and clinical circumstances requiring consideration [7].

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Glucose regulation also varies across circadian phase. Experimental protocols separating behavioral cycles from internal time show lower glucose tolerance in the biological evening, while misalignment adds a distinct adverse influence [8]. Modeling of glucose and insulin responses suggests that the evening circadian effect is driven substantially by reduced beta-cell responsiveness, whereas misalignment predominantly reduces insulin sensitivity [9]. These findings caution against describing every increase in postprandial glucose as insulin resistance. Clock time, biological phase, and the timing of meals and metabolic testing are relevant to interpretation.

Sleep dimensions associated with insulin resistance

Acute and sustained sleep restriction

Controlled human experiments provide some of the clearest causal evidence for the acute effects of sleep restriction, although sample sizes and generalizability are limited. In nine healthy adults, one night with four hours of sleep opportunity reduced clamp-derived insulin sensitivity and impaired suppression of endogenous glucose production [10]. The tightly controlled setting supports a direct effect, but the severe exposure and small sample limit extrapolation to habitual community sleep.

More sustained, moderate restriction improves ecological relevance. A randomized crossover study of 38 women compared six weeks of adequate sleep with a nightly reduction of approximately 1.5 hours. Fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR) increased, without evidence that adiposity changes mediated the effect; the HOMA-IR response was more pronounced after menopause [11]. Oral glucose tolerance test (OGTT)-derived measures did not significantly change in the overall sample. Because fasting indices rather than clamps drove the principal inference, the result should be interpreted as deterioration in estimated insulin sensitivity. A separate crossover experiment in postmenopausal women also found impaired clamp-derived insulin sensitivity after four nights of restriction, although only nine women were analyzed [12].

These studies extend earlier predominantly male experiments, but do not establish that menopause uniformly amplifies susceptibility. Across trials, responses depend on restriction severity, baseline sleep, energy balance, and the measurement used. A systematic review supports adverse effects of sleep restriction on several insulin-sensitivity outcomes while also reporting heterogeneity between methods and tissue-related endpoints [4].

Long sleep duration

Evidence is predominantly prospective and observational; causality remains uncertain. The association between long sleep and diabetes risk is less readily interpreted as causal. Prospective data show a U-shaped relationship, with the lowest observed risk around seven to eight hours [2]. Long reported sleep may instead indicate illness, depression, inactivity, fragmented sleep, increased time in bed, or an evolving metabolic disorder. Statistical adjustment cannot fully resolve these possibilities. There is insufficient evidence to recommend deliberate sleep curtailment to improve insulin sensitivity in otherwise well long sleepers. Clinically, unusually long or nonrestorative sleep warrants assessment of its cause.

Fragmentation and slow-wave sleep

Small human experiments support a physiological effect; consistency and clinical translation are limited. Selective suppression of slow-wave sleep without reducing total sleep duration impaired insulin sensitivity and glucose tolerance in a small human experiment, with insufficient compensatory insulin secretion [13]. Experimental fragmentation across stages also reduced insulin sensitivity in 11 healthy participants and increased sympathetic activity and morning cortisol [14].

Nevertheless, fragmentation effects are not consistently reproduced across the sparse intervention literature. The broader synthesis did not find uniformly adverse effects for every architecture manipulation [4]. Acoustic or mechanical arousals may themselves activate stress pathways, and experimentally suppressed slow-wave sleep differs from age-related variation. These data support the metabolic relevance of sleep continuity and depth without establishing a clinical indication to pharmacologically increase a particular stage.

Subjective sleep quality and insomnia

Prospective observational evidence supports an association, with substantial phenotype heterogeneity. Difficulty initiating or maintaining sleep predicts diabetes in prospective studies, but symptom-based measures combine heterogeneous exposures [1]. Insomnia may involve hyperarousal and distress even when objective duration is relatively preserved; conversely, objectively short sleep may occur without prominent complaints. Depression, pain, medications, alcohol, and established diabetes can influence both perceived sleep quality and metabolism. The association is therefore compatible with causation, shared determinants, and reverse causality. Treating clinically significant insomnia is justified by its burden, while its independent effect on insulin action remains less firmly established than that of experimentally imposed sleep restriction.

Sleep irregularity, chronotype, and shift work

Cohort evidence supports associations with diabetes incidence; laboratory evidence addresses selected components of circadian disruption. Rotating night-shift cohorts demonstrate an association with incident diabetes that is attenuated, but not eliminated, after adjustment for body mass index [15]. Evening chronotype is likewise associated with higher diabetes risk in middle-aged women, with substantial attenuation after accounting for lifestyle factors [16]. Device-based prospective data also link variable sleep duration to incident diabetes [17]. These exposures are related but should not be treated as interchangeable: chronotype reflects preferred timing, irregularity describes variability, and shift work imposes a broader occupational and behavioral exposure.

Laboratory studies strengthen the circadian interpretation. Forced desynchrony produced higher glucose despite higher insulin [18], and experiments with similar restricted sleep durations found additional adverse effects during misalignment [19]. Nevertheless, observational risk estimates also capture meal timing, socioeconomic conditions, occupational stress, and physical activity. A favorable association with regular sleep does not establish that regularizing schedules alone prevents diabetes.

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Obstructive sleep apnea

Observational and acute experimental evidence supports interacting pathways, without establishing the metabolic effect of treating chronic OSA. Obstructive sleep apnea (OSA) combines upper-airway obstruction, intermittent hypoxia, recurrent arousals, and variable sleep loss. In a community cohort, severe OSA predicted incident diabetes after adjustment for both body mass index and waist circumference [20]. This supports a contribution beyond measured anthropometry, but residual differences in visceral fat and other determinants remain possible.

Experimental intermittent hypoxia during wakefulness reduced insulin sensitivity in healthy volunteers, providing evidence for a hypoxia-related pathway independent of experimentally disrupted sleep [21]. However, acute simulated hypoxia cannot fully reproduce chronic OSA. Apnea severity, hypoxic burden, arousal frequency, and adiposity may exert different effects. The evidence favors interacting pathways rather than assigning all metabolic risk either to obesity or to apnea alone.

Pathophysiological mechanisms

Direct human experimental evidence

Sleep-debt, fragmentation, and hypoxia experiments demonstrate autonomic or endocrine changes alongside altered glucose regulation. Cortisol responses depend on timing and protocol, and are not universally elevated [3,14,21]. Human adipocyte experiments show reduced insulin-stimulated Akt signaling after restriction, while clamp and tracer studies identify impaired hepatic and peripheral responses [10,22]. These findings support biological plausibility, without identifying a single obligatory mediator.

Human substrate and behavioral pathways

Sleep restriction increased nocturnal nonesterified fatty acids in healthy men; their rise correlated with impaired insulin sensitivity [23]. This is consistent with increased lipid delivery to liver and muscle, but correlation does not prove mediation or identify the molecular pathway in those tissues.

Experimental sleep loss can also increase food intake beyond the energetic cost of prolonged wakefulness [24]. Energy balance may therefore amplify longer-term risk alongside acute physiological effects. Hormonal changes in leptin and ghrelin vary with feeding conditions and should not be treated as universal responses.

Associative and preclinical mechanisms

Sleep disturbance is associated with inflammatory markers, but pooled experimental deprivation data do not consistently show elevations of standard circulating markers [25]. Oxidative stress and immune pathways remain plausible, especially during hypoxia and reoxygenation, but detailed mediation is incompletely established in humans.

Animal CLOCK/BMAL1 disruption supports an islet-clock mechanism, but does not reproduce human insomnia or shift work [26]. Human circadian experiments distinguish effects on secretion from effects on sensitivity [8,9]. Glucose can remain normal when beta-cell compensation is adequate; insulin concentration alone also reflects clearance. Preclinical mechanisms should therefore be separated from demonstrated clinical treatment effects.

Assessment of insulin resistance and sleep

The hyperinsulinemic-euglycemic clamp quantifies glucose requirements during insulin infusion and is a reference method for insulin action [27]. Its interpretation depends on insulin dose, achieved concentrations, steady-state conditions, and normalization. Tracers and multistep protocols distinguish endogenous glucose production from glucose disposal; lipolysis measures add information on adipose responses. A single high-dose clamp does not characterize every organ equally.

HOMA estimates basal insulin resistance from fasting glucose and insulin [28], but reflects a modeled fasting equilibrium rather than direct tissue measurement. Assay variation, beta-cell dysfunction, and treatment complicate interpretation; there is no universal diagnostic HOMA-IR threshold [29]. Oral glucose tolerance test indices, including the Matsuda index, provide dynamic estimates but depend on secretion, clearance, and gastrointestinal physiology [30]. Intravenous minimal models offer complementary information. Continuous glucose monitoring characterizes glycemia and variability, not insulin sensitivity itself.

Sleep questionnaires capture experiences that physiological recordings cannot replace. The Pittsburgh Sleep Quality Index (PSQI) assesses perceived sleep quality [31], whereas the Insomnia Severity Index (ISI) measures insomnia-related symptoms and impairment [32]. Sleep diaries and actigraphy characterize habitual timing and variability over multiple days; actigraphy may classify quiet wakefulness as sleep and does not directly measure sleep stages [33]. Polysomnography measures architecture, arousals, and respiratory events but a single night may not represent habitual schedules. OSA questionnaires support risk assessment rather than diagnosis; appropriate home testing or polysomnography is required [34]. Metabolic studies should document actual sleep change, testing phase, recent sleep history, and meal timing.

Table 1 summarizes the interpretation and limitations of commonly used metabolic and sleep measurements [27,28,29,30,31,32,33,34].

Interpreting experimental and clinical evidence

Measure	What it estimates	What it does not establish
Clamp with appropriate tracers [27]	Insulin-stimulated disposal and organ-related responses	Universal tissue sensitivity independent of dose, insulin exposure, or protocol.
HOMA-IR [28,29]	Modeled fasting insulin resistance	Direct tissue action; universal diagnosis or treatment threshold.
OGTT indices [30]	Dynamic estimates integrating oral glucose responses	Pure insulin action independent of secretion, clearance, or absorption.
HbA1c and CGM	Chronic glycemia or glucose patterns	Insulin sensitivity or beta-cell function in isolation.
PSQI and ISI [31,32]	Subjective quality and insomnia symptoms	Objective sleep duration or an OSA diagnosis.

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Actigraphy and diary [33]	Habitual sleep timing, duration, variability	Sleep stages; reliable discrimination of quiet wakefulness in every patient.
PSG and appropriate home testing [34]	PSG: architecture and respiratory events; home testing: selected respiratory parameters	Habitual multiweek patterns; home tests do not fully reproduce PSG.

Table 1: What metabolic and sleep measures estimate

This table summarizes commonly used metabolic and sleep assessment methods, the physiological or clinical parameters they estimate, and their main interpretative limitations. It highlights the importance of distinguishing direct measurements from surrogate markers when evaluating the relationship between sleep disturbances and insulin resistance.

Experimental manipulation supports causality for selected short-term exposures, whereas cohorts establish temporality and clinical relevance over longer periods. Neither design answers every question. Small experiments often exclude obesity, comorbidity, medications, and established diabetes. Cohorts better represent habitual exposures but depend on imperfect measurements and incomplete confounder control. Associations with incident diabetes cannot be translated directly into the magnitude of a change in insulin sensitivity.

Body weight is particularly complex: it may confound a sleep association, mediate an effect of sleep loss, or modify the response. Adjustment for adiposity is thus not synonymous with proving a weight-independent mechanism. Controlled feeding and within-person designs strengthen inference, while sustained real-life studies require careful mediation analyses. Differences between acute experimental deprivation and years of habitual short sleep also mean that exposure induction and exposure reversal need not have symmetric effects. Tables 2 and 3 summarize these distinctions. Figure 1 presents a conceptual framework linking sleep exposures, candidate pathways, and distinct metabolic outcomes

Dimension	**Main metabolic finding**	**Evidence and principal limitation**
Short sleep	Experimental reduction in sensitivity; prospective diabetes association	Human manipulation supports short-term causality; habitual exposure and long-term effects differ. [1,2,4,10,11]
Long sleep	Higher observed diabetes incidence	Prospective association; illness, inactivity, reporting error, and reverse causality remain plausible. [2]
Reduced slow-wave sleep	Lower sensitivity without shorter total sleep	Small acoustic-suppression experiment; limited external validity. [13]
Fragmentation	Adverse findings in individual experiments	Sparse and inconsistent intervention evidence; arousal-related stress is difficult to separate. [4,14]
Insomnia and poor quality	Association with incident diabetes	Subjective phenotypes, distress, comorbidity, and bidirectionality complicate attribution. [1]
Irregularity and evening chronotype	Prospective diabetes associations	Lifestyle attenuation; device recordings capture a limited interval. [16,17]
Shift work and misalignment	Epidemiological risk and experimental glucose impairment	Occupational exposure includes meals, sleep loss, and stress; laboratory protocols isolate only selected components. [9,15,18,19]
OSA	Severe OSA predicts diabetes after anthropometric adjustment	Residual adiposity confounding; experimental hypoxia supports an additional pathway. [20,21]

Table 2: Sleep dimensions and metabolic evidence

This table summarizes the main dimensions of sleep, including sleep duration, sleep continuity, circadian timing, and obstructive sleep apnea, and their associations with insulin resistance and metabolic outcomes. It distinguishes findings from observational studies, experimental investigations, and clinical interventions while highlighting the principal limitations of the available evidence.

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Study	Population and design	Exposure and outcome	Main finding and limitation
Spiegel 1999	11 young men; laboratory comparison	Six nights of restricted opportunity; glucose and endocrine testing	Impaired glucose tolerance; small, severe, short-term exposure. [3]
Donga 2010	9 healthy adults; within-person comparison	One restricted night; clamp with tracer	Impaired hepatic and peripheral responses; very small acute experiment. [10]
Tasali 2008	9 healthy adults; crossover experiment	Three nights of slow-wave suppression; IVGTT	Reduced sensitivity without shorter sleep; artificial architecture manipulation. [13]
Zuraikat 2024	38 women; randomized crossover	Six weeks of mild restriction; fasting and OGTT indices	Higher fasting insulin and HOMA-IR without adiposity mediation; surrogate primary inference. [11]
Singh 2023	9 postmenopausal women analyzed; crossover	Four restricted nights; clamp	Reduced sensitivity; limited sample and restriction duration. [12]
So-ngern 2019	21 adults completed; randomized crossover	Two-week extension; OGTT and fasting indices	Overall null result; benefit in 8-person per-protocol subgroup. [35]
Hartescu 2022	18 men with overweight or obesity; randomized trial	Six-week extension; fasting indices and glucose monitoring	Improved selected metabolic markers; small sample and surrogate sensitivity assessment. [36]
Beals 2026 [37]	31 randomized; 29 completed (15 habitual, 14 extension); adults with overweight or obesity	Approximately six-week extension; clamp and tracers	Sleep improved; no multiorgan sensitivity benefit detected; limited precision. [37]
Pamidi 2015 [38]	39 adults with prediabetes and OSA; randomized trial	Two weeks of supervised overnight CPAP; OGTT and IVGTT	Improved sensitivity and glucose response; intensive adherence limits routine applicability. [38]
Groeneveld 2024	57 adults with type 2 diabetes; randomized trial	Online CBT-I; HbA1c and symptoms	No significant intention-to-treat glycemic benefit; incomplete intervention uptake. [39]

Table 3: Selected Experimental and Intervention Studies on Sleep and Metabolic Outcomes

This table summarizes selected experimental and interventional studies investigating the effects of sleep restriction, sleep extension, circadian disruption, and sleep-related therapeutic interventions on insulin sensitivity and glucose metabolism. It highlights the study designs, principal metabolic findings, and methodological limitations relevant to interpreting the available evidence.

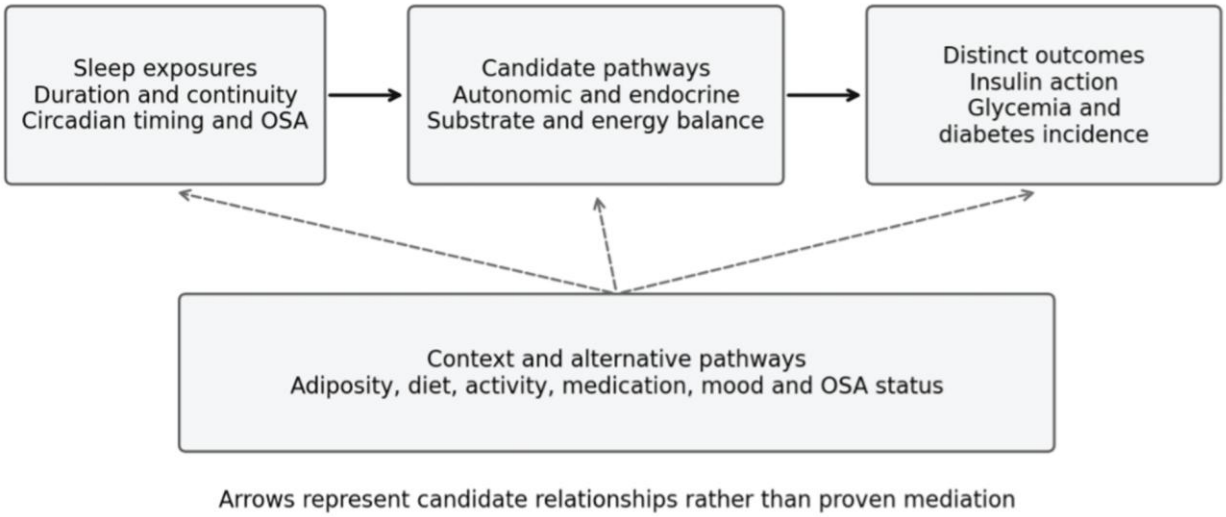


Figure 1: Conceptual framework linking sleep disturbances and metabolic outcomes

This conceptual diagram illustrates the proposed relationships between sleep duration, sleep continuity, circadian disruption, potential physiological mechanisms, and metabolic outcomes, particularly insulin resistance. The arrows represent proposed relationships rather than established causal pathways.

Interventions and therapeutic implications

Sleep extension and recovery sleep

Intervention evidence is inconsistent and mostly small. An uncontrolled study associated extension with improved fasting sensitivity [43]. So-ngern et al. analyzed 21 of 22 randomized participants and found no overall metabolic benefit; an eight-person adherence subgroup had lower HOMA-IR (adjusted difference −0.50, 95% confidence interval (CI) −0.89 to −0.11), a hypothesis-generating result vulnerable to selection bias [35]. In Hartescu et al., 18 men were randomized; the primary endpoint was actigraphic sleep duration, not insulin sensitivity. HOMA-IR

changes were −0.51 (95% CI −0.98 to −0.03) in the extension arm and +0.28 (−0.20 to 0.76) in controls. These are arm-specific changes, not the confidence interval of a treatment contrast [36].

Beals et al. randomized 31 adults with overweight or obesity, insulin resistance, and habitual short sleep; 29 completed follow-up (14 extension, 15 habitual sleep). After approximately six weeks, sleep increased by 1.1 h/night in the extension arm (95% CI 0.8 to 1.4), versus 0.0 h/night (−0.2 to 0.2) in controls. Multiorgan insulin sensitivity did not improve detectably [37]. The numerical adjusted clamp contrast was not extracted from the accessible report; the absence of a detectable difference should not be interpreted as equivalence. This small trial evaluates one program and phenotype; it cannot exclude modest effects or establish general ineffectiveness of sleep extension.

In 80 adults with overweight, a two-week extension program increased sleep by approximately 1.2 h/night and reduced estimated energy intake by 270 kcal/day versus control (95% CI −393 to −147) [44]. This supports an energy-balance pathway, not direct proof of improved insulin action. Laboratory weekend recovery did not fully prevent dysregulation when restriction resumed; that protocol does not establish that recovery sleep has no benefit [45].

Insomnia treatment

Cognitive behavioral therapy for insomnia (CBT-I) is recommended for chronic insomnia; sleep hygiene alone is not an adequate sole treatment [46]. In Groeneveld et al., 57 adults with type 2 diabetes were randomized (29 CBT-I, 28 usual care), with glycated hemoglobin (HbA1c) assessed as the primary outcome at three and six months. Intention-to-treat analyses did not detect a glycemic benefit; only about half completed CBT-I [39]. The limited uptake constrains interpretation. The numerical intention-to-treat HbA1c contrast was unavailable for verification; per-protocol findings cannot substitute for the randomized comparison. Symptom improvement does not establish improved insulin sensitivity.

Continuous positive airway pressure (CPAP) and metabolic outcomes

In Pamidi et al., 39 adults with prediabetes and OSA were randomized to supervised eight-hour nightly CPAP or oral placebo for two weeks. The primary OGTT glucose-area outcome improved by −1,276.9 mg/dL·min (95% CI −2,392.4 to −161.5); the secondary intravenous glucose tolerance test (IVGTT) sensitivity contrast was +0.77 $(mU/L)^{-1}\cdot min^{-1}$ (95% CI 0.03 to 1.52) [38]. Near-complete supervised overnight exposure limits routine applicability, and secondary outcomes were not adjusted for multiplicity. A larger type 2 diabetes trial found no HbA1c benefit [47], while a smaller six-month trial reported improvement [48]. These outcomes and populations should not be pooled conceptually as one insulin-sensitivity result.

Herth et al. included 11 randomized trials overall (964 participants); the HbA1c analysis used nine trials (807 participants). The pooled difference was −0.24 percentage points (95% CI −0.43 to −0.06), with substantial heterogeneity (I^2 = 71.25%). Excluding an outlier reduced the estimate to −0.16 points (−0.28 to −0.03; I^2 = 39.30%) [40]. Longer nightly CPAP use was associated with greater reduction in trial-level meta-regression, which does not establish a randomized dose-response effect. The modest average glycemic benefit may matter differently according to baseline control; it neither demonstrates diabetes prevention nor proves restored insulin sensitivity. Table 4 summarizes the quantitative intervention findings and their limitations.

Study and population	Design and exposure	Outcome	Estimate and precision	Adherence and limitation
So-ngern 2019 [35] 22 randomized; 21 analyzed	Crossover; extension versus habitual sleep; 2 weeks	Fasting indices and OGTT	Overall null. In 8-person subgroup: HOMA-IR −0.50 (95% CI −0.89 to −0.11).	Subgroup achieved >6 h/night; +60 min/night. Adherence selection; no general treatment effect.
Hartescu 2022 [36] 18 men; overweight or obesity	Parallel; 10 extension versus 8 controls; 6 weeks	Primary: actigraphic sleep. Secondary: HOMA-IR	HOMA-IR change: −0.51 (−0.98 to −0.03) versus +0.28 (−0.20 to 0.76). Arm-specific CIs.	Sleep change +79 versus +6 min. Very small sample; surrogate sensitivity measure; attrition not verified.
Beals 2026 [37] 31 randomized; 29 completed	Extension versus habitual sleep; about 6 weeks	Clamp and tracer assessment of multiorgan insulin action	No detectable between-group benefit. Adjusted clamp contrast and CI not numerically extracted.	14 extension; 15 control; 1 withdrawal per arm. Sleep +1.1 h (CI 0.8 to 1.4) versus 0.0 h. Limited precision.
Tasali 2022 [44] 80 adults; overweight	Extension versus habitual sleep; 2 weeks; 40 per arm	Primary: objectively estimated energy intake	Between-group difference −270 kcal/day (95% CI −393 to −147).	Sleep +1.2 h/night versus control (CI 1.0 to 1.4). Energy outcome; no direct sensitivity conclusion.
Groeneveld 2024 [39] 57 adults; type 2 diabetes	Online CBT-I (29) versus usual care (28); 3 and 6 months	Primary: HbA1c	No significant ITT glycemic benefit. Numerical ITT contrast and CI not available for verification.	About half completed CBT-I. Uptake and losses constrain inference; PP results do not replace ITT.
Pamidi 2015 [38] 39 adults; prediabetes and OSA	26 CPAP versus 13 placebo; 2 weeks	Primary: OGTT glucose AUC. Secondary: IVGTT sensitivity	AUC −1,276.9 mg/dL·min (CI −2,392.4 to −161.5). Sensitivity +0.77 (CI 0.03 to 1.52).	8 h/night supervised. One placebo withdrawal; 5 CPAP withdrawals or intolerance. Endpoint denominators vary. Secondary multiplicity.
Herth 2023 [40] 11 trials; 964 participants overall	CPAP versus inactive control; varying durations	HbA1c: 9 trials; 807 participants	−0.24 percentage points (CI −0.43 to −0.06); I^2 71.25%. Sensitivity analysis: −0.16 (−0.28 to −0.03).	Use varies; trial-level adherence association. Heterogeneity and small-study effects; glycemia is not insulin sensitivity.

Table 4: Quantitative evidence for selected interventions

This table summarizes quantitative findings from selected clinical intervention studies evaluating the effects of sleep-related interventions on insulin sensitivity, glucose metabolism, and other metabolic outcomes. It presents the reported effect estimates and highlights differences in study populations, intervention characteristics, and outcome measures. These findings should be interpreted in light of methodological limitations and the heterogeneity of the available evidence.

All CIs are 95%. NR or unverified values are not evidence of zero effect. IVGTT sensitivity units for Pamidi are $(mU/L)^{-1}\cdot min^{-1}$.

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Circadian and integrated strategies

In simulated night work, restricting eating to daytime prevented the deterioration in glucose tolerance observed with nighttime eating [41]. This supports meal timing as a modifiable circadian factor, but long-term effectiveness in actual shift workers remains unproven. Regular sleep opportunities and feasible schedule adjustments are reasonable, although trials directly demonstrating improved insulin action through regularization alone remain limited.

Weight-directed therapy is a separate intervention category. Tirzepatide improved apnea severity and weight in adults with obesity and OSA in SURMOUNT-OSA [42]. Direct weight and metabolic effects prevent attribution of benefit specifically to sleep improvement. These findings support integrated care rather than a sleep-specific mechanism.

Implications for clinical practice

Sleep assessment can be incorporated into consultations for obesity, prediabetes, and type 2 diabetes by asking about habitual duration, weekday-weekend differences, night work, insomnia, snoring, witnessed apnea, and daytime impairment. ADA guidance supports screening and appropriate referral [5]. A short diary can clarify patterns; targeted questionnaires assist assessment without replacing diagnostic evaluation.

Management should match the phenotype: create adequate sleep opportunity for behavioral restriction, offer CBT-I for chronic insomnia, and investigate suspected OSA through the appropriate diagnostic pathway [7,34,46]. Pain, mood symptoms, medications, nocturia, and glucose-related sleep disruption also merit consideration. Follow-up should assess symptoms, actual sleep change, adherence, and conventional metabolic outcomes. Routine HOMA-IR testing solely to monitor sleep counseling is not established [29]. Sleep care complements nutrition, physical activity, weight management, and indicated diabetes treatment; its symptomatic benefit remains valuable even when HbA1c is unchanged.

Clinical pathway

Clinical assessment should begin by asking about opportunity, duration, regularity, insomnia, snoring, witnessed apnea, and daytime impairment; a questionnaire is a risk assessment, not a diagnosis [5,34]. The relevant sleep phenotype should then be identified: insufficient opportunity → behavioral counseling; persistent insomnia with daytime consequences → clinical assessment and CBT-I; suspected OSA → appropriate home testing or polysomnography [7,34,46]. Referral is warranted when marked sleepiness, witnessed apnea, complex cardiorespiratory disease, suspected hypoventilation, or persistent symptoms require medical or sleep-specialist evaluation [34]. Follow-up should address outcomes separately: monitor symptoms and adherence, then conventional glycemic and weight outcomes. Maintain indicated diabetes care; do not assume a change in HOMA-IR or HbA1c proves a sleep-specific mechanism [29].

Limitations, controversies, and research priorities

The literature is limited by small experiments, short interventions, heterogeneous sleep definitions, and incompatible metabolic endpoints. Recent female-specific studies improve representation, but age, menopausal status, ancestry, and comorbidity remain incompletely examined. Objective cohorts reduce reporting bias without eliminating confounding or the limitations of a brief recording period. Narrative selection and variable full-text access also constrain this review.

Future trials should enroll adults with objectively confirmed sleep deficits and characterize OSA, medications, adiposity, diet, and activity. Randomized comparisons should document achieved duration and timing, distinguish intention-to-treat from adherence analyses, and incorporate organ-specific physiology when feasible. HbA1c change, insulin sensitivity, and diabetes incidence should be prespecified as separate endpoints. Longer studies are needed to determine whether improvements persist and whether sleep interventions reduce incident diabetes beyond established preventive measures. The 2026 null extension trial makes identification of responsive phenotypes particularly relevant [37].

Five messages for clinical practice

Assess duration, regularity, insomnia, and OSA symptoms when evaluating metabolic risk [5]. Short-term experimental insulin resistance is not equivalent to clinical diabetes or proof of future disease [4,10]. Improving sleep is worthwhile even when insulin sensitivity or HbA1c does not measurably improve [37,39]. Treat insomnia and OSA using established pathways, while maintaining indicated metabolic treatment [34,40,46]. Interpret HOMA-IR cautiously and keep insulin sensitivity, glycemia, and diabetes incidence as separate outcomes [27,28,29,30].

Conclusions

Controlled human experiments support an adverse effect of selected sleep restrictions and circadian disturbances on insulin action. Longer-term clinical associations and treatment responses remain heterogeneous. Assess sleep, diagnose and treat established disorders, and maintain standard metabolic care; reliable reversal of insulin resistance or prevention of diabetes through sleep treatment remains unproven.

Declarations

Ethics approval: Ethics committee approval was not required for this narrative review of published literature; no new human or animal participant research was conducted.

Author contributions: Sanae Chakdoufi, Amal Moumen, and Asmae Chadli contributed to the literature search, critical analysis and interpretation of the scientific evidence, manuscript preparation, and critical revision of the article. All three authors reviewed and approved the final manuscript and agree to be accountable for its content.

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Data availability: No new datasets were generated for this narrative review. The cited publications are listed in the references.

References

1. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA: Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2010, 33:414-420. 10.2337/dc09-1124
2. Shan Z, Ma H, Xie M, et al.: Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care. 2015, 38:529-537. 10.2337/dc14-2073
3. Spiegel K, Leproult R, Van Cauter E: Impact of sleep debt on metabolic and endocrine function. Lancet. 1999, 354:1435-1439. 10.1016/S0140-6736(99)01376-8
4. Sondrup N, Termannsen AD, Eriksen JN, et al.: Effects of sleep manipulation on markers of insulin sensitivity: a systematic review and meta-analysis of randomized controlled trials. Sleep Med Rev. 2022, 62:101594. 10.1016/j.smrv.2022.101594
5. American Diabetes Association Professional Practice Committee for Diabetes. 5: Facilitating positive health behaviors and well-being to improve health outcomes: Standards of Care in Diabetes-2026. Diabetes Care. 2026, 49:89-131. 10.2337/dc26-S005
6. Borbély AA, Daan S, Wirz-Justice A, Deboer T: The two-process model of sleep regulation: a reappraisal. J Sleep Res. 2016, 25:131-143. 10.1111/jsr.12371
7. Watson NF, Badr MS, Belenky G, et al.: Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. Sleep. 2015, 38:843-844. 10.5665/sleep.4716
8. Morris CJ, Yang JN, Garcia JI, et al.: Endogenous circadian system and circadian misalignment impact glucose tolerance via separate mechanisms in humans. Proc Natl Acad Sci U S A. 2015, 112:2225-2234. 10.1073/pnas.1418955112
9. Qian J, Dalla Man C, Morris CJ, Cobelli C, Scheer FAJL: Differential effects of the circadian system and circadian misalignment on insulin sensitivity and insulin secretion in humans. Diabetes Obes Metab. 2018, 20:2481-2485. 10.1111/dom.13391
10. Donga E, van Dijk M, van Dijk JG, et al.: A single night of partial sleep deprivation induces insulin resistance in multiple metabolic pathways in healthy subjects. J Clin Endocrinol Metab. 2010, 95:2963-2968. 10.1210/jc.2009-2430
11. Zuraikat FM, Laferrère B, Cheng B, et al.: Chronic insufficient sleep in women impairs insulin sensitivity independent of adiposity changes: results of a randomized trial. Diabetes Care. 2024, 47:117-125. 10.2337/dc23-1156
12. Singh P, Beyl RA, Stephens JM, et al.: Effect of sleep restriction on insulin sensitivity and energy metabolism in postmenopausal women: a randomized crossover trial. Obesity (Silver Spring). 2023, 31:1204-1215. 10.1002/oby.23739
13. Tasali E, Leproult R, Ehrmann DA, Van Cauter E: Slow-wave sleep and the risk of type 2 diabetes in humans. Proc Natl Acad Sci U S A. 2008, 105:1044-1049. 10.1073/pnas.0706446105
14. Stamatakis KA, Punjabi NM: Effects of sleep fragmentation on glucose metabolism in normal subjects. Chest. 2010, 137:95-101. 10.1378/chest.09-0791
15. Pan A, Schernhammer ES, Sun Q, Hu FB: Rotating night shift work and risk of type 2 diabetes: two prospective cohort studies in women. PLoS Med. 2011, 8:e1001141. 10.1371/journal.pmed.1001141
16. Kianersi S, Liu Y, Guasch-Ferré M, et al.: Chronotype, unhealthy lifestyle, and diabetes risk in middle-aged U.S. women: a prospective cohort study. Ann Intern Med. 2023, 176:1330-1339. 10.7326/M23-0728
17. Kianersi S, Wang H, Sofer T, et al.: Association between accelerometer-measured irregular sleep duration and type 2 diabetes risk: a prospective cohort study in the UK Biobank. Diabetes Care. 2024, 47:1647-1655. 10.2337/dc24-0213
18. Scheer FAJL, Hilton MF, Mantzoros CS, Shea SA: Adverse metabolic and cardiovascular consequences of circadian misalignment. Proc Natl Acad Sci U S A. 2009, 106:4453-4458. 10.1073/pnas.0808180106
19. Leproult R, Holmbäck U, Van Cauter E: Circadian misalignment augments markers of insulin resistance and inflammation, independently of sleep loss. Diabetes. 2014, 63:1860-1869. 10.2337/db13-1546
20. Nagayoshi M, Punjabi NM, Selvin E, et al.: Obstructive sleep apnea and incident type 2 diabetes. Sleep Med. 2016, 25:156-161. 10.1016/j.sleep.2016.05.009
21. Louis M, Punjabi NM: Effects of acute intermittent hypoxia on glucose metabolism in awake healthy volunteers. J Appl Physiol (1985). 2009, 106:1538-1544. 10.1152/japplphysiol.91523.2008
22. Broussard JL, Ehrmann DA, Van Cauter E, Tasali E, Brady MJ: Impaired insulin signaling in human adipocytes after experimental sleep restriction: a randomized, crossover study. Ann Intern Med. 2012, 157:549-557. 10.7326/0003-4819-157-8-201210160-00005
23. Broussard JL, Chapotot F, Abraham V, et al.: Sleep restriction increases free fatty acids in healthy men. Diabetologia. 2015, 58:791-798. 10.1007/s00125-015-3500-4
24. Markwald RR, Melanson EL, Smith MR, et al.: Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. Proc Natl Acad Sci U S A. 2013, 110:5695-5700. 10.1073/pnas.1216951110
25. Irwin MR, Olmstead R, Carroll JE: Sleep disturbance, sleep duration, and inflammation: a systematic review and meta-analysis of cohort studies and experimental sleep deprivation. Biol Psychiatry. 2016, 80:40-52. 10.1016/j.biopsych.2015.05.014
26. Marcheva B, Ramsey KM, Buhr ED, et al.: Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes. Nature. 2010, 466:627-631. 10.1038/nature09253

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27. DeFronzo RA, Tobin JD, Andres R: Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979, 237:E214-E223. 10.1152/ajpendo.1979.237.3.E214

28. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985, 28:412-419. 10.1007/BF00280883

29. Wallace TM, Levy JC, Matthews DR: Use and abuse of HOMA modeling. Diabetes Care. 2004, 27:1487-1495. 10.2337/diacare.27.6.1487

30. Matsuda M, DeFronzo RA: Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care. 1999, 22:1462-1470. 10.2337/diacare.22.9.1462

31. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989, 28:193-213. 10.1016/0165-1781(89)90047-4

32. Bastien CH, Vallières A, Morin CM: Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med. 2001, 2:297-307. 10.1016/S1389-9457(00)00065-4

33. Smith MT, McCrae CS, Cheung J, et al.: Use of actigraphy for the evaluation of sleep disorders and circadian rhythm sleep-wake disorders: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2018, 14:1231-1237. 10.5664/jcsm.7230

34. Kapur VK, Auckley DH, Chowdhuri S, et al.: Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017, 13:479-504. 10.5664/jcsm.6506

35. So-ngern A, Chirakalwasan N, Saetung S, Chanprasertyothin S, Thakkinstian A, Reutrakul S: Effects of two-week sleep extension on glucose metabolism in chronically sleep-deprived individuals. J Clin Sleep Med. 2019, 15:711-718. 10.5664/jcsm.7758

36. Hartescu I, Stensel DJ, Thackray AE, et al.: Sleep extension and metabolic health in male overweight/obese short sleepers: a randomised controlled trial. J Sleep Res. 2022, 31:e13469. 10.1111/jsr.13469

37. Beals JW, Smith GI, Farabi SS, et al.: Sleep extension improves sleep health but not insulin sensitivity in people with overweight or obesity who maintain habitual short sleep schedules. Diabetes Care. 2026, 49:740-745. 10.2337/dc25-2083

38. Pamidi S, Wroblewski K, Stepien M, et al.: Eight hours of nightly continuous positive airway pressure treatment of obstructive sleep apnea improves glucose metabolism in patients with prediabetes. A randomized controlled trial. Am J Respir Crit Care Med. 2015, 192:96-105. 10.1164/rccm.201408-1564OC

39. Groeneveld L, Beulens JWJ, Blom MT, et al.: The effect of cognitive behavioral therapy for insomnia on sleep and glycemic outcomes in people with type 2 diabetes: a randomized controlled trial. Sleep Med. 2024, 120:44-52. 10.1016/j.sleep.2024.05.029

40. Herth J, Sievi NA, Schmidt F, Kohler M: Effects of continuous positive airway pressure therapy on glucose metabolism in patients with obstructive sleep apnoea and type 2 diabetes: a systematic review and meta-analysis. Eur Respir Rev. 2023, 32:230083. 10.1183/16000617.0083-2023

41. Chellappa SL, Qian J, Vujovic N, et al.: Daytime eating prevents internal circadian misalignment and glucose intolerance in night work. Sci Adv. 2021, 7:eabg9910. 10.1126/sciadv.abg9910

42. Malhotra A, Grunstein RR, Fietze I, et al.: Tirzepatide for the treatment of obstructive sleep apnea and obesity. N Engl J Med. 2024, 391:1193-1205. 10.1056/NEJMoa2404881

43. Leproult R, Deliens G, Gilson M, Peigneux P: Beneficial impact of sleep extension on fasting insulin sensitivity in adults with habitual sleep restriction. Sleep. 2015, 38:707-715. 10.5665/sleep.4660

44. Tasali E, Wroblewski K, Kahn E, Kilkus J, Schoeller DA: Effect of sleep extension on objectively assessed energy intake among adults with overweight in real-life settings: a randomized clinical trial. JAMA Intern Med. 2022, 182:365-374. 10.1001/jamainternmed.2021.8098

45. Depner CM, Melanson EL, Eckel RH, et al.: Ad libitum weekend recovery sleep fails to prevent metabolic dysregulation during a repeating pattern of insufficient sleep and weekend recovery sleep. Curr Biol. 2019, 29:957-967. 10.1016/j.cub.2019.01.069

46. Edinger JD, Arnedt JT, Bertisch SM, et al.: Behavioral and psychological treatments for chronic insomnia disorder in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021, 17:255-262. 10.5664/jcsm.8986

47. Shaw JE, Punjabi NM, Naughton MT, et al.: The effect of treatment of obstructive sleep apnea on glycemic control in type 2 diabetes. Am J Respir Crit Care Med. 2016, 194:486-492. 10.1164/rccm.201511-2260OC

48. Martínez-Cerón E, Barquiel B, Bezos AM, et al.: Effect of continuous positive airway pressure on glycemic control in patients with obstructive sleep apnea and type 2 diabetes. A randomized clinical trial. Am J Respir Crit Care Med. 2016, 194:476-485. 10.1164/rccm.201510-1942OC

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