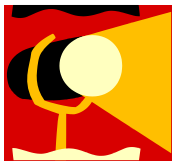
Spotlight on Sleep Medications



The human body has adapted to diurnal variations in sunlight with an innate, physiologic, sleep-wake cycle. Deviations from this circadian rhythm can have functional consequences. Recent survey data from the National Sleep Foundation determined that individuals reporting good health were shown to sleep on average 30 more minutes per night than those with poor health.[1] Individuals who rated their general health as excellent were twice as likely to report very good sleep quality. Those individuals reporting **good mental health** were also **three times more likely to report very good quality of sleep** (Figure 1). Indeed, they went on to identify poor sleep quality as associated with severe stress and increased physical pain.[1]

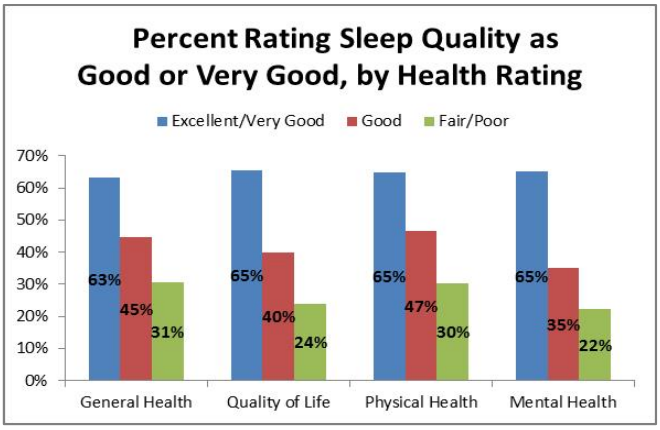


Figure 1. Good health is related to good sleep.

Difficulties in the initiation and/or maintenance of sleep (dyssomnia) and the inability to sleep (insomnia) are common, with one third of adults describing troublesome episodes.[2,3] While behavioral changes via cognitive-behavioral therapy have the best results for frequent insomnia (70-80% efficacy)[4-6], augmentation with a sleep medication may be warranted. The most common sleep medications include zolpidem, zaleplon, eszopiclone, ramelteon, suvorexant and various benzodiazepines[2], with side-effects ranging from dizziness and headaches to prolonged drowsiness and sedation during normal waking hours. These medications are included on the Genecept Assay®. Our companion test, Mindful DNA™, assesses genes related to sleep disturbance and provides key recommendations for non-pharmacologic therapies when appropriate. For example, restless leg syndrome is often an undiagnosed contributor to insomnia (present in 3-4% of adults)[1] and Mindful DNA assesses genetic risk for this condition via a gene called *MEIS1*.

The Genecept Assay assesses genetic polymorphisms that may affect an individual's response to medications used to treat sleep disorders. Most of these medications are metabolized by the CYP450 enzymes. For example, the CYP3A4/5 enzymatic pathway is a common means of metabolizing some of the frequently used benzodiazepines such as alprazolam and clonazepam. If CYP3A4/5 genotype or drug-drug interactions are a concern, another benzodiazepine, temazepam, bypasses this pathway. The Genomind Drug Interaction Guide (G-DIG)® online drug-gene interaction checker can assist in evaluating these medications for optimal drug selection. Among the non-benzodiazepines, zolpidem, eszopiclone and suvorexant are primarily metabolized via CYP3A4/5; therefore caution with CYP3A4/5 inhibitors or inducers should be considered when prescribing.[7, 10, 11] Zaleplon is primarily metabolized via aldehyde oxidase, and CYP3A4/5 to a lesser extent.[8,9] Ramelteon, a melatonin receptor agonist, is metabolized primarily via CYP1A2, and serum levels may increase dramatically in the presence of inhibitors of this enzyme, such as fluvoxamine.[12] Trazodone is the second most prescribed medication for sleep, though it is not FDA approved for this use.[1] While this practice continues, evidence is scarce with primarily insignificant data. Therefore trazodone is not recommended by the American Association of Sleep Medicine.[13, 14]

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