



REVIEW

# Valerian for Sleep: A Systematic Review and Meta-Analysis

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## ABSTRACT

Insomnia affects approximately one-third of the adult population and contributes to increased rates of absenteeism, health care use, and social disability. Extracts of the roots of valerian (*Valeriana officinalis*) are widely used for inducing sleep and improving sleep quality. A systematic review of randomized, placebo-controlled trials of valerian for improving sleep quality is presented. An extensive literature search identified 16 eligible studies examining a total of 1093 patients. Most studies had significant methodologic problems, and the valerian doses, preparations, and length of treatment varied considerably. A dichotomous outcome of sleep quality (improved or not) was reported by 6 studies and showed a statistically significant benefit (relative risk of improved sleep = 1.8, 95% confidence interval, 1.2-2.9), but there was evidence of publication bias in this summary measure. The available evidence suggests that valerian might improve sleep quality without producing side effects. Future studies should assess a range of doses of standardized preparations of valerian and include standard measures of sleep quality and safety. © 2006 Elsevier Inc. All rights reserved.

**KEYWORDS:** Herb; Alternative medicine; Insomnia; Sleep; Meta-analysis; Systematic review

Insomnia is one of the most common complaints among adults. Numerous surveys conducted in countries around the world report that approximately 30% to 40% of adults have problems initiating or maintaining sleep.<sup>1-3</sup> A smaller percentage of adults report severe problems (10%-15%), but the prevalence of severe, chronic sleep problems increases to 25% in the elderly.<sup>2</sup> Insomnia is also more common in patients with chronic medical problems and is found in up to 69% of patients enrolled in primary care clinics.<sup>4</sup>

Approximately 40% of adults with insomnia have used either over-the-counter medication or alcohol to help induce sleep, and approximately one-quarter have used prescription medications at least once.<sup>1</sup> There is only limited evidence to support the efficacy of many of the commonly used medi-

cations for insomnia, including antihistamines, chloral hydrate, barbiturates, tryptophan, and melatonin.<sup>5</sup> Although benzodiazepines are known to be effective for insomnia, the clinical benefit is small (<1 hour of increased sleep) and similar to that found with exercise therapy alone.<sup>6</sup> Moreover, chronic benzodiazepine therapy for sleep is associated with several negative side effects, including cognitive impairment and an increased risk of motor vehicle accidents, falls, and fractures.<sup>5</sup>

The extract of the root of valerian (*Valeriana officinalis*), a flowering plant, has been widely used to treat sleeping disorders in Europe for decades.<sup>7</sup> Valerian is becoming increasingly popular in the United States as a self-prescribed treatment for insomnia. In a national survey conducted in 2002, 1.1% of the adult population in the United States, or approximately 2 million adults, reported using valerian in the past week.<sup>8</sup> If valerian is an effective treatment for insomnia, it may be an important treatment alternative because it is relatively inexpensive and without known side effects. We sought to clarify the efficacy of valerian for improving sleep quality by conducting a sys-

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tematic review and meta-analysis of all prior randomized, controlled trials.

## METHODS

We conducted a search of PUBMED, EMBASE, IBIDS, BIOSIS, and the Cochrane Library (through June 2005) using the keywords “valerian,” “valeriana,” and “baldrian” and retrieved and screened all relevant publications in all languages. Studies were included if they were randomized, placebo-controlled trials of valerian reporting some measure of sleep quality.

Two authors independently abstracted all relevant data including study quality, which was assessed with a commonly used scale (the Jadad scale; range: 0-5, higher scores indicate better quality).<sup>9</sup> No single measure of sleep quality was reported in all studies. The most commonly reported outcome of sleep quality was a simple dichotomous measure (sleep quality improved or not), and studies reporting this outcome were combined using both a fixed-effects (Mantel-Haenszel method) and a random-effects (DerSimonian and Laird method) model. Heterogeneity of pooled studies was assessed with the Q statistic.<sup>10</sup> A funnel plot was used to examine the correlation between study outcome (relative risk) and standard error, and a statistical test of this relationship was performed using Kendall's tau.<sup>11</sup>

## RESULTS

Our search yielded a total of 370 articles. Sixteen randomized, controlled trials, examining a total of 1093 patients, satisfied all inclusion criteria. The characteristics of the individual studies are shown in Table 1. (Studies are arranged in order of decreasing sample size). The sample size for most of the studies was small, with 8 of the studies examining fewer than 25 patients.<sup>12-19</sup> The severity of insomnia in study participants was generally not well defined, although most studies included otherwise healthy patients with some self-reported sleep problems. Two studies were limited to elderly patients,<sup>13,20</sup> and 1 study enrolled only children with intellectual deficits.<sup>16</sup> One study was a combination of multiple n-of-1 studies, rather than a traditional randomized, controlled trial.<sup>17</sup> One study was a randomized, controlled trial that recruited and enrolled all patients entirely over the Internet.<sup>21</sup>

The average study quality was 3.4 (95% confidence interval [CI], 3.0-3.9, 0-5 scale), indicating important methodologic problems in the included studies. There was significant variation in study design, including variations in valerian preparation and dosing, length of treatment, and outcome assessment (Table 1). Valerian doses ranged from

225 to 1215 mg per day, excluding the 1 study involving children whose doses were based on weight.<sup>16</sup> Only 2 of the 16 studies stated that the valerian extract was standardized to a specific percentage of valerianic acids.<sup>17,21</sup>

There was no single sleep quality outcome measure reported by all of the included studies. Seven studies<sup>12-14,16,19,22,23</sup> used a visual analog scale to assess change in sleep quality among participants. Five of these 7 studies<sup>12-14,19,23</sup> reported that there was no statistically significant improvement in the visual analog scales in the valerian group compared with the placebo group. The remaining 2 studies<sup>16,22</sup> noted improvements in the valerian groups but did not present enough information to determine whether the changes were statistically significant compared with the placebo group. The statistical presentation of the data did not allow pooling of this outcome measure.

The most commonly reported outcome measure that could be combined was a dichotomous outcome of sleep quality (sleep improved or not), which was reported in 6 of the 16 studies.<sup>20,21,23-26</sup> With the more conservative random-effects model to pool these data, the use of valerian was found to almost double the chance of sleeping better when compared with placebo (relative risk of improved sleep = 1.8, 95% CI, 1.2-2.9) (Figure 1). The studies were heterogeneous, which is clear from a visual inspection of Figure 1, in which the Jacobs study is the only one showing no effect. Because the Jacobs study used a unique, Internet-based design, we performed a sensitivity analysis and found that there was no significant heterogeneity when this study was excluded from the meta-analysis (relative risk = 1.9, 95% CI, 1.6-2.3, *P* value for heterogeneity = .3).

An examination of the funnel plot (Figure 2) reveals that there is a relationship between study size (as measured by standard error of the mean) and treatment effect (relative risk of a better sleep), which is confirmed by the statistical test Kendall's tau (*P* < .01). This suggests that publication bias may be present, which occurs when negative studies are less likely to be published than positive studies, often resulting in an absence of small negative studies, as shown in Figure 2. The test for publication bias was still positive even when the Jacobs study was excluded (*P* = .03).

Nine of the included studies reported the effect of valerian on “subjective sleep onset latency,” which is defined as the self-reported time it takes to fall asleep (Table 2).<sup>12,14-20,25</sup> The methods used to examine this outcome varied considerably, and only 4 studies reported the actual difference in minutes that it took participants to fall asleep. Of these 4 studies, 2 reported a nonsignificant

## CLINICAL SIGNIFICANCE

- Valerian is commonly used to improve sleep.
- Patients taking valerian had an 80% greater chance of reporting improved sleep compared with patients taking placebo; however, there was evidence of publication bias.

**Table 1** Randomized, Controlled Trials of Valerian for Sleep

First Author, Year	No. of Participants	Participant Population	Mean Age (y)	Dose	Duration	Quality Score*	Subjective Sleep Quality Measure	Sleep Quality Result	Sleep Quality Improvement?†
Jacobs, 2005 <sup>21</sup>	270	Adults with anxiety or insomnia recruited from Internet advertisements	41	600 mg qhs extract	28 d	5	Dichotomous (sleep improved or not)	89% of valerian group improved 86% of placebo group improved	No
Jansen, 1977 <sup>26</sup>	150	Geriatric inpatients with sleep disturbance	79	100 mg tid extract	30 d	3	Dichotomous (very good, good, a little better vs no improvement, worse)	85% of valerian group improved 51% of placebo group improved	Yes
Leathwood, 1982 <sup>25</sup>	128	52% good sleepers, 48% poor sleepers; health status not reported	NR	400 mg qhs dried root	1 day	3	Dichotomous (slept better or not)	43% of valerian group slept better 25% of placebo group slept better	Yes
Vorbach, 1996 <sup>24</sup>	121	Non-organic insomnia requiring medication	47	600 mg qhs dried root	28 d	5	Dichotomous (good sleep or not)	66% of valerian group had a good sleep 26% of placebo group had a good sleep	Yes
Cerny, 1999 <sup>23</sup>	98	Healthy volunteers	34	360 mg qhs + 80 mg lemon balm extract	30 d	3	Visual analog scale	33% of valerian/lemon balm group improved 9.4% of placebo group improved	Yes
Kuhlmann, 1999 <sup>22</sup>	91	Healthy subjects	41	600 mg qhs extract	14 d	3	Visual analog scale	7.4% increase in valerian group 4.5% decrease in placebo group	No
Kamm-Kohl, 1984 <sup>20</sup>	80	Elderly patients with a nervous impairment of behavior	NR	90 mg tid	14 d	3	Dichotomous (sleep improved or not)	74% of valerian group improved 33% of placebo group improved	Yes
Delsignore, 1992 <sup>27</sup>	40	Patients with minor anxiety symptoms and emotional tension disturbances	51	100 mg tid	21 d	2	Dichotomous (insomnia improved or not)	81% of valerian group with insomnia improved 50% of placebo group with insomnia improved Complete data not reported	NR
Farag, 2003 <sup>18</sup>	25	Healthy volunteers with sleep-onset insomnia	37	320 mg + other herbs qhs	4 d	3	St Mary's Hospital Sleep Questionnaire	Data not shown	NR
Coxeter, 2003 <sup>17</sup>	21	Adults with chronic insomnia; combined n-of-1 trials	54	225 mg qhs extract	21 d	4	Proportion of treatment success	0.49 proportion of success with valerian over placebo	No

**Table 1** Randomized, Controlled Trials of Valerian for Sleep (continued)

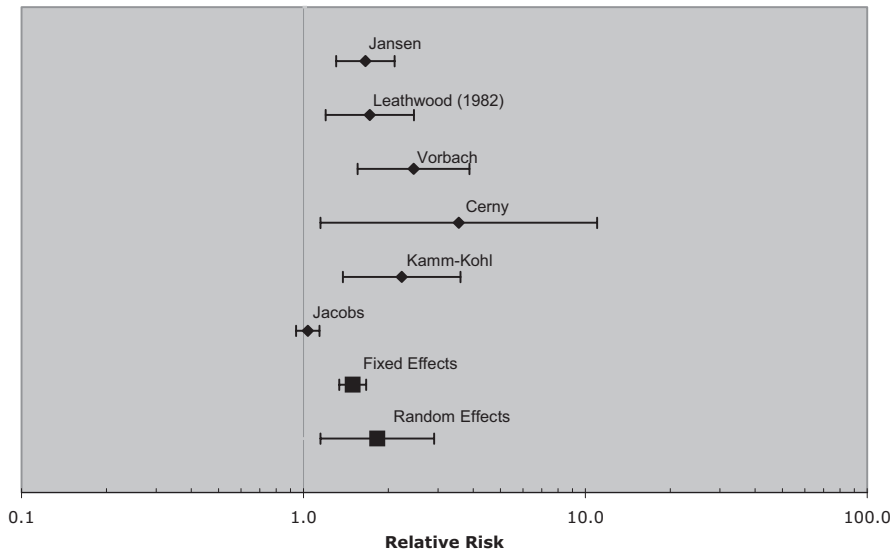
First Author, Year	No. of Participants	Participant Population	Mean Age (y)	Dose	Duration	Quality Score*	Subjective Sleep Quality Measure	Sleep Quality Result	Sleep Quality Improvement?†
Diaper, 2004 <sup>19</sup>	16	Healthy adults with a mild sleep complaint	56	300 or 600 mg qhs extract	1 day	3	Visual analog scale, posttreatment score (0-100)	Valerian 300 mg = 48.1 Valerian 600 mg = 51.5 Placebo = 47.9	No
Donath, 2000 <sup>12</sup>	16	Healthy subjects with insomnia	49	600 mg qhs extract	14 d	3	Visual analog scale	10% increase in valerian group 15% increase in placebo group	No
Schulz, 1994 <sup>13</sup>	14	Healthy elderly women with insomnia	62	405 mg tid extract	8 d	3	Visual analog scale	No difference between groups Data not shown	No
Balderer, 1985 <sup>14</sup>	10	Healthy subjects	33	450 mg or 900 mg qhs dried root	1 day	4	Visual analog scale	No difference between groups Data not shown	No
Leathwood, 1985 <sup>15</sup>	8	Healthy subjects with insomnia	45	450 or 900 mg qhs dried root	1 day	3	9-point scale (9 is best score)	Valerian 450 mg score = 5.8 Valerian 900 mg score = 5.2 Placebo score = 5.0	No
Francis, 2002 <sup>16</sup>	5	Children with intellectual deficits and sleep disturbances	11	20 mg/kg dried root qhs	14 d	5	Visual analog scale (by parents)	Baseline score = 5.3 Valerian score = 7.5 Placebo score = 6.7	No

NR = not reported.

\*Quality was assessed using the Jadad scale (0-5 points).

†Sleep quality improvement indicates a statistically significant benefit in the reported subjective sleep quality measure.

Dichotomous Outcomes for Sleep Quality (sleep improved or not)



**Figure 1** Meta-analysis of 6 studies reporting dichotomous outcomes for sleep quality (sleep improved or not). The dichotomous outcome (improved sleep or not) is presented as the relative risk for reporting improved sleep in the valerian group. Risk ratios greater than one indicate a benefit in the valerian group. Point estimates are represented by diamonds (with first author names) for individual studies and by squares for the summary estimates. Vertical lines represent 95% confidence intervals [CIs].

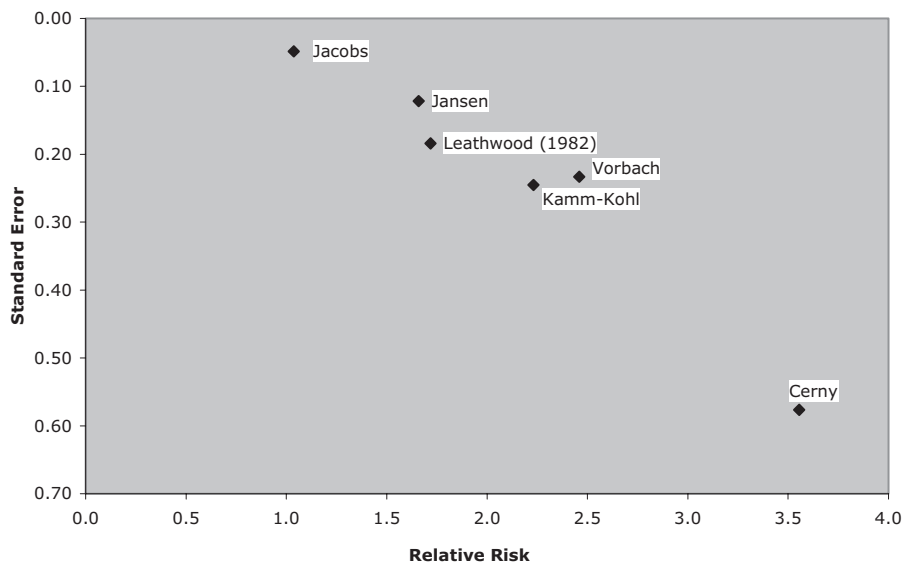
improvement in subjective sleep-onset latency of 17.7 minutes<sup>16</sup> and 15 minutes,<sup>12</sup> and 2 reported significant improvements of 16.7 minutes<sup>18</sup> and 14 minutes.<sup>14</sup> Because of the limited statistical presentation of data in the individual studies, this outcome could not be pooled to create a summary measure.

Eight of the trials included a measurement of hang-over effect the morning after study medication was

given,<sup>12,13,15,17,19,22,24,25</sup> and 6 of those studies reported results.<sup>12,15,17,19,22,25</sup> All showed no difference between the valerian and placebo groups in terms of sleepiness the next morning. The variation in assessment and presentation of this outcome measure also prevented statistical pooling of the results.

Five of the included studies used polysomnographic sleep recordings to evaluate the effects of valerian on

Funnel plot of studies reporting a dichotomous outcome of sleep quality



**Figure 2** Funnel plot of studies reporting a dichotomous outcome of sleep quality. The funnel plot shows the relationship between study size (as measured by standard error, with larger standard errors indicating smaller studies) and study outcome (as measured by relative risk). The visual inspection of the graph suggests an absence of small negative studies (low relative risk, bottom left), which is supported by the statistical test for publication bias, Kendall’s tau ( $P = .03$ ). The points are labeled with the first author name.

**Table 2** Studies Reporting the Effect of Valerian on Sleep-Onset Latency

First Author, Year	No. of Participants	Subjective Sleep Latency Outcome	Sleep Latency Result	Statistical Significance
Leathwood, 1982 <sup>25</sup>	128	No. who went to sleep more rapidly/ total No. of participants	Placebo: 29/128 Valerian: 47/128	Yes $P = .01$
Kamm-Kohl, 1984 <sup>20</sup>	80	No. with improved falling asleep/total No. of participants	Placebo: 10/39 Valerian: 33/39	Yes $P < .001$
Farag, 2003 <sup>18*</sup>	25	Mean No. of minutes to fall asleep (SD)	Placebo: 74.1 min (69) Valerian: 57.4 min (51) Mean decrease: 16.7 min (44.8)	Yes $P = .003$
Coxeter, 2003 <sup>17</sup>	21	Proportion of success (95% CI)	43% (29-57)	No
Diaper, 2004 <sup>19</sup>	16	Visual analog score from 0-100 (100 = best) (SD)	Placebo: 49.7 (11.1) Valerian 300 mg: 47.0 (10.8) Valerian 600 mg: 49.5 (8.3)	No
Donath, 2000 <sup>12*</sup>	16	Median No. of minutes to fall asleep (1st-3rd quartiles)	Baseline: 60.0 min (30.0-90.0) Placebo: 60.0 min (30.0-105.0) Valerian: 45.0 min (17.5-75.0)	No
Balderer, 1985 <sup>14*</sup>	10	Mean No. of minutes to fall asleep (SEM)	Placebo: 23 min (5) Valerian 450 mg: 18.5 min (8) Valerian 900 mg: 9 min (3)	Yes $P < .01$
Leathwood, 1985 <sup>15</sup>	8	9-point scale, 9 is best score (SD)	Placebo: 4.9 points (0.4) Valerian 450 mg: 4.3 points (0.4) Valerian 900 mg: 4.9 points (0.3)	No
Francis, 2002 <sup>16*</sup>	5	Mean No. of minutes to fall asleep, reported by parents (SD)	Baseline: 41.1 min (21.0) Placebo: 39.1 min (34.7) Valerian: 23.4 min (13.4)	No

SD = standard deviation; CI = confidence interval; SEM = standard error of mean.

\*Of four studies reporting subjective sleep-onset latency in minutes, two reported statistically significant benefits.

sleep.<sup>12-15,19</sup> There were no consistent, statistically significant changes in any of these outcome measures, which included sleep efficiency index, sleep period time, time in each of the stages of sleep, measured sleep-onset latency, rapid eye movement sleep-onset latency, and number of arousals.

Adverse events were not consistently assessed or reported. Of the 16 studies, 5 reported that there were no adverse events,<sup>15,16,18,26,27</sup> and 8 reported various side effects in both groups with no statistically significant difference in the frequency of adverse events between the valerian and placebo groups.<sup>12,17,19,20,22-25</sup> Two studies did not report any results on adverse events.<sup>13,14</sup> Only 1 study<sup>21</sup> reported a statistically significant increase in any adverse event (diarrhea), which occurred in 18% of patients in the valerian group compared with 8% of patients in the placebo group ( $P = .02$ ).

## DISCUSSION

Valerian is the most commonly used herbal product to induce sleep in both the United States and Europe.<sup>7,28,29</sup> We identified 16 studies that examined the effect of valerian on sleep quality, but eight of the studies were small (<25 patients)<sup>12-19</sup> and most had significant methodologic problems. In addition to the low average study quality score, which measures problems related to the conduct or description of randomization, blinding, and participant with-

drawal,<sup>9</sup> there were numerous other problems that limit the ability to draw conclusions about the safety and efficacy of valerian. These limitations include the lack of use of standard measures of subjective sleep quality,<sup>30,31</sup> inadequate statistical presentation of data, wide variation in the dose and duration of valerian treatment, and limited assessment of side effects. Because of these numerous problems, the summary estimates of this meta-analysis should be interpreted with caution.

By pooling the most commonly reported sleep quality measure, we found that valerian had a statistically significant effect on the relative risk of improved sleep (1.8, 95% CI, 1.2-2.9). Only 6 of the 16 identified studies reported a dichotomous outcome measure of sleep and could be included in the summary measure. However, these studies were all relatively large, accounting for 72% of all patients studied, and therefore may provide a reasonable summary estimate of the effect of valerian in the identified studies. Because both the funnel plot and the accompanying statistical test (Kendall's tau) were positive, there is evidence for publication bias, which suggests that small negative studies may have been unpublished and not located by our review, potentially leading to an overestimate of the effect of valerian.

Although nine studies reported the effect of valerian on subjective sleep-onset latency, a summary measure could not be created because of the variable presentation of data.



Overall, 4 of these 9 studies reported a statistically significant benefit, and all four studies reporting the outcome in minutes found at least a trend favoring valerian.

There was a large variation in the dose of valerian used in the identified studies. Doses ranged from 225 mg to 1215 mg per day, and only 2 of the studies specifically stated that the herb was standardized to a specific amount of valerianic acid, which is believed to be one of the most biologically active components of the herb.<sup>32</sup> Although there is clearly not enough evidence to define the optimum amount of valerianic acid that should be present in a given dose of the herb, the use of standardized products in clinical trials of valerian might improve the reproducibility and clinical relevance of the results. The variation in the dose of valerian in these studies is also reflected in products sold in the United States. Thirteen valerian products commonly used in this country were evaluated by a reference laboratory, and the recommended doses ranged from 75 to 3000 mg per day; most of the standardized extracts were standardized to 0.8% valerianic acids.<sup>33</sup>

The poor overall methodology observed in these studies is a common problem in clinical trials of herbal products.<sup>34</sup> Methodologic problems are also common in randomized, controlled trials of pharmaceutical drugs used to treat insomnia. Many of these studies incompletely report results<sup>35</sup> and use a variety of different outcome measures, making it difficult to compare the efficacy of different agents.<sup>36</sup> It is possible that the methodologic flaws in the studies included in this systematic review led to invalid results in individual studies, and the only way to address this concern is to conduct new, high-quality clinical trials.

In addition to evidence from clinical trials, there is some intriguing historical and basic science evidence regarding the efficacy of valerian. Several different species of *Valeriana* have been used for sedation and sleep in many different cultures throughout the world, including *V. wallichii* in India and *V. angustifolia* in China and Japan.<sup>7</sup> Also, several studies have shown that components of valerian inhibit the breakdown of gamma-aminobutyric acid in the brain and induce sedation and a decrease in central nervous system activity in mice.<sup>7</sup> The presence of this plausible mechanism of action lends support to the limited clinical trial data.

Valerian may be a more attractive option than other sleeping agents because of the lack of hangover effect. Of the six studies that reported a measure of morning feeling, all reported no difference between valerian and placebo.<sup>12,15,17,19,22,25</sup> Similarly, a previous randomized, controlled trial of valerian, which was excluded from this review because a sleep quality outcome was not reported, found that valerian had a hangover effect equal to placebo and less than the benzodiazepine flunitrazepam.<sup>22</sup>

Although only 1 of the included studies<sup>21</sup> identified a statistically significant increase in an adverse event in the valerian group (diarrhea), it is not possible to reach definitive conclusions regarding the safety of valerian on the basis

of this review. Most studies did not describe the process of identifying, recording, or analyzing adverse events, as recently recommended.<sup>37</sup> Similarly, because the included studies had small sample sizes and lasted 1 month or less, they do not have sufficient power to rule out even relatively common adverse events.

## CONCLUSION

This systematic review suggests that valerian may improve sleep quality, but methodologic problems of the included studies limit the ability to draw firm conclusions. Because of the significant limitations of the identified studies, we believe that larger randomized, controlled trials that adhere to established quality guidelines<sup>38</sup> and have adequate power to assess changes in standard, subjective measures of sleep quality<sup>30,31,39</sup> and overall quality of life are necessary. These studies should evaluate valerian products that are standardized to specific levels of the suspected active ingredients and should focus on detecting possible adverse effects, including the development of tolerance and withdrawal effects. Given the high prevalence of insomnia worldwide and the associated morbidity and economic costs, future studies of valerian should assume a high priority.

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