Quetiapine and CBT-I for Insomnia in Elderly Veterans with Stable Affective Disorders: A Pilot Study

Rayan K. Al Jurdi, MD[1,2] William M. Schmitz, Jr., PsyD;[3] Nancy J. Petersen, PhD[1,2,4]
Ken L. Woods, BS[1,2] and Quang X. Nguyen, PhD[1,2]

Abstract

The aim of this study is to assess the feasibility of conducting a full scale investigation and to obtain preliminary data regarding the efficacy of quetiapine (Seroquel) versus group cognitive behavioral therapy (CBT-I) for the treatment of insomnia secondary to an affective disorder in elderly patients. Sixteen veterans aged 60 and above were randomized to receive six-sessions of CBT-I or quetiapine at progressively increasing dose to maximum of 50 mg daily. Subjects were assessed at study entry, 4 week and 8 week intervals. Results for global sleep quality reveal a significant effect of Time, indicating that the overall sample improved Pre-treatment to Posttreatment, with no significant difference between the two groups. There was no effect of Time, Group, or Group x Time interaction for perceived daytime sleepiness. In conclusion, analysis of recruitment and retention data and robust between- and within- group effect size estimates suggest that a full scale investigation regarding the efficacy of quetiapine versus CBT-I for the treatment of insomnia in elderly veterans with co-morbid affective disorder is both feasible and warranted.

Introduction

A cursory review of the epidemiological data in the general population over the past quarter century reveals remarkably stable prevalence rates for insomnia. Sleep problems such as insomnia are a common occurrence in Western societies, with surveys finding that between 30–50% of individuals report having some sleep problems.[1–5] When applying the more stringent DSM-IV criteria for insomnia, the rates remain high at 9–19% in adulthood[4–6] and up to 21–25% in older populations.[7,8] In their survey of three communities in the United States, Foley and colleagues[2] found that between 23–34% of respondents had symptoms of insomnia, with 7–15% rarely or never feeling rested after waking up in the morning. The rate of insomnia is even more inflated in clinical populations,

reportedly between 21–50%.[5,7,9,10] In older populations, it has been estimated that disturbances of sleep afflict more than half of the people 65 and older who live at home and about two-thirds of those who live in long-term care facilities.[11]

Deleterious sequelae of insomnia include cognitive impairment (sustained attention and alertness),[12] mood disturbance that possibly leads to depression[13] and mania,[14] and sleepiness/fatigue.[12] For older males, insomnia may be a greater predictor of mortality and nursing home placement than age, problems with activities of daily living (ADL), cognitive impairment, depression, income, or living alone.[15]

The majority of research pertaining to the treatment of insomnia has focused on "primary insomnia"; that is, insomnia not associated with or secondary to either a mental or medical illness. Although this has been critical for establishing the efficacy of both pharmacological and nonpharmacological treatments for insomnia, it has left a void for clinicians, since the majority of individuals who complain of sleep problems do so in the context of a co-morbid medical or psychiatric condition.[5,16,17] The National Institutes of Health (NIH)[5] noted that the paucity of research examining secondary insomnia is striking given that most cases of insomnia are co-morbid with other conditions. The majority of individuals diagnosed with insomnia at sleep disorders centers are labeled as having secondary insomnia,[16] with Ohayon[18] estimating that 60% of people with insomnia had secondary insomnia. According to Petit and colleagues,[10] this may be even more typical in older patients. Conditions that are often co-morbid with sleep disturbances such as insomnia include mood and anxiety disorders, substance abuse, attention deficit/hyperactivity in children, dementia, and a variety of physical health problems.[5]

Although the literature addressing secondary insomnia is still in its infancy, an impressive volume of work has been accumulated regarding the efficacy of psychosocial and pharmacological treatments for primary insomnia. With regard to psychosocial treatments, there is a sizeable amount of evidence in the literature that supports the efficacy of cognitive behavioral therapy based interventions (CBT-I). CBT-I combines cognitive-behavioral and behavioral therapy techniques into a structured intervention package, typically including procedures such as sleep restriction, stimulus control, cognitive restructuring of dysfunctional beliefs and attitudes about sleep and sleep loss, and sleep hygiene education. Several meta-analyses have found CBT-I to produce moderate to large effects on subjective sleep outcomes.[19–23] Furthermore, these benefits were found for both younger and older populations.[19,23] Often,

[1] Michael E. DeBakey VA Medical Center, Houston, Texas.
[2] Baylor College of Medicine, Houston, Texas.
[3] Southeast Louisiana Veterans Health Care System, Baton Rouge, Louisiana.
[4] Houston Health Services Research and Development Center of Excellence, Houston, Texas.
Rayan K. Al Jurdi, MD, MHCL-116CMHP, Michael E. DeBakey VAMC, 2002 Holcombe Blvd., Houston, TX 77030, Correspondence to; Rayan.Aljurdi@med.va.gov.

treatment gains were noted to continue from post-treatment to follow-up.[5,20,21]

Although the meta-analyses conducted thus far have been specific to the treatment of primary insomnia, researchers have more recently turned their attention to the treatment of secondary insomnia. For example, Smith and colleagues[17] found CBT-I to be effective in treating insomnia that was determined to be secondary to either medical or psychiatric disorders. Additionally, they determined that by improving sleep, CBT-I might also indirectly improve the principal medical or psychiatric disorder that led to the insomnia initially. Lichstein[16] evaluated the efficacy of four CBT-I sessions in elderly patients with multiple co-morbid psychiatric (mostly depression and anxiety disorders) and medical illnesses (mostly chronic pain), with 57% of subjects reporting clinical improvement compared to 19% in the control group. These findings have led some to claim that the initial treatment of insomnia in older patients, in most cases, should consist of behavior modification,[24] a key component in CBT-I.

Antipsychotics such as quetiapine have been increasingly used "off label" to treat insomnia. Philip et al.[25] reported that only 28.5% of psychiatric inpatients receiving quetiapine had an FDA approved indication. Quetiapine was often used on an as needed basis for agitation or insomnia, with the most common dose being 50 mg.

Quetiapine is an atypical antipsychotic that shows high affinity to the histamine (H1) receptor, α1 adrenergic receptors, and serotonergic 5-HT2a receptors. It has a low affinity for dopamine D2 and D1 receptors and little binding to muscarinic and other serotonergic receptors. The sedating qualities of quetiapine are likely related to its antihistaminic, antiadrenergic, and antidopaminergic effects. Dopamine has been shown to play an important role in the sleep/wake cycle, as studied in patients with Parkinson's disease.[26]

Quetiapine has shown positive effects on sleep in studies of patients with bipolar depression,[27] unipolar depression,[28] and post traumatic stress disorder (PTSD).[29] All three studies used quality of sleep as the outcome measure, assessed by the Pittsburgh Sleep Quality Index. Todder et al.[28] found no statistically significant association between the objective sleep measurements and the clinical status of depression, postulating that the positive effects on sleep were not influenced by improvement of clinical depression symptoms. Cohrs et al.[30] studied the effects of quetiapine on sleep in healthy subjects (i.e. no diagnosis of insomnia, affective, or other psychiatric disorder). They used polysomnography and subjective sleep measures to assess the effect of quetiapine at doses of 25 mg and 100 mg. Both doses significantly increased total sleep time, sleep efficiency, and percentage of sleep in stage 2. Larger improvements in sleep quality were seen in the augmentation of antidepressant treatment with higher doses of quetiapine (mean > 360 mg/day), compared to lower doses (mean < 210 mg /day).[31]

Quetiapine has often been used to treat mania, psychosis, depression, aggression, hostility, delirium, and PTSD in elderly patients, all of which have sleep related disturbances as common symptoms. Although medications can provide symptom relief, they can also expose frail patients, such as the elderly, to increased risk of unwanted and sometimes severe, adverse effects. Quetiapine is generally well tolerated.[32] However, somnolence, hypotension, dizziness, extrapyramidal symptoms, and tardive dyskinesia have been reported.[33,34]

The efficacy of quetiapine for insomnia in the elderly with major affective disorders has not been assessed. Given the increased "off-label" use of atypical antipsychotics, such as quetiapine, to treat insomnia in elderly patients and the paucity of data in this area, systematic investigations are needed to determine the efficacy of these medications. The purpose of this pilot study was two-fold. The primary aim was to explore the feasibility of conducting a full scale study with regard to recruitment and retention of participants. A secondary aim was to obtain preliminary data regarding the efficacy of quetiapine versus group cognitive behavioral therapy (CBT-I) for the treatment of insomnia secondary to an affective disorder in elderly patients.

Methods

Participants

A convenient sample of 16 participants were recruited for this study from psychiatry ambulatory services, primary care, geriatric clinics, and sleep lab referrals at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas.

Inclusionary criteria included 1) age greater than or equal to 60 years; 2) history of major affective disorder (e.g. bipolar disorder type I or type II or major depressive disorder); 3) difficulty starting or initiating sleep four or more times per week for at least three months; and 4) Global Pittsburgh Sleep Quality Index (PSQI)[35] score of greater than five.

Exclusionary criteria included 1) Patients in an acute mood episode (mania, hypomania, mixed, depression) as assessed by the Structured Clinical Interview for DMS-IV Axis I disorders (SCID-I)[36]; 2) Patients with sleep disruptive medical problems, including sleep apnea, restless leg syndrome, periodic limb movement, parasomnia, congestive heart failure, chronic pain and chronic obstructive pulmonary disease, as assessed by medical history and medical record review; 3) Patients with schizophrenia, primary anxiety disorder, and active substance abuse as determined by the SCID-I; 4) Patients on or with history of failure or intolerance to quetiapine; 5) Patients with total score of greater than eight on the Alcohol Use Disorders Identification Test (AUDIT-C)[37]; 6) Patients with dementia, brain degenerative diseases, cognitive disorders, and Mini-Mental Status Examination (MMSE)[38] score of less than or equal to 24; and 7) Patients on concurrent sedating medications that would confound interpretation of the results. Sedating medications must be present and with stable dosage for at least 14 days prior to enrollment in the study. If the medication was not prescribed as a primary sleep aid, it was continued. The rationale was that patients may need these medications, and the initial sedating effect would have reached a plateau by 14 days. However, medications prescribed specifically for insomnia were discontinued, as they were not effective for participants who otherwise met inclusion and exclusion criteria for the study. Medications were tapered as clinically indicated after the participants signed informed consent and prior to baseline assessment.

Procedure

Potential participants were given information regarding the purpose of the study, expectations, activities, and issues of confidentiality. Of the 123 individuals screened, 16 met the study criteria and were randomly assigned to an 8-week

treatment protocol that involved either the quetiapine or the CBT-I arm of the study.

Participants randomized to the quetiapine arm were prescribed 12.5 mg at bedtime daily. The dose could be increased by 12.5 mg on a weekly basis for a maximum of 50 mg a day, depending on tolerance and response. Participants received a weekly phone call from a study physician to assess the need for medication change, evaluate side effects, and provide weekly contact.

Participants randomized to the CBT-I arm participated in one of a series of "CBT for Insomnia" groups that consisted of eight one-hour weekly sessions conducted by a licensed clinical psychologist with training and expertise in CBT. The manualized protocol was adapted from the work of Morin and Espie[12] and Morin[39] and included an introductory session (i.e. program overview; definition of insomnia; basic facts about sleep; CBT conceptualization of insomnia; introduction to sleep diary), two sessions on behavioral strategies (e.g. stimulus control; sleep restriction; emphasis on concepts of consistency and association), two sessions on cognitive strategies (e.g. discussion of relation between thoughts, feelings and behavior; goals/targets of cognitive therapy; keeping realistic beliefs about sleep and sleep loss), one session on sleep hygiene (e.g. lifestyle and bedroom factors), one session on relaxation and pre-sleep routine, and one final session for course review, questions, and feedback. Participants were asked to complete a daily sleep diary for review at each session.

This pilot study utilized various instruments to assess participants' sleep characteristics, psychiatric symptoms, and general health at three evaluation periods: Pre-treatment (Baseline), Mid-treatment (four weeks), and Post-treatment (eight weeks). The PSQI is a commonly used, 9-item self-report questionnaire that assesses sleep quality and disturbances over a one month period. The nine individual items generate seven "component" scores (Sleep Quality, Sleep Latency, Sleep Duration, Sleep Efficiency, Sleep Disturbances, Sleep Medication, and Daytime Dysfunction), with the Global PSQI score representing the sum of the seven component scores. Higher scores denote poorer sleep quality. The Epworth Sleepiness Scale (ESS)[40] is an 8-item survey that measures participants' perception of daytime sleepiness. A total score is achieved by summing the eight items, with higher scores indicating greater daytime sleepiness.

A trained rater blind to participants' group assignment administered these instruments at the three evaluation points. Participants received $15 at each assessment period, totaling $45 if they completed all three assessments.

Results

Participant Recruitment and Retention

As the primary aim of this pilot study was to assess feasibility in order to design an adequately powered, full scale study to compare the efficacy between quetiapine and CBT-I for the treatment of insomnia in elderly patients, recruitment and retention data will be described first. A total of 107 patients were excluded from this study at the time of screening. The most common reasons for exclusion included active mood disorder episode (21.5%), presence of COPD or asthma (15.9%), presence of sleep apnea (10.3%), and participants' already taking quetiapine (9.4%). Two participants underwent initial

assessment and fulfilled criteria, but refused the assigned randomization to the CBT-I arm.

With regard to retention, only three of the eight participants in the quetiapine group completed all eight weeks of the study. Three participants were dropped from the study, as one reported severe sedation at the lowest recommended dose of 12.5 mg, a second observed no benefit with progressive increase to the maximum dose of 50 mg (and wished to discontinue), and a third developed an acute manic episode while in the study and stopped all medications. Two participants were essentially "lost to follow-up," as they did not present for their assessment at eight weeks, despite repeated phone contact and reminders from study personnel. However, records indicate that they did continue to take the medication, despite not coming for their final assessment. Of note, the mean doses of quetiapine at weeks four and eight were 26.9 mg (N = 7) and 45.8 mg (N = 3), respectively. With regard to the CBT-I group, only one participant withdrew from the study, reportedly due to unexpected change in work schedule.

Multivariate analyses of variance (MANOVA) revealed no significant Pre-treatment differences between the three participants in the quetiapine group who completed the study, the two participants who were "lost to follow-up," and the three participants who were dropped from the study, with regard to age, the Global PSQI, the seven PSQI components, and the ESS, F (10,2) = 380, p = .879. Additionally, a MANOVA revealed no significant Pre-treatment differences between the 10 participants who completed the study versus the six who did not, with regard to the same variables, F(9,6) = 1.47, p = .330.

Descriptives and Pre-Treatment Comparisons

Descriptive statistics were computed for the demographic and primary variables, including the Global PSQI, the seven PSQI components, and the ESS, at Pre-treatment for the entire sample (N = 16), as well as each group (see Table 1). The sample was 100% male.

Analyses were conducted to examine whether the quetiapine and CBT-I groups significantly differed at Pre-treatment on the demographic and dependent measures. To account for multiple comparisons, threshold for statistical significance was set to a more stringent criterium of p < .01. As the P-values indicate in Table 1, independent samples t-test revealed no significant difference between the two groups with regard to age, t(14) = .20, and Chi-square analyses using Fisher's Exact Test (test for homogeneity of proportions) revealed no significant differences between the two groups with regard to race, x^2 (1, N = 16) = .29 or diagnosis, x^2 (1, N = 16) = .29. T-tests indicated that the two groups did not significantly differ on the Global PSQI, t(14) = .91, PSQI Sleep Quality, t(14) = .48, PSQI Sleep Latency, t(14) = 1.07, PSQI Sleep Duration, t(14) = .61, PSQI Sleep Efficiency, t(14) = −.67, PSQI Sleep Disturbance, t(14) = .51, PSQI Sleep Medications, t(14) = −.57, PSQI Daytime Dysfunction, t(14) = 2.26, and the ESS, t(14) = −.14.

Repeated Measures Analyses

Mixed model repeated measures analyses of variance were conducted to assess the effect of the treatment manipulation (quetiapine versus CBT-I; between-subjects effects) over time (within-subjects effects). Due to the small sample size of this

Table 1. Pre-Treatment Sample Characteristics and Comparisons between the Quetiapine and CBT-I Groups

Variable	(CBT-I; N = 8)			(Quetiapine; N = 8)			(Total; N = 16)				
Race	n(%)			n(%)			n(%)			P	
White	6 (75.0%)			5 (62.5%)			11 (68.7%)			1.000	
Black/Hispanic	2 (25.0%)			3 (37.5%)			5 (31.3%)				
Diagnosis											
Depression	5 (62.5%)			6 (75.0%)			11 (68.7%)			1.000	
Bipolar	3 (37.5%)			2 (25.0%)			5 (31.3%)				
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	P	d
Age	68.0	8.0	61.0–86.0	67.3	7.4	60.0–81.0	67.6	7.4	60.0–86.0	.8481	.10
Global PSQI	16.6	2.3	13.0–19.0	15.6	2.1	13.0–18.0	16.1	2.2	13.0–19.0	.3787	.46
PSQI Sleep Quality	2.6	0.5	2.0–3.0	2.5	0.5	2.0–3.0	2.6	0.5	2.0–3.0	.6420	.24
PSQI Sleep Latency	2.9	0.4	2.0–3.0	2.5	0.9	1.0–3.0	2.7	0.7	1.0–3.0	.3026	.54
PSQI Sleep Duration	2.9	0.4	2.0–3.0	2.8	0.5	2.0–3.0	2.8	0.4	2.0–3.0	.5536	.30
PSQI Sleep Efficiency	2.4	0.7	1.0–3.0	2.6	0.7	1.0–3.0	2.5	0.7	1.0–3.0	.5125	−.34
PSQI Sleep Disturbance	1.8	0.5	1.0–2.0	1.6	0.5	1.0–2.0	1.7	0.5	1.0–2.0	.6186	.26
PSQI Sleep Medications	2.0	1.4	0.0–3.0	2.4	1.2	0.0–3.0	2.2	1.3	0.0–3.0	.5749	−.29
PSQI Daytime Dysfunction	2.1	0.6	1.0–3.0	1.3	0.9	0.0–2.0	1.7	0.9	0.0–3.0	.0401	1.13
ESS	5.6	3.3	2.0–11.0	6.0	6.7	0.0–21.0	5.8	5.1	0.0–21.0	.8884	−.07

pilot study, analyses were conducted only on the mean scores of the Global PSQI and the ESS. Regarding the Global PSQI, results reveal a significant effect of Time, $F_{(2,20)} = 16.47$, $p < .0001$, with no significant effect of Group or Group x Time interaction, indicating that the overall sample improved from Pre-treatment to Post-treatment, with no significant difference between the two groups. Results for the ESS reveal no significant effect of Time, Group, or Group x Time interaction. Figure 1 and Figure 2 show changes in the two measures over time. As can be seen in Figure 2, the difference in ESS between the CBT-I group and the quetiapine group was fairly large at eight weeks, but this finding was likely not detected as statistically significant because the quetiapine group had only three participants at that time point.

Effect Size Estimates

Both between and within group effect size estimates (Cohen's *d*) were calculated for the Global PSQI, the seven PSQI components, and the ESS, at all three assessment periods (Pre-treatment, Mid-treatment, and Post-treatment). These estimates provide useful information regarding the magnitude of the difference between group mean scores that can assist in designing a sufficiently powered, full scale study. In general, effect sizes of .2, .5, and .8 are considered small, medium, and large, respectively.[41] As can be seen in Table 2, medium to large effect sizes were found for both groups for several of the outcome variables from Pre-treatment to Mid-treatment, and from Mid-treatment to Post-treatment.

The CBT-I group had large effect sizes for the Global PSQI and all seven PSQI components in the expected direction from Pre-treatment to Post-treatment (i.e. mean scores were lower at Post-treatment than at Pre-treatment). For the quetiapine group, medium to large effect sizes were found for the Global PSQI and five PSQI components (Sleep Quality, Sleep Latency,
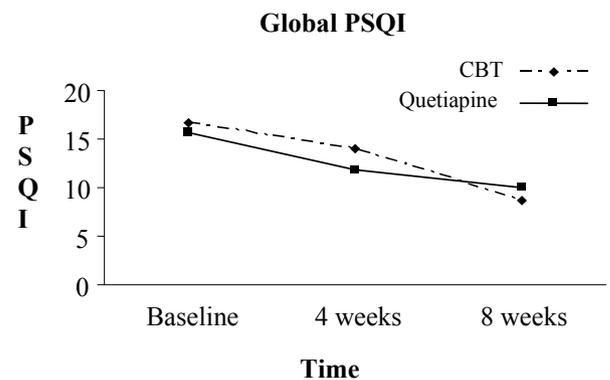

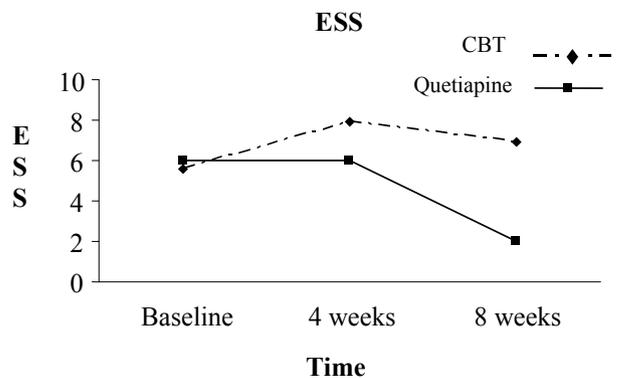**Fig. 1.** Mean PSQI scores for over time.

Fig. 2. Mean ESS scores for over time.

Table 2. Within-Group Effect Size Estimates for PSQI and ESS (Cohen's *d*)

Variable	Pre- to Mid- Treatment (Baseline to 4 Weeks)		Mid- to Post- Treatment (4 Weeks to 8 Weeks)		Pre- to Post- Treatment (Baseline to 8 Weeks)	
	CBT-I	Quetiapine	CBT-I	Quetiapine	CBT-I	Quetiapine
Global PSQI	.78	1.12	1.30	.51	2.46	2.93
Sleep Quality	.56	1.08	.78	.90	1.98	3.44
Sleep Latency	1.26	.59	.86	−1.17	2.31	−.54
Sleep Duration	.70	1.68	.67	.37	1.54	2.79
Sleep Efficiency	.54	.77	1.08	.84	1.56	2.06
Sleep Disturbance	.20	.60	.60	.00	.80	.57
Sleep Medications	.07	.22	1.02	.06	1.14	.30
Daytime Dysfunction	.31	−.35	.49	.70	.90	.33
ESS	−.56	.00	.19	.64	−.29	.66

Note: Positive numbers indicate change in expected direction.

Sleep Duration, Sleep Efficiency, and Sleep Disturbance), all in the expected direction, with the exception of Sleep Latency. The ESS had a medium effect size in the expected direction.

Table 3 displays the between group effect size estimates. At Mid-treatment (Week 4), medium to large effect sizes were found for the Global PSQI and four PSQI components, all in the direction favoring the quetiapine group. At Post-treatment (Week 8), medium to large effect sizes were found for the Global PSQI, five PSQI components, and the ESS, with three of the estimates in the direction favoring the CBT group. It should be noted that, due to the small number of participants who completed the study in the quetiapine group, effect size estimates at Post-treatment should be interpreted with some caution, as they may be unstable.

Discussion

The primary goal of this pilot study was to assess the feasibility of conducting a full scale investigation comparing the efficacy of quetiapine versus CBT-I for the treatment of secondary insomnia in elderly individuals. With regard to recruitment, this study successfully enrolled the target number of participants within the specified timeframe of four months, despite the fairly stringent inclusionary/exclusionary criteria. An examination of the ratio of patients enrolled in the study to patients referred indicates a proportion of 13%. A perusal of the primary reasons for exclusion from the study indicates that about 25% of patients were excluded due to medical conditions (COPD, asthma, sleep apnea). In a full scale study, it may be fruitful to reconsider this criterium. Although problems such as COPD, asthma, and sleep apnea (and others) may be disruptive to sleep, this does not preclude the possibility of an insomnia treatment, such as quetiapine or CBT-I, having a positive impact, even with the presence of these problems. These medical conditions could serve as covariates in the larger study.

With regard to retention, five of the eight participants in the quetiapine group did not complete all eight weeks of the study (versus only one participant in the CBT-I group). However, two of those participants were dropped from the study due to intolerance or no response to the medication, essentially

Table 3. Between-Group Effect Size Estimates for PSQI and ESS (Cohen's *d*)

Variable	Mid-Treatment (4 Weeks)	Post-Treatment (8 Weeks)
Global PSQI	**.49**	<u>.39</u>
Sleep Quality	**.43**	**.80**
Sleep Latency	.00	<u>1.77</u>
Sleep Duration	**.95**	**.65**
Sleep Efficiency	.10	.09
Sleep Disturbance	**.80**	.19
Sleep Medications	.13	<u>1.15</u>
Daytime Dysfunction	**.40**	**.91**
ESS	.31	**.98**

Note: Bolded numbers indicate difference favoring quetiapine. Underlined numbers indicate difference favoring CBT-I.

representing a failure of the treatment (25%). Two participants did not present for their final assessment, although they did continue taking the medication, representing "lost to follow-up" attrition (25%). In a larger scale investigation, recruitment efforts may benefit from taking into account the treatment failure/attrition rates found in this pilot study and (over) sample accordingly. Additionally, a full scale study may benefit from including a procedure to conduct follow-up assessments via phone, as a back-up to in-person assessments. The appropriateness of such a procedure depends on several factors, including the types of instruments used. Due to the structure of the PSQI and the ESS, it is conceivable that both can be administered over the phone, if needed.

A secondary goal of this pilot study was to obtain preliminary data regarding the relative efficacy of quetiapine versus CBT-I for the treatment of insomnia in elderly veterans with co-morbid affective disorder. The results indicate that both groups demonstrated improvement in overall sleep quality from Pre-treatment to Post-treatment as measured by the Global

PSQI, with no significant differences between the two groups. Daytime sleepiness as measured by the ESS did not change significantly over time and did not differ between the groups. This finding and others that are non-significant may be due to the small sample size of this pilot study.

Effect size estimates were calculated to assist in designing a larger scale study with sufficient power to detect group differences. Medium to quite large within and between group estimates for the Global PSQI, the various PSQI components, and the ESS suggest that a full scale study with a larger sample size would increase the likelihood of detecting differences at a statistically significant level. A review of the within group effect sizes from Pre-treatment to Mid-treatment, and from Mid-treatment to Post-treatment, reveals a notable trend (Table 2). From Pre-treatment to Mid-treatment, the effect sizes for the quetiapine group tend to be consistently larger than those of the CBT-I group. However, from Mid-treatment to Post-treatment, the estimates for the CBT-I group were larger on several of the outcome measures. This finding, along with the pattern of the between group effect size estimates, is not surprising. Given that CBT-I is a self-management approach that involves learning and practicing sleep promoting behaviors and changing ineffective routines, it is reasonable that participants in this group would, on average, take longer to experience significant changes. Thus, it would be important for a larger scale study to include a follow-up assessment period to evaluate the longer term impact of both interventions.

The search for effective treatments for insomnia continues to be an important endeavor, as the negative consequences experienced at the individual level are also felt at the societal level. It has been estimated that the direct and indirect costs associated with insomnia figure in the billions of dollars per year,[5,42] part of which is related to the fact that those with insomnia have been found to have higher health care utilization.[5] In fact, the direct costs of assessing and treating insomnia in the United States were estimated to be about 14 billion dollars in 1995.[43] Moreover, despite research documenting the efficacy of nonpharmacological treatments, as well as reports indicating patients' preference for behavioral over pharmacological interventions,[44–46] medications continue to be a popular choice in the treatment of insomnia. Although pharmacotherapy has been found to be effective in the treatment of insomnia, there is also concern about side effects and long-term use. It is particularly important to investigate the efficacy of medications that are prescribed "off label" to treat insomnia, such as atypical antipsychotics like quetiapine.

The findings of this pilot study suggest that conducting a full scale investigation regarding the efficacy of quetiapine versus CBT-I for the treatment of insomnia in elderly veterans with co-morbid affective disorder is both feasible and warranted. A full scale study would benefit from increased sample size, possible modification of exclusionary criteria, and a follow-up assessment period.

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Disclosure

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