REVIEW

OPEN

The management of sleep disorders in dementia: an update

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Purpose of review
Sleep disorders in dementia cause distress and may lead to families being unable to care for someone with dementia at home. Recent Cochrane reviews found no interventions of proven effectiveness. There was no effect of light therapy and moderate evidence that melatonin was ineffective both given without knowledge of the patient's circadian rhythm. The current article updates this review by considering newer publications on interventions for sleep disorders or abnormalities of the sleep–wake cycle in people with dementia living in the community.

Recent findings
We searched electronically for new primary research, reviews and meta-analyses and identified 258 articles published between 15/12/2015 and 14/06/2017 on sleep and dementia; 43 of them on nonpharmacological or pharmacological treatments. Fifteen articles reported on the management of sleep disturbances in people with dementia, living at home. Those using pharmacological treatments (melatonin, psychotropic medications, donepezil, memantine) encompassed a meta-analysis, two double-blind RCTs, two uncontrolled trials, two population-based studies, and one case report. The studies of behavioural interventions comprised five uncontrolled trials, one case series, and one qualitative study. We also included three recent reviews on the management of sleep disturbances in Alzheimer's disease; pharmacotherapies for sleep disturbances in dementia, and dementia prevention, intervention and care. None of these found a treatment that showed definitive effectiveness, although there is preliminary work about nonpharmacological interventions, which can be built on.

Summary
Clinically effective, safe treatment of sleep disturbances in dementia remains an unresolved challenge. Given the importance of sleep and the many consequences of its disruption, well designed controlled trials are needed to determine acceptable and cost-effective treatment strategies that work for sleep disturbances.

Keywords
dementia, intervention, sleep, sleep disorders, treatment

INTRODUCTION

Sleep disorders are common in dementia [1,2], with problems including difficulty falling asleep or staying asleep, sleep fragmentation, wandering and excessive daytime sleepiness. Sleep is one of the cornerstones of human wellbeing, and reduced or poor-quality night-time sleep can significantly impact daytime functioning and quality of life [3]. Over the coming years, the aging population will lead to a dramatic rise globally in the number of individuals living with dementia [4]; approximately two-thirds of them in the community. Carers find disturbed sleep particularly difficult as their own sleep is often affected and this impacts their quality of life [5,6]. For those who wish to continue caring at home, paid night-time care can be unaffordable. If the primary carer reduces hours at work or stops working altogether, this has consequences for societal economics as well as personal finances. Clinical and cost-effective ways to improve disrupted sleep in people with dementia are needed for the benefit of those affected, their families, communities,

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KEY POINTS

- The causes of sleep disorders in dementia are complex and multiple strategies may be needed for their successful treatment.
- Research into potential management strategies – both nonpharmacological and pharmacological – has not produced convincing proof of efficiency.
- Emerging evidence suggests multicomponent interventions might work, but controlled trials are needed to determine their acceptability and cost effectiveness and clinical effectiveness.

societies, health and social care systems and global economics. Treating sleep disorders may not only improve wellbeing, daytime functioning and quality of life of those living with dementia, but as they are thought to increase amyloid deposition it is possible that treatment might slow the progression [7▪▪]. Recent Cochrane reviews found no effective treatments for sleep disorders, and in particular found that light therapy [8] and melatonin [9▪▪] did not show efficacy in trials. However, other options include psychological and behavioural interventions and pharmacological treatments. The need for treatments that work and can be used over the long-term, therefore seems pressing.

TYPES OF SLEEP DISORDERS AND THEIR CAUSES

Insomnia, difficulty falling asleep or staying asleep, or sleeping at irregular times can have many causes. Most are secondary, but there are primary sleep disorders such as sleep apnoea, but these are outside the remit of our review. Within dementia, the causes of sleep disorders can be – as in people without dementia – physical health conditions, pain or discomfort, medications or anxiety or depression. In addition, there are often disturbances of the circadian rhythm. The endogenous circadian rhythms play a critical role in controlling sleep. External 'zeitgebers' including light, daytime activity and physical exercise and meal times help to entrain the circadian sleep–wake rhythm to the 24-h day. Circadian rhythm disorders include advanced (early sleep onset and offset) and delayed (late sleep initiation and rise time) phase disorders and irregular sleep–wake rhythm, which includes brief bouts of sleep and wakefulness throughout the day [10,11].

The neurodegenerative changes in dementia and the deposition of amyloid and tau may affect the structure and functioning of relevant brain networks [12,7▪▪]. In addition, alterations to the suprachiasmatic nucleus (SCN) and pineal gland and SCN–pineal gland functional disconnection can impair melatonin production and release [11,12]. As melatonin secretion is regulated by a 24-h circadian rhythm, it is also susceptible to disruption by inadequate zeitgebers (particularly light) and diminished rest–activity amplitude [12]. Sleep and circadian rhythm disorders may also contribute to the reduction of Aβ42 in cerebrospinal fluid observed in the preclinical stages of Alzheimer's disease, and increase cerebral amyloid burden [12,13]. It is suggested that sleep disturbances promote the neurodegenerative cascade because of malfunction of the glymphatic system, which clears the brain of neurotoxic products such as Aβ42 during nocturnal sleep [14]. The multifactorial aetiology of sleep disturbance in an individual with dementia may mean that complex strategies to treat it may be necessary.

LITERATURE SEARCH STRATEGY

We searched PubMed on 14/06/2017 for evidence regarding the management of sleep disorders in people with dementia living at home, from articles published in English between 15/12/2015 and the search date. Search terms were: sleep, sleep–wake, circadian, dementia and Alzheimer*. We filtered the initial results using terms management, therapy, intervention, treatment, efficacy, effects and medic*. We found 238 papers, from which we excluded irrelevant studies based on the abstract. Of the 43 papers that were about behavioural or pharmacological treatments for sleep disorders in dementia, 15 fulfilled the inclusion criteria.

RECENT REVIEWS

A recent report by the Lancet Commission on dementia found no definitive evidence to recommend a particular therapy to treat sleep disorders but noted that preliminary data suggested a nonpharmacological approach combining tailored light therapy with sleep hygiene measures might help [15]. A Cochrane review on pharmacotherapies [9▪▪] also found no definitive randomised controlled trial (RCT) evidence of improvements in actigraphy measures for melatonin, trazodone or ramelteon. Trazodone 50 mg at night showed some potential for increased nocturnal sleep time and sleep efficiency in Alzheimer's disease, but confirmation awaits a larger trial. Notably, no RCTs were found of medications such as hypnotics that are widely prescribed for sleep problems in dementia. Another recent review concluded that evidence of efficacy

overall remained scarce and new drugs that work on mediating or modulating the circadian clock may need to be developed [16▪]. In the following section, we have reviewed more recent developments in this field.

ADVANCES IN NONPHARMACOLOGICAL MANAGEMENT OF SLEEP DISORDERS IN DEMENTIA

The potential of a variety of psychological and behavioural therapies has been investigated: mixed methods, bright light therapy and music therapy with movement. Table 1 lists all studies reviewed here.

Mixed methods

A 5-week uncontrolled trial investigated feasibility of a new sleep intervention in 15 community-dwelling pairs of patients (aged ≥ 65) and carers living together [17]. This involved timed light therapy, physical exercise (walking, yoga-style stretches and movement, a senior's exercise DVD) and a 'sleep support handbook' for sleep education. Objective (7-day actigraphy) and subjective (Pittsburgh Sleep Quality Index, PSQI [24]; Sleep Disorders Inventory, SDI [25]) sleep measures, symptoms of dementia and impact of caregiving were compared between baseline and follow-up. Structured participant feedback was additionally sought. Nine (60%) dyads completed the trial. Of these, six people with dementia showed some improvement in night-time sleep efficiency and five some improvement in PSQI scores over time. The article additionally presents case studies and suggests feasibility of the approach. However, the sample size was small, 40% did not complete the trial and there was no control group. This intervention may need more work on acceptability before a larger effectiveness trial.

Another study examined the feasibility of a group version of the home-based caregiver sleep education programme NITE-AD [26], which focuses on the impact of aging and dementia on sleep, using strategies including light, exercise, sleep hygiene, problem solving and goal setting. It was delivered by a trained sleep educator over 6 weeks and consisted of four group workshops and two reinforcement phone calls [18]. Half (7/14) of the patient–carer dyads completed the 6-week programme. Four carers withdrew before and three carers during the intervention. The results, using SDI to measure outcome, found some improvement on all items for the people with dementia, particularly in getting up during the night and awakening the carer. Three of six carers with possible major depression showed a reduction in depression severity. The carers felt supported by the intervention and intended to continue applying the strategies. However, this was not an RCT, and the small sample size and dropout mean more work is needed.

Table 1. Results of trials testing nonpharmacological treatments

Study	Strategy	Control group	Participants	Outcomes
Gibson *et al.* [17]	Mixed (light therapy, exercise, sleep education)	None	Fifteen community-dwelling dyads of carers and people with dementia	40% Dropout Six participants improved
Tewary *et al.* [18]	Sleep education program for caregivers	None	Fourteen people with dementia (and carers)	50% Dropout Improved sleep problems
Sekiguchi *et al.* [19]	Bright light therapy 1 h daily for 2 weeks	None	Seventeen people with dementia (people with Alzheimer's disease, 8; people with vascular dementia, 4; DLB, 5)	Improved sleep disturbance in 4/17 mild-to-moderate patients with Alzheimer's disease
Lai *et al.* [20]	Music with movement	Not applicable	Results not available	Not known
Krolak-Salmon *et al.* [21]	Multidisciplinary team intervention	None	424 people with dementia	Overall neuropsychiatric symptoms reduced in 329 people with data
Lazarou *et al.* [22]	Smart home/assistive technology	None	Four people with dementia	Improved sleep
Kodama *et al.* [23]	Physical activity reference values for a good sleep–wake pattern	None	117 older community-dwelling participants; 52 with dementia	51–55 min activity per day needed

DLB, people with dementia with Lewy bodies.

Bright light therapy

One study recruited 17 participants (eight with Alzheimer's disease, four with vascular dementia, five with dementia with Lewy bodies, DLB) to explore light therapy's potential for sleep management at different dementia stages [19]. Participants were asked to sit in front of the light box every day for 2 weeks from 9.00 to 10.00 a.m. Reduction in sleep disturbances was observed in four participants, all with mild-to-moderate Alzheimer's disease and a relatively short duration of illness. The authors concluded that whether light therapy is an effective strategy could depend on the type and severity of dementia, but that a larger study is needed to confirm this.

Activity and music intervention

One article reported on the development of a music-with-movement intervention to reduce anxiety and promote sleep in older people with early-stage dementia (Clinical Dementia Rating 0.5–1) [20]. This manual-based intervention combines motor imitation activities (e.g. making swimming movements with arms) or Tai Chi exercises with listening to familiar music while also playing an instrument. Singing along to songs is also encouraged. It is intended to be delivered by a family caregiver at least three times per week for 12 weeks, with each session lasting 30 min. No results are available at this stage.

Mobile care team intervention

Although not primarily developed to improve sleep in dementia, The Alzheimer Cooperative Valuation in Europe study [21] investigated the potential effectiveness of a multidisciplinary mobile care team for behavioural disorders using nonpharmacological, pharmacological and medico-social interventions to reduce hospitalisation and neuropsychiatric symptoms. This study included 424 consecutive patients (Clinical and Research Memory Centre, Lyon, France) aged 84 ± 7 years living at home or in a nursing home. They used the difference between planned hospitalisations (in the absence of the mobile team) and actual hospitalisations over 30 days to calculate 'hospitalisation sparing'. The Neuropsychiatric Inventory (NPI) [27] total from both time points, including the sleep subscale, was available for 329 patients. The mean score decreased from 45.8 to 29.9 ($P < 0.001$), but the change in sleep scores is not given.

Intervention using technology

One study [22] used assistive technology to support four people with dementia, within a smart home environment system enabling continuous remote monitoring. Wearable, sleep, object motion, presence and utility usage sensors were installed to detect sleep patterns, physical activity and activities of daily living. Targeted psychosocial interventions were designed to improve cognitive function and quality of life, based on feedback from the system and clinical observations. Improvements in sleep were detected, but the study was small and uncontrolled so gave little indication of potential generalisability.

Other

Another study aimed to determine how much daily moderate-to-vigorous physical activity (MVPA) is needed for normal circadian rest–activity rhythm [23]. They used 7-day actigraphy (Actiwatch2, Philips Respironics Inc., Andover, Massachusets, USA) in 117 older community-dwelling people with ($N = 52$) and without ($N = 66$) dementia. Daily MVPA conducive to a good sleep–wake pattern was 51 min for inter-daily variability and 55 min for relative amplitude. These values may be useful in developing interventions incorporating physical activity.

ADVANCES IN PHARMACOLOGICAL MANAGEMENT OF SLEEP DISORDERS

We reviewed the latest studies on pharmacological treatments for sleep in people with dementia. Table 2 lists relevant publications since December 2015. We have commented on effectiveness, but psychotropic drugs also have side effects including hypotension, dizziness and falls [36], which can preclude their use in many people.

Melatonin

A meta-analysis of double-blind, placebo-controlled RCTs of melatonin in Alzheimer's disease (until 01/03/2016) included seven trials, with study periods of 10 days to 24 weeks [28]. Sleep was assessed by actigraphy in all. Melatonin for patients with Alzheimer's disease was not superior to placebo in the primary outcome, sleep efficiency ($N = 287$, standard mean differences; SMD: 0.14, 95% confidence intervals; CI −0.17–0.44, $P = 0.38$), but was in total nocturnal sleep time ($N = 305$, SMD: 0.26, 95% CI 0.01–0.51, $P = 0.04$). Dropout rates were similar in the treatment and placebo groups ($N = 453$, risk ratio $= 0.77$, 95% CI 0.51–1.16, $P = 0.21$). The Cochrane review of RCTs, as discussed above, found no significant effect of melatonin on sleep efficiency.

Antidepressants and sedatives

A Spanish population study of trazodone investigated first prescription between 2002 and 2011 in

Table 2. Results of trials testing pharmacological treatments

Study	Treatment	Control group	Participants	Outcomes
Wang *et al.* [28]	Melatonin	Placebo-controlled randomised trials (meta-analysis)	453 with dementia (305 with Alzheimer's disease; 287 with primary outcome)	Negative primary outcome sleep efficiency ($N=287$), but improved nocturnal sleep time ($N=305$)
Macías Saint-Gerons *et al.* [29]	Trazodone	Naturalistic study of Spanish population	11 766 individuals aged over 65 years	Increased use of trazodone for dementia and sleep problems
Iaboni *et al.* [30]	Dispensing of drugs with sedative properties (benzodiazepines, trazodone, quetiapine)	Naturalistic study of Canadian population	1 181 469–1 603 809 individuals Aged over 66 years with drug benefit 2002–2013	Increased use of trazodone and decreased use of benzodiazepines over time, especially in those with dementia
Scoralick *et al.* [31]	Mirtazapine, 15 mg	Placebo-controlled randomised trial	24 with Alzheimer's disease	Increased daytime sleepiness Did not increase sleep efficiency or nocturnal sleep time
Leonpacher *et al.* [32▪]	Citalopram, 30 mg (secondary analysis)	Placebo-controlled randomised trial	186 with Alzheimer's disease	Increase in the severity of sleep disturbances in those with these present at week 9
Altınyazar *et al.* [33]	Agomelatine, 25 mg	No control, case study	A 91-year-old woman with Alzheimer's disease	Improved both insomnia and depression
Kazui *et al.* [34]	Donepezil, 5 mg	24 healthy controls	16 DLB (8 with sleep disturbances at baseline)	Inconclusive but tendency towards decreased sleep disturbances in DLB at 14 weeks
Ishikawa *et al.* [35]	Memantine, 20 mg	None	12 with Alzheimer's disease	Improved sleep and was well tolerated

DLB, people with dementia with Lewy bodies.

11 766 individuals aged 65 and over. This showed that dementia (20.36%) and sleep disorders (16.22%) were the most common therapeutic indications, after only depression (21.41%) [29]. Its use increased five-fold in 2002–2011. The median dose was 100 mg/day. Another population-based survey of older adults in Ontario, Canada compared patterns of trazodone and benzodiazepine dispensing to older adults (≥66 years) from January 2002 to March 2013 ($N=1\,181\,469$–$1\,603\,809$) [30]. Whereas trazodone dispensing increased over time, that of benzodiazepine decreased, especially in those with dementia, both in community and long-term care settings.

A randomized, double-blind, placebo-controlled trial investigated the safety and efficacy of mirtazapine 15 mg/day at 9.00 p.m. in the treatment of sleep disorders in 24 community-dwelling patients with Alzheimer's disease for 2 weeks [31]. Those treated with mirtazapine had increased daytime sleepiness without improvement in sleep efficiency or the duration of nocturnal sleep on actigraphy. In a planned secondary analysis of the CitAD study, a double-blind, placebo-controlled RCT assessed citalopram 30 mg/day in Alzheimer's disease over 9 weeks [32▪]. Those given citalopram who had sleep disturbances present at week 9, showed an increase in their severity.

A case report [33] suggested agomelatine 25 mg/day as a potential treatment for insomnia: a 91-year-old woman with Alzheimer's disease and a 20-year history of insomnia showed decreased sleep fragmentation and daytime sleepiness after a month.

Dementia medications

One study investigated whether donepezil 5 mg daily for 14 weeks could help to alleviate sleep disturbances (assessed using actigraphy) and sleep symptoms such as dream enactment in 16 people with DLB [34]. Eight patients had sleep disturbances at baseline. The results from this small sample suggested that donepezil treatment reduced sleep disturbances and night-time activity/wakefulness.

An uncontrolled trial investigated memantine 20 mg/day for sleep in 12 patients with Alzheimer's disease (aged 79 ± 4 years) using polysomnography at baseline and after 4 weeks [35]. There were significant increases in total sleep time, sleep efficiency and time in stage II sleep, and decreases in night-time awakening, periodic limb movement and time in stage I sleep. As this was a small study and not controlled, the results are inconclusive.

CONCLUSION

Sleep disorders in dementia affect emotional and physical health, may worsen cognitive symptoms, and reduce quality of life for those with dementia

and their family members. They also add to dementia costs as people are admitted to care homes. Interventions that work are needed. However, most recent studies have been exploratory, and definitive evidence is lacking. To date, as the aetiology of sleep disturbance is mixed, the most promising interventions appear to be multicomponent. Further research with adequately powered trials of such interventions or medication is needed before evidence-based clinical practice recommendations can be made on managing sleep disorders in dementia. In the meantime, clinicians will continue to use evidence derived from trials in other conditions, or from their clinical experience.

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Conflicts of interest

K.K. and G.L. are currently working on DREAMS START, an acceptability and feasibility RCT of a multicomponent intervention for sleep disorders in dementia.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Moran M, Lynch C, Walsh C, *et al.* Sleep disturbance in mild to moderate Alzheimer's disease. Sleep Med 2005; 6:347–352.
2. Dauvilliers Y. Insomnia in patients with neurodegenerative conditions. Sleep Med 2007; 8(Suppl 4):S27–S34.
3. Kyle SD, Espie CA, Morgan K. '... Not Just a Minor Thing, It Is Something Major, Which Stops You From Functioning Daily': quality of life and daytime functioning in insomnia. Behav Sleep Med 2010; 8: 123–140.
4. Prince M, Comas-Herrera MA, Knapp M, Guerchet M, Karagiannidou MM. World Alzheimer Report 2016: improving healthcare for people living with dementia coverage, quality and costs now and in the future. London, UK: Alzheimer's Disease International. Available online at: https://www.alz.co.uk/research/WorldAlzheimerReport2016.pdf.
5. McCurry SM, Logsdon RG, Teri L, Vitiello MV. Sleep disturbances in caregivers of persons with dementia: contributing factors and treatment implications. Sleep Med Rev 2007; 11:143–153.
6. Gehrman P, Gooneratne NS, Brewster GS, *et al.* Impact of Alzheimer disease patients' sleep disturbances on their caregivers. Geriatr Nurs 2017; 1–6.
7. ■■ Holth JK, Patel TK, Holtzman DM. Sleep in Alzheimer's disease–beyond amyloid. Neurobiol Sleep Circadian Rhythm 2017; 2:4–14.
A review discussing how amyloid, tau and comorbid disease affect the brain and how this might impair sleep regulation in Alzheimer's disease.
8. Forbes D, Blake CM, Thiessen EJ, *et al.* Light therapy for improving cognition, activities of daily living, sleep, challenging behaviour, and psychiatric disturbances in dementia. In: Forbes D, editor. Cochrane Database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2014 .
9. ■■ McCleery J, Cohen DA, Sharpley AL. Pharmacotherapies for sleep disturbances in dementia. In: McCleery J, editor. Cochrane Database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2016.
A systematic review of placebo-controlled randomised trials of pharmacological treatments used for sleep disoders in dementia. Assessed effects and adverse effects.
10. Cooke JR, Ancoli-Israel S. Normal and abnormal sleep in the elderly. Handb Clin Neurol 2011; 98:653–665.
11. Pavlova M. Circadian rhythm sleep-wake disorders. Contin Lifelong Learn Neurol 2017; 23:1051–1063.
12. Ju Y-ES, Lucey BP, Holtzman DM. Sleep and Alzheimer disease pathology–a bidirectional relationship. Nat Rev Neurol 2014; 10:115–119.
13. Ju Y-ES, McLeland JS, Toedebusch CD, *et al.* Sleep quality and preclinical Alzheimer disease. JAMA Neurol 2013; 70:587–593.
14. Wu Y-H, Swaab DF. Disturbance and strategies for reactivation of the circadian rhythm system in aging and Alzheimer's disease. Sleep Med 2007; 8:623–636.
15. Livingston G, Sommerlad A, Orgeta V, *et al.* Dementia prevention, intervention, and care. Lancet 2017; 1–62.
16. ■ Urrestarazu E, Iriarte J. Clinical management of sleep disturbances in Alzheimer's disease: current and emerging strategies. Nat Sci Sleep 2016; 8:21–33.
A previous review highlighting the lack of evidence of efficacy and the need to develop drugs with new mechanisms of action.
17. Gibson RH, Gander PH, Dowell AC, Jones LM. Nonpharmacological interventions for managing dementia-related sleep problems within community dwelling pairs: a mixed-method approach. Dementia 2016; 1–18.
18. Tewary S, Cook N, Pandya N, McCurry SM. Pilot test of a six-week group delivery caregiver training program to reduce sleep disturbances among older adults with dementia-innovative practice. Dementia 2016; 1–10.
19. Sekiguchi H, Iritani S, Fujita K. Bright light therapy for sleep disturbance in dementia is most effective for mild to moderate Alzheimer's type dementia: a case series. Psychogeriatrics 2017; 1–7.
20. Lai CKY, Lai DLL, Ho JSC, *et al.* Interdisciplinary collaboration in the use of a music-with-movement intervention to promote the wellbeing of people with dementia and their families: development of an evidence-based intervention protocol. Nurs Health Sci 2016; 18:79–84.
21. Krolak-Salmon P, Roubaud C, Finne-Soveri H, *et al.* Evaluation of a mobile team dedicated to behavioural disorders as recommended by the Alzheimer Cooperative Valuation in Europe joint action: observational cohort study. Eur J Neurol 2016; 23:979–988.
22. Lazarou I, Karakostas A, Stavropoulos TG, *et al.* A novel and intelligent home monitoring system for care support of elders with cognitive impairment. J Alzheimers Dis 2016; 54:1561–1591.
23. Kodama A, Kume Y, Tsugaruya M, Ishikawa T. Deriving the reference value from the circadian motor active patterns in the "nondementia" population, compared to the "dementia" population: what is the amount of physical activity conducive to the good circadian rhythm. Chronobiol Int 2016; 33:1056–1063.
24. Buysse DJ, Reynolds CF, Monk TH, *et al.* The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28:193–213.
25. Tractenberg RE, Singer CM, Cummings JL, Thal LJ. The Sleep Disorders Inventory: an instrument for studies of sleep disturbance in persons with Alzheimer's disease. J Sleep Res 2003; 12:331–337.
26. McCurry SM, Gibbons LE, Logsdon RG, *et al.* Nighttime insomnia treatment and education for Alzheimer's disease: a randomized, controlled trial. J Am Geriatr Soc 2005; 53:793–802.
27. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology 1997; 48(5 Suppl 6):S10–S16.
28. Wang Y-Y, Zheng W, Ng CH, *et al.* Meta-analysis of randomized, double-blind, placebo-controlled trials of melatonin in Alzheimer's disease. Int J Geriatr Psychiatry 2017; 32:50–57.
29. Macías Saint-Gerons D, Huerta Álvarez C, García Poza P, *et al.* Trazodone utilization among the elderly in Spain. A population based study. Rev Psiquiatr Salud Ment 2016; 1–8.

30. Iaboni A, Bronskill SE, Reynolds KB, *et al.* Changing pattern of sedative use in older adults: a population-based cohort study. Drugs Aging 2016; 33:523–533.
31. Scoralick FM, Louzada LL, Quintas JL, *et al.* Mirtazapine does not improve sleep disorders in Alzheimer's disease: results from a double-blind, placebo-controlled pilot study. Psychogeriatrics 2017; 17:89–96.
32. Leonpacher AK, Peters ME, Drye LT, *et al.* Effects of citalopram on ■ neuropsychiatric symptoms in Alzheimer's dementia: evidence from the CitAD study. Am J Psychiatry 2016; 173:473–480.
An analysis from a placebo-controlled randomised trial importantly reporting negative effects of citalopram on sleep.
33. Altınyazar V, Kiylioglu N. Insomnia and dementia: is agomelatine treatment helpful? Case report and review of the literature. Ther Adv Psychopharmacol 2016; 6:263–268.
34. Kazui H, Adachi H, Kanemoto H, *et al.* Effects of donepezil on sleep disturbances in patients with dementia with Lewy bodies: An open-label study with actigraphy. Psychiatry Res 2017; 251:312–318.
35. Ishikawa I, Shinno H, Ando N, *et al.* The effect of memantine on sleep architecture and psychiatric symptoms in patients with Alzheimer's disease. Acta Neuropsychiatr 2016; 28:157–164.
36. Forlenza OV, Loureiro JC, Pais MV, Stella F. Recent advances in the management of neuropsychiatric symptoms in dementia. Curr Opin Psychiatry 2017; 30:151–158.

