

Sleep in Care Homes

Adam L Gordon and John RF Gladman

Division of Rehabilitation and Ageing, University of Nottingham, UK.

Correspondence to:

Dr Adam Gordon

Room B98,

Division of Rehabilitation and Ageing,

Medical School,

Queens Medical Centre,

Nottingham.

NG7 2UH.

E-mail: adam.gordon@nottingham.ac.uk

Telephone: +44 115 823 0236

Fax: + 44 115 823 0231

This paper has been accepted for publication and will appear in a revised form, subsequent to peer review and/or editorial input by Cambridge University Press, in **Reviews in Clinical Gerontology** published by Cambridge University Press. Cambridge University Press hold the copyright.

Summary

Sleep problems in older adults are common and disturbance in sleep is associated with increased mortality. These problems are more pronounced in the care home population because of institutional factors and a high prevalence of frailty and comorbidity. This article reviews the randomized controlled trials undertaken to address sleep problems in care homes. These suggest that standalone therapies – oral melatonin and light therapy – have no effect on sleep but that combination treatments – physical exercise plus sleep hygiene, physical exercise plus sleep hygiene plus light and melatonin plus light – may have positive effects. These effects are more marked for daytime arousal than nocturnal sleep. Practical considerations for care homes are how to maximise light exposure, incorporate exercise into daily routines and minimize night-time disruption for residents. Trials undertaken so far are compromised by small sample size and inappropriate randomization strategies and further research is therefore required.

Keywords (using MeSH headings)

Sleep; Nursing Homes; Residential Facilities; Homes for the Aged; Randomized Controlled Trials as

Topic

Introduction

Sleep problems in older adults are common: up to 42% of people over 65 report problems in initiating or maintaining sleep(1). Problems with sleep in older people have been comprehensively reviewed elsewhere(2) and are due to medical problems(3-6), an increased prevalence of specific sleep disorders(7, 8) and age-related changes in circadian rhythm(9). Care home residents are, however, an extreme case – they have a higher prevalence of frailty and cognitive impairment than their community dwelling counterparts(10), have lower levels of physical activity(11), have daily routines altered to fit with institutional timetables and spend much of their time indoors(12). All of these variables may influence circadian rhythm.

In this article we consider sleep problems specifically in the care home population and present findings from randomized controlled trials (RCTs) of interventions undertaken to improve the quality of sleep in this cohort, including evaluations of pharmacological, physical, sleep hygiene, light and combination therapies. We also consider implications for practice and future research.

Search Strategy

This work comprises part of a larger literature review of RCTs conducted in the care home setting. Three databases were consulted, with different search terms and limits used for each based upon those available. Medline (1950-June 2009) was searched for the search terms “Nursing Home”, “Residential Facilities” and “Homes for the Aged”, combined using the “OR” command. Results were limited for English language and randomized controlled trials. The Allied and Complementary Medicine Database (AMED) (1985-June 2009) was searched for “Nursing homes”, “Long term care” and “Residential facilities” combined using the “OR” command and “Randomized controlled trial” using the “AND” command. The British Nursing Index and Archive (BNI) (1985-June 2009) was searched for “Nursing Homes”, “Residential Care” and “Long-term care”. 563 articles were identified from Medline and AMED and 3161 from BNI – it was not possible to limit the results from this database further as no filter for RCTs was available. Abstracts were reviewed by a single reviewer for

descriptions of interventions evaluated using RCTs in residential, nursing or care homes. 339 articles met these criteria and were read in full. From these, articles reviewing interventions for sleep in care home residents were used to compile the current review.

What is a care home?

Long-term care facilities are given different titles depending on the country in which they operate. A care home is defined in the United Kingdom as, “an establishment [which] provides accommodation, together with nursing or personal care, for persons who are or have been ill, who have or have had a mental disorder, who are disabled or infirm, or are or have been dependent on alcohol or drugs” (13). The majority of homes care for residents with frailty and physical dependency, with those caring for people with learning difficulties, alcohol or drug dependency and mental health problems separated by specialist registration. All care homes provide support with activities of daily living but are classified as either residential care homes or care homes with nursing depending on whether they provide dedicated 24-hour professional nursing care. When the sector is considered as a whole, only 8.6% of residents are under 70, with 76% overall requiring assistance with their mobility or being immobile, 78% having at least one form of mental impairment and 71% suffering incontinence(10). Although most developed countries have a care home equivalent, the model of separate residential and nursing care is far from universal(14). Despite these differences, we present in this article findings which we believe are applicable across national boundaries.

The problem of sleep in care homes

Sleep is often fragmented in care home residents. A study of 200 residents, conducted in 1989, gathered recordings of sleep-wake cycles using a portable Respitrace-Medilog device(15). This was carried by the participant, and used thoracic and abdominal inductance bands to measure respiration, tibialis electromyography to record hypnagogic leg myoclonus and a wrist transducer to measure arm and hand activity. Recordings averaging 15.4/24 hours per subject were obtained and

revealed that subjects averaged a relatively normal 7 hours 58 minutes asleep and 7 hours 28 minutes awake. However in the sleep periods, they spent no more than 39.5 minutes per hour asleep, whilst 50% of subjects woke up more than twice per hour. It was noted that residents compensated by catnapping during normal waking hours.

There are several reasons for disturbed sleep patterns amongst care home residents. They are, for the most part, old and older people experience a higher prevalence of sleep disorders. This is attributed to an accumulation of general medical conditions associated with insomnia (heart failure(3), Parkinson's Disease(4), dementia(5), depression(6)), a higher prevalence of sleep-specific disorders such as sleep apnoea(8) and restless leg syndrome(7), and age associated changes in sleep-wake cycle which result in early morning wakening and difficulty maintaining sleep. The latter are attributed in part to degenerative changes in the suprachiasmatic nucleus of the hypothalamus, commonly referred to as the pacemaker of circadian rhythm(2).

Circadian rhythms are set by "zeitgebers" (from German, literally meaning "time givers") – including bright light and physical activity – to which care home residents have limited exposure. Bright light exposure during the day, of 2000 lux or more, helps maintain circadian rhythm. Yet data recorded using wrist worn photosensors from 66 care home residents recorded a median exposure of only 10 minutes per day of light above 1000 lux intensity(12) compared with average exposures amongst young adults of 58 minutes per day(16) and healthy older people of 60 minutes per day(17) above 2000 lux. Activity also helps maintain circadian rhythm. Yet data gathered from 95 care home residents using motion sensors to measure activity levels found that unrestrained residents spent most of their time immobile –83.5% of measurements recorded participants sitting or lying flat(11).

Regimens designed to facilitate care delivery in care homes, such as night-time continence checks, disturb residents' sleep. A study of 100 residents across four nursing homes, using bedside monitors to record night-time noise and light levels, recorded 32 noises per resident per night at the volume

of loud speech (60 decibels) or louder(18). Another study using similar technology in 225 residents from 10 homes revealed 22% of waking episodes to be associated with noise alone, 10% with light or light and noise and 10% with incontinence care routines. 76% percent of all incontinence care practices resulted in awakenings(19).

Disturbed sleep is detrimental. A survey of 1526 64-99 year olds recording falls, health and socio-economic variables, demonstrated a strong positive correlation between falls and night-time sleep problems(20). Focussing specifically on care home residents, a retrospective case note analysis of 507 deaths in 1557 residents established standardized mortality rates for commonly presenting problems and showed a hazard ratio of 1.9 (95% CI 1.3-2.8) for excess day time sleepiness (the correlate of night-time sleep disruption)(21). This finding is supported by a prospective study of 272 Japanese long-term geriatric hospital patients (the equivalent of UK care home residents(14)), which recorded sleep-patterns over two weeks using 2-hourly observations at baseline and showed a hazard ratio at 2-year follow-up of 1.6 (95% CI 1.5-2.4) for those with night time insomnia and 1.8 (95% CI 1.2-2.8) for those with sleep-onset delay(22).

Given that sleep quality is so poor amongst care home residents and that this is likely to be detrimental to their health, it is unsurprising that research has focussed on treatments to improve the quality and quantity of sleep in this cohort.

Pharmaceutical interventions

Hypnotics have been shown to increase sleep duration in the older population(23) and, despite their considerable side-effect profile, they are still recommended by some expert authorities for treatment of short-term insomnia in this age group(24). It is likely, however, that they have little role in treating care home residents with insomnia. A randomized controlled crossover trial comparing temazepam with diphenhydramine – a first generation antihistamine available over the counter – and placebo in 14 care home residents reported reduced sleep latency (time between

going to bed and sleep onset) for both hypnotics but no advantage in terms of duration of sleep, number of awakenings or time spent awake(25). In addition, participants scored higher in terms of cognitive function testing (word lists, cancellation tests, digit span and digit symbol substitution) whilst receiving placebo – indicating significant hangover effects from both drugs. These findings are supported by a cohort study of 145 US nursing home residents recording baseline medication use and self-reported sleep complaints. There was no demonstrated association between hypnotic prescribing and presence/absence of sleep complaints at either baseline or six month follow-up(26). Therefore, even before the considerable side-effect profile of hypnotics(27) in frail older people is considered, there is little to justify their widespread use. This has led to a search for alternative pharmacological treatments, with specific focus on melatonin and the melatonin-receptor agonist, ramelteon(28). Of these, only melatonin has been tested in the care home population.

Melatonin is an endogenous hormone produced in the pineal gland, with its secretion mediated by stimulation from the suprachiasmatic nucleus in response to light. A nocturnal peak in melatonin secretion is clearly demonstrable in young subjects and is thought to have a role in initiating sleep(29). Older people have both lower levels of circulating melatonin – measured through serum levels and excretion of serum metabolites – and a diminished nocturnal peak(30, 31). Exogenous melatonin has been shown to be effective in promoting shifts in circadian rhythms(32), leading to the hypothesis that it may have a role in normalising sleep/wake cycles in older people with insomnia.

Only one RCT has evaluated melatonin as a standalone therapy in the care home population. This selected 41 residents with Alzheimer's disease (National Institute of Neurological and Communicative Disorders and Stroke criteria) and randomized them to receive either melatonin or placebo for 10 days. Sleep efficacy (the proportion of the time in bed spent asleep) was measured using actigraphy, where motion and light sensors are worn in a wrist-watch type device – a method validated against EEG recordings for ascertainment of sleep in care home residents(33). Agitation

was recorded using the Cohen Mansfield Agitation Inventory (CMAI) immediately before and after treatment. No significant difference was found for either outcome measure. Although at odds with findings from small cohort studies(34, 35), these findings are supported by a non-care home placebo-controlled trial of melatonin in 157 older patients with Alzheimer's disease, where no effect on sleep efficacy was demonstrated(36).

The authors of these studies have queried whether the negative results were a consequence of either the supra-physiological doses of melatonin employed or the phase-shift in circadian rhythm prominent in Alzheimer's disease. It might, for example, be necessary to administer melatonin at a different time of day than in the non-demented population to promote improved sleep efficacy. There remains, however, no evidence to support melatonin as a standalone therapy in care home residents. However, there is evidence, as discussed later in the article, to promote its use as part of a multi-component intervention.

Turning up the light

Light is a potent zeitgeber and, given that care home residents are relatively light-deprived, there has been considerable interest on how light therapy affects sleep.

Bright light therapy, using electric light boxes, affects circadian rhythm in older people. Evening bright light delays sleep onset such that people fall asleep later and morning bright light advances the onset, leading to earlier onset of sleep(37). Non-demented older people are characteristically tend to fall asleep earlier than normal controls(38) and therefore potentially could benefit from evening bright light. People with Alzheimer's disease tend to fall asleep later(39) and could potentially benefit from morning light.

There have been two RCTs of light as a standalone therapy in a care home setting. In the first of these(40) 77 care home residents with a mean MMSE of 12.8 were randomized to receive either evening bright light therapy, morning bright light therapy, daytime sleep restriction – where

residents were kept awake by study staff – or evening dim light. Evening dim light was the control intervention. Light therapies were delivered using medical-grade light boxes, with bright light at 2500 lux intensity and dim light at 50 lux. Day and night time activity levels were measured using actigraphy. No difference between groups was detected and there was no within group difference in activity between baseline and follow-up. A non-significant tendency for morning bright-light to delay the onset of sleep was noted.

The second study selected 46 residents with Alzheimer's disease (mean MMSE 6.7) who were randomized to receive either morning bright light or normal light exposure(41). A naturalistic approach was adopted by encouraging residents in the intervention arm to undertake activities either outdoors or in a bright room, with light levels recorded to ensure adequate exposure. When light levels were less than 2500 lux for an hour or more , top-up treatment was provided using light boxes. Sleep efficacy and day and night activity levels were recorded by actigraphy. There was no difference between groups when the intervention cohort was considered as a whole but positive effects were noted on a subgroup analysis of those individuals (n=13) who had the most profound sleep disturbance at baseline, with their 10 most active hours occurring at a time they would be expected to be sleeping. For this group there was a statistically significant improvement in rest-activity ratios, night-time sleep efficacy and sleep duration by comparison with controls.

Thus light therapy has little evidence to support its use in the care home population as a standalone therapy, except perhaps in patients with dementia and profound sleep-wake cycle disruption.

Multicomponent interventions

It is unsurprising that standalone therapies, either melatonin or light, have little influence over sleep or circadian rhythms in the care home population, given that the causes are likely to be multifactorial. Furthermore, the suprachiasmatic nucleus undergoes degenerative change in advanced old age and this is particularly marked in Alzheimer's disease(42). It has therefore been

proposed that older patients, particularly those with Alzheimer's disease, will be less sensitive to individual zeitgebers such as light exposure or circulating melatonin levels. A response has been to combine individual therapies in the hope that their influence on sleep is summative – melatonin, for example, might prime an individual to respond to bright light therapy(43). Three multicomponent interventions have been described in the care home setting and have, for the most part, been more successful than standalone therapies.

Combination 1 – Physical exercise and sleep hygiene

The mechanism of the association between physical exercise and sleep is poorly understood but is likely to be mediated through an effect on overall physical fitness rather than an immediate effect of the exercise, with improved physical fitness resulting in improved quality of sleep(44).

Functional Incidental Training is incorporated into daily care home routines by encouraging participants to undertake repetitions of routine activities such as sit-to-stand transfers following toileting and therefore has intuitive advantage over, potentially more artificial, structured exercise programmes. It has been shown to improve physical endurance in an RCT of 76 nursing home residents(45) and hence, putatively, might have a role in improving sleep.

A post-hoc analysis of two RCTs, one involving Functional Incidental Training and the other involving a programme of rowing, walking or wheelchair-propulsion based exercises, showed no benefit for either intervention on sleep(46). The authors attributed this to the possible disruptive effects of light and noise associated with routine night-time checks on residents. A subsequent study allowed for this by combining a 14 week Functional Incidental Training programme with 1 week of sleep-hygiene in the form of a "quiet at night programme"(46). In this staff were advised to wear quiet shoes, minimise entries into residents' rooms, use a flash-light rather than overhead lighting when doing so and not to awaken a patient for continence checks unless they had been asleep for four consecutive one-hourly reviews. 29 participants were randomized to receive either Functional

Incidental Training plus quiet at night or the quiet at night intervention alone. Sleep efficacy, the proportion of daytime spent asleep and agitation levels all improved in the intervention arm. However the study was noted to be inconclusive due to technical issues, most importantly the small sample size and inadequate randomization which led to the intervention subjects having markedly poorer sleep at baseline.

Combination 2 – Physical exercise, sleep hygiene and light

In a further augmentation of their protocol and in an attempt to address the sample-size issue these authors conducted a second study evaluating functional incidental training, this time combined with both sleep hygiene and light exposure(47). The intervention comprised five days of daytime Functional Incidental Training, coupled to a quiet at night programme and 30 minutes per day of bright outdoor light exposure, confirmed using a handheld meter as being 30 minutes at $\geq 10,000$ lux. Control subjects received usual care. 118 participants were individually randomized. Actigraphy recordings demonstrated no effect on the duration of sleep or number of night-time awakenings, however the duration of night-time awakenings was significantly, if slightly, shorter. A more significant finding was an 11% reduction in the proportion of the day spent asleep and a resultant improvement in rest-activity ratios(48). Two specific issues draw this analysis into question – residents were randomized individually, rather than by home, with the possibility that those receiving usual care were partially exposed to the intervention through cross-contamination; and the possibility that social interaction alone acts as a zeitgeber could not be excluded by the use of a usual care control.

Combination 3 – Melatonin and light

The combination of melatonin and bright-light has also been tested(43). Fifty patients were randomized to receive bright morning light and evening oral melatonin, bright morning light and evening oral placebo or usual care, with sleep recorded using actigraphy. When compared with

controls, those receiving both light and melatonin showed higher daytime activity levels, fewer and a shorter duration of daytime sleep episodes and a more normal sleep-wake ratio. There was, however, no effect on night-time sleep. Light and placebo had no effect on sleep, however, the small sample size meant that the study was underpowered to detect such an effect and it is possible that a larger study may have revealed a positive, if smaller magnitude, effect for light alone.

Conclusions

We have summarised in this article the RCT-generated evidence base for sleep interventions in care homes. There is little to suggest that hypnotic drugs, or other standalone therapies that have been tested – bright light therapy and oral melatonin – have any overall benefit. Combination therapies seem to be more effective with Functional Incidental Training plus sleep hygiene, Functional Incidental Training plus light plus sleep hygiene and melatonin plus light all having positive effects. These effects are seen predominantly during the day – with residents staying awake for longer and being more physically active whilst doing so. This improvement in daytime arousal may be positive by allowing improved participation in daytime activities and improving quality of life measures as a consequence(35, 43). What is not clear, however, is whether it has any meaningful effect on the more dangerous associations of impaired sleeping – falls and mortality. It is not, in fact, clear what the causal relationship is between sleep and these variables and whether sleep interventions, even if effective, can have any influence over them.

It is difficult to make any concrete recommendations based upon current research in care homes because of technical issues with the RCTs undertaken. All are small and have used individual rather than cluster randomization, with implications for cross-contamination. Several studies have issues with poorly chosen control interventions that make it difficult to interpret the true meaning of their results. Also, whilst it is clear that older patients with and without dementia have differing circadian rhythm disturbances, it is not clear that these groups have been considered separately in several of the studies undertaken.

Further research is required if proper sense is to be made of how to manage sleep in care homes. Nevertheless, there are practical lessons to note from what is already known. There is no good evidence that there are any useful drug therapies for sleep disturbance in this group and reasons to believe that they are largely ineffective. The evidence that non-pharmacological interventions are effective is not strong either. Standalone interventions do not seem to work, so we propose that a sleep strategy must be comprehensive and tackle more than one issue at once. Physical activity seems to have a positive influence on sleep and this effect can be achieved with relatively low levels of exertion that could easily be achieved as part of a care home activity programme. Light exposure seems to help patients sleep and the examples from the research of this being achieved by outdoors sun exposure could be easily delivered as part of care home routines. Finally attempts to reduce night-time disruption are important. This latter concept will trouble many care home practitioners because of the tension between providing good pressure care through regular continence checks and leaving patients to sleep. The optimum regimen that allows both issues to be safely addressed is yet to be established and is a potential focus for future research.

Conflict of Interests

The authors declare that they have no conflict of interests.

References

1. Foley DJ, Monjan AA, Brown SL, et al. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep*. 1995;18(6):425-32.
2. Ancoli-Israel S, Ayalon L. Diagnosis and Treatment of Sleep Disorders in Older Adults. *Focus*. 2009 January 1, 2009;7(1):98-105.
3. Katz DA, McHorney CA. Clinical correlates of insomnia in patients with chronic illness. *Arch Intern Med*. 1998;158(10):1099-107.

4. Garcia-Borreguero D, Larrosa O, Bravo M. Parkinson's disease and sleep. *Sleep Med Rev.* 2003;7(2):115-29.
5. Vitiello MV, Prinz PN, Williams DE, Frommlet MS, Ries RK. Sleep disturbances in patients with mild-stage Alzheimer's disease. *J Gerontol.* 1990;45(4):131-8.
6. Quan SF, Katz R, Olson J, et al. Factors associated with incidence and persistence of symptoms of disturbed sleep in an elderly cohort: the Cardiovascular Health Study. *Am J Med Sci.* 2005;329(4):163-72.
7. Ohayon MM, Roth T. Prevalence of restless legs syndrome and periodic limb movement disorder in the general population. *Journal of Psychosomatic Research.* 2002;53(1):547-54.
8. Ancoli-Israel S, Kripke DF, Klauber MR, et al. Sleep-disordered breathing in community-dwelling elderly. *Sleep.* 1991;14(6):486-95.
9. Bliwise DL. Sleep in normal aging and dementia. *Sleep.* 1993;16(1):40-81.
10. Bowman C, Whistler J, Ellerby M. A national census of care home residents. *Age Ageing.* 2004 November 1, 2004;33(6):561-6.
11. MacRae PG, Schnelle JF, Simmons SF, Ouslander JG. Physical Activity Levels of Ambulatory Nursing Home Residents. *Journal of Ageing and Physical Activity.* 1996;4(3).
12. Shochat T, Martin J, Marler M, Ancoli-Israel S. Illumination levels in nursing home patients: effects on sleep and activity rhythms. *Journal of Sleep Research.* 2000;9:373-9.
13. Great Britain Department of Health. Care Standards Act 2000. London: Stationery Office; 2001.
14. Ribbe MW, Ljunggren G, Steel K, et al. Nursing Homes in 10 Nations: A Comparison Between Countries and Settings. *Age Ageing.* 1997 January 1, 1997;26(suppl_2):3-12.
15. Ancoli-Israel S, Parker L, Sinaee R, Fell RL, Kripke DF. Sleep Fragmentation in Patients From a Nursing Home. *Journal of Gerontology.* 1989 January 1989;44(1):M18-M21.
16. Espiritu RC, Kripke DF, Ancoli-Israel S, et al. Low illumination experienced by San Diego adults: Association with atypical depressive symptoms. *Biological Psychiatry.* 1994;35(6):403-7.

17. Campbell SS, Kripke DF, Gillin JC, Hrubovcak JC. Exposure to light in healthy elderly subjects and alzheimer's patients. *Physiology & Behavior*. 1988;42(2):141-4.
18. Schnelle JF, Ouslander JG, Simmons SF, Alessi CA, Gravel MD. The nighttime environment, incontinence care, and sleep disruption in nursing homes. *J Am Geriatr Soc*. 1993;41(9):910-4.
19. Cruise PA, Schnelle JF, Alessi CA, Simmons SF, Ouslander JG. The nighttime environment and incontinence care practices in nursing homes. *J Am Geriatr Soc*. 1998;46(2):181-6.
20. Brassington GS, King AC, Bliwise DL. Sleep problems as a risk factor for falls in a sample of community-dwelling adults aged 64-99 years. *J Am Geriatr Soc*. 2000;48(10):1234-40.
21. Dale MC, Burns A, Panter L, Morris J. Factors affecting survival of elderly nursing home residents. *Int J Geriatr Psychiatry*. 2001;16(1):70-6.
22. Manabe K, Matsui T, Yamaya M, et al. Sleep Patterns and Mortality among Elderly Patients in a Geriatric Hospital. *Gerontology*. 2000;46(6):318-22.
23. Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ*. 2005 November 19, 2005;331(7526):1169-.
24. Bloom HG, Ahmed I, Alessi CA, et al. Evidence-based recommendations for the assessment and management of sleep disorders in older persons. *J Am Geriatr Soc*. 2009;57(5):761-89.
25. Meuleman, JR, Nelson R, Clark RL, Jr. Evaluation of temazepam and diphenhydramine as hypnotics in a nursing-home population. *Ann Pharmacother*. 1987 September 1, 1987;21(9):716-20.
26. Monane M, Glynn RJ, Avorn J. The impact of sedative-hypnotic use on sleep symptoms in elderly nursing home residents[ast]. *Clin Pharmacol Ther*. 1996;59(1):83-92.
27. Ray WA, Thapa PB, Gideon P. Benzodiazepines and the risk of falls in nursing home residents. *J Am Geriatr Soc*. 2000;48(6):682-5.
28. Roth T, Stubbs C, Walsh JK. Ramelteon (TAK-375), a selective MT1/MT2-receptor agonist, reduces latency to persistent sleep in a model of transient insomnia related to a novel sleep environment. *Sleep*. 2005;28(3):303-7.

29. Zeitzer JM, Daniels JE, Duffy JF, et al. Do plasma melatonin concentrations decline with age? *The American Journal of Medicine*. 1999;107(5):432-6.
30. Magri F, Sarra S, Cinchetti W, et al. Qualitative and quantitative changes of melatonin levels in physiological and pathological aging and in centenarians. *J Pineal Res*. 2004;36(4):256-61.
31. Skene DJ, Swaab DF. Melatonin rhythmicity: effect of age and Alzheimer's disease. *Experimental Gerontology*. 2003;38(1-2):199-206.
32. Wyatt JK, Dijk D-J, Ritz-de Cecco A, Ronda JM, Czeisler CA. Sleep-facilitating effect of exogenous melatonin in healthy young men and women is circadian-phase dependent. *Sleep*. 2006;29(5):609-18.
33. Ancoli-Israel S, Clopton P, Klauber MR, Fell R, Mason W. Use of wrist activity for monitoring sleep/wake in demented nursing-home patients. *Sleep*. 1997;20(1):24-7.
34. Cardinali DP, Brusco LI, Liberczuk C, Furio AM. The use of melatonin in Alzheimer's disease. *Neuro Endocrinol Lett*. 2002;23 Suppl 1:20-3.
35. Cohen-Mansfield J, Garfinkel D, Lipson S. Melatonin for treatment of sundowning in elderly persons with dementia - a preliminary study. *Archives of Gerontology and Geriatrics*. 2000;31(1):65-76.
36. Singer C, Tractenberg RE, Kaye J, et al. A multicenter, placebo-controlled trial of melatonin for sleep disturbance in Alzheimer's disease. *Sleep*. 2003;26(7):893-901.
37. Klerman EB, Duffy JF, Dijk DJ, Czeisler CA. Circadian phase resetting in older people by ocular bright light exposure. *J Investig Med*. 2001;49(1):30-40.
38. Carrier J, Monk TH, Reynolds CF, Buysse DJ, Kupfer DJ. Are age differences in sleep due to phase differences in the output of the circadian timing system? *Chronobiol Int*. 1999;16(1):79-91.
39. Satlin A, Volicer L, Stopa EG, Harper D. Circadian locomotor activity and core-body temperature rhythms in Alzheimer's disease. *Neurobiol Aging*. 1995;16(5):765-71.

40. Ancoli-Israel S, Martin JL, Kripke DF, Marler M, Klauber MR. Effect of Light Treatment on Sleep and Circadian Rhythms in Demented Nursing Home Patients. *Journal of the American Geriatrics Society*. 2002;50(2):282-9.
41. Dowling GA, Hubbard EM, Mastick J, et al. Effect of morning bright light treatment for rest-activity disruption in institutionalized patients with severe Alzheimer's disease. *Int Psychogeriatr*. 2005;17(2):221-36.
42. Swaab DF, Fliers E, Partiman TS. The suprachiasmatic nucleus of the human brain in relation to sex, age and senile dementia. *Brain Res*. 1985;342(1):37-44.
43. Dowling GA, Burr RL, Van Someren EJW, et al. Melatonin and bright-light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. *J Am Geriatr Soc*. 2008;56(2):239-46.
44. Driver HS, Taylor SR. Exercise and sleep. *Sleep Medicine Reviews*. 2000;4(4):387-402.
45. Schnelle JF, MacRae PG, Ouslander JG, Simmons SF, Nitta M. Functional Incidental Training, mobility performance, and incontinence care with nursing home residents. *J Am Geriatr Soc*. 1995;43(12):1356-62.
46. Alessi CA, Schnelle JF, MacRae PG, et al. Does physical activity improve sleep in impaired nursing home residents? *J Am Geriatr Soc*. 1995;43(10):1098-102.
47. Alessi CA, Martin JL, Webber AP, et al. Randomized, controlled trial of a nonpharmacological intervention to improve abnormal sleep/wake patterns in nursing home residents. *J Am Geriatr Soc*. 2005;53(5):803-10.
48. Martin JL, Marler MR, Harker JO, Josephson KR, Alessi CA. A multicomponent nonpharmacological intervention improves activity rhythms among nursing home residents with disrupted sleep/wake patterns. *J Gerontol A Biol Sci Med Sci*. 2007;62(1):67-72.