The Regional Committee on Health Research Ethics

Title

LED light's effect on sleep, circadian rhythm, and well-being in people living in elderly housing: a cross-over non-blinded randomized trial.

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Trial site

Sundhedshuset; Sundhedshuset Albertslund and Plejecentret Alberthøj, Skolegangen 1, 2620 Albertslund,

Project period

Data collection will commence in September 2016 and end in February 2017, followed by data analysis until February 2018.

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Project description

LED light's effect on sleep, circadian rhythm, and well-being in people living in elderly housing.

Background

Europe is undergoing a demographic change with a rapidly growing population of 65 years+. This challenges public services of municipalities and hospitals as the ageing citizens need care and treatment due to an age-related decline in physical and mental capacity. Also, a growing proportion of elderly citizens spend the last part of their life in elderly housing facilities, where they have access to specialized caretaking provided from the municipality (1).

In Denmark, municipalities like Albertslund are experiencing a growing need for sufficient and customized housing, which can support the elderly citizens in sustaining well-being and health along with preventing functional decline (2). The transition from living in one's private home to an elderly housing can be experienced as a loss of independence, where use of supportive well-fare technology is suggested as a remedy (3). However, any kind of well-fare technology must be tested for significant benefits and drawbacks to its end-users in everyday life before being introduced to larger group of users. Not least, because of the technologies' impact on the residents' and their families' possibilities of creating an individualized living area (4).

<u>Circadian adjusted LED-based lighting (CALED) as a well-fare technology</u>

To date, the designs of lighting systems in elderly housing are primarily made to support visual acuity for staff and secondly to minimize risk of falling in hazardous areas such as staircases (5). However, to obtain proper visual sharpness and better contrast, people of older age require heightened light levels due to age-related failing vision. Furthermore, inappropriate light at night disrupts not only sleep but also the timing of the circadian rhythm, with negative consequences on cognition and emotions (6). LED, a two-lead semiconductor light source with a lower energy consumption, a wider spectrum of wavelengths than incandescent light sources, and better contrast and faster switching, is therefore being increasingly considered for use in hospitals and elderly housing (5). With LED it is possible to intensify indoor lighting without increasing glares from shiny surfaces that can disturb safe mobility of the elderly residents (7).

The technological development in recent years has added the possibility of adjusting LED to a 24-hour circadian rhythm (henceforth: CALED (circadian adjusted LED-based lighting) that reflects the rhythm of outdoor daylight. The eye is the human body's receptive organ for light. It´s highly specific photoreceptive retinal structures project not only to the visual cortex for image processing but to a number of brain regions modulating basal physiology, such as the circadian master pacemaker, which adjusts its activity to light and regulates internal timing of physiological processes. Through these pathways, light information is relayed to regions throughout the brain, i.e. the amygdala, known to mediate stress and anxiety responses (8).

Elderly people have higher demands on quality and quantity of light as their body has to cope with immobility, pathologies and age-related functional decline (9). In addition to meeting the age-related demands for intensified light, a normalized circadian rhythm can positively influence mood, cognition, alertness, sleep and internal rhythms (10). Interestingly, lighting based on LED has been shown to improve the quality of sleep and to improve well-being in the elderly (11–13).

However, for frail and demented elderly intensifying the light may not have the same benefits due to a severely disturbed 24-hour circadian rhythm related not just to age but also to cognition (14).

Light's effects on quality of sleep and cognition

Nearly half of elderly over the age of 65 residing in nursing home facilities suffers from sleep disorders which is associated with depression and hypnotic drugs intake affecting their quality of life (15). Chronic sleep complaints have been associated with excessive daytime sleepiness and may result in impaired cognition, confusion, and psychomotor retardation all of which may be misinterpreted as dementia. Also, sleep disorders impacting persons with dementia include insomnia, excessive fatigue, circadian rhythm misalignment, and sleep behavior disorder. Untreated sleep disorders may exacerbate cognitive and behavioral symptoms in patients with dementia and are a source of considerable stress for family members. When left untreated, sleep disturbances may also increase the risk of injury at night, delirious episodes and compromise health-related quality of life (16,17).

Also, in demented elderly living in assisted care facilities a tailored lightning intervention has been shown to improve sleep quality and reduce depression and agitation (18) and the rest-activity rhythm has been shown to be associated with well-being (19). Moreover, previous studies have suggested that disrupted circadian rhythm and sleep quality are associated with episodes of delirium (20,21). Delirium is a neurocognitive disorder which occurs in up to 70% of elderly long-term care residents depending on diagnostic criteria and on the prevalence of dementia (22). Elderly with dementia and frailty are particularly disposed to developing delirium, and it has been suggested that the prevalence of delirium increases with pre-existing dementia (23). Persistent delirium is a significant independent predictor of 1-year mortality after acute hospitalization, and resolving delirium seems to diminish mortality (24).

Especially in people with dementia it can be challenging to prevent, diagnose and treat episodes of delirium, because delirium and behavioral symptoms of dementia are often co-exiting and misinterpreted with implications for the management of these symptoms by nursing home staff (25). This creates the potential risk for non-treatment of underlying causes of delirium such as infections, dehydration, malnutrition and adverse pharmacological events (22).

A study has shown that persons with delirium present more wandering/trying to leave, sleep problems, and irrational behavior, putting them at risk of needing restraining to prevent falls and complications (26). Restraining is disruptive to the well-being of elderly, families and staff. Therefore, any well-fare technology that may decrease episodes of delirium, and thereby restraining, is highly warranted and should be evaluated for its benefits and drawbacks (27). Particularly since little is known about how changes to the habitual environment, including lighting, influences delirium and mobility in terms of acute or temporal changes in sleep-wake and wandering behaviour, and delirium (28,29).

Thus, the possible effect of CALED on well-being, defined as physical and mental functioning, calls for an evaluation of CALED in persons with various levels of dementias and in frail elderly, before this new technology can be recommended for implementation in elderly housing on a general scale. Therefore, we wish to investigate whether an intervention of CALED targeting sleep quality and circadian rhythm has a different manifestation in a group of frail elderly compared to elderly with dementia. Also, we wish to investigate whether an association between disrupted circadian rhythm, sleep quality and delirium exists, as suggested by other studies (20,21).

Aim and objectives

The aim of the present trial is to investigate the effects of CALED on sleep quality, well-being and delirium in the two groups of elderly living in elderly housing: a group of frail elderly with mobility disabilities and a group of elderly with dementia. We hypothesise that CALED has a positive effect on sleep quality, well-being and delirium in both frail elderly and elderly with dementia.

Trial participants

We wish to include elderly (+65) who have been referred by the municipality of Albertslund to a residence in the elderly housing called "Sundhedshuset" in Albertslund, Denmark. "Sundhedshuset" has two types of elderly housing, one housing type designed for elderly with mobility disability, who have no need of assistance in their everyday living, and their spouses, and another housing type designed for people with various levels of dementia and a substantial need for support and nursing from staff.

Both housings are currently being considered for CALED, starting with a test installation in 15 flats for frail elderly and 9 rooms for people with dementia.

Also, a control group of elderly with mobility disability will be recruited to provide an indication of effect not associated with CALED such as seasonal impacts and other events ex. replacements in staffing.

Inclusion and exclusion criteria

Inclusion criteria

15 frail elderly (+65) and 9 elderly (+50) with dementia, who live in the flats/rooms that have been chosen for a test installation of CALED, will be invited to participate. The installation of CALED will be on one floor of the residential area of "Sundhedshuset".

Exclusion criteria

Terminal illness with an expected life time of 3 months

Trial design

The trial will be conducted as a cross-over non-blinded randomized trial. Due to the technical requirements, CALED will only be installed in 24 elderly housing facilities, limiting the number of participants receiving the intervention to 24.

Residents accepting participation will be divided into the following groups (numbers are the maximal possible for each group): 15 frail elderly receiving CALED as an intervention (group A), 9 people with dementia receiving CALED as an intervention (group B), and 15 frail elderly not receiving CALED during the trial as a control group (group C).

Group A and group B will each be randomized to 2 subgroups (A1+A2 and B1+B2). A1 and B1 will start out as intervention groups, and A2 and B2 as control groups. The trial period will be 16 weeks with both 8 weeks of intervention and 8 weeks of control. The first 8 weeks (week 1-8) are denoted period 1 and the last 8 weeks (week 9-16) are denoted period 2. The randomization is conducted after baseline assessments by the drawing of a sealed envelope containing the instruction: *Intervention at Baseline* or *Delayed Intervention* equivalent to subgroup 1 (A1 and B1) and 2 (A2 and B2).

Subgroup C will function as a control group throughout the trial (Table 1).

Table 1

Participants	*No*	*Week 0*	*Randomization*	*No*	*Week 1-8 Period 1*	*Week 9-16 Period 2*
Group A, frail elderly receiving CALED	15	Baseline	Subgroup A1	8	Intervention	Control
			Subgroup A2	7	Control	Intervention
Group B, residents with dementia receiving CALED	9	Baseline	Subgroup B1	4	Intervention	Control
			Subgroup B1	5	Control	Intervention
Group C, frail elderly not receiving CALED	15	Baseline	Non	15	Control	Control

The trial will consist of two trial periods commencing respectively in the fall of 2016 (Pilot 1) and in the fall of 2017 (Pilot 2). CALED will be installed as a test installation in 24 residences and will be used on a voluntary basis, with the consent of the residents and/or their relatives. Findings from the test installation (the present trial) will be a basis for considering full scale installation in the entire housing facility comprised of approx. 100 living quarters. The commercially available CALED will be installed in collaboration with the company Zumtobel as appointed supplier. Zumtobel will calibrate light intensity (lux), color temperature (Kelvin) and wavelength (nm) according to the latest industry-based knowledge about the light phase-response curve for elderly (30).

In between the trial periods CALED will be used as regular lighting in "Sundhedshuset", why a wash-out period of 4 weeks will be added to the trial design depicted in Table 1 before Period 1 and before commencing the trial in 2017. Conducting the trial twice adds a possibility of further optimization of the induced CALED based on an interim analysis. Depending on the findings from the analysis, supplemental interventions targeted sleep quality, cognition or delirium may be suggested in the form of an additional protocol.

Recruitment process

Residents living in the flats/rooms chosen for CALED, and residents eligible for the control group, will be asked for participation in a randomized order by a coordinating nurse associated with "Sundhedshuset". The coordinating nurse will conduct a trial orientation session, where relatives are welcome to participate. Relatives of the incapacitated residents will be invited to participate. During the orientation session participants will be given the possibility of discussing their specific concerns about participation in the trial. Complete details of the trial will be given and questions from participants will be answered. In addition, information about the trial will be given to participants in writing. Informed consent will be obtained after min. 24-hours reflection time. Differentiated consent forms will be provided to the group of incapacitated residents determined for their relatives and GP's with specific information about proxy-consent following paragraph 19 in the Danish Committee Law. Request for consent through GP's will be forwarded only after consent from relatives.

Ethical considerations

There is a lack of evidence based knowledge to the benefits and drawbacks of welfare technologies as CALED on sleep quality, well-being and delirium for elderly with dementia. This creates the potential risk for inappropriate adaptation of the commercially available technology in elderly housing facilities. With the present trial we wish to uncover some of the considerations' municipalities should make before and during installation.

Also, as descried under Recruitment process, special considerations are being made towards the participation of the incapacitated residents, because their participation is crucial to the aim of the present trial. The considerations comprise the full involvement of their relative in order to address individual needs. Also, the trial has been designed to limit the control group to frail elderly to limit the number of incapacitated participants. Regardless of any consent given, the incapacitated residents can withdraw from the project by verbal or non-verbal utterances across the project's timeline under the responsibility of the principal investigator.

All eligible elderly residents will be interviewed by the coordinating nurse in a quiet meeting room offered by "Sundhedshuset" or in their private housing facility, following the orientation session and requested reflection time. The residents have the full right to have a spouse or relative present at the interview, and the right to consider participation for 24 hours before giving their consent. Both oral and written informed consent will be obtained. All individuals have the right to retract their consent at any time during the trial without giving any reason.

The trial follows the possible health related effect of a well-fare technology based on lighting, which is installed on a voluntary basis in the elderly housing facilities. The trial presents no intervention in treatment terms and bears no risk of medical side effects. Also, the funding bodies will have no authority over study design, collection and interpretation of data or the writing of manuscripts.

The trial adheres to the law for protection of patient' information and will obtain permission from Danish Data Protection Agency (Datatilsynet) in the Capital Region and will be registered at clinicaltrials.gov.

<u>Collaboration</u>

The trial takes place in collaboration between the municipality of Albertslund, Clinical Research Centre at Amager Hvidovre Hospital and Gate 21, a consortium for developing solutions for lighting. The long term objective of the collaboration is to create an environment between researchers, the elderly living in the municipality along with relatives and staff with the overall aim of creating a platform for evidence based knowledge for selecting and testing well-fare technologies designated elderly housing.

Researchers from Aalborg University will conduct a socio-anthropological survey in the elderly housing with focus on the technical application in the purpose of adding a comprehensive perspective to the final results. Consent for this survey will be obtained by the researchers from Aalborg University. Data from the two studies will not be pooled on an individual level.

The project will be organized with a steering committee, a head of the steering committee and a project group with a project leader. The steering committee will cover health professionals in two healthcare sec-

tors, specialists in internal medicine, sleep and inflammation and a representative of "Sundhedshuset". A GP representing one or several of the residents with dementia will be invited to join the steering committee.

Outcome measures

The trial participants will be assessed at baseline, and after 4, 8, 12 and 16 weeks, respectively. The test panel will consist of questionnaires, functional and cognitive tests, and a blood sample for detecting underlying causes of delirium and illness' during the trial. A full test panel will be used at baseline, after 8 weeks and after 16 weeks; with a smaller test panel being used after 4 weeks and 12 weeks. The tests are supplemented by sensory data from wrist and leg worn monitors in weeks 1, 4, 8, 9, 12 and 16. An overview of the outcomes to be assessed is presented in Table 2.

Table 2

Variables	**Baseline**	**4-week**	**8-week**	**12-week**	**16-week**
Primary outcome; quality of sleep					
PSQI; total sleep time	x	x	x	x	x
Secondary outcomes: sleep efficiency, mobility and immunological status					
1. Actigraphy, Actiwatch; sleep and wake activity	x	x	x	x	x
2. ESS; daytime sleepiness	x	x	x	x	x
3. Biomarkers; immunological status	x	x	x	x	x
4. CAM; delirium and confusion	x	x	x	x	x
5. MoCA, MMSE; cognition	x	x	x	x	x
6. MDI; depression	x		x		x
7. ActivePal; mobility	x	x	x	x	x
8. EQ-5D; well-being	x		x		x
9. ADL; self-efficacy;	x		x		x
Additional variables					
10. Registration; medication	x		x		x
11. IVI-test; vision	x				x
12. MNA; nutritional status	x		x		x

PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale; CAM: Confusion Assessment Method; MoCA: Montreal Cognitive Assessment; MMSE_ Mini Mental State Examination; MDI: Major Depression Inventory; EQ-5D: EuroQol; ADL: Activities of Daily Living; MNA: Mini Nutritional Assessment

Primary outcome measure

The primary outcome will be change in the Pittsburgh Sleep Quality Index (PSQI) between the intervention and the control (31). The PSQI) is a measure of sleep quality consisting of 19 self-report items. The participants indicate the amount of sleep obtained as well as factors interfering with their sleep. The PSQI assesses subjective sleep efficiency, sleep latency, sleep duration, sleep quality, sleep disturbance, use of sleep medication and daytime dysfunction due to sleepiness. The subscale scores are summed to a total score of 0 to 21 with higher scores indicating poorer sleep quality and with a score of >5 being indicative of poor sleep (31).

Secondary outcome measures

The secondary outcomes will be:

1) Sleep and wake activity by the Actiwatch Spectrum (Philips Respironics, Bend, OR, USA) which is a wrist worn monitor containing a solid-state "Piezo-electric" accelerometer. The Actiwatch will be worn on the wrist of the non-dominant hand for 7 consecutive days, and will measure total sleep time (TST: the amount of time the participant spends sleeping while in bed), sleep latency (SL: time from getting to bed until falling asleep), wake after sleep onset (WASO: minutes awake during a sleep period after the initial onset of sleep, and sleep variability (SV: inter-day variability in TST). All parameters will be measured between 10 pm and 7 am. Also, number of naps between 7am and 10 pm will be assessed.

2) Daytime sleepiness by the Epworth Sleepiness Scale (ESS) (32). The ESS is an 8-item self-report measure in which participants indicate the likelihood of dozing off or falling asleep in eight different conditions. Responses are summed to a total score from 0 to 24. Higher scores indicate greater sleepiness.

3) Inflammatory and infectious biomarkers based on previous evidence about their role in delirium and well-being, and their usefulness in reflecting illness and e.g. nutritional conditions: immunological parameters (c-reactive protein (CRP), soluble urokinase plasminogen activating receptor (suPAR), white blood cell counts and inflammatory receptors, cytokines and chemokines (33,34)); endocrinological parameters (cortisol, melatonin, leptin and glucose) (35); parameters involved in diagnostics of delirium (albumin, phosphate, magnesium, sodium and potassium[1]) (36).

4) Delirium by the Confusion Assessment Method (36), which is a 4-criteria test for the identification of delirium in accordance with the DSM delirium criteria; the 4 criteria are: 1) acute change in mental status with a fluctuating course, 2) inattention, 3) disorganized thinking, and 4) altered level of consciousness. Delirium is considered present if criteria 1 and 2 are present and criteria 3 or 4.

5) Cognition by the Mini Mental State Examination (MMSE) (37) and the Montreal Cognitive Assessment (MoCA) (38); where MMSE is an 11-item cognitive test with a maximum score of 30, with lower scores indicating more severe cognitive problems. The cut point established for the MMSE defines 'normal' cognitive function and is set at 24. MoCA is a cognitive screening measure covering 7 cognitive domains using a total score of 30 with a cut-off of less than 26 to signify impairment.

6) Depression by the Major Depression Inventory (MDI) (39,40); The MDI contains items that cover the ICD-10 symptoms of depression including DSM-IV major depression symptoms as well. The MDI contains 10 items with a maximal score of 50. A score of 20-24 denotes mild depression, 25-29 moderate depression and 30 or above major depression.

7) 24-h mobility will be measured by an activPAL3™ activity monitor (PAL Technologies Ltd., Glasgow, UK). The participant will be asked to wear an activPAL3™ on the thigh, 24h/day, for five one week periods: week 1, week 4, week 8, week 9, week 12 and week 16. The activPal3™ accelerometer measures time spent sitting/lying, standing and walking, the number of steps taken, cadence and the number of sit-to-stand and stand-to-sit transitions (41–43).

8) Health related quality of life by the EuroQol (EQ-5D-3L) (44); which is a three level version of the EQ-5D measuring health-related quality of life by assessing aspects of physical, mental and social functioning with three response levels. Physical functioning is encompassed in mobility and a self-care item, social functioning in a usual activities item, and mental functioning in an anxiety/depression item.

9) Activities of daily living (ADL) by the Barthel Index 20 (BI) (45); which is a performance evaluation tool assessing a person's capacity to perform 10 daily tasks without assistance and provides a summed, overall BI score (0-20 points) that reflects the patient's level of independence.

<u>Additional variables</u>

[1] Diagnostics for delirium, www.sundheds.dk

Descriptive variables and possible confounders and modifiers will be collected and will include: sex, age, chronical illnesses, education, hospital admissions, medications, visual impairment by the Lindcon Optical Group table based on the Danish social classification system for visual impairment (category 0, A-D) (46), and nutritional state by the Mini Nutritional Assessment (MNA) (47).

Data

Data collection

All data collection and assessments will be performed at "Sundhedshuset" by trained staff under the instruction and supervision of the primary investigator. Date and time of all assessments will be noted. Blood samples (approximately 20 ml) will be taken on 5 occasions in the "Sundhedshus" and by trained staff under the supervision of the primary investigator. Date and time of blood sampling will be documented.

Blood samples will be transported to Hvidovre Hospital for analysis after collection and analysed routinely at the Biochemistry Department for all parameters excluding non-routine analyses such as cytokines and chemokines which will be analysed after week 16 and before Pilot 2. Any additional plasma will be stored in a biobank for further analysis to the purpose of the present trial and application to the Scientific Committee.

Data management

All case report forms will be checked for errors and missing data by the assessor before being archived in a trial database and all paper-based versions will be locked in a filing cabinet in a locked room to ensure confidentiality. The primary investigator will have access to the full dataset, containing no information about group allocation, and co-investigators will have access as needed. Data management will follow the rules of the Danish Data Protection Agency.

Statistics and power calculations

Power calculation

The number of participants who can be exposed to CALED is given by the municipality's capacity for installing CALED in "Sundhedshuset" which is in 24 residences. A power calculation for the Pittsburgh Sleep Quality Index based on a paired t-test with an alpha of 0.05, 24 pairs, a correlation of 0.8, a stand deviation of 5.6 (18) showed it possible to detect a minimal clinical difference of 2 with a power of 0.76. This does not account for possible drop-outs, but we expect that the inclusion of 15 control participants not exposed to CALED will increase power. Moreover, we expect that a maximum of 3 citizens will not want to participate.

Descriptive data and outcome analysis

Data will be presented as means with standard deviations, medians with inter-quartile ranges or frequencies with percentages depending on the distribution of the variable.

The primary analysis for the primary outcome will be performed using the SAS procedure PROC MIXED (dif (intervention-control)).The difference in the PSQI scores between the intervention period and the control period will be analysed using mixed models, with treatment (intervention and control) and period (period 1 and period 2) as fixed effects and the participant identification as random effect. Secondly, the models will be adjusted for baseline PSQI scores.

The primary analysis will follow the intention-to-treat principle using multiple imputations in case of missing outcome measures. For the secondary outcomes, similar analyses will be performed. Moreover, all analyses will be repeated using adjustments for baseline vision. All models will be investigated for goodness-of-fit (linearity, variance homogeneity and normal distribution of residuals) by visual inspection of plots and remodelling will be performed accordingly. All statistical tests will be performed using SAS (SAS Institute Inc., Cary, NC, USA) and p values ≤0.05 will be considered statistically significant.

Budget and financial conditions

Installation and calibration of the CALED has been funded by The ElForsk foundation and are being conducted in collaboration between Aalborg University, Zumtobel and the municipality of Albertslund. The present trial will be mutually financed in collaboration between municipality of Albertslund and Clinical Research Centre at Amager Hvidovre Hospital. The grant from the ElForsk foundation will cover expenditure's for analyzing blood samples.

	2016	**2017**	**AHH**	**Albertslund**	**Gate 21**
Scientific project manager, part time	100.000	400.000	100.000	400.000	0
Project coordinator, health care on-site	150.000	150.000		300.000	
Sampling and testing	50.000	100.000	50.000		100.000
Publication costs		20.000	20.000		
Overall costs	300.000	670.000	170.000	700.000	100.000

Expenditures in DKK

Communication and publication plan

The results will be published in peer reviewed international journals. The results and learnings from the project will be disseminated to residents and staff in "Sundhedshuset" using evidence based knowledge about implementation through the research conducted at Clinical Research Centre, and to a wider audience through the activities off Gate 21. The scientific results will also be disseminated through teaching activities and conference presentations of the investigators.

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