AUS DEM LEHRSTUHL FÜR PSYCHIATRIE
PROF. DR. RAINER RUPPRECHT

DER FAKULTÄT FÜR MEDIZIN
DER UNIVERSITÄT REGENSBURG

Assessment of the Acceptance of a specialized granulate blanket on patients with moderate to severe dementia and sleep disturbances

Inaugural – Dissertation
zur Erlangung des Doktorgrades
der Medizin

der
Fakultät für Medizin
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Deutsche Zusammenfassung:

Demenz ist eine weltweit zunehmende Erkrankung. Da die Behandlungsmöglichkeiten derzeit begrenzt sind, ist es umso wichtiger die Lebensqualität der Demenzkranken und ihrer Angehörigen zu erhalten.
Schlafstörungen sind eine häufige Komorbidität der verschiedenen Demenzarten, da die degenerativen Prozesse der Demenz auch die für gesunden Schlaf verantwortlichen Hirnareale schädigen. Basierend auf der Theorie der sensorischen Integration entwickelten wir die Idee, den Nachtschlaf von Demenzkranken durch den Einsatz von Granulatdecken zu verbessern. Um dies weiter zu untersuchen, wurde eine prospektive klinische Studie mit 100 Patienten durchgeführt, bei der die Schlafqualität und -quantität von Patienten mit mittelschwerer bis schwerer Demenz beim Schlafen mit einer Ganulatdecke im Vergleich zum Schlafen mit einer normalen Decke untersucht wurde. Für eine sichere Durchführung dieser Studie waren einige Vorarbeiten erforderlich. Diese Arbeit ist eine vorbereitende Studie, die die Akzeptanz der Granulatdecke ermittelt und den Zusammenhang zwischen der Akzeptanz und dem Schweregrad der Demenz, der Außentemperatur, dem Geschlecht und dem Alter untersucht.
Die Ergebnisse dieser Studie zeigten eine allgemein gute Akzeptanz der Granulatdecken und bestätigten zudem, dass die Decken sehr sicher sind. Dies ist eine wichtige Voraussetzung für unsere Hauptstudie.
Bezüglich der Abhängigkeit der Akzeptanz von den Cofaktoren (Alter, Schwere der Demenz, Außentemperatur und Geschlecht) konnten wir keinen statistisch relevanten Zusammenhang nachweisen. Die deskriptiven Statistiken zeigen eine tendenziell schlechtere Akzeptanz bei heißen Außentemperaturen und bei zunehmender Schwere der Demenz. Insgesamt ergibt sich jedoch kein relevantes Ausschlusskriterium für die Nutzung der Granulatdecken.

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1. Introduction

1.1 Epidemiology

Dementia has become a significant public health problem.

With a prevalence of approximately 50 million people worldwide and 10 million new cases every year, dementia is rated the 7th leading cause of death around the world and among the top three in high income countries. (1)

The estimated global economic cost caused by dementia was over $948 billion US dollars in the year 2018 and is estimated to hit 2 trillion US dollars by 2030. (2)

However, these numbers are about to rise, as demographic change leads to an increasing number of older people. The World Health Organisation (WHO) estimates that the prevalence of 50 million people will have doubled by 2030 and even tripled by 2050, with a majority of people coming from low and middle-income countries. (1)

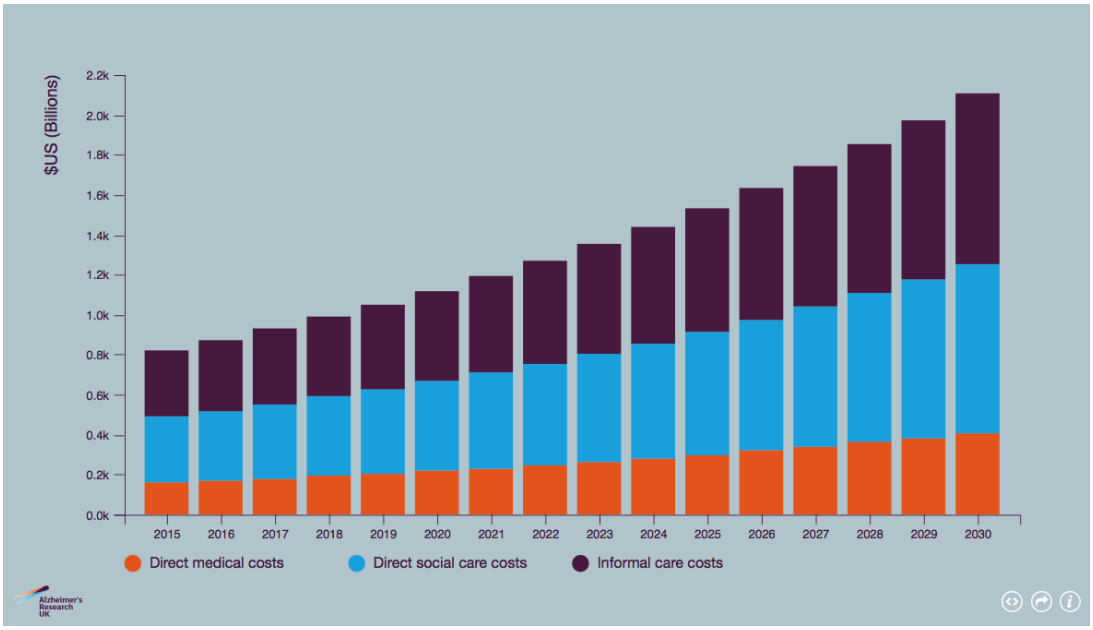


Figure 1: Estimated global costs due to dementia through the years 2015 to 2030, divided into direct medical costs, direct social care costs and informal care costs

Regarding these upcoming problems, researchers around the world are searching for a cure for diseases leading to the syndrome of dementia. Most medications which are currently on the market can only reduce symptoms and may improve quality of life for some patients, but it is unclear if they can stop the progression of the disease. (3)

Meanwhile, two drugs to treat especially Alzheimer´s disease offer at least some reason for hope for patients with this form of dementia. The drugs are called Donanemab and Lecanemab

and both work in similar ways. They are antibodies directed at the beta-amyloid protein. They bind to the amyloid plaques so that those plaques can be removed by the body´s immune system. Current studies propose that Lecanemab can reduce the amount of amyloid build-up in the brain shown in a Positron Emission Tomography (PET). (4)

In April of 2025 Lecanemab has been approved by the European Medicines Agency (EMA), it had been approved in the USA and several Asian countries and Israel in 2023; The antibody drug Donanemab is currently being examined for approval in Europe.

While showing moderately less decline of cognition in initial trials, it is associated with adverse events and has to be further tested in larger trials.

Unfortunately, these drugs are not yet available for everyone. Thus, it is still very important to reduce the consequences and burdens which are associated with dementia and to try to keep the quality of life of the patients and caregivers high, using pharmacological and non-pharmacological treatment.

1.2 Types of dementia

The word dementia comes from the Latin word “demens”, which means “without sense” or “being out of one´s mind.” Dementia describes a syndrome characterized by progressive memory loss that interferes with day-to-day life and causes impairment of other cognitive functions, such as orientation in place and time or decline of emotional control or motivation. (5)

It is often a close family member or the patient himself who notices the beginning cognitive decline in everyday life. (6)

Yet, setting the exact etiological diagnosis of early dementia is not simple, as dementia has various forms with quite heterogenous etiologies. (7)

Most types of dementia develop slowly, with an expected survival time of up to 10 years. The progression can fluctuate or steadily worsen over time and there are even cases which rapidly end fatally, all depending primarily on the underlying cause of dementia. (8)

1.2.1 Alzheimer´s disease

In 1901, the German psychiatrist Alois Alzheimer was the first to report about a 51-year-old woman who showed symptoms of memory loss, insomnia, paranoia and anxiety. After her death five years later, Alzheimer found neurofibrillary tangles and senile plaques in her brain. This

marked the discovery of the new disease “presenile dementia”, which was later named Alzheimer´s disease. (9)

Nowadays, representing about 70% of all cases of dementia, Alzheimer’s disease (AD) is the most common cause of dementia. (10) Currently, 6% of all people over 65 years of age are diagnosed with Alzheimer´s disease, with the incidence and prevalence of AD increasing exponentially with age. (11)

1.2.1.1 Subtypes

Approximately 90 – 95% of the AD cases are sporadic. (6) The sporadic form of AD is typically a disease of increased age.
However, the other 5% suffer from the rare form of early onset dementia, which occurs before the age of 65. (12) Some of these early onset forms seem to have a familial component, often showing autosomal dominant mutations in the genes encoding for the amyloid precursor protein (APP), presenilin 1 (PSEN1) and presenilin 2 (PSEN 2). (10)
Apart from the classic presentation of Alzheimer´s disease, there are some types without the typical presentation which are referred to as atypical forms of Alzheimer´s disease. (11)
Examples for atypical presentations include a posterior variant, primary progressive aphasia and a frontal variant of AD, each accompanied by damage in the related brain region.
Patients with the posterior variant often first report visual impairment, with symptoms like agnosia, neglect, alexia and limb apraxia.
Primary progressive aphasia is associated with language difficulties with a relative sparing of cognitive memory functions in early stages. Typical symptoms include problems in word finding and impairment in sentence repetition.
Lastly, patients suffering from the frontal variant of AD show early behavioral changes. Progressive apathy or behavioral disinhibition are common symptoms. (11) (13)

Apart from the above-mentioned special types of Alzheimer´s disease, the coexistence of AD pathology and other pathological changes, mostly of vascular origin, is common and identifies as mixed Alzheimer´s dementia. Criteria for diagnosing a mixed dementia of Alzheimer´s and vascular type are clinical presentation, preferably together with evidencing biomarkers of typical or atypical Alzheimer´s pathology, plus the detection of a pathology related to a stroke (vascular lesions, microangiopathy) in the MRI or signs of an acute stroke.

This mixed form is becoming more and more important, as the incidences are rising, especially in people of increased age with more comorbidities. (13) (14) (15) (16)

1.2.1.2 Pathology

The molecular pathology of AD is complex and not completely understood, but there are seminal histological features. (17) Histological damage begins even before the clinical onset. Preclinically, the amyloid ß peptides aggregate into amyloid plaques, which accumulate in the brain, leading to long term neuron loss. (11)
The other pathophysiology concerns the tau protein, which is normally responsible for the stabilization of the microtubule in the cytoskeleton network of the neurons. In the course of Alzheimer´s pathology, abnormal hyperphosphorylation of the tau protein occurs, which results in the formation of neurofibrillary tangles, consisting of aggregated tau protein .These tangles disturb the function of the microtubule, impair axonal transport and lead to synaptic and neuronal harm. (18) (10) (6)

1.2.1.3 Diagnostics

Alzheimer´s disease is still predominantly diagnosed upon the clinical symptoms.
The classic symptoms are memory loss, especially of the short-term memory, followed by progressive deterioration of language and executive dysfunction. (19)
The spectrum of deficits in AD are likely related to the affected brain structures. In the early stages of the classical variant AD, especially the pyramidal layer of the subiculum and hippocampus are infested with the accumulated amyloid deposits. This explains the early impairment of the short-term episodic memory, which is processed and retrieved in the hippocampus. (20) (13) (21)
As the pathology advances into other areas of the brain in later stages of the disease, more and other symptoms are presented by the patients. In the intermediate state, memory loss also applies to remote memory and the patients have more and more difficulties in naming objects and persons. These symptoms worsen in the severe state. In this state, the patients are typically not capable of accomplishing their everyday life on their own any more. (6)

Apart from cognitive impairment, 60 – 80% of AD patients display neuropsychiatric symptoms. (22) Depression is one of the typical and early mental disorders and applies to up to 30% of

patients with Alzheimer´s disease. Additionally, they can show hallucinations and delusions, due to limbic and paralimbic atrophy. (23) Other neuropsychiatric symptoms which usually develop in later stages include aggression, anxiety and sleep disturbances. (6) (11) (17)
These neuropsychiatric symptoms are not only problematic for the patient, but are also a heavy burden for family members and caregivers. (24)

The diagnosis of Alzheimer´s disease can be supported by the examination of biomarkers. These biomarkers can be found in cerebrospinal fluid (CSF) and in the amyloid positron emission tomography (PET). Biomarkers in CSF include the concentration of Beta-Amyloid 1-42 (Aß1-42), total tau protein and phospho-tau protein. Aß 1-42 reversely reflects the amyloid burden of the brain, which means a low CSF Aß concentration is a sign for highly active AD pathology. Even better than the isolated determination of CSF Aß 1-42 reduction is the analysis of the reduction of the Aß1-42/Aß 1-40 ratio. It shows sensitivities of up to 96% for detection of AD. This biomarker can be found even before symptom onset. The other CSF biomarkers T-tau (total tau) and p-tau (phosphorylated tau) directly reflect the neurofibrillary tangles in the brain. To increase the accuracy of AD diagnosis all three biomarkers should be determined combined; low Aß1-42 levels and high T-tau and p-tau concentrations in the CSF are considered a sensitive and specific diagnostic criterion for Alzheimer´s disease.
Furthermore, there is a way to identify amyloid and tau in PET scans of the brain. Amyloid PET is a validated pathophysiological marker for fibrillar amyloid and therefore an increased retention in amyloid tracer PET can be indicative of AD pathology. (13) (18) (25)
In conclusion, all these biomarkers indicate Alzheimer pathology and are needed for the diagnosis of pathophysiologically approved Alzheimer dementia. (26)

1.2.1.4 Risk factors

Although the cause of Alzheimer´s disease is not certain, there are some risk factors which are linked to the disease. Sporadic AD, for example, is probably due to multifactorial genetic and environmental risk factors. (10)
The first risk factor is increasing age, as Alzheimer dementia is typically a disease of older age. (17) Other risk factors include cerebrovascular diseases, high blood pressure, type 2 diabetes, body weight and plasma lipid levels, smoking and traumatic head injuries. (27)
The risk of getting AD is also increased in families with cases of this disease. Not only the early onset type, but also the sporadic form has a genetic component. This is demonstrated by the

ApoE4 gene. (28)

Physiologically, Apolipoprotein E (ApoE) is a cholesterol carrier that is responsible for lipid transport and injury repair in the brain. There are three existing alleles of this ApoE gene on chromosome 19: E2, E3 and E4. Many studies have shown that the presence of ApoE4 allele is the strongest genetic risk factor for AD. Individuals with one E4 allele (in comparison with people with no E4 allele) are four times more likely to develop AD, people with both E4 genes eight times more likely. (6) (29) Although the risk of AD is higher, if a person has the Apo E4/E4 genotype, the genetic testing of this allele is not yet recommended as a screening method for Alzheimer´s disease. (16)

1.2.2 Vascular dementia

Vascular dementia is the second most common form of dementia after Alzheimer´s disease. The prevalence of this dementia type rapidly increases from about 2%-3% in the age group of 70 – 75-year-old people to 20% – 25% among those aged 85 and over, which demonstrates that vascular dementia is predominantly a problem of higher age. (30) (31)

Vascular changes of the brain resulting in cognitive impairment of at least one cognitive function is defined as vascular cognitive impairment (VCI). The most severe form of VCI is vascular dementia (VaD). (32) The classification of VCI is more difficult than for AD. It is based on the onset of cognitive impairment, the location, type, number and size of brain lesions (cortical or subcortical, single or multiple stroke, lacunar), the mechanisms of vascular change (ischemic or hemorrhagic), the size of involved vessels (small or large vessels) and the origin of vascular disease (atherosclerosis, arteriosclerosis, inflammation or genetic). (14)

Since there are many different forms and clinical presentations of VCI, there is no generally accepted scheme for diagnosis of vascular dementia. So, in order to diagnose a VCI, evidence of a cognitive impairment and of a stroke in the past or other cerebrovascular damages are needed. (33) (34)

1.2.2.1 Symptoms

Although there is a large overlap in symptoms between Alzheimer´s disease and VaD, the clinical presentation and process of cognitive change is much more variant in VaD. This variable

clinical manifestation is related to the different types and locations of damage in the brain seen in vascular dementia. (34) (14)
Frequent symptoms of vascular dementia include a decrease of the executive functions, memory loss, impaired attention and reduced verbal fluency, which can often also be seen in AD.
Other typical features of VaD are gait disturbances, dysarthria, dysphagia, urinary incontinence, pseudobulbar palsy, lower body parkinsonism, minor stroke symptoms and vertigo. The extent and expression of these symptoms can vary.
(33) (14) (35)
Similar to AD patients, patients with vascular dementia also face neuropsychological problems such as depression and apathy, whereas delusion and hallucinations are less prominent in vascular dementia. (34)

VaD often progresses stepwise with fluctuation, whereas the cognitive and behavioral decline in AD is more gradual. These alternations of cognition, alertness and attention are a key feature of vascular dementia.(14) (36)

1.2.2.2 Pathology

In contrast to Alzheimer´s disease, the pathology of VCI relies on different causes and there are many theories about the entity of this disease.

The idea of a vascular pathology connected with cognitive impairment is quite old. One of the first published hypotheses, which was proposed by Hachinski in 1974, suggested that the occurrence of multiple small or large cerebral infarcts is responsible for vascular dementia. He called this form multi-infarct dementia. (37) More than ten years later, Hachinski recognized that also diffuse white matter lesions, called leukoaraiosis, were frequently correlated with cognitive impairment, even more commonly than the multiple infarcts.
In 1996, Loeb and Meyer postulated classification of the different forms of vascular dementia:

Type 1 is the aforementioned multi-infarct dementia, which was previously described by Hachinski. It stipulates that the cognitive impairment is the result of different cerebral infarcts, which accumulate and lead to destruction of brain mass. (35)

Type 2: strategically placed infarcts. For this type, only one infarct in a critical region of the

brain is needed to trigger cognitive detriment. These critical regions are those which are especially important for cognitive functions, such as the frontal lobe, thalamus, basal ganglia or angular gyrus. (38) (35)

Type 3: multiple, subcortical lacunar infarcts. This is the most common subtype of VCI. (39) A lacune indicates a lesion smaller than 1.5 cm in diameter. So subcortical lacunar infarcts are small microangiopathic infarcts due to arteriosclerosis. (6)

Type 4: vascular dementia due to leukoaraiose. It is defined as a bilateral symmetric change in the cerebral hemispheric white matter, which is often found in a CT and MRI. (40) Many diseases can lead to these cerebral changes.
One example is Binswanger´s subcortical arteriosclerotic leuko-encephalopathy. This form of vascular dementia is the result of atherosclerosis of the arteries that feed the subcortical white matter, leading to a restricted blood flow in this area. (41) Binswanger disease is often associated with stroke risk factors like hypertension. (39) (6)

Type 5: Type 5 presents a mixture of Type 1, 2 and 3, often also referred to as the "shotgut method." Many small, diffuse lesions combine, leading to the destruction of a critical mass of brain and therefore trigger vascular dementia. (35) (39)

Type 6: single or multiple hemorrhagic cerebral lesions. More rarely, vascular dementia can also be the consequence of one or more intracerebral hemorrhages, which are usually induced by hypertension, ruptured aneurysms, or vasospasm.

Type 7: genetically induced subcortical dementias.
Firstly, the subcortical damage can be induced by cerebral amyloid angiopathy (CAA). CAA is defined as the accumulation of aggregated amyloid peptide, mostly of the ß type, in small cerebral vessels, especially those penetrating the cortex, eventually leading to lobar intracerebral hemorrhages, cortical infarction and dementia. These amyloid aggregations are expected to have a genetic relation and can be found in 10-30% of all brain biopsies and even more frequently in elderly people. (35) (38) (42) (43)Secondly, anoften underrated, reason for subcortical vascular dementia is CADASIL. CADASIL stands for cerebral autosomal dominant arteriopathy with subcortical infarcts and leucencephalopathy and is caused by a mutation in the NOTCH 3 gene. This mutation induces direct microvascular damage leading to different

clinical appearances like migraines, psychiatric diseases (e.g. depression, bipolar disease) and strokes which can ultimately lead to dementia. (44) (35) (33)

Lastly, Type 8: mixed dementia, here as the combination of Alzheimer´s dementia and vascular dementia, was already mentioned in chapter 1.2.1

1.2.2.3 Risk factors

Vascular dementia is predominantly associated with vascular and lifestyle risk factors and therefore can at least partially be prevented.
Vascular risk factors include age, hypertension, dyslipidemia, diabetes, smoking, cardiovascular disease, atrial fibrillation, hyperhomocysteinemia, systemic inflammation and sleep apnea. In reducing these risk factors for elderly people the prevalence of dementia can be reduced by 50%. (14)
A stroke in the past is also an alarming risk factor for vascular dementia. About 30% of stroke patients develop a cognitive dysfunction within the following 3 years. (38) (35)
The prevention of VCI lies mainly in the identification and treatment of these risk factors. (10) (14)

1.2.3 Lewy Body dementia and Parkinson´s dementia

Dementia with Lewy Bodies (DLB) and also Parkinson´s disease dementia (PDD) are common types of neurodegenerative dementias.(10)
Although Dementia with Lewy Bodies and Parkinson´s dementia are not the same disease, they originate from the same pathology, as both are a type of alpha synucleopathy and will be reviewed together. (45)

Parkinson´s disease (PD) is usually primarily associated with movement disorders, but up to 70% of patients with PD eventually develop dementia in the course of the disease (usually 10 or more years after initial motor symptoms). (46) (47)
DLB had been underrated for a long time and is now being diagnosed more frequently, even though it is not always easy to differentiate from AD. This is firstly due to partly similar clinical presentation and secondly, AD and DLB can occur combined, as a mixed pathology.

1.2.3.1 Symptoms

DLB and PD dementia have overlapping symptoms. The only significant difference is the point of onset. In DLB, dementia often indicates the onset of the disease, later followed by the typical parkinsonian motor signs. In contrast, Parkinson´s disease dementia is diagnosed when cognitive decline develops in the course of an already well-established Parkinson´s disease, one or more years after the onset of PD. (45)

The main clinical symptom and core criterium of both diseases is cognitive impairment. Especially attention, executive functions and visuo-spatial skills are affected early in the course of DLB, with memory loss, which usually is the initial symptom of AD, following at a later stage. (48)

Other clinical core criteria are essential in diagnosing DLB and PD.
Firstly, there are fluctuations of cognitive malfunction. This is a very common sign, with prevalence of up to 80%. Episodes of spontaneous alterations in cognition, attention and arousal can be variable in duration, severity and type. They can last seconds to days and may reach from a slight decline in daily life activities to incoherent speech, motor arrest, variable attention and even clearly reduced consciousness. This feature often turns out to be quite challenging for clinicians, but also for caregivers and family. (49) (50)

Another typical clinical feature of DLB and PD dementia are visual hallucinations. These are usually well-formed and often feature people or animals. Visual hallucinations are a good diagnostic criterion to help differentiate between Lewy Body dementia, where they occur in earlier stages of the disease, and Alzheimer´s dementia, where they sometimes occur in late stages of the disease. (50) (23) (6)
REM-associated sleep behavior disorder also belongs to the core clinical features. It is a form of parasomnia in which the normal paralysis of REM sleep is impaired, leading to enactment of dreams and hence possible injury of patients themselves or their bedpartner. (49) (48)

The last core criterion is parkinsonism. Ninety percent of DLB patients and all PD dementia patients show spontaneous parkinsonian symptoms such as bradykinesia, limb rigidity and rest tremor. (50) (51)

1.2.3.2 Pathology

DLB and PD dementia are characterized by the development of Lewy Bodies and Lewy neurites, which consist of aggregated alpha-synuclein, a protein expressed at pre-synaptic terminals of neurons. (51)
Due to neuroinflammatory processes, these alpha-synuclein proteins can be overexpressed and misfolded and in consequence accumulate into Lewy Bodies. (52) (53)
At some point, these aggregations lead to neuron loss, resulting in widespread damage in certain regions of the brain. These regions are mainly the brainstem, substantia nigra, limbic system and the anterior frontal, occipital and temporal lobes. (54) (55)

1.2.3.3 Diagnostics

Apart from the clinical core criteria mentioned above, there are other diagnostic ways to debunk a DLB or PDD.
The 2017 consensus report of the DLB Consortium has updated the diagnostic biomarkers.
They state that there are indicative and supportive biomarkers. If an indicative biomarker and at least one core clinical criterion are found in a patient, probable DLB should be diagnosed. These indicative markers include reduced DAT (dopamine active transporter) uptake in basal ganglia in SPECT (single photon emission computed tomography) or PET CT. Additionally, reduced uptake on metaiodobenzylguanidine myocardial (MIBG) scintigraphy can be seen in Lewy body dementia, as sympathetic cardiac innervation is reduced in patients with this form of dementia. Lastly, polysomnographic confirmation of REM sleep without atonia can help lead to the diagnose of DLB.

In addition to the indicative biomarkers, the Consortium has determined other supportive biomarkers, which can be spotted in EEG, CT or PET and can help with the diagnosis, but do not have clear diagnostic specificity. (50)

1.2.4 Frontotemporal dementia

One of the rather rare forms of dementia is the frontotemporal dementia (FTD), which is characterized by degeneration in the frontal and temporal lobe and is also known as “Pick´s

disease." Similar to early onset AD, most cases of FTD occur between the age of 45 and 64. (56)

The disease can be categorized into two main subtypes, depending on the presented clinical features: the behavioral variant FTD and the primary progressive aphasia (PPA), which itself can again be subclassified into three variants: the semantic variant PPA (sv-PPA), the nonfluent variant and the logopenic variant (this variant is sometimes also caused by AD pathology). The behavioral variant FTD is the most common, at about 50%. (57) (58)

1.2.4.1 Symptoms

Contrary to the other types of dementia, early memory loss and problems in orientation are not the main factors of FTD. The core features of FTD concern behavior, cognition and neurological changes. (56)

Patients with behavioral variant FTD show early behavioral disinhibitions, which can present as loss of manners, loss of sympathy for others, apathy or impulsivity. Also, hyperorality or change in diet can be an early symptom of the behavioral variant. (58) (59)

In primary progressive aphasia, impairment of language is paramount. Whereas agrammatism and inconsistent speech sound errors are most prominent in the nonfluent variant PPA, the semantic variant presents with impaired single word comprehension and severe naming problems. (60)

As the disease progresses, the differences in the variants meld and the course becomes more uniform, with patients eventually showing global cognitive impairment and motor deficits, including parkinsonism. (58)

1.2.4.2 Pathology

The underlying cause of FTD is frontotemporal lobar degeneration, including neuronal loss, gliosis and microvascular changes. (58)

The pathology of frontotemporal dementia is similar to that of Alzheimer´s disease because it also relies on protein deposit in certain regions of the brain. The pattern of deposit and the structure of the protein are heterogenic and depend on the clinical variant.

The most frequent form of pathology, which can also be seen in AD, are aggregations of hyperphosphorylated tau protein. This is often found in patients with the behavioral variant

FTD. (56) (51)

The other frequently found pathology consists of abnormally phosphorylated and ubiquinated TDP- 43 protein. Normally, TDP- 43 protein is an RNA- binding protein of normal cells, but through the phosphorylation and ubiquination, it forms neuronal cytoplasmic inclusions, which finally lead to neurodegeneration. (61)

Although most cases of frontotemporal dementia are sporadic, FTD has a highly genetic component. More than 10% of FTD patients show an autosomal dominant pattern and approximately half of them have a family history of dementia. The most common genes which are associated with FTD are MAPT, GRN and C9ORF72. (57)

1.2.5 Other forms of dementia syndrome

Apart from neurodegenerative or vascular causes, there are many other pathologies which can lead to a dementia syndrome, some of them even reversible. These will just be briefly mentioned, as discussing them in detail would go beyond the scope of this paper.

Predominantly, medications which could induce cognitive impairment and arousal problems as side effects and also metabolic diseases, such as thiamine or vitamin B12 deficiency or hyperthyroidism, may lead to cognitive disturbance which can fulfill the criteria for setting the syndromological diagnosis of a dementia syndrome. (62)

Furthermore, intoxications can cause dementing symptoms. Alcohol-induced dementia, heavy metal intoxication and other drugs often lead to persistent cognitive impairment severe enough to be described as dementia. Further, structural brain lesions can also indicate the diagnosis of dementia. These brain damages can result from tumors, trauma or normal pressure hydrocephalus and other neurological illnesses.(63)

Another important trigger for dementia are infections. Neurosyphilis, Creutzfeld-Jakob disease, HIV and the Cytomegalovirus can all lead to impaired memory and attention. (6)

It is important to also have these pathologies in mind, as many of them are reversible under appropriate treatment, contrary to the neurodegenerative dementias.

1.3 Sleep Disturbances

1.3.1 Normal sleep

It is commonly known that healthy sleep is important for our body functions and for our

neuropsychological well-being. It is proposed that sleep is essential for promoting body growth, saving and restoring energy, regulating body temperature, metabolism and immune functions and consolidation of memory. (55)

Our sleep cycle is divided into various stages. Firstly, two types of sleep can be differentiated: Non-rapid eye movement (NREM) sleep and rapid eye-movement (REM) sleep. (64) According to the American Academy of Sleep Medicine, NREM sleep again can be divided into three subgroups. Stage N1, which is the transition between wakefulness and sleep, Stage N2, with typical findings of sleep spindles and k-complexes on the EEG and Stage N3, which is also known as slow wave sleep. (65) This slow wave stage is referred to as deep sleep and is important for the consolidation of declarative memory. (55)
In a normal eight-hour sleep cycle, people have five to six NREM-REM cycles, with each cycle lasting about 90-120 minutes. (55)

For all these cycles to run smoothly, a complex regulation system is needed. The main regions of the brain where sleep and circadian rhythm are regulated are the anterior hypothalamus, reticular activating system, suprachiasmatic nucleus and pineal gland. (47)
On the one hand, sleep is induced by inhibiting neurons of the ventrolateral preoptic area, which shut down the arousal system. (66)
On the other hand, the circadian rhythm regulates the sleep/wake cycle. The central regulator of the circadian rhythm is the suprachiasmatic nuclei (SCN). It gets input from the retina, which detects light. As a result, the SCN synchronizes the biological clock to the day-night cycle. (67) (68)
The circadian rhythm not only induces sleep, but also regulates other cycles, like the rise and fall of body temperature, heart rate, blood pressure and release of different hormones. (67)
One of these hormones is melatonin. It is a metabolite, which is produced in the pineal gland and plays a key role in the regulation of sleep. Melatonin levels are high at night and low at sunrise, which explains its function as the “sleeping hormone.” (69)
Although the circadian rhythm is precisely regulated, it changes as age increases. Even healthy elderly people have a decreased quantity and quality of sleep, with more fragmentation of sleep and frequent daytime naps. (70)
Additionally, the sleep architecture itself changes in older subjects. They spend more time in sleep stages N1 and N2, and the amount of slow wave sleep and REM sleep declines, in comparison to younger people. (55)

1.3.2 Sleep disturbances in dementia

Dementia not only influences memory, but also the behavior of the patient, which results in behavioral and psychological symptoms of dementia, or BPSD for short. Common BPSD are aggression, depression, anxiety, apathy, motor abnormalities, disinhibition, agitation, eating disorders and sleeping disturbances. (71)
In addition to sleep changes, which normally occur with increasing age, the neurodegenerative changes of dementia raise the severity, frequency and time of onset of sleep disturbances indementia patients, compared to healthy people of the same age. (67) (72)

The significant sleeping disorders of people with dementia include insomnia, hypersomnolence, circadian rhythm disfunction, sleep apnea, motor disturbances and parasomnias. These will be described in detail later in this paper. (10)
Additionally, people with dementia often have nighttime behavioral changes such as sleepwalking, day/night confusion, getting up frequently, nightmares and hallucinations. These behavioral changes can be especially onerous for caregivers and often lead to institutionalization. At more than 20%, sleeping problems are one of the primary reasons for nursing home administration, and it is cited that nearly two thirds of nursing home residents complain about chronic sleeping disturbances. (73) (67)

However, sleep disturbances could play an even bigger role in dementia than previously expected.
Like the dementia-associated pathology itself, sleeping problems can appear years before typical cognitive decline, which may indicate a predictive factor of sleep disturbances in dementia. (51) Furthermore, there is increasing evidence of the bidirectional relationship between sleep disorders and the pathophysiology of neurodegenerative dementia types. Current research states that decreased sleep directly and adversely affects the course of dementia. (19) (10)

1.3.2.1 Causes of sleeping disturbances

The etiology of sleep disturbances in demented persons is multifactorial, including environment, behavior, medication, comorbidities, neurodegeneration and others. (19)

Firstly, the cause of a sleeping disturbance can be categorized into internal (patient-related) and external (environmental) factors. (10)

1.3.2.1.1 Internal factors

Starting off with the internal factors, many neuronal or metabolic changes of AD and other types of dementia contribute to decreasing sleep quality and quantity.
These changes themselves can lead to sleep disorders, for instance insomnia, which are then referred to as a primary sleep disorder, whereas a secondary sleep disorder is the result of the symptoms of an underlying somatic or psychiatric illness. (74)
One pathological change in dementia which could lead to a primary sleep disorder are alterations in melatonin production. The plasma concentration of melatonin declines with age, resulting in a dropped peak of nighttime melatonin release, which can lead to a misalignment of the circadian rhythm. Studies have shown that these melatonin levels are especially low in patients with an Apo E4/E4 AD. (75) (67)
These decreased melatonin levels could result from reduced optical transmission in the elderly, due to visual dysfunctions such as cataracts or retinopathies or the lack of daylight for impaired patients. (75) (19) If fewer signals go out of the retina and reach the SCN, less melatonin is produced. Other studies say that the lower melatonin levels in AD patients, compared to other people of the same age, are a consequence of a dysfunctional noradrenalin and serotonin regulation, which is often seen in Alzheimer´s disease. (76)

Even the physiopathology of dementia itself is a key factor in sleeping disturbances. Amyloid-ß, for instance, which is responsible for the pathology of AD, can exacerbate sleeping problems. (77)
It was suggested that Aß accumulations disrupt NREM sleep, especially the slow wave stage, and induce changes in clock genes, such as PER2 and BMAL1 (51) (10)
But not only does the Aß contribute to sleeping problems, there is also evidence that tau pathology is present in many sleep centers of the brain, which ultimately leads to dysregulation of sleep. (51)
All in all, the neurodegeneration induced by dementia affect neurons which are involved in the regulation of sleep and wakefulness, such as the neurons in the SCN, which function as a main sleep center. This can lead to shifts in sleep patterns, sleep disruptions and changes in the circadian rhythm. (72)

Closely linked to these neurodegenerations in dementia are sleep apneas, which will be discussed in detail in 1.3.2.3.1.

Patients with dementia also often suffer from secondary sleep disturbances, due to other underlying illnesses. Demented people are generally elderly and often have many comorbid medical conditions. Chronic diseases, such as ischemic heart disease, diabetes, renal failure, pulmonary disorders and multiple medications to treat these, contribute to decreased sleep quality. (78)
Unfortunately, even medications prescribed to hinder symptoms of Parkinson dementia can lead to daytime sleepiness and fragmented sleep. (47)
In addition to chronic diseases, psychiatric diseases have to be considered as well, as over 50% of people with dementia have symptoms of depression or dysthymia, which can both lead to sleep maintenance problems. (19) (79)

1.3.2.1.2 External factors

External factors are often overlooked but they are not uncommon causes of sleeping problems in demented people and should certainly be managed.
Increased ambient lighting during sleeping time, excessive noise, an excessively warm or cold sleep environment and late intake of caffeine can be seen as external disruptive factors of sleep. Also, patients with AD typically have a more sedentary indoor lifestyle with less access to daylight and physical exercise, which can lead to shifts in the circadian rhythm. (10) (78) (68)

1.3.2.2 Consequences of sleeping problems

Why is it so important to manage sleep disturbances in demented people?
Sleeping problems are not only a burden for dementia patients themselves and their caregivers, but also have physical and mental consequences for the patient. Untreated sleeping disturbances lead to increased morbidity and mortality. (78) Chronic sleeping problems are associated with morbidities such as respiratory symptoms, cardiac insufficiency, hypertension and a decreased immune system. (46)
Also, impaired night sleep will have an impact on the daily performance of the patient. Patients can show daytime sleepiness, irritability, headache, depression and deterioration of motor and cognitive functions, which decreases their already limited daily life skills. (80) (10)

It was also found that restricted sleep attenuates beneficial effects of sleep on declarative memory consolidation and increases the formation of false memory. (55)
Finally, there are many studies indicating that sleep disturbances increase the concentration of Amyloid-ß, leading to accelerated neurodegenerative changes. This topic will further be reviewed in Section 4.4. (51)

1.3.2.3 Different types of sleep disturbances

1.3.2.3.1 Sleep disturbances in Alzheimer´s disease

The accompanied sleeping disturbances of AD are the most familiar, as AD is the most common form of dementia. Therefore, Chapter 1.3.2.3 will concentrate mainly on the sleep disturbances of AD and then provide information about sleeping problems in other dementia forms.

Over 60% of patients with mild cognitive impairment and AD suffer from sleep disorders of some kind, mostly insomnia and sleep apnea. (55) These sleeping problems can be found years before cognitive symptoms begin, very likely because the pathology of AD emerges around 10 years before the patients show any symptoms. (46)

The insomnia and excessive daytime napping can be a result of a shifted circadian rhythm. Shift of the circadian sleep/wake rhythm can be severe in patients with AD and may lead to complete day/night sleep pattern reversals. Indicators for the circadian dysfunction in AD patients include core body temperature phase delay and amplitude decrease, clock gene phase changes and changes in sleep regulating hormones, for example, decreased nocturnal melatonin and increased hypocretin (wake promoting hormone) (51) (81)
Studies show that circadian rhythm dysfunctions were found in patients with AD regardless of whether they live in an institution or at home. (78)

Sleep apnea is another very common sleep disturbance of older age. A study from 2014 has shown that 50% of the adults older than 50 years suffer from some kind of sleep-related breathing disturbance and in AD patients over 70% are affected. (82) (80)
On the one hand there is the obstructive sleep apnoe syndrome resulting from anatomical cause due to collapse of the pharyngeal muscles. On the other hand there is the central sleep apnoe syndrome. Both can occur in people with dementia.
Degeneration of respiratory neurons of the brain stem and the supramedullary respiratory

pathway in the course of the dementia syndrome may trigger the central sleep apnea syndrome and other respiratory problems affecting sleep in the demented. (10) (75) Sleep apnea is a syndrome characterized by repeated stagnation of breathing during sleep for at least 10 seconds. This can result in episodes of hypoxemia and multiple brief awakenings at night, leading to excessive daytime sleepiness and impaired day-time functioning. Apneas lead to changes in sleep architecture, especially decreased REM sleep and SWS. Secondary to the sleep reduction, sleep apnea can also lead to cognitive impairment, personality changes, morning headaches and depression. (75) (73)
Major risk factors for sleep apnea include male gender, obesity and increased age. (81)
Although the obstructive sleep apnea syndrome can often be treated well with a so-called CPAP device, the use of this device is often not possible for patients with cognitive impairments, due to reduced compliance.

Apart from insomnia and sleep apnea, other common sleeping problems associated with AD include decreased slow wave and REM sleep, increased day time napping and sundowning. Sundowning is a phenomenon which can be described as an increase of agitation, confusion, anxiety and aggressiveness in the late afternoon or evening. (47) (75)

Quantitatively reduced REM sleep is typical for AD. While the mean REM sleep episode duration is decreased, the total number of REM sleep episodes and REM sleep latency remains intact. (75)

1.3.2.3.2 Sleep disturbances in vascular dementia and frontotemporal dementia

It is assumed that approximately 80% of patients with vascular dementia show sleeping disturbances. Numbers are similar in patients with frontotemporal dementia. (55)
The types of sleeping problems which can be found during the course of these two types of dementia are quite similar to those of AD patients, and include insomnia, disrupted sleep/wake cycles, decreased sleep quality, daytime sleepiness and sleep apnea.
Having said this, one aspect of these sleeping problems which differs from the other dementias is the frequency of the types of sleep disturbances.
Insomnia was found to be 2.5 times more frequent in VaD patients compared to AD patients and sleep apnea was two times more frequent in VaD patients than in those with AD. (78) (46)

1.3.2.3.3 Sleep disturbances in Lewy Body dementia and Parkinson's disease

Sleeping problems are a present issue in the α-synucleinopathies.

With over 90% of patients affected, dementia with Lewy bodies and Parkinson dementia are the two dementia forms which are most frequently accompanied by sleep disturbances. As the pathology of these two diseases is so similar, they also show very similar sleeping disturbances. (46)

Insomnia, including prolonged sleep latency, increased sleep fragmentation and waking up early in the morning, is a central problem for PD and DLB patients. Also, daytime sleepiness and sleep apnea are reported in patients with PD and DLB as well as AD and VaD. (47) (46) (78)

However, apart from these sleeping disturbances, which are also common in AD and VaD patients, DLB and PD are characterized by specific sleep conditions, which help in differentiating these diseases from AD and other forms of dementia. These specific conditions include movement disorders during sleep and REM sleep behavior disorder. (51) (10)

1.3.2.3.3.1 Restless legs syndrome

Restless legs syndrome (RLS) is a common movement disorder during sleep of older age. Approximately 6% of people with dementia suffer from this movement disorder, with an especially high prevalence of up to 20% in patients with Lewy Body dementia and Parkinson dementia. (78) (83)

RLS is a sleep-related movement disorder with a circadian pattern, characterized by unpleasant leg sensations and the urge to move the legs during periods of inactivity, mostly at bedtime. (83) In addition, 80% of patients with RLS complain of periodic limb movements of sleep (PLMS), which are defined as periodic episodes of repetitive and highly stereotyped limb movements that occur during sleep. (84) (75)

The pathophysiology of RLS is not yet fully understood, but the syndrome can either be idiopathic, normally with an earlier onset, or secondary. Secondary RLS is associated with various diseases including iron deficiency, renal failure, pregnancy and parkinsonism. (85) (83)

The consequences of RLS can be severe. Sleep onset and sleep maintenance insomnia, depression, anxiety and even increased cardiovascular risk are possible. (85)

1.3.2.3.3.2 REM sleep behavior disorder

REM sleep behavior disorder (RBD) is a very specific and predictive sleep disturbance of α-synucleopathies. The clear majority of individuals affected from idiopathic RBD appear to be at risk of developing an α-synucleopathy, such as PD or DLB, whereas the interval between initial RBD symptoms and disease onset can reach up to 15 years. (67) (46)
RBD is characterized by repeated episodes of dream enactments with excessive motor activity and sometimes vocalization, which emerge mostly in the second half of night sleep, during the REM sleep phase, resulting out of the loss of REM sleep atonia. The patients often have nightmares involving animals or people, which they act out by punching, kicking and screaming. These actions can be harmful to the patients themselves and their bedpartners. (86) (75) (78)

1.3.3 Therapy of sleep disturbances in dementia

Sleep disturbances in people with dementia are not only onerous for patients themselves but are also a major burden for caregivers and family members. Apart from that, decreased sleep quality has been shown to worsen the cognitive state, leading to a sharp deterioration of the dementia symptoms. (75)

So, it is imperative to find a way to improve the nighttime sleep of people with dementia with the aim of treatment being the preservation of quality of life for the patients and the caregivers.

There are different ways to approach solving these sleeping problems. The therapeutic approaches can primarily be divided into non-pharmacological treatment and pharmacological treatment. It is important to try to exhaust all possibilities of non-pharmacological treatment before starting drug therapy, as the latter often has side effects or interactions with other drugs. (78)

1.3.3.1 Pharmacological treatment

There are many different pharmacological ways to handle sleeping problems. The main groups of sleep improving medications are benzodiazepines, antidepressants, melatonin, antipsychotics and Z-drugs. (80) Every group has certain advantages and disadvantages, and their use should

be discussed individually for every patient. However, these will not be discussed in this paper, as its main topic is non-pharmacological treatments. Only after strictly non-pharmacological treatments do not show the anticipated success should a medical therapy of the sleeping disturbances be considered.

1.3.3.2 Non-pharmacological treatment

Non-pharmacological interventions are especially convenient, as they have lower risks than medication and can be used in combination without the risk of interactions.
There are many different non-pharmacological approaches to improve sleep quality and quantity. This chapter will focus on three main concepts: behavioral measures, bright light therapy and Sensory Integration (SI).

1.3.3.2.1 Behavioral measures

Changes and corrections of the circadian behavior is a simple way to solve sleeping problems. (47) Important measures to begin with are paying attention to sleep hygiene. This means especially maintaining regular bedtime and rising time. Further, caregivers should limit naps during the day to a maximum of 30 minutes. During the day, patients should exercise at least 30 minutes every day, ideally outside in natural light. Many studies show that daytime activities in natural lighting can have a beneficial effect on sleep in nursing home residents with dementia. (47)
Also, a consistent dinner time and avoiding caffeine and alcohol can be helpful for patients with sleeping problems. At night, patients should have access to a pleasant sleeping environment with minimal noise, minimal ambient light and a comfortable temperature. (72) (78) (75)
If these interventions are not effective enough, patients can also try sleep restriction, progressive muscle relaxation, biofeedback or meditation. These are also known to be effective for older adults with sleeping disturbances, however are not easy to implement in patients with dementia. (80) (46)

1.3.3.2.2 Bright light therapy

An established intervention is bright light therapy (BLT). It can be considered as a form of sensory integration (see below), but because it is used more commonly, it will be discussed separately.

Institutionalized older adults, especially those with dementia, often have very little daily exposure to sunlight, which can be a cause of the sleeping problems. (67) Timed daily exposure to bright light has been shown to improve nighttime sleep by significantly reducing nocturnal sleep fragmentation, increasing daytime wakefulness and consolidating rest/active patterns. Patients who receive greater than 2500 lux of blue light in the morning show less phase delay in sleep, whereas evening bright light therapy is most beneficial for older adults with sleep maintenance problems. All in all, studies have proven that BLT has a positive impact on the sleep quality of patients with AD. (68) (19) (47)

Bright light therapy is an intervention without any known side effects which can easily be integrated in everyday life and is already successfully being used for patients suffering from depression. (80)

1.3.3.2.3 Sensory Integration

Sensory Integration is a theoretical concept which was developed by the American therapist Jean Ayres in the 1950s. Ayres defined Sensory Integration as "the organization of sensations for use." (87)

Most information about our body and the surrounding environment is registered by multiple sensory systems, including the five senses: the olfactory, auditory, visual, gustatory and tactile systems, as well as the proprioception and the vestibular systems. Our brain has the ability to integrate all these different sensations, putting them together to a coherent percept which allows us to react in an appropriate way. All this happens unintentionally. (88) (89)

However, sensory processing can be impaired, and this might result in various functional problems, which Ayres labeled *sensory integration dysfunction (SID)*. (90)

Sensory integration dysfunction is based on the proposition that functional performance deficits originate from a failure to correctly process and integrate sensory information of the body, including the correct intake of information, then filtering out the unnecessary information and processing the necessary information to come to an appropriate response. Individuals can be over-sensitive to sensory input but also under-sensitive or even both. Some people suffering from SID may experience problems in integrating inputs from one particular sense, others from more than one sense. These dysfunctional integrations of sensory input can result in subjective discomfort and lead to inattentiveness and stereotypical behavior. (91)

Sensory integration treatment is a method of intervention. It is a non-pharmacological intervention which refers to different techniques that try to stimulate the senses of the patient.

It can be used for many different age groups and for many different pathologies. There are various forms of sensory integration treatment, including, for example, weighted vests or blankets, which provide additional tactile input and are said to release stress and anxieties. (91) Also included are aromatherapy, music therapy, massage and others. (92)
Given the plastic reorganizational processes, cognitive changes and also the impairment of the sensory organs during normal aging, it seems logical that sensory integration processes decline in elderly humans. (93)
Regarding dementia, sensory integration interventions have generally been found to be helpful, especially in terms of reducing sleep disturbances, agitation, depression, apathy and anxiety symptoms. (71)
For example, "Snoezelen" is a multi-sensory behavior therapy developed by two Dutch therapists in the 1970s, which is based on Ayres theory. It combines the input of different senses in one environment, such as a room with music, smells, bright light, colors and different tactile stimulants. Patients can then try to actively concentrate on one sense and train their sensory integration processing. Studies have shown that this can decrease the appearance of stereotypical behavior in patients suffering from dementia. (94)

All this said, while some studies show positive outcomes for Sensory Integration treatment, up to now no published studies have specifically investigated the scientific background of Ayres sensory integration theory. (95)
Summarized, Sensory Integration is mostly seen more as a hypothesis than a fact by many experts.

1.3.3.2.3.1 The granulate blanket from the company Protac

The manufacturer of the special granulate blankets used in our trial is the Danish company Protac. They are specialized in "developing and manufacturing a variety of unique sensory integration products that serve the need of people with physical disabilities and sensory impairment." (96)
Their range of products, among others, includes weighted vests, ball cushions, ball filled chairs and the aforementioned granulate blankets and ball blankets.

The rationale of the use of a weighted ball blanket (used instead of a classic bed blanket) is based on the theory of Sensory Integration Disturbances, described above. (96). According to this theory, a disturbance of awareness of one´s own body and its sensory inputs is an important

cause of motoric restlessness and of accompanied sleep disturbance in patients with various neuropsychiatric disorders. Based on this premise, the usage of weighted blankets should stimulate both the sensation of touch and the proprioception.

Receptors located in skin, muscles and joints provide information about the position and movement of limbs to create an awareness of the position of the body, which is called proprioception. If tactile and proprioceptic information is not provided, it results in restlessness. The weight and the changing pressure of the plastic balls or granulates give the skin, muscles and joints a certain resistance, which helps the brain understand the calming information on the localization and boundaries of the body. Both the stimulation of the tactile sense and the proprioception increase the awareness of one´s own body and can contribute to a sense of security, which is why the weighted blankets can help provide a calm night sleep.

Children with neuropsychiatric disorders (especially autism spectrum disorders - ASD and attention deficit hyperactivity disorder - ADHD) represented the primary target population of patients for the use of sensory integration therapy products, such as weighted blankets. However, empirical experience with the use of a weighted blanket on some patients with dementia (including in our Department) also showed positive effects on the quality and quantity of night sleep and secondarily on the behavioural disturbances during the day. Such effects could however not be observed in all patients. It remains unclear whether there are specific groups of patients with dementia who benefit from the use of a weighted blanket during the night more than the others. Also, it is not known if there are some specific co-factors which are important for the therapeutic effect and for the acceptance of the blanket by patients of dementia. And finally, if a positive effect on the quality of the night sleep could be found, it would be of interest to know whether the pattern of daily activity in these patients is also positively affected.

These questions led us to the decision to conduct a study on the effectiveness of weighted blankets in improving sleep of patients with advanced dementia and concomitant sleep disturbances.

1.4 The idea behind the study

For a long time, staff members on the ward have been aware of the effect of a good night's sleep on the daytime performance of patients suffering from dementia. So, it has always been a goal to provide these patients with the best rest possible. For a few years now, weighted blankets and

special beanbags designed for disabled people, have been used on this ward of the Department of Psychiatry and Psychotherapy and have shown an empirical positive effect on the sleep of some patients.

Through this observation, the idea for our main study was born. The main study is supposed to evaluate the effect of weighted blankets on the quality and quantity of sleep of patients with a dementia syndrome suffering from sleeping disturbances. In order to examine this, some preparatory considerations had to be completed, which led to the necessity of preparatory studies like this one.

To find out whether conducting this kind of study would even be possible on this special group of patients, we had to assess the acceptance of the weighted granulate blanket beforehand. The blankets are heavy and can feel unfamiliar, so immediate acceptance is not as self-evident as it may seem, especially with patients suffering from dementia. They generally show a lower level of compliance for any intervention and often have a more skeptical attitude towards the unknown due to their lack of comprehension.

This preparatory study primarily examined whether sleeping with a granulate blanket is tolerated by patients with moderate to severe dementia and sleep disturbances. Apart from that, this work should also answer the questions as to whether there are any specific factors/cues which could help to anticipate the response or effect and the tolerability of granulate blanket use during night sleep on people with dementia.

All in all, two preparatory studies with resulting publications were initiated before the start of the main study. The first one dealt with the collection and the processing of the actigraphic data and this one examined the acceptance of the granulate blanket. Results of actigraphic data study will not be discussed, and the course of the preparatory study is discussed in the following.

2. Material and methods

2.1 Course of the study

This study is a preparatory study for our main clinical trial. Our main trial is a randomized, monocentric, double-blind controlled trial, designed to evaluate the efficiency of the use of weighted blankets for improving the quality and quantity of night sleep and daily activity in patients with moderate to severe dementia suffering from sleep disturbances.

As can be seen in the diagram (Figure 2), our research started in September of 2017 with the study of the efficiency of the actigraphic measurements. This study was initiated by another

student. She tested the handling of the actigraphy watches and determined the suitable measuring periods in one day. Additionally, she developed an Excel chart, allowing us to calculate the overall sleep efficiency of one patient out of the raw data recorded from the actigraphic watch.

My work for our project started in April of 2018. At first, the collection of actigraphic data for the actigraphy preparatory study had to be completed in April and May of 2018. A short planning period followed, in which we tested the logistics of the subsequent studies (use of actigraphic watch and granulate blanket) and also developed a table including the research criteria of the various types of dementia (Figure 2), which was then used to determine the type and severity of dementia for our potential study patients. After the ethics committee reviewed and accepted our study proposal, testing on the tolerance of the granulate blanket was initiated. During this time, the development of a randomization list, the study protocol, and the marginal conditions on the execution of the main trial were completed. In July of 2018 our main double-blind, randomized study started. As we were still examining the tolerance of the granulate blanket during that period of time, those two studies continued in parallel for approximately 14 months. In August 2019, the preparatory study was concluded with 62 included patients.

The testing for the main study was finished in November 2019 after 90 patients had been included.

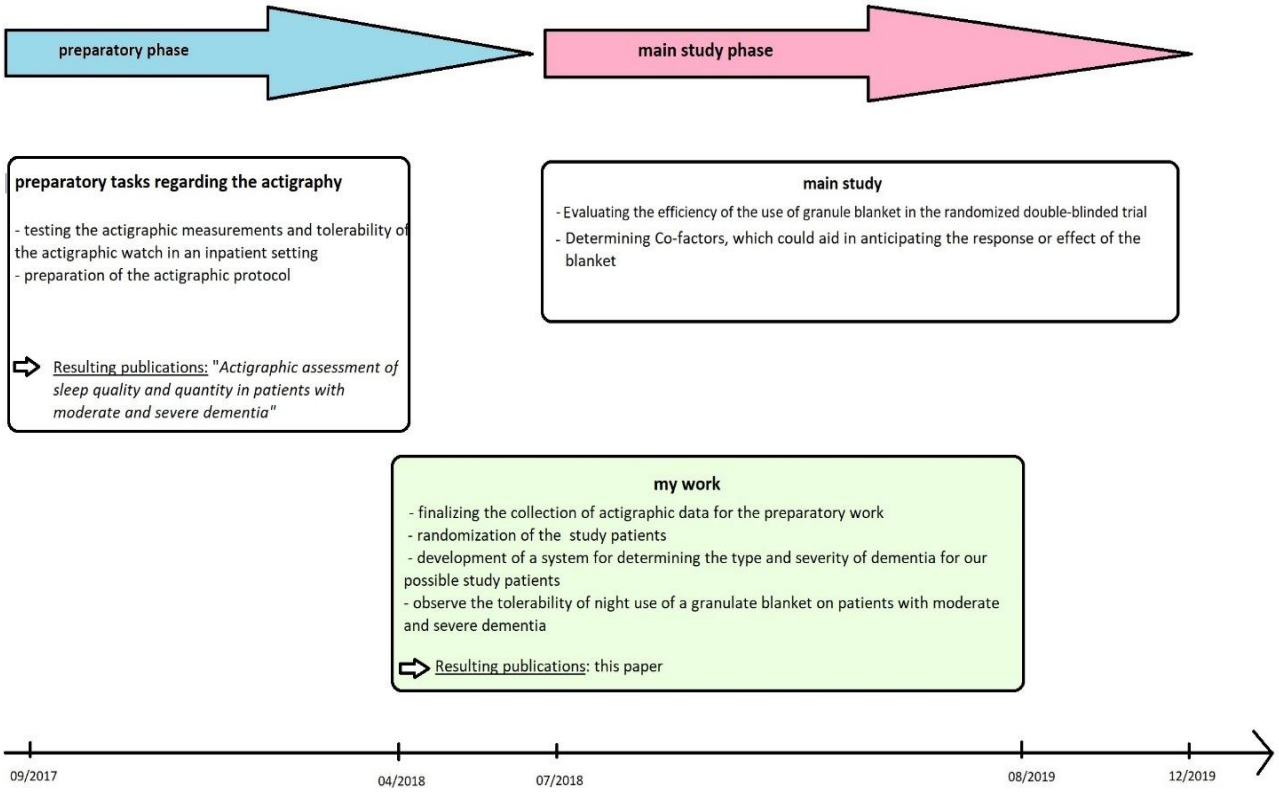


Figure 2: Timetable of the studies

2.2 Material

2.2.1 Institution

The study took place in the locked geropsychiatric unit of the Center for Geriatric Psychiatry, Department of Psychiatry and Psychotherapy of the University of Regensburg at the medbo Bezirksklinikum in Regensburg, Germany.

This ward holds 26 beds in 12 rooms. The rooms are mostly double rooms. Every day is divided into 3 shifts for the nursing staff. The medical staff of this ward are consultants in psychiatry and neurology as well as residents in psychiatry. Further staff members include neuropsychologists, occupational therapists, psychotherapists and social workers.

2.2.2 Patients

The majority of patients admitted to the locked unit suffer from advanced dementia with various behavioral disturbances. Patients with delirium with or without underlying dementia as well as geriatric patients with severe psychosis or affective disorders are also treated at this unit. The

mean duration of stay of a patient in this unit is 16 days, with a range from one day up to a few months. All of the admitted patients were screened for suitability for inclusion in the trial. Patients over 50 years of age with moderate or severe stage of any type of neurodegenerative or vascular dementia or alcohol-induced dementia and concomitant sleep disturbances were chosen as our study population. These patients were selected based on the primary and secondary inclusion criteria developed previously (these are described below).

The weighted blanket used in the study is certified as a medical device in the European Union and had already been routinely in use at the department. All patients who were evaluated for inclusion in the study would also be considered to get the blanket as part of routine measures for sleep improvement outside of the study situation. Hence, the only intervention in the present study was the systematic random decision about providing the weighted blanket to an individual patient. Because all patients considered for inclusion in the study suffered from advanced dementia, an informed consent was acquired from the legal representatives of the patients (see appendix, Figure 24).

2.2.3 The granulate blanket from Protac

The granulate blanket used for the trial is from the manufacturer Protac A/S in Denmark. In our study, a weighted blanket type named "Protac Granulate Blanket" was used. This model is filled with small polypropylene granules. According to the producer, it should alleviate anxiety and restlessness and is especially suitable for elderly people with dementia, who often do not accept a classical ball blanket filled with bigger plastic balls. This is also the same type of weighted blanket which had already been in routine use in our department. (99)

The model we chose weighed 5 kg. In comparison, the normal blanket on the ward weighs around 2 kg.

The blanket is covered in an incontinence covering and a bed sheet over that. The bed sheet is the same as for the normal blankets of the ward. The granulate blanket cannot be distinguished from a normal blanket just by sight, as you can see comparing Fig. 7 and Fig. 9. Four granulate blankets, including incontinence covers, were borrowed from Protac. In addition, a special on-site training session with a demonstration of the correct use of the granulate blanket was conducted by Protac for all members of the investigator team and nursing staff of the study center.



Figure 3: Granulate blanket without cover



Figure 4: Close-up of the granulate pockets



Figure 5: Granulate blanket with incontinence cover



Figure 6: Breathing holes in incontinence cover



Figure 7: Granulate blanket with incontinence cover and standard bed sheet



Figure 8: Person sleeping unter granulate blanket



Figure 9: Normal blanket with standard blanket sheet



Figure 10: Person sleeping under normal blanket

2.3 Methods

2.3.1 Inclusion criteria

2.3.1.1 Primary inclusion criteria

In order to be included in this trial, the selected patient had to be rated with an at least moderate to severe dementia of a neurodegenerative type (Alzheimer's disease, Lewy Body dementia, Parkinson-associated dementia, frontotemporal dementia), of vascular origin or alcohol dementia.

To confirm the diagnosis, the ward physicians and the consultant neurologist/psychiatrist were consulted. Subsequently, every patient was assessed according to the set of diagnostic criteria designed prior to this study. These diagnostic criteria were also used in the main clinical trial. Our diagnostic criteria were based on the research criteria for the different types of dementia, which were incorporated in the newly-developed MS Excel table. For illustration purposes, part of this table is attached here.

Diagnosekriterien nach NIA-AA für Alzheimer Demenz	Allgemeine Demenzkriterien: kognitive oder verhaltensbezogene Symptome liegen vor, die	das Funktionieren bei Alltagsaktivitäten beeinträchtigen (J/N)	1	1	1
		eine Verschlechterung im Vergleich zum vorherigen Zustand darstellen (J/N)	1	1	1
		nicht durch ein Delir oder eine psychische Erkrankung erklärbar sind (J/N)	1	1	1
		Eindeutige Hinweise auf kognitive Störung in Eigen- und Fremdanamnese und objektiver Bewertung der kognitiven Leistung durch kognitive Testung oder klinische Untersuchung; wenn nicht eindeutig, neuropsychologische Testung (J/N)	1	1	1
		Mindestens zwei der folgenden kognitiven Bereiche beeinträchtigt: a) Gedächtnisfunktion b) Verstehen und Durchführung komplexer Aufgaben, Urteilsfähigkeit c) räumlich-visuelle Funktionen d) Sprachfunktionen e)Veränderung im Verhalten ("Persönlichkeitsänderung")	1	1	1
		Welche?	a, b, e	a,b,	a,b,e
	Wahrscheinliche Demenz bei Alzheimer-Krankheit	Allgemeine Demenzkriterien erfüllt (J/N)	1	1	1
		Langsamer Symptombeginn über Monate bis Jahre (J/N)	0	1	1
		Eindeutige anamnestische oder beobachtete kognitive Verschlechterung (J/N)	1	1	1
		Erste und deutliche Symptome sind **a) anamnestische Variante** (Defizit der episodischen Gedächtnisfunktion + 1 weiteres Defizit in anderer kog. Domäne **b) nonanamnestische Varianten** (sprachbezogen, visuell-räumlich oder exekutiv)	1	1	1
		Welche?	a	a.	a
		Keine substanzielle zerebrovaskuläre Erkrankung (Beginn d. kognitiven Störung zeitlich verbunden mit Schlaganfall; multiple Infarkte; große Infarkte; schwere Veränderungen der weißen Substanz) (J/N)	1	1	1
		Keine deutlichen Symptome für Lewy-Körperchen-Demenz (J/N)	1	0	1
		Keine deutlichen Symptome der frontotemporalen Demenz (J/N)	1	1	1
		Kein Hinweis für andere Ursachen der kognitiven Störung	1	1	1
		Wahrscheinliche Demenz bei Alzheimer Krankheit (J/N)	**1**	**1**	**1**
	Mögliche Demenz bei Alzheimer-Krankheit	**Atypischer Verlauf** (typ. Symptomausprägung aber plötzlicher Beginn/ anamnest. Angaben zum Verlauf nicht ausreichend / nicht ausreichende objektive Dokumentation der Verschlechterung)	0	0	0
		Was genau atypisch?			
		Ätiologisch gemischte klinische Präsentation (typ. Symptomausprägung aber mit zerebrovaskulärer Erkrankung ODER zus. Deutliche Symptome der Lewy-Body-Demenz ODER zus. Hinweis für andere Erkrankungen / Med.-Einnahmen mit erheblichen Effekten auf die Kognition)	0	1	0
		Welche andere Komponente (und genau welche Aspekte/Symptome)?		Parkinson	
		Mögliche Demenz bei Alzheimer-Krankheit (J/N)	**0**	**1**	**0**
	Wahrscheinliche Demenz bei Alzheimer-Krankheit mit Evidenz für den pathophysiologischen Prozess	Wahrscheinliche Demenz bei Alzheimer-Kranheit nach klinischen Kriterien	**1**	**1**	**1**
		ß-Amyloid 42/40	**X**	**X**	**X**
		Tau	**X**	**X**	**X**
		Phospho-Tau	**X**	**X**	**X**
		cMRT typisch (disproportionale Atrophie des medialen, basalen und lateralen temporalen und des medialen parietalen Cortex)	**X**	**X**	**X**
		FDG-PET typisch (erniedrigter FDG-Uptake im temporoparietalem Kortex	**X**	**X**	**X**
		Biomarkern sich widersprechend oder unspezifisch			
		Biomarkern mit intermediärer Spezifität - a) ß-Amyloid positiv+Tau grenzwertig oder nicht verfügbar, oder b) ß-Amyloid grenzwertig oder nicht verfügbar+Tau positiv			
		Biomarkern typisch (ß-Amyloid+Tau positiv)			
		Wahrscheinliche Demenz bei Alzheimer-Krankheit mit Evidenz des pathophysiologischen Prozesses (J/N)			
	Mögliche AD mit Evidenz Pathophysiologie	Mögliche Demenz bei Alzheimer-Kranheit nach klinischen Kriterien			
		Biomarkern typisch (ß-Amyloid+Tau positiv)	**X**	**X**	**X**
		Mögliche Demenz bei Alzheimer-Krankheit mit Evidenz des pathophysiologischen Prozesses (J/N)			
	Demenz wahrscheinlich nicht durch die Alzheimerkrankheit bedingt	Klinische Kriterien für die Demenz bei Alzheimerkrankheit treffen nicht zu	0	0	0
		Klinische Kriterien für die wahrscheinliche oder mögl. Demenz bei AD treffen zu, es liegen aber ausreichende Hinweise für eine andere Ursache der Demenz vor (z.B. HIV-Demenz, M. Huntington)	0	0	0
		Welche?			
		Klinische Kriterien einer möglichen Demenz bei Alzheimerkrankheit treffen zu, aber sowohl Amyloid-Marker als auch die Marker für neuronale Schäden sind negativ	X	X	X
		Alzheimer Demenz unwahrscheinlich (J/N)	**0**	**0**	**0**

Table 1: Research criteria for Alzheimers´disease
Each of the three columns on the right side represents one patient, anonymized through a patient ID
1 = yes, 0 = no, X = unknown

We combined the ICD 10 criteria for dementia and the research criteria for Alzheimer´s disease, Lewy Body dementia, frontotemporal dementia, primary progressive aphasia and vascular dementia. The table also included criteria for secondary forms of dementia, including alcohol-induced dementia. To recognize the presence of delirium, delirium criteria from the "Diagnostic and Statistical Manual of Mental Disorders," Part 5 (DSM 5), were also listed in the table. In addition, the table included indicating criteria of a depression in order to exclude patients with pseudodementia. Lastly, the Hachinksi score, the MMSE, imaging methods, biomarkers and neurological items were added to the table.

1. General dementia criteria: cognitive or behavior-related symptoms are existent, which…

- Impair functioning in the daily routine (Yes or No)
- Represent a degradation compared to a previous condition (Y/N)
- Are not explainable by another psychiatric disease (Y/N)
- Exhibit definite evidence of cognitive impairment in the patients' own and other anamnesis and objective evaluation of their cognitive performance through cognitive testing or clinical examination; if not definitive, neuropsychological testing (Y/N)
- Show impairment of at least two of the following cognitive skills: a) memory, b) understanding and performing complex tasks, ability to judge c) spatial-visual functions d) speech e) change in behavior
- Which of these?

→ General dementia criteria fulfilled? (Y/N)

2. Probable dementia through Alzheimer´s disease

- Slow onset of symptoms over a period of months to years (Y/N)
- Clear anamnestic or observed cognitive impairment (Y/N)
- The initial and obvious symptoms are a) anamnestic type: deficit of the episodic memory + one other deficit in another cognitive domain. b) non-anamnestic type: concerning speech, spatial-visual functions or executive features
- Which of these?
- No substantial cerebrovascular disease (Onset of the cognitive dysfunction chronologically

connected to a stroke, multiple infarctions; major infarctions; heavy change in the white matter) (Y/N)
- No clear symptoms of Lewy Body dementia (Y/N)
- No clear symptoms of frontotemporal dementia (Y/N)
- No evidence of another cause of the cognitive dysfunction

→ Probable dementia through Alzheimer's disease (Y/N)

3. Possible dementia through Alzheimer's disease

- Atypical course of disease: typical symptoms, but with sudden onset/anamnestic information on the course is not adequate/insufficient objective documentation of the impairment (Y/N)
- What exactly is atypical?
- Aetiologically mixed clinical presentation: typical symptoms, but combined with a cerebrovascular disease OR additionally symptoms of Lewy Body dementia OR additional evidence of another disease/medication effecting cognition (Y/N)
- Which other components were seen?

→ Possible dementia through Alzheimer's disease (Y/N)

4. Probable dementia through Alzheimer's disease with evidence of the pathophysiological process :

- Probable dementia through Alzheimer's disease according to the clinical criteria (Y/N)
- ß-Amyloid 42/40:
-Tau-protein
- Phospho-tau-protein
- Typical cMRI (disproportional atrophy of the medial, basal and lateral temporal cortex and the medial parietal cortex)
- Typical FDG-PET (decreased FDG-uptake in the temporoparietal cortex)
- Biomarkers contradict each other or are unspecific
- Biomarkers with intermediate specificity – a) ß-amyloid positive + tau marginal or not available or b) ß-amyloid marginal or not available + tau positive
- Biomarkers typical (ß-amyloid + tau positive)

→ Probable dementia through Alzheimer's disease with evidence of the pathophysiological process (Y/N)

5. Possible dementia through Alzheimer's disease with pathophysiological evidence

- Probable dementia through Alzheimer's disease according to the clinical criteria (Y/N)
- Biomarkers typical (ß-amyloid + tau positive)

→ Possible dementia through Alzheimer's disease with evidence of the pathophysiological process (Y/N)

6. Dementia probably not due to Alzheimer's disease

- Clinical criteria of Alzheimer's dementia do not apply (Y/N)
- Clinical criteria of the probable and possible dementia through Alzheimer's disease apply, but there is sufficient evidence for another cause of the dementia (HIV-dementia, Huntington's disease…) (Y/N)
- Which of these?
- Clinical criteria of the possible or probable dementia through Alzheimer's disease apply, but amyloid and markers for neuronal damage are negative (Y/N)

→ Alzheimer's disease unlikely (Y/N)

Every patient, who was chosen to participate in our trial was listed in this table, in order to ensure the diagnosis. Part of my work was developing and checking these criteria.

2.3.1.2 Secondary inclusion criteria

Out of the pool of patients who met the primary inclusion criteria, only patients fulfilling also the secondary inclusion criteria were picked. This meant patients showing a sleep disturbance during their stay at the ward. These were determined based on the daily entries in our computer system, which were written by the observing nursing staff. Our team developed the following scoring system for the purpose of this study. It is based on the routine controls on the patients done daily by the staff.

At the end of each night shift, sleep and activity of each patient was described, scored and assigned to one of seven categories.

1	Patient was sleeping the whole night
2	Patient was sleeping for more than half of the night, with short interruptions

3	Patient was sleeping for more than half of the night, but woke up too early
4	Patient was sleeping for more than half of the night, but fell asleep too late
5	Patient was sleeping for less than half of the night, without motor agitation
6	Patient was sleeping for less than half of the night, with motor agitation
0	Special cases, without assignment to any of the above listed situations

Table 2: Classification of sleep quality and quantity

Besides this standardized documentation system, an additional description of the night activity was documented if necessary. Additionally, each day the night staff was consulted in person about the night sleep of that patient, especially to clarify any uncertainties.

Patients in categories 2-6 were selected and approved for participation in the study.

2.3.2 Exclusion criteria

Some patients had to be excluded due to comorbidities or other factors which would have falsified the results.

Firstly, patients suffering from a type of dementia other than the aforementioned were not included in the study (e.g. dementia accompanying Huntington´s disease, Neurosyphilis or Creutzfeld Jakobs disease). Patients with Pseudodementia were also not included (Patients with pseudodementia manifest cognitive deficits which result from other diseases like depressionand are potentially reversible.)

Another exclusion criterion was immobility, either in connection with physical inability or as the consequence of (extremely rare) temporary use of five-point restraint. These patients were not given the granulate blanket, because they eventually would not have been able to uncover themselves.
If a patient was discharged from the locked gerontopsychiatric unit earlier than after two nights of study interval, he/she was also excluded from the study group.

Another aspect for exclusion were safety reasons. Although the blanket cover has holes in its upper (cranial) part to ensure proper breathing, patients who were seen to place the blanket over

their head with the potential (albeit minimal) danger of suffocation were immediately excluded from the study and the staff exchanged the weighted granulate blanket for the normal blanket.

The presence of one or more of the mentioned exclusion criteria resulted in the patient not being included in the study or being excluded in hindsight.

2.3.3 Decision on inclusion

After applying the inclusion and exclusion criteria on each patient, the patients who were suitable for our study were included into the study as long as their caregivers gave their permission. As only two patients were able to take part in the study per study night, some patients (although qualified for joining the study) were not immediately enrolled in the study process but had to wait for their "study nights."

The patient who was going to sleep with a granulate blanket was randomly chosen. To ensure a bias free inclusion, a randomization list was used to choose whether the trial participant would sleep with a granulate blanket or be part of the control group and sleep with a normal blanket. This randomization list randomized the use of a normal blanket or the weighted blanket for 150 patients according to their ID.

At first, we had to collect preparatory data to ensure our main study could be conducted unobstructedly. For this we focused only on the acceptance of the blanket among our study patients. Twenty-six patients were merely part of this preparatory work, before our preparatory study (this work) and the main study ran in parallel.

2.3.4 Evaluation of severity of dementia

For most patients, the severity of dementia was determined as a team effort including the nursing staff, the doctors and the ward psychologist. As a supporting method to give us a rough estimate on whether the patient could be used as a test patient, we used the mini-mental state exam (MMSE). The MMSE is a question battery of 20 questions regarding orientation, retentiveness, calculating, speech and executive and visual functions. The maximum score that can be reached in the MMSE is 30 points, which means that no cognitive impairment was found. Patients who reached an MMSE score of 30 to 21 points were considered to have a mild stage of dementia. Patients reaching a score of 20 to 11 points were estimated to have a moderate stage of dementia, and lastly patients with an MMSE score of 10 and under were considered to

suffer from a severe stage of dementia. (97) (98) (see Figure 16 in Appendix) The resulting mini-mental status score (MMSE score) together with the estimation of the responsible ward members enabled us to classify the severity of dementia into three groups: mild, moderate and severe dementia. As only patients with moderate to severe dementia were included in our study, only these two categories are represented in the study. (An exception was made for one patient who reached an MMSE score of 21 points but was rated as having a moderate stage of dementia by the ward psychiatrist using the Global Deterioration Scale). As the MMSE only gives an estimation about the severity of dementia, the MMSE serves more as a rough classification. We always also considered the staff estimation in the severity categorization, but for better chance of display, we used the MMSE score for our following statistics.

If the patient showed a form of dementia other than Alzheimer's disease, he/she could also be chosen for the trial even if the MMSE score was not < 21, provided that the Global Deterioration scale was rated ≥ 5. The Global Deterioration Scale (GDS) is a scale for assessment of primary degenerative dementia. Broken down into 7 stages, 1 having the least cognitive impairment and 7 the most, it gives an overview of the cognitive function of a patient with a primary degenerative dementia. The grading of the patients into this GDS scale was done by the ward medical staff based on their own observations as well as information from patients' relatives and the nursing staff. The GDS was also used for patients for whom the MMSE was not possible to apply, due to language or hearing difficulties. In our study this was the case for two patients.

2.2.5 Data collection, documentation and evaluation

The selected study patient was supposed to sleep with the weighted blanket for three whole nights, starting at approximately 7 p.m. and ending at approximately 6 a.m.
To receive this information about acceptability of the blanket, we referred to the data which was collected by the ward staff members especially during the night shift.
Every day, the nurses of the late shift were informed about who was the participant of our study for that day. Additionally, this information was noted in the computer system. The nurses of the late shift were responsible for giving the weighted blanket to the selected patient at approximately 7 p.m. and then also covering the patient with the blanket. They then informed the night shift about the selected patient.
The night shift regularly checked on the patient (at least three times during the period between 10 pm and 6 am) and observed whether he or she was still covered with the weighted blanket.

At the end of the night shift, the sleep and activity of each patient was described, scored and assigned to one of the seven categories described in 2.3.1.2 .

To reinforce the collected data, the nursing staff of the next morning was questioned about the tolerance of the weighted blanket, and, if necessary, this information was added to the report. Additionally, the staff documented the reasons for non-tolerance if these were expressed by the patient.
Based on this documentation, the tolerance of the weighted blanket of the selected patient for each night was estimated.

The tolerance was graded into three categories:

1	Patient tolerated the weighted blanket the whole night
2	Patient tolerated the blanket for most of the time, but uncovered himself a few times
3	Patient did not tolerate the weighted blanket at all

Table 3: Tolerance categories

The information regarding the tolerance was then listed in an Excel table with the patient´s ID number and later inserted in the SPSS table.

2.3.7 Data processing using binary logistic regression

After looking at the descriptive statistics of the study, we wanted to statistically test the correlation between acceptance and independent variables like gender, severity of dementia and temperature. For this we used a binary logistic regression, which forecasts the probable values for the acceptance depending on the independent variables.
Our null hypothesis is that the acceptance is not influenced by independent variables. The goal of this test is to reject the null hypothesis in favor of the rival hypothesis, which states that the independent variables indeed have an influence in the acceptance of the granulate blanket.
The dependent binary variable is the acceptance of the blanket for two or more nights with the values of yes (the patient accepted the blanket for at least two nights) or no (the patient accepted the blanket for only one or none of the nights). The independent variables which were tested

for dependence included the gender of the patients, the severity of dementia and the outdoor temperature. To do so, we converted the severity and the outside temperature into ordinal scaled values, as seen in 3.2 .

The logistic regression predicts the probability for the dependent variable to have the value of 1. Through calculation of the Odds Ratio, the binary logistic regression can also determine the difference in the probability of the dependent variable being 1 (acceptance) in correlation with the different independent variables.

Therefore it gives us an idea on which variables have a positive or negative influence on the acceptance of the granulate blanket.

2.3.6 Measuring the temperature

A few months after initiating our preparatory study, it occurred to us that a few patients were neglecting the granulate blanket because they were getting too warm under it. As the summer of 2018 was an exceptionally hot summer anyway, we had to take the outdoor temperature into consideration.

This information was drawn from the “Deutscher Wetterdienst.” The temperatures we used for our documentation were sent to us from the meteorological station in Regensburg, which is located at an elevation of 2 meters and provided the exact local temperature for every half hour of a day. For our study, we chose the temperature recorded at 7 pm, because this was the time when the patients were brought to bed and covered with the granulate blanket. As our ward was equipped with a heating system, the temperature in the patient´s rooms during colder weather was kept relatively constant between 20°C and 24°C. However, without an air conditioning system, the room temperatures in the warmer months of the year could be higher, depending on the outside temperature. On the few days where the weather and the room temperature in the ward were extremely hot, the team decided to interrupt the study for these days to prevent patients from overheating.

2.3.7 Preparatory study objectives

Primary objective:

Determining whether sleeping with a granulate blanket is tolerated by patients with moderate to severe dementia and sleep disturbances.

Secondary objectives:

To find out whether there are any specific factors/cues which could help to anticipate the response/effect and the tolerability of granulate blanket use during night sleep. Collecting the reasons why the blanket was not tolerated.

3. Results

3.1 Demography of the patient collective

A total of 62 patients were primarily included in the study.
The expected duration of the study involvement of each patient was three nights. Of the 62 included patients, only 55 completed this full duration of three study nights. Three patients only slept with the blanket for one night and four patients were able to complete two study nights. This was due to an early release out of our locked ward (four patients), a restraining of the patient, and, respectively, reduced vigilance (three patients).
Looking at the reasons for exclusion during any night of trials, there was a five-point restraint for three nights (33.3%), early release for three nights (33.3%) and reduced vigilance with a possible risk to the patient during three nights (33.3%).

3.1.1 Gender distribution

Our patient cohort consisted of 32 women (51.6%) and 30 men (48.4%).

3.1.2 Age distribution

To be included in our study, patients had to be at least 50 years old. There was no upper age limit. The average age of the study participants was 80.2 years, whereas the average age of the female participants was slightly higher, at 81.4 years, than the average age of male participants, at 79.2 years.

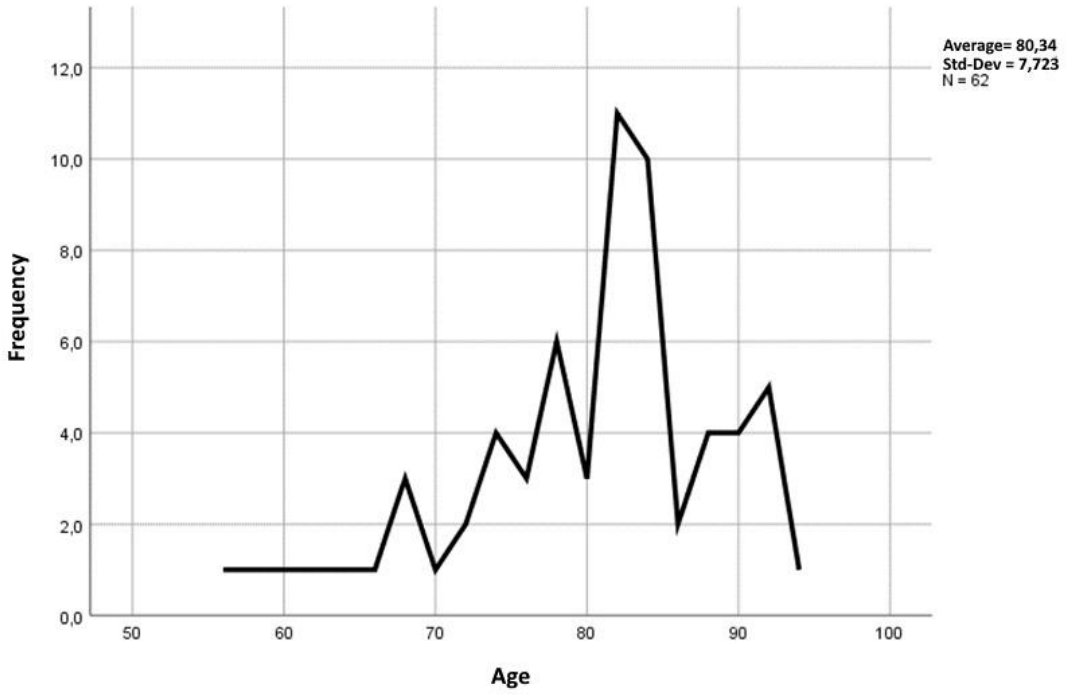


Figure 11: Distribution of age

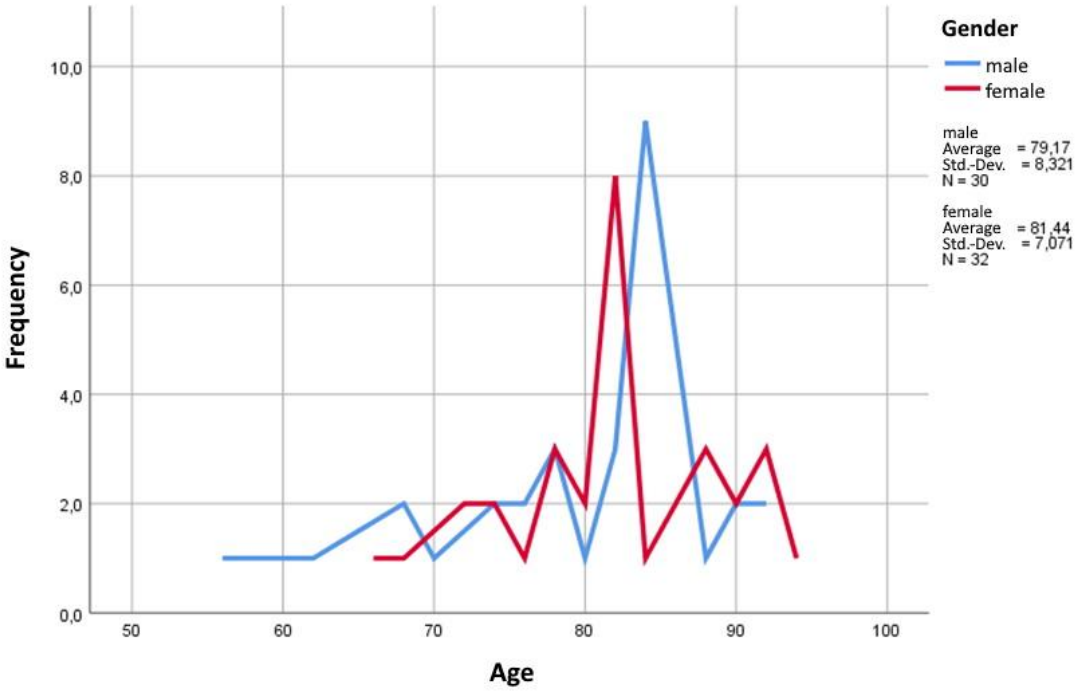


Figure 12: Age distribution depending on the gender

3.1.3 Distribution of dementia types

To compare the tolerance of the weighted blanket between the different types of dementia, every patient was assigned a dementia category including

AD = Alzheimer´s dementia
AD + Alk = mixed dementia with components of Alzheimer´s dementia and alcohol-induced dementia
AD + LBD = mixed dementia with components of Alzheimer´s dementia and Lewy body dementia
Alcohol = Alcohol-induced dementia
Other = other forms of dementia, not further defined
FTD = frontotemporal dementia
LBD = Lewy body dementia
AD + VaD = mixed dementia with components of Alzheimer´s dementia and vascular dementia
PD = Parkinson's dementia
PPA = primary progressive aphasia
Secondary = any form of secondary dementia, other than alcohol-induced or vascular dementia
VaD = vascular dementia

Overall, the most frequent type of dementia in our study was Alzheimer´s dementia, with 32 patients (51.6%), followed by the mixed dementia with Alzheimer´s and vascular components, at 13 patients (21.0%). The other types of dementia only represent a small percentage. Our study group did not include patients assigned to the categories of Parkinson´s dementia, pure alcohol-induced dementia, frontotemporal dementia or secondary dementia.

Types of dementia

		Frequency	Percentage
	AD	32	51.6
	LBD	3	4.8
	VaD	4	6.5
	Mixed AD+VaD	13	21.0
	AD + LBD	5	8.1
	AD + Alcohol	4	6.5
	Other	1	1.6
	Total	62	100.0

Table 4: Distribution of the different types of dementia

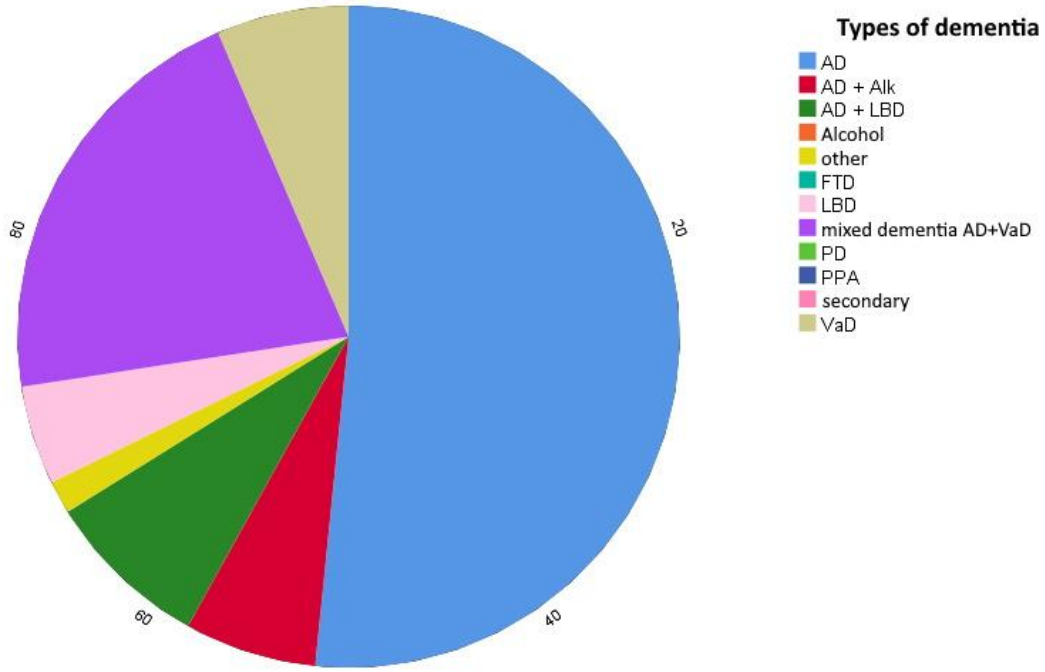


Figure 13: Distribution of the types of dementia

3.2 Descriptive statistics of other variables

3.2.1 Severity of dementia

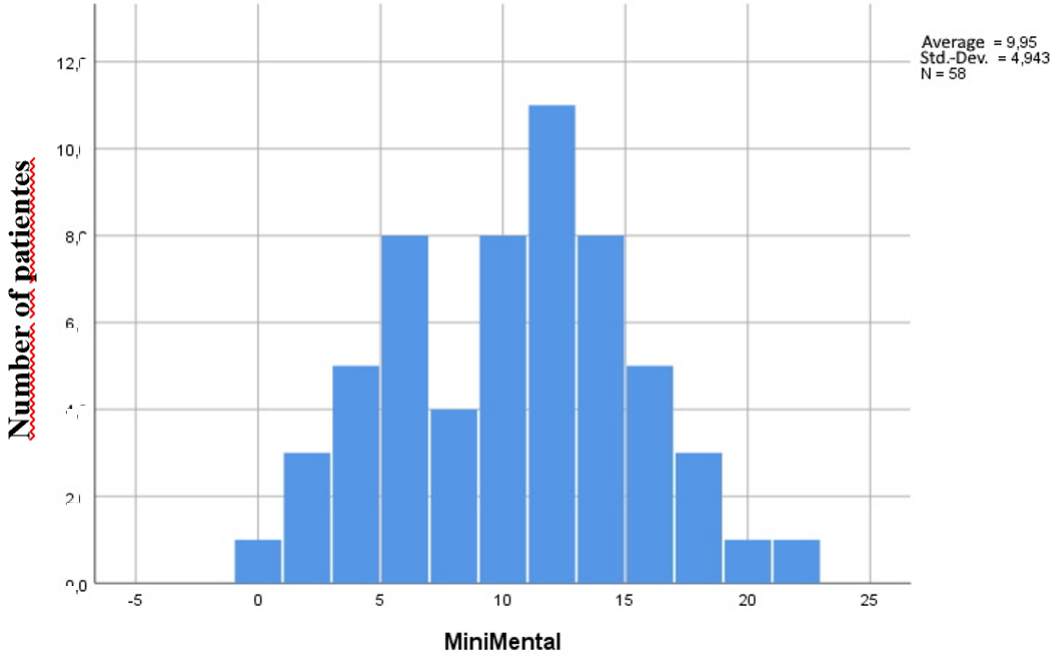


Figure 14: Distribution of Mini-Mental State Exam Scores

Looking at the severity of dementia, 29 (50%) of these 58 patients were categorized in the stage of moderate dementia and 29 (50%) in the stage of severe dementia. The remaining 4 patients categorized with the GDS were all assigned a GDS Score of 6 (severe cognitive decline) which put them in Category 1, severe dementia.

Severity of dementia

Severity stage		Number of patients	Percentage
	Severe	33	53.2
	Moderate	29	46.8
	Total	62	100.0

Table 5: Frequency distribution of moderate and severe dementia

1 = MMSE Score of 0-10, severe dementia 2 = MMSE Score of 11- 20, moderate dementia

3.2.2 Measurement of the outside temperature

During the preparatory stage of this study, it was noticed that many patients who did not tolerate the weighted blanket were complaining about it being too warm. As our study was conducted over different seasons, including hot weather during summertime, our team decided to also look at the outside temperature during the examined nights. At first the temperature of each individual night at 7 pm was noted. Based on this temperature we assigned every study night to a temperature category ranging from normal temperature to hot temperature. The lowest measured outside temperature was -3.7°C and the highest was 29.9°C.

Temperature category	**Temperature in ° C**
Normal temperature	-4 – 19.9°C
Warm temperature	20.0 – 24.9°C
Hot temperature	25°C – 30°C

Table 6: Temperature categories based on the outside temperature in °C as measured by the Deutscher Wetterdienst for Regensburg at 7 pm

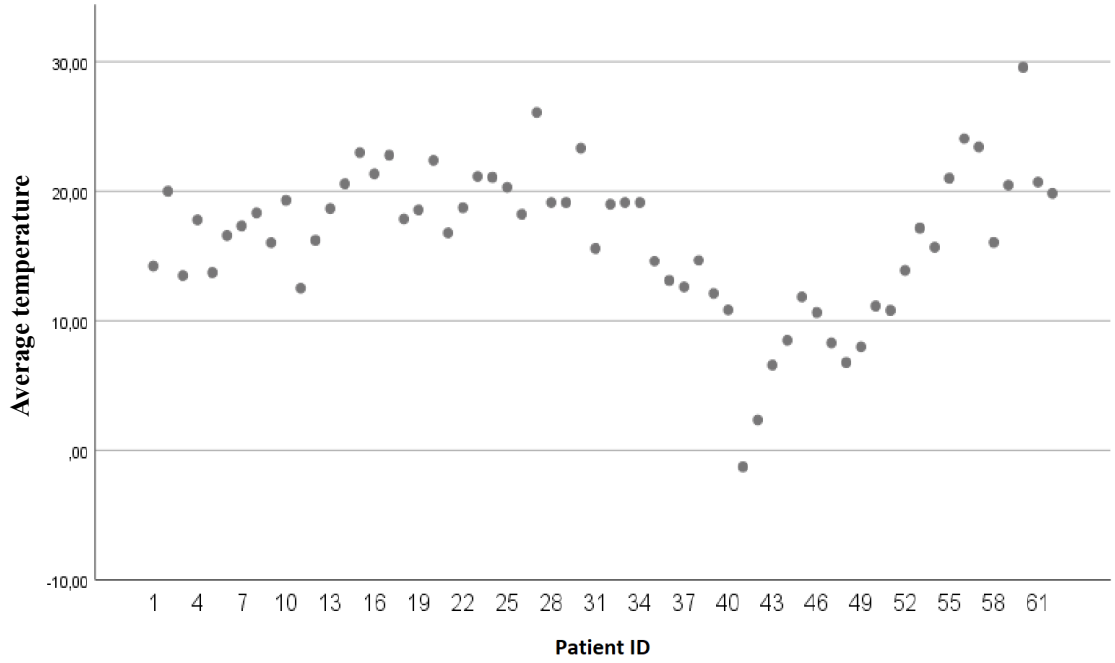


Figure 15: Temperature profile over the course of the study

Temperature category		Number of nights	Percentage
	Normal	45	72.6
	Warm	15	24.2
	Hot	2	3.2
	Total	62	100.0

Table 7: Distribution of temperature categories

1 = normal temperature
2 = warm temperature
3 = hot temperature

Overall, examination of the evening temperature showed a pleasant temperature for the majority of trial nights. Of course, the optimal sleeping temperature is an individual measure and can vary from patient to patient.

3.3 Acceptance of the granulate blanket

As mentioned in Section 2.1.3 The granulate blanket from Protac, the acceptance of the

granulate blanket was divided into three categories: 1) acceptance of the blanket during the whole night, 2) mostly accepting the blanket with uncovering a few times and 3) non-acceptance of the granulate blanket for most of the night. At first, we looked at each night individually.

Acceptance during first study night

		Number of patients who…	Percentage
	Tolerated it the whole night	38	61.3
	Uncovered themselves a few times, overall tolerated	9	14.5
	Did not tolerate the blanket	15	24.2
	Total	62	100.0

Table 8: Acceptance during the first night

tolerated it the whole night = Category 1
uncovered themselves a few times, overall tolerated= Category 2
did not tolerate = Category 3

Acceptance during second study night

	Number of patients who…	Percentage
Tolerated it the whole night	32	51.6

	Uncovered themselves a few times, overall tolerated	11	17.7
	Did not tolerate	16	25.8
	Total nights	59*	95.2

Table 9: Acceptance during the second night

* Three patients could not be evaluated in their second night as explained in Section 3.1, hence the number of patients evaluated in the second night is lower than the number of patients in the first night

Out of the 62 patients, 59 proceeded in the study and completed the second night. Three patients were not able to complete the second night due to various reasons, mentioned above.

Acceptance during third study night

		Number of patients who…	Percentage
	Tolerated it the whole night	32	51.6
	Uncovered themselves a few times, overall tolerated	9	14.5
	Did not tolerate	14	22.6
	Total nights	55*	88.7

Table 10: Acceptance during the third night
**Five patients could not be evaluated in their third night as explained in section 3.1, hence the number of patients evaluated in the third night is lower than the number of patients in the first and second night*

After that, we looked at each patient and determined their overall acceptance over the course of the three trial nights. We assumed that Category one (acceptance during the whole night) and Category two (mostly acceptance with a few times of uncovering) could both be seen as overall acceptance of the granulate blanket and only Category three (non-acceptance for most of the night) as non-acceptance.

If a patient was in the acceptance category one or category two for at least two out of the three nights, he/she was judged as accepting the granulate blanket in this part of the analysis.

Acceptance during two or more nights

		Frequency	Percentage
	Yes	45	72.6
	No	17	27.4
	Total	62	100.0

Table 11: Overall acceptance during two or more nights

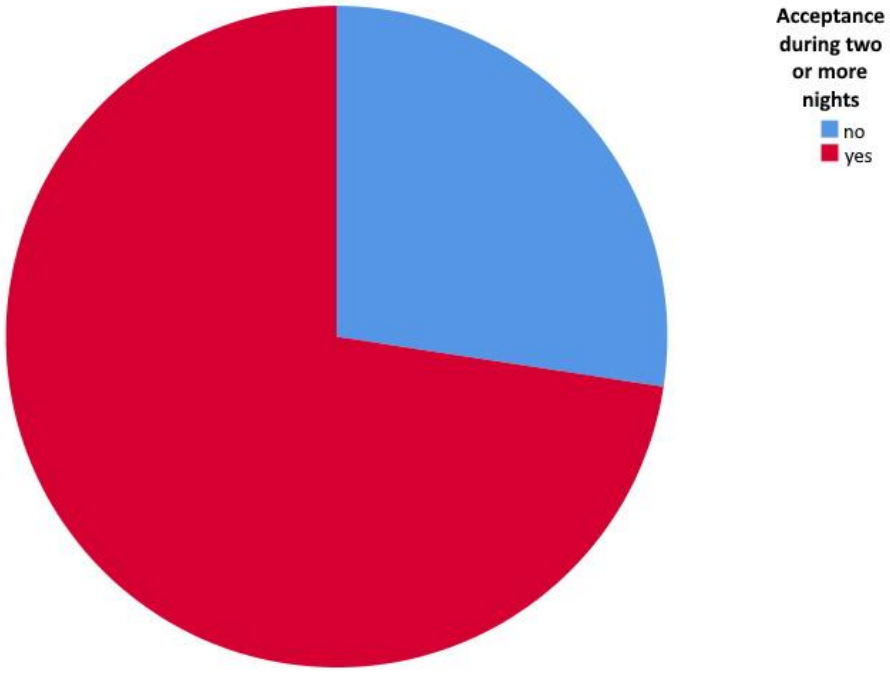


Figure 16: Distribution of acceptance during two or more nights

According to the frequencies of acceptance, the granulate blanket was accepted by 72.6% of

the patients, whereas only 27.4 % of the patients did not accept the blanket.
For a more detailed analysis, in Figure 27 we show how many patients accepted the granulate blanket for how many nights.

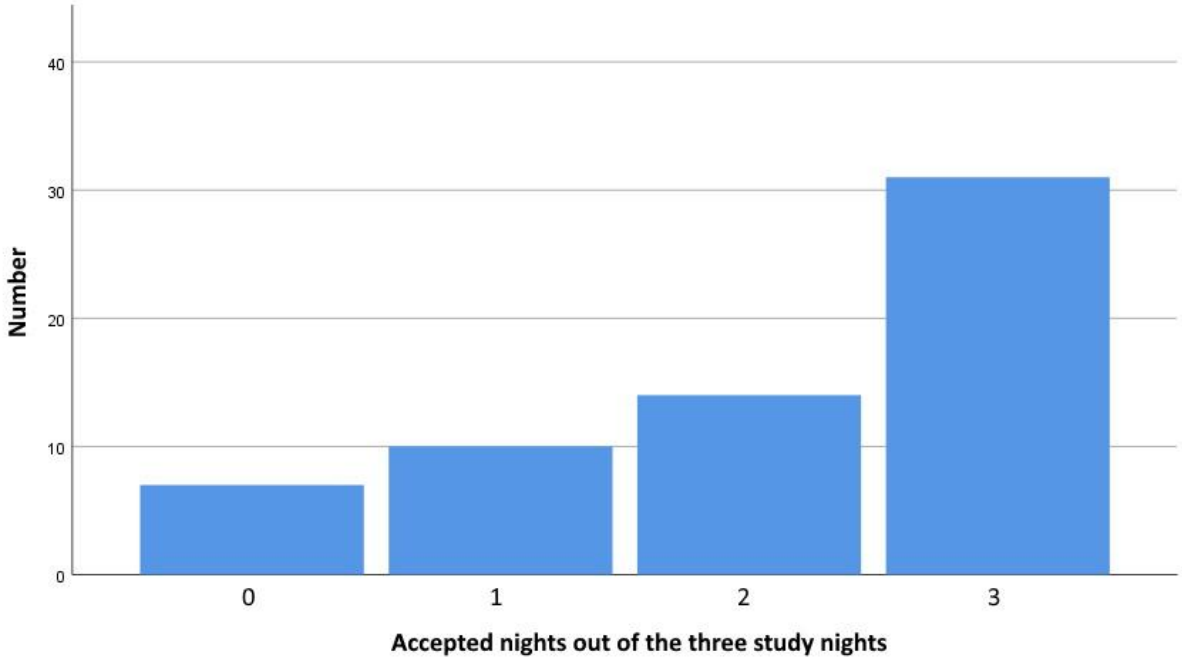


Figure 17: Number of nights during which granulate blanket was accepted

Seven patients (11.3%) did not accept the granulate blanket for any night. Ten patients (16.1%) accepted the granulate blanket for one night and 14 patients (22.6 %) accepted it for two nights. The remaining 50%, or 31 patients, accepted the blanket for the full three trial nights. It has to be mentioned that out of the seven patients with no accepted night, two were excluded from the trial. Out of the patients with one accepted night, three patients were excluded from the trial for one night and lastly out of the patients with two accepted nights, three patients had to be excluded from the trial for one night.

3.2.1 Reasons for non-acceptance

While seeing that the overall acceptance of the granulate blanket is good, we wanted to find and analyze reasons for non-acceptance.

First of all, we collected information from the patients themselves and from the nursing staff on the wards as to what reasoning the patients gave for not wanting to sleep with the weighted blanket.

Because not all patients of our study collective were able to give an explanation due to their stage of dementia, only the statement of a few patients, especially those with moderate dementia, could be recognized in this trial. On their periodic check-ins on the patients, the nursing staff not only examined the acceptance of the blanket, but would also ask the patients about their reasons for non-acceptance, or the patients would mention it on their own (if their communication skills allowed this). Then the nursing staff would note the acceptance category and also, if available, added the reasoning for non-acceptance into the report.

The most common reason for non-acceptance expressed by the patients was that the blanket was too heavy. The other reason which was mentioned often was that the granulate blanket was too warm and the patients were sweating during the night.

These reasons were documented by the nursing staff. Exact numbers cannot be determined due to the severe dementia of some subjects.

3.3 Examination of the correlations

To get an objective view of the reasons for non-acceptance, we also examined the correlation between the age, the temperature, gender and the stage of dementia on the one side and the acceptance of the granulate blanket on the other side.

3.3.1 Correlation between age and acceptance

To examine if there was any difference in acceptance depending on the age of the patients, the age of the patients who accepted the blanket (for two or more nights) was compared to the age of patients who did not accept the blanket.

Acceptance depending on the age of the patients

Acceptance during two or more nights	Average	N	Standard deviation
Yes	80.1	45	8.0
No	81.0	17	7.1
Total	80.34	62	7.7

Table 12: Average age of patients with overall acceptance and non-acceptance

As seen in Table 14, there is no big difference (0.91 years) in the mean age of patients who accepted the blanket to patients who did not accept the blanket during the nights.

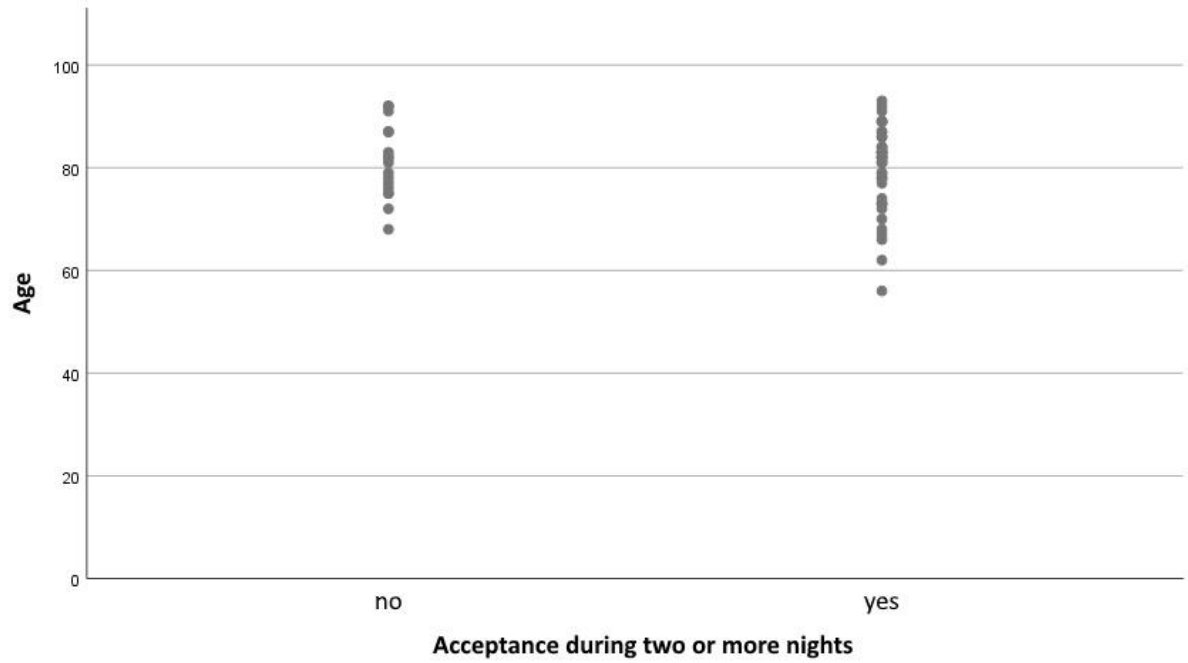


Figure 18: Scattering of the age in the categories acceptance and non-acceptance

3.3.2 Correlation between gender and acceptance

		Acceptance during two or more nights		
		No	Yes	Total
Gender	Male	7	23	30
	Female	10	22	32
Total		17	45	62

Table 13: Distribution of acceptance and non-acceptance of the blanket in men and women

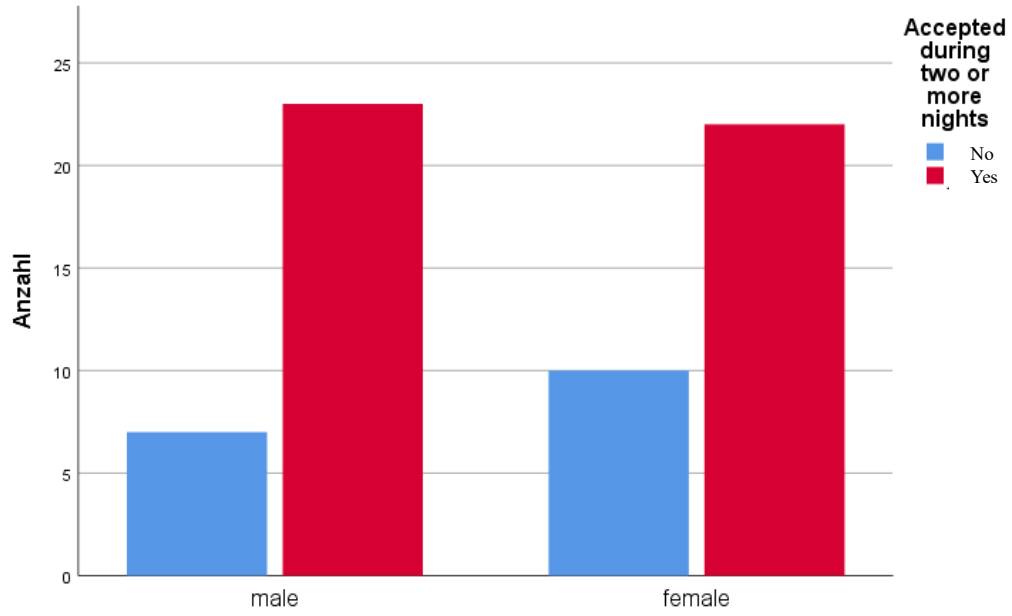


Figure 19: Bar graph showing the acceptance during two or more nights depending on the gender

Out of the 30 men in the study, 76.67 % accepted the blanket for two or more nights. For the women, 68.76% accepted the blanket for at least two nights.

3.3.3 Correlation between severity of dementia and acceptance

		Acceptance during two or more nights		
		No	Yes	Total
Severity of dementia	Severe	9	24	33
	Moderate	8	21	29
Total		17	45	62

Table 14: Distribution of acceptance depending on the severity of dementia

In the group of patients with severe dementia, 72.7 % accepted the granulate blanket for at least two nights. With almost the identical percentage, 72.4 % of the patients with moderate dementia accepted the blanket for two or more nights. Therefore, the acceptance of the blanket was similar in both severity groups.

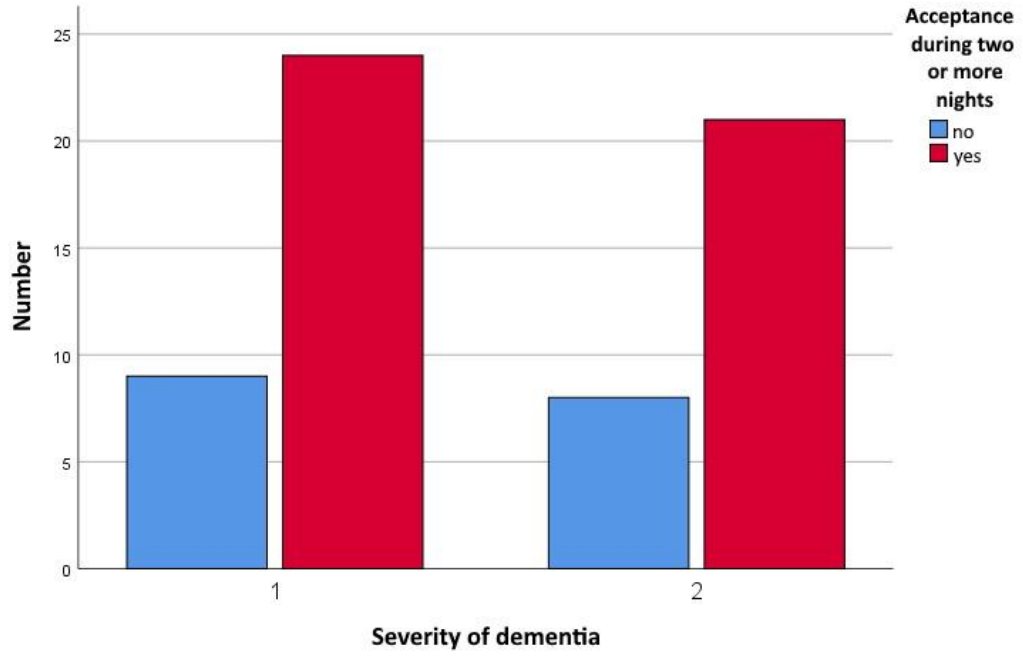


Figure 20: Bar graph of acceptance depending on the severity of dementia

Group 1 = severe dementia
Group 2 = moderate dementia

3.3.4 Correlation between outside temperature and acceptance

3.3.4.1 Correlation between outside temperature and acceptance for each individual night

Temperature category 1 compared to acceptance during Night 1

Acceptance Night 1			Tolerated the whole night	Uncovered themselves a few times, overall tolerated	Not tolerated	Total
Temperature Category 1	1	N	25	8	13	46
		% of all	40.3%	12.9%	21.0%	74.2%
	2	N	12	1	1	14
		% of all	19.4%	1.6%	1.6%	22.6%
	3	N	1	0	1	2
		% of all	1.6%	0.0%	1.6%	3.2%
Total		N	38	9	15	62
		% of all	61.3%	14.5%	24.2%	100.0%

Table 15: Acceptance depending on temperature category night 1

temperature category 1= normal temperature
2 = warm temperature
3 = hot temperature

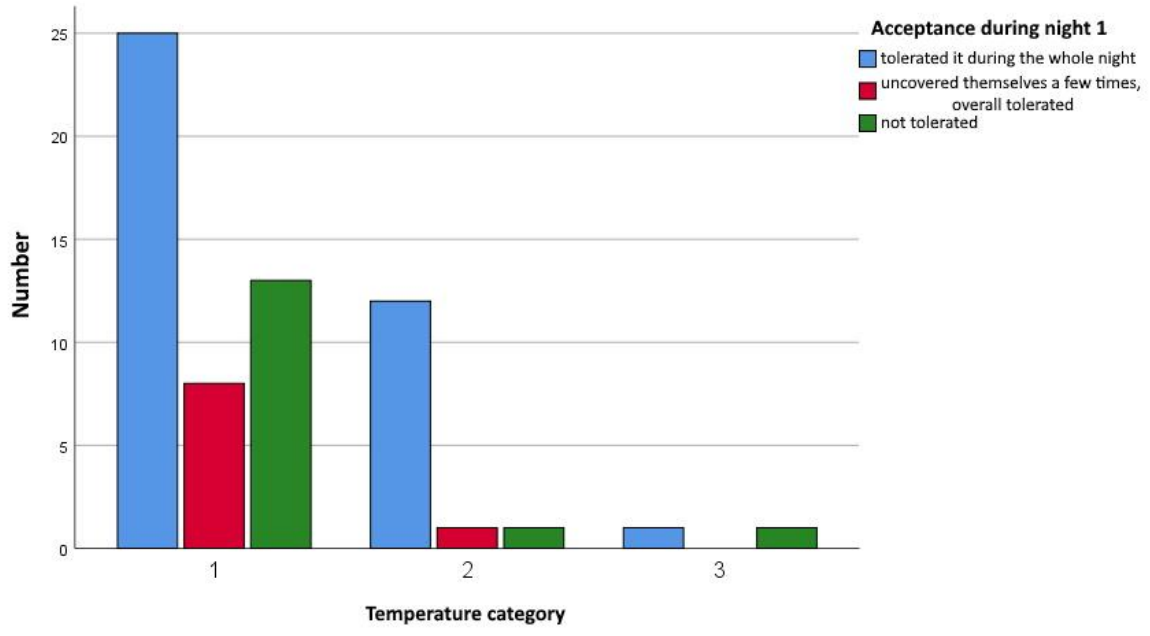


Figure 21: Acceptance during Night 1 in the temperature category 1

Looking at the first night of the trial, there were 46 nights with a normal temperature, 14 with warm temperature and two with hot temperature. Out of the nights with normal temperature, 33 of the 46 nights (71. 7%) fell into the acceptance category 1 or 2, which are considered accepted. The warm nights were accepted by 92.9% (13 of 14 nights) of patients. During the hot nights, one night was accepted and the other one was not.

Temperature category 1 compared to acceptance during Night 2

Acceptance Night 2			Tolerated the whole night	Uncovered themselves a few times, overall tolerated	Not tolerated	Total
Temperature cat. 2	1	N	21	10	12	43
		% of all	35.6%	16.9%	20.3%	72.9%
	2	N	9	1	4	14
		% of all	15.3%	1.7%	6.8%	23.7%
	3	N	2	0	0	2
		% of all	3.4%	0.0%	0.0%	3.4%
Total		N	32	11	16	59
		% of all	54.2%	18.6%	27.1%	100.0%

Table 16: Acceptance depending on temperature category Night 2

During the second night, there were 43 nights with a normal temperature in which 72.1% of subjects (31 nights) slept fully or almost fully with the blanket. In the warm temperature category, 71.4% (10 out of 14 nights) of the nights were accepted. In the hot temperature nights, all of them were accepted.

Temperature category 3 compared to acceptance during Night 3

Acceptance during Night 3			Tolerated the whole night	Uncovered themselves a few times, overall tolerated	Not tolerated	Total
Temperature cat. 3	1	N	21	8	7	36
		% of all	38.2%	14.5%	12.7%	65.5%
	2	N	11	1	6	18
		% of all	20.0%	1.8%	10.9%	32.7%
	3	N	0	0	1	1
		% of all	0.0%	0.0%	1.8%	1.8%
Total		N	32	9	14	55
		% of all	58.2%	16.4%	25.5%	100.0%

Table 17: Acceptance depending on temperature category Night 3

The acceptance for the third night shows similar results. The nights with the normal temperature had 80.6 % (29 of 36) accepted nights. The nights with warm temperature had 66.7% (12 of 18) accepted nights. And the only night in the hot temperature category was not accepted.

Overall, the observation of the nights individually showed that all of the nights were accepted at an equal rate, not really dependent on the outside temperature. The temperature category 3 with the hot temperature is difficult to interpret, as only 2.8% of the nights fall into this category.

3.3.4.2 Correlation between outside temperature and overall acceptance

Temperature category compared to acceptance during two or more nights

		Acceptance during two or more nights		
		No	Yes	Total
Temperature category	1	13	32	45
	2	3	12	15
	3	1	1	2
Total		17	45	62

Table 18: Distribution of acceptance depending on the outside temperature category

1 = normal temperature
2 = warm temperature
3 = hot temperature

During the hot temperature, 50% (1of 2) of the patients did not accept the granulate blanket. Due to the small number of nights with a hot temperature, these results cannot be significantly examined.

During the warm nights, despite the warm temperature, 80% (12 of 15) of the patients accepted the blanket for two or more nights, therefore only 20% did not accept the blankets. For the nights with a normal mean temperature, 71% (32 of 45 patients) accepted the granulate blanket.

Overall, the statistics did not show a difference in acceptance depending on the outside temperature on that evening. However, we were able to find a subjective difference in acceptance. To our team and the staff, it seemed as if the blanket was denied more often during the hot temperatures than during normal temperatures. This effect could also be influenced by individual opinions and was not shown by the statistic results.

3.4 Estimation of the occurrence of the acceptance depending on the independent variables through a binary logistic regression

3.4.1 Binary logistic regression with categorical data

Independent categorical variables

		Frequency	Parameter codes (1)
Temperature category	normal*	45	0
	warm*	17	10
Severity of dementia	severe	33	1.0
	moderate	29	0
Gender	male	30	1.0
	female	32	0

Table 19: Independent variables

* The number of nights with an average hot temperature were too few (2 nights) for an inclusion into the binary logistic regression, so we decided to count these as warm nights for this part of the statistics

The table of independent categorical variables gives us the chance to verify that every category has enough values to be considered for this calculation. The parameter codes show us which of the two categories of each variable was taken as the reference category.
The first step of SPSS is to calculate the equation with a constant without using the independent variables to create an intercept-only model.

Classification Table[a,b]

			Predicted		
			Acceptance during two or more nights		Percentage
	Observed		No	Yes	Correct
Schritt 0	Acceptance during two or more nights	No	0	17	0
		Yes	0	45	100
	Overall Percentage				72.6

a. The cut value is .500 *

* This means that if the probability of a case being classified into the "yes" category is greater than .500, then that particular case is classified into the "yes" category.

Variables in the Equation

		Regression coefficient B	Standard Error	Wald	df	Sig.	Exp(B)
Step 0	Constant	.973	.285	11.692	1	.001	2.647

Variables not in the Equation

			Wert	df	Sig.
Step 0	Variables	Gender1)	.488	1	.485
		Severity of dementia (1)	.001	1	.978
		Temperature category (1)	.178	1	.673
	Total		.789	3	.852

In the next step, SPSS calculates the independent variables into the equation to compare the intercept-only model to the new Block 1 model with the independent variables to see if this model is an improvement compared to the intercept-only model. For this, it uses a Chi-square independent test, which is called Omnibus test in SPSS.

Omnibus-Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	.797	3	.850
	Block	.797	3	.850
	Model	.797	3	.850

In order to show that the new Block 1 model is an improvement compared to the intercept-only model, the statistical significance would have to be under 0.05. As it is over 0,05, this predicts that the Block 1 model is not statistically significant and should not be used instead of the intercept-only model. Nevertheless, the logistic regression was completed.

Model Summary

Step	-2 Log-Likelihood	Cox & Snell R-Square	Nagelkerkes R-Square
1	72.039[a]	.013	.018

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001

The explained variation in the dependent variable based on our model ranges from 1.3% to 1.8%, depending on whether you reference the Cox & Snell R2 or Nagelkerke R2 methods, respectively.

Hosmer-Lemeshow-Test

Step	Chi-square	df	Sig.
1	.489	5	.993

The Hosmer-Lemeshow Test tests the null hypothesis that predictions made by the model fit perfectly with observed group memberships. A chi-square statistic is computed comparing the observed frequencies with those expected under the linear model. The chi-square for this model is nonsignificant, which indicates that the data fit the model well.

Contingency table for Hosmer-Lemeshow-Test

		Acceptance during two or more nights = no		Acceptance during two or more nights = yes		
		Observed	Predicted	Observed	Predicted	Total
Step 1	1	3	3.108	6	5.892	9
	2	4	4.002	8	7.998	12
	3	1	1.077	3	2.923	4
	4	2	1.813	5	5.187	7
	5	4	3.249	9	9,.751	13
	6	2	2.642	9	8.358	11
	7	1	1.109	5	4.891	6

Classification Table[a]

	Observed		Predicted: Acceptance during two or more nights		Percentage Correct
			No	Yes	
Step 1	Acceptance during two or more nights	No	0	17	.0
		Yes	0	45	100.0
	Overall Percentage				72.6

a. The cut value is 0.500

Variables in the Equation

		Regression coeffience B	Standard errorr	Wald	df	Sig.	Exp(B)	95% Coefficient for EXP(B) Lower	Upper
Step 1[a]	Gender(1)	.459	.589	.607	1	.436	1.583	.499	5.025
	Severity of dementia(1)	.053	.580	.008	1	.928	1.054	.338	3.282
	Temperature category(1)	.358	.672	.284	1	.594	1.431	.383	5.344
	Constant	.640	.547	1.368	1	.242	1.896		

a. Variables entered in Step 1: Gender, Severity of dementia, Temperature category

Correlation Matrix

		Constant	Gender(1)	Severity of dementia(1)	Temperature category(1)
Step 1	Constant	1.000	-.588	-.604	-.354
	Gender(1)	-.588	1.000	.119	.157
	Severity of dementia(1)	-.604	.119	1.000	-.048
	Temperature category(1)	-.354	.157	-.048	1.000

After completing the binary logistic regression, the last table shows us that the expected influence on acceptance, as predicted in the chi-square-test, is not statistically significant. All of the marked significance coefficients are larger than 0.05, which makes them not statistically significant. This means that, according to this statistical model there is no significant influence on the acceptance of the blanket by the independent variables, and the null hypothesis that the dependent variable (the acceptance) does not correlate with the independent variables (gender, severity state and temperature), cannot be rejected. Therefore, we are not allowed to use the other results of the logistic regression as they would not be correct.

3.4.2 Binary logistic regression with metric data

To rule out that the statistically insignificant outcome resulted from using ordinal variables and not metric variables, we used the same binary logistic regression with independent variables and metric values. For this, we used the mean temperature of the three nights for the temperature, the mini-Mental Status Examination score for the severity of dementia and as a third metric independent variable we used the age of the patients.

Summary

Unweighted cases[a]		N	Percent
Selected cases	Included in the analysis	58	93.5
	Missing cases	4	6.5
	Total	62	100.0
Not selected cases		0	.0
Total		62	100.0

Because four patients' dementia severity was not scored with the MMST, these 4 values were not included in the calculation.

Omnibus Tests of Model Coefficients

	Chi-square	df	Sig.

Step 1	Step	.506	3	.918
	Block	.506	3	.918
	Model	.506	3	.918

Variables in the Equation

		Regression coefficient B	Standard error	Wald	df	Sig.	Exp(B)	95% Coefficient for EXP(B) Lower	Upper
Step 1	Age	-.021	.040	.291	1	.590	.979	.906	1.058
	MiniMental	.001	.061	.000	1	.992	1.001	.887	1.129
	Mean Temperature	-.024	.053	.206	1	.650	.976	.879	1.084
	Constant	3.081	3.313	.865	1	.352	21.771		

a. Variables entered in Step 1: Age, MiniMental, Mean Temperature

Put in a nutshell, we found that even with using metric values instead of ordinary ones, the differences still came out as not statistically significant. The marked values show a significance coefficient of larger than 0.05, which makes the correlation insignificant and therefore the binary logistic inconclusive.

4. Discussion

4.1 Summary of main findings

This study is a preparatory study for our main study, "Studying the effectiveness of a granulate blanket in improving sleep quality and daytime activity in patients with moderate to severe dementia and sleeping disorders." Our main study examines the effect on the quality and quantity of sleep when using a granulate blanket during the night on patients with moderate to severe dementia and sleeping problems. To ensure the fluent process of this main study, a preparatory study was conducted which examines the acceptance of this granulate blanket during the course of three nights in patients with moderate to severe dementia. For this the patients slept with the granulate blanket over a course of three nights, when possible, and it was noted how they tolerated the granulate blanket and if there were any relevant factors influencing the acceptance.

The main questions asked in this preparatory study were:

Primary objective:

Determining, whether sleeping with a granulate blanket is tolerated by patients with moderate to severe dementia and sleep disturbances.

Looking at the primary objective, this preparatory study showed that a predominant number (72.6%) of patients with moderate to severe dementia did accept and tolerate the granulate blanket. This was an important requirement for our main study as it proves that the blanket is a safe and suitable treatment, even for patients with dementia.

Secondary objectives:

To find out whether there are any specific factors/cues which could help to anticipate the effect and the tolerability of granulate blanket use during night sleep; collecting the reasons why the blanket was not tolerated.

Secondly, our study was not able to determine a certain group of patients who significantly did not tolerate the granulate blanket, nor did we find any specific factors that statistically showed an impact on the effect or tolerability of the granulate blanket. Reasons for non-acceptance, which were verbally expressed by the patients, were often that the blanket was too warm or too heavy for their personal preference.

On top of our main study objectives, we also gained an initial insight into the effects of the granulate blanket on the sleep quality and quantity of the study participants. As the results of the actigraphy have not been interpreted yet, the effect can only be assumed based on what the patients themselves and the staff of the ward have observed and reported. According to them, there were certain patients who especially profited from the use of a granulate blanket. The night shift nurses reported that some of the patients showed a decrease in the frequency of nocturnal awakenings and night wanderings, which led to a decrease of day-night reversal symptoms. In addition, some patients, predominantly those with moderate dementia, verbally expressed their liking for the granulate blanket and that they had the impression of better sleep through this blanket. However, it has to be noted that these effects were only found for certain patients and other patients did not show any improvement while using the blanket. Of course, the real data of our main study still has to be evaluated, but it looks like the effect of the blanket is individual and is hard to predict based on specific factors or features.

4.2 Discussing the materials and methods

4.2.1 Discussing the study patients

The initially planned minimum age of 60 was lowered to 50 years at the outset of the study, as we discovered that there was a non-negligible number of potential patients with sleeping problems and early onset dementia on our ward.
With an overall average age of 80 years, the age group chosen for our study also gave us a better representation of the general average age of people with moderate to severe dementia.

The distribution of sex was fairly even, with almost 50% men and women. This represents the average gender distribution on our geriatric psychiatric ward.

62 patients were included in the preparatory study. Although the study could have been extended, the number of study patients was sufficient to demonstrate a trend in the acceptance of the weighted blanket. It was more important that this information was collected over the course of one year. We started collecting data in April 2018 and ended data collection in May 2019, so we included all four seasons in the study timeframe. As the weather is typically warmer in spring and summer, this could have led to less tolerance due to the warming blanket being too hot for some patients. Also, the changing amount of sunlight and the time spent outside could have influenced the depth of sleep and therefore also the acceptance of the weighted blanket. If we had only included one season, or if the study had included more summer than winter months, this would have biased the results.

4.2.2 Discussing the study center

The study was conducted in a closed gerontopsychiatric unit of the Department of Psychiatry and Psychotherapy of the University of Regensburg.
This clinic is a widespread psychiatric clinic with 626 beds and a catchment of two local districts. Therefore, patients with many different pathologies can be found here, which would have allowed us to include rare cases of dementia. Nevertheless, we did not find patients with PPA or frontotemporal dementia in our study participants. This is either due to the low number of patients with these types or the lack of correct diagnosis on our ward.
The patients admitted to the closed unit are predominantly patients with moderate or severe dementia or also other types of psychiatric illnesses suited for the objective of the study.
In the future, a study for patients with light to moderate dementia could be indicated. For this

purpose, an open geriatric psychiatric unit may be more appropriate.

Looking at the ward itself, it also could have influenced the acceptance of the blanket.
This ward is responsible for all psychiatric patients over 50 years of age (in some rare cases also patients younger than 50 are admitted, for example with early onset dementia) having a psychiatric illness and the risk of constituting any danger to themselves or any other person and requiring accommodation in a closed unit. Consequently, all patients wander around the ward a lot and they often disturb their fellow patients, including at night, which could have adversely affected the night sleep of a patient with a weighted blanket. However, a similar situation can be found in other clinical units or even in nursing homes, where these blankets will also find use.

The form of data collection can also be discussed. For our documentation, we only used the observations of the nursing staff and other members of the ward team. And although the night staff used a standardized observation pattern and a standardized documentation system, this form of observation is still quite subjective. The fact of whether a blanket is tolerated over the course of the night or if the blanket was rejected due to some reason can certainly be determined only by checking on the patient several times, so this procedure was adequate for this pilot study.
In order to get a more precise observation, including the exact times of uncovering and recovering or the overall movement in bed with a granulate blanket, video surveillance throughout the night would be a better approach. For video surveillance, we would have had to hang up video cameras in every room in a spot out of reach of the patients. This would have exceeded the financial framework of our study. Additionally, it would have been a time-consuming method. Not only viewing the video material the next day, but also getting the declaration of consent to film the patient takes major effort and would have called for another member X.

Lastly, the discussion of material and methods will focus on the material. We chose granulate blankets from the producer Protac from Denmark. The blanket is divided into 40 chambers which are filled with polypropylene granulates and weighs 5.5 kg. The company Protac also produces other weighted blankets, but this granulate blanket was chosen for our trial because Protac recommends this model for adults with sleeping problems and agitation, which dementia patients often have. (99)

Former studies tested weighted vests for children with ADHD, but as we wanted to improve the night sleep of patients with dementia, weighted vests would not have been as suitable as weighted blankets.

4.2.3 Discussing the statistics

First of all, we tried to reduce the risk of making a Type II error by choosing an appropriate sample size. Different studies recommend a minimal sample size of approximately 10 caseloads per predictor. (101) (102)
Secondly, the requirements for a binary logistic regression were tested. Our dependent variable was a nominal variable with exactly two possible values (accepted and not accepted).
Linearity was tested using the Box-Tidwell procedure. Bonferroni correction was applied to all terms in the model. All variables were found to follow a linear relationship.

For the first attempt at the binary logistic regression, we used categorical independent variables. One of these was the mean Temperature category, determined by taking the average temperature during the three study nights and deriving the overall temperature category from it. This step is not fully accurate as we wanted to look at the likelihood of accepting the blanket depending on the outside temperature during that study night. By taking the average temperature of all three nights, the direct relation between outside temperature and acceptance can be lightly distorted. All in all, we still chose this method, as the temperature differences between all three study nights were never larger than 8°C.

4.3 Discussing the results

As this study shows, the use of weighted blankets is tolerated overall by patients with moderate to severe dementia.
The study was not able to find a specific group of patients who predominantly did not tolerate the blanket. There was no statistically significant influence on acceptance by the severity of dementia, the gender of the patient or the outside temperature. This can be due to insufficient sample size and also the uneven distribution of the various categories. In the category of the outside temperature, for instance, only five out of the 180 study nights were assigned to Category 3 “hot temperature”, which makes it hard to determine a significant difference between these categories.

Overall, the primary results of our main study show that the use of granulate blankets can improve the quality and quantity of sleep in patients with moderate to severe dementia and sleeping disturbances. However, the effect is very individual and does not apply to every patient. And this effect, of course, is dependent on the acceptance of the blanket during the night.

On the one hand, this provides an open foundation for our main study, as we do not have to exclude certain groups of age, severity of dementia or nights with a higher temperature due to a significantly higher rate of unacceptance in these groups. On the other hand, this shows that acceptance is more likely dependent on individual preferences. Patients who did not tolerate the blanket either expressed their dislike verbally or they simply placed the blanket aside or on the floor, so that no patients were forced to use the blanket if they did not want it. Therefore, the use of a granulate blanket can easily be tried for any patient with sleeping disorders and the acceptance can be tested without forcing the patients.

Another positive point which was revealed in this study was the safety aspect. The staff of our ward never had to remove the blanket from a patient's room because the patient had placed the blanket over his/her head; they only removed the blanket for three patients as a preventative measure, as these patients had suffered from reduced vigilance during the day. This demonstrates that the granulate blanket is a safe method, even for people with dementia. Of course, the risk of suffocation cannot be disregarded, especially in patients with limited mobility. However, in our trial the impression was given that if the patients were supervised while covering themselves with the blanket and checked on every few hours, the risk of suffocation through a granulate blanket can be minimized. Sleeping with a granulate blanket can be a safe and easy way to improve sleep quality and quantity.

After demonstrating the statistics of our study, the study endpoint, the methods and material and the overall result will now be revisited and critically reflected.

In the present study, the tolerance of weighted granulate blankets by patients with moderate to severe dementia and sleeping problems was examined. A prospective clinical trial was used, because this is the first study that focusses on the use of granulate blankets on patients suffering from dementia and there was no available data concerning this question.

4.4 Comparing our results to the outcome of similar studies.

The number of studies on weighted or granulate blankets is limited. There have been other studies, which examined the effect and the tolerance of the weighted blanket during night sleep, but as mentioned above, primarily children with neuropsychiatric disorders (especially autism spectrum disorders - ASD and attention deficit hyperactivity disorder - ADHD) represented the target population of patients.

For this group, there is an exhaustive body of literature discussing the effectiveness of various sensory-based interventions - see e.g. May-Benson und Koomar 2010; Zimmer und Desch 2012 for review. (103) One study by Hvolby und Bilenberg from 2011 for example examines the effectiveness of use of weighted ball blankets during night sleep in pediatric patients with ADHD. A significant improvement of various parameters of sleep had been found. While a positive effect on the motor restlessness and on the quality of night sleep in geriatric patients with dementia has been anticipated, to our knowledge, there is not a single high-quality scientific study examining such effects in this group of patients. (104)

Although it is rather inaccurate to compare the result of a study on children with the results of a study conducted on dementia patients, all of the studies show that the blanket was accepted by the majority of study participants, which is also what we observed in our study. One other study from 2014 found that, although in this study the use of the weighted blanket did not improve the sleep quality of children with ASD, the weighted blanket was favored by children and parents, and blankets were well tolerated over this period. (105) “Seventy-three patients were randomized, and 6 were subsequently excluded. Four could not tolerate or declined to use the weighted blanket.” (105)

In any case, there have been studies looking at the use of weighted blankets on adults. A study by D. Dickson, L. Gantt and M. Swanson, which was released a few years prior, looked at the effectiveness of weighted blankets on patients with psychiatric illnesses in an emergency department. Since the patients were not examined during night sleep, this study is not ideal for comparison. However, in this study, the patients demonstrated a high tolerability of the weighted blanket and expressed positive feedback: (106)

> The participants who used the WB responded to two questions: ‘What did you like about the WB study?’ and ‘Did it seem to help, why or why not?’(see Table 3). The responses provided here are direct written quotes from the participants including their spelling

errors. For the first question, the participants stated, ‘it was relaxing,’ ‘it was good time to relax,’ ‘the calmness that the weighted blanket (undecipherable word) worked,’ ‘it’s somewhat helpful,’ ‘good reflection,’ ‘nice to know myself more,’ ‘it was calm, felt like a hug,’ ‘it was simple and straight forward,’and ‘I liked the weighted blanket.” (106)

Another finding of our study involved the safety of granulate blankets. As mentioned prior, during the course of this study, there was no situation where a patient was at risk of suffocation through the use of the granulate blanket and the precautions, we took prior to the study by excluding patients with a higher risk of suffocation appeared to have been very effective.
The work of Champagne and Mullen from the year 2015 evaluated the effectiveness and safety of weighted blankets with adults during an inpatient mental health hospitalization. To determine the safety of the weighted blankets, the vitals sign of the patients were monitored during the time the blanket was used. The vital signs included: pulse, blood pressure and pulse oximetry. The analysis of the vital signs showed that almost all of the patients stayed within the safe range for blood pressure and pulse and none of the patients fell below the pulse oximetry level of 90% and therefore stayed within the safe oxygen level range. In conclusion, the study states that the use of their weighted blanket did not cause any negative effect on physiological safety in terms of blood circulation or oxygen supply.
It also affirms: “This study verifies the previous results of the authors, which indicated that the use of a WB was safe for 100% and effective for 60% of the adult participants.” (107)

It must be noted that the model of weighted blanket used in the study of Champagne and Mullen weighed 30 pounds (approx. 14 kg), whereas our model was much lighter at only 5 kg. But nevertheless, the results regarding the safety of the use of a weighted granulate blanket were identical and with an even lighter blanket it is safe to say that a weighted granulate blanket is a low-risk form of therapy and can be safely used for our main study.
There has been one recent study which focuses on the use of a weighted blanket in patients with dementia. However, that work from Naramura and Yamauchi from 2021 only studied the effectiveness of the usage of a weighted blanket for one person with severe dementia, so this cannot be considered as a representative study. Nonetheless, the study found that the sleeping hours of this patient increased, and the frequency of nocturnal awakening decreased after the usage of the weighted blanket. The authors suggest that the effect of the blanket increased over the course of time. For this study, the patient slept with the blanket over a time period of five months, and the positive effects were even more significant after five months compared to after

one month of usage. They also propose that the effectiveness of the blanket can be further enhanced by combining it with lifestyle therapy, including environmental and psychological adjustments. (108)
To take the findings of this study up, a longer trial period could be used to show the long-term acceptance and effectiveness of the granule blanket in a further study.

4.5 Outlook on future studies

In total, this study was able to show that the usage of a granulate blanket during night sleep is widely accepted by patients with moderate to severe dementia and is not significantly influenced by age, gender, severity of dementia or outside temperature. However, there are still some aspects that could have been examined regarding these findings.
Firstly, other internal or external influencing factors on the acceptance should be taken into consideration and examined in further studies. Internal influencing factors include the height and weight of patients, as this could introduce the need for a different type of blanket, and also other internal factors like the comorbidities and medication of the patient. Prescribing a patient sedative medication could strongly influence the acceptance and the effects of the granulate blanket.
External factors should also be revisited. Not only the outside temperature, but also the temperature in the rooms should be looked at, as these can vary depending on the solar radiation.
Solar radiation is not the only influence on the patients´ sleep ; the exposure to sunlight during the day together with exercise also affect the patients' sleep. Many different studies indicate that a certain amount and the correct timing of exposure to sunlight and physical exercise have a positive effect on the quality and quantity of night sleep and could therefore manipulate the effectiveness results of the granulate blanket. (109) (110) Nevertheless, we found our study set-up to be sufficient to answer our study endpoints.

Another very interesting issue within this topic is the effect of sleep deprivation on the development of neurodegenerative illnesses like dementia.

In this work, the negative impact of dementia on the quality and quantity of sleep of elderly people was discussed, but some recent studies assume that this relationship is bidirectional.
In the beginning, scientists discovered an association between sleep and the accumulation of

amyloid-ß (Aß), which is the driving cause of Alzheimer's disease, in mice. Soon they realized that, also in humans, increased wakefulness and sleep disturbances lead to increased Aß production and deposition and to a decreased Aß clearance. The levels of Aß 40 and Aß 42 have been shown to be consistently higher during wakefulness and lower during sleep. (75) (10) This theory was supported by the findings of Kang and Lim, who showed a direct Aß plaque decrease after treatment with an orexin receptor antagonist. Orexin is a peptide produced in the hypothalamus which stimulates arousal and wakefulness. (107)
These studies found out that, even in healthy young adults, morning Aß42 levels increase after a single night of sleep deprivation. (51) A similar effect on the tau protein, which is also a key factor in the development of dementia, has been suggested. (51)

Especially a decrease of slow wave sleep is supposed to have the strongest effect on increased levels of Aß release. On the other hand, this slow wave sleep is predominantly decreased in patients with diagnosed dementia, which shows the direct negative effect of Aß accumulation on sleep quality and quantity. (111) (19)
The bidirectional relationship between sleep and the pathophysiology of dementia should be investigated further as it could be a key feature in prevention and maybe even treatment of dementia.

5. Conclusion

5.1 Overall conclusion

Overall, it was found that sleeping with a granulate blanket was accepted by patients with moderate to severe dementia. Reasons for non-acceptance were often that the blanket was either too warm or too heavy for the patients' personal preference. However, we were not able to find a correlation between a specific age group or severity of dementia and the acceptance of the granulate blanket. The outside temperature could have played a role in acceptance, but we were not able to find a significant correlation between high outside temperature during the night and non-acceptance. This consequently serves as a basis for our main study, as we have shown that the effectiveness of the granulate blanket will not be decisively disrupted by the non-acceptance of the blanket.

Additionally, this study indicates that the use of granulate blankets is a safe treatment option. There was no significant risk of suffocation, even in patients with severe dementia and

behavioral disorders. The exclusion criteria chosen prior to the study, which are also used for our main study, are sufficient in limiting the risks in using the granulate blanket.

As this preparatory study ran partly simultaneously to the main study, an early insight into the effect of the blanket and therefore our main study was revealed. Subjectively speaking (based on information from the night staff or the patients themselves), the patients who did accept the blanket for all of the nights often had an improvement in their sleep quality and/or quantity.

To sum it all up, although the acceptance and the effect of these granulate blankets were mostly positive, it is very individual, and while some patients did not enjoy the heavy sensation on their body while sleeping, others did subjectively and also objectively sleep better during the study nights.

5.2 Future outlook

The future of weighted blankets is bright. The industry of weighted and granulate blankets is growing and the interest in these kinds of blankets is increasing. More companies are producing weighted blankets and more types of weighted or granulate blankets are being developed to fit the needs of every person.

As seen in our results, a weighted blanket is often accepted by patients with dementia and can improve their night sleep. With more and more companies releasing their own type of weighted blanket, this makes them more affordable to purchase. This will make it easier for hospitals, nursing homes and even private people to purchase a weighted blanket and just try it out to see if it is tolerated by the user and can bring positive effects.

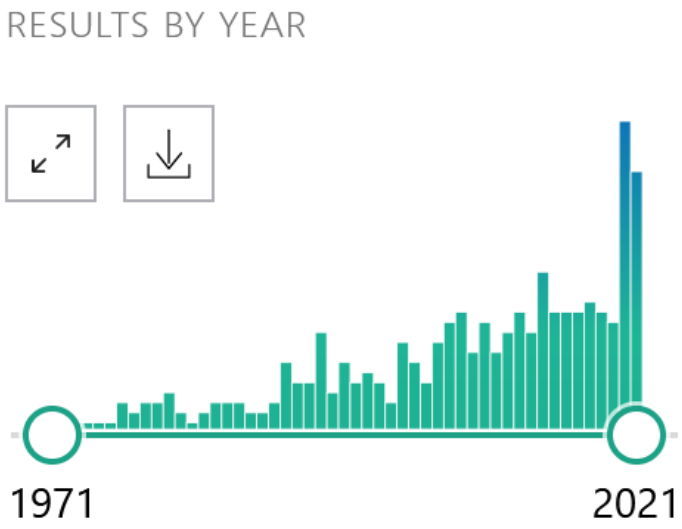


Figure 22: Result by year for the search term "weighted blanket" on the pubmed website

The graph in Figure 14 shows the results by year on the internet site pubmed.ncbi.nlm.nih.gov when searching for the words “weighted blanket.” 2020 and 2021, the results for this topic have almost tripled. Looking at 2019, there were 10 publications including the words “weighted blanket,” whereas in 2020 the number of results rose to 30.

Looking into the future, these blankets should also be tried in patients with a mild form of dementia or even patients with sleeping disorders due to other illnesses.
Patients with a mild form of dementia could actively ask for the blanket and can also better reflect on whether using it improves their night sleep and their daytime performance. Patients with milder cognitive illnesses can also give a more precise reason for non-acceptance if they did not tolerate sleeping with a weighted blanket. This information can then be used to improve the acceptance of the blankets in inpatient settings.
Apart from buying a granulate blanket as a hospital or as a private person, I think nursing homes are another institution which could surely profit from the purchase of a few granulate blankets, which their residents could use as needed.
In my opinion, providing these weighted granulate blankets for nursing homes could be a useful investment. If the possible non-acceptance of the blanket is a barrier for purchase for a nursing home or a private person, maybe the companies producing these blankets could offer a loan system, where patients or institutions have the opportunity to try the blankets and give them back after a certain period of time, much like the company Protac, which kindly lent us some granulate blankets for our study.
Many caretakers of the study patients on our ward were very interested in purchasing a granulate blanket for the people for whom they were caring. This shows that the demand is high, and the caretakers and families of patients with dementia and sleeping problems are desperately searching for solutions, ideally without the use of prescription drugs. Therefore, the granulate blanket is not only a safe but also an easy way to help not only the patients themselves but also their caregivers and families.

6. Appendix

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Bezirksklinikum Regensburg

Zentrum für Altersmedizin der Klinik und Poliklinik für Psychiatrie und Psychotherapie der Universität Regensburg

Chefarzt
Prof. Dr. med. Stephan Schiekofer

Information für gesetzliche Vertreter von Teilnehmerinnen und Teilnehmer

Sehr geehrte Dame, sehr geehrter Herr,

wir möchten Sie über die Studie **„Untersuchung über die Effektivität der Benutzung einer Granulat-Decke (Firma Protac A/S, Dänemark) zur Verbesserung der Schlafqualität und der Tagesaktivität bei Patienten mit mittelschwerer bis schwerer Demenz mit Schlafstörungen“** informieren.

Bitte lesen Sie sich die folgenden Anmerkungen zur Durchführung der Studie aufmerksam durch. Sie können dem aufklärenden Mitarbeiter alle Fragen stellen, die Sie eventuell im Zusammenhang mit der Studie haben.

Die Studie wird auf der Station 23B des Zentrums für Altersmedizin der Klinik und Poliklinik für Psychiatrie und Psychotherapie der Universität Regensburg durchgeführt. Herr MUDr. F. Barinka PhD (Funktionsoberarzt, Zentrum für Altersmedizin; Klinik für Psychiatrie und Psychotherapie der Universität Regensburg am Bezirksklinikum Regensburg) ist Leiter der Studie, Frau Tamara Finger (Stationsärztin, gleiche Klinik) ist stellvertretende Leiterin der Studie.

Zweck der Studie

Patientinnen und Patienten mit Demenz leiden häufig unter Schlafstörung, teilweise bis zur vollständigen Tag/Nachtumkehr. Zeitgleich sind durch häufig zahlreiche Vorerkrankungen und das fortgeschrittene Alter der Patienten der medikamentösen Behandlung der Schlafstörung Grenzen gesetzt.

Wir möchten in dieser Studie herausfinden, in wie weit sich der Nachtschlaf mit einer sogenannten Granulat-Decke (eine beschwerte, mit Granulat aus Polypropylen gefüllte Bettdecke) positiv beeinflussen und die

Medizinische Einrichtungen des Bezirks Oberpfalz - KU (Anstalt des Öffentlichen Rechts)

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Tagesmüdigkeit sich so reduzieren lässt. Das Wirkprinzip der Granulat-Decke beruht auf der Theorie sogenannten „Sensorischen Integration". Man geht davon aus, dass eine mangelhafte Wahrnehmung des eigenen Körpers dessen Grenzen eine Ursache motorischer Unruhe sein kann. Durch eine beschwerte Granulat-Decke kann über die Druckrezeptoren der Haut der eigene Körper ggf. wieder besser wahrgenommen werden und die Decke kann möglicherweise so beruhigend wirken und motorischer Unruhe entgegenwirken.

Diese Granulat-Decke ist ein Medizinprodukt und ist für die Benutzung zur Verbesserung des Schlafes offiziell durch entsprechende Behörden zugelassen (CE Kennzeichen als Medizinprodukt der Klasse I - niedrigster Gefährdungspotenzial, entsprechend der europäischen Medizinprodukterichtlinie 93/42/EWGund), und darf auch in Deutschland frei verkauft werden. Solche Decken werden auf der Station 23B für diesen Zweck (Verbesserung des Schlafes bei Patienten mit Demenz und vorliegender Schlafstörung) bereits seit mehreren Jahren benutzt.
Das Ziel der Studie ist somit nicht die Testung eines neuen Produktes, sondern genauere Untersuchung der Effektivität der Anwendung dieses Produktes und Untersuchung, welche Faktoren dabei möglicherweise eine Rolle spielen (wie z.B. Typ der Demenz)

Sicherheitsaspekte

Durch die Teilnahme an der Studie entstehen für den Patienten keine wesentlichen Belastungen oder Risiken. Alle angewendeten Produkte (Granulat-Decke und Aktigraphiegerät) werden auf der Station 23B bereits routinemäßig im klinischen Alltag nach Ermessen des ärztlichen Teams und/oder des pflegerischen Teams angewendet.

Beschreibung von Ablauf der Studie und der hierbei erhobenen Daten des Patienten

Im Folgenden erklären wir den Ablauf der Studie.

1. Patienten mit mittelschwerer bis schwerer Demenz und einer vorhandenen Schlafstörung (diese wird mittels der pflegerischen Dokumentation erfasst) werden zufällig ausgewählt und erhalten zur Messung der Aktivität ein sogenanntes Aktigraphiegerät, welches aussieht wie eine gewöhnliche Armbanduhr, über 5 Tage und 5 Nächte angelegt. Ein Teil der Patienten erhält nachts die Granulat-Decke, der andere Teil nicht. Auch die Untersucher wissen nicht, wer die Granulat-Decke in der Nacht hatte und wer nicht (sogenannte verblindete Studie). Zwischen den beiden Gruppen von Patienten gibt es hinsichtlich der medikamentösen und anderen nicht-medikamentösen Therapien keinerlei Unterschiede.

4. Patienten, die eine Infektion mit Fieber haben, sehr aggressiv oder nicht gehfähig sind, werden von der Teilnahme ausgeschlossen.

5. Nach 5 Tagen/Nächten wird die Teilnahme des Patienten an der Studie automatisch beendet.

6. Folgende Daten werden von dem Patienten erhoben:

   - Bei allen Patienten im Rahmen des Aufenthaltes zum Aufnahmezeitpunkt routinemäßig durchgeführten körperlichen, neurologischen und psychiatrischen Untersuchungsbefunde.

   - Die standardisierte pflegerische Dokumentation des Nachtschlafverhaltens der Patienten.

   - Ergebnisse von (im Rahmen der Diagnostik) weiterführenden Untersuchungen, wie EEG, CT, MRT, Blutuntersuchungen und ggf. Liquoruntersuchungen (="Nervenwasser"-Untersuchungen). Hierbei ist ausdrücklich zu erwähnen, dass diese Untersuchungen nicht explizit wegen der Studienteilnahme erfolgen, sondern bei allen Patienten nur bei Notwendigkeit zur Diagnostik erfolgen.

   - Ergebnisse von neuropsychologischen Testungen zur Erfassung des Demenzgrades und der daraus resultierenden Einschränkungen im alltäglichen Leben (Mini-Mental- Status -Test, Uhren-Test, Global Deterioration Skala, Neuropsychiatric Inventory Fragebogen und ähnliche).

   - Angaben der Angehörigen oder des Pflegeteams (bei Patienten aus einem Pflegeheim) zum bisherigen Verlauf der Erkrankung (Fremdanamnese)

Die Daten werden allen Mitgliedern des Untersucherteams zugänglich gemacht. Es werden keine Patienten Daten an externe Stellen (Hersteller der Granulat-Decke usw.) übermittelt. Alle erhobenen Daten, die zum Zwecke der Auswertung der Studienergebnisse benötigt werden, werden anonymisiert, so dass sie später keinem Patienten mehr eindeutig zugeordnet werden können. Somit können auch Ihnen als gesetzlichem Vertreter abschließend die persönlichen Studienergebnisse des Teilnehmers nicht mitgeteilt werden. Aber mit der Teilnahme wird ein wichtiger Beitrag geleistet, die nicht-medikamentöse Behandlung von Schlafstörungen bei Demenz ggf. zu verbessern.

Die Studie ist den international anerkannten ethischen Grundsätzen für die medizinische Forschung am Menschen verpflichtet.
Die Teilnahme ist freiwillig und kann jederzeit abgebrochen werden. Die Nichtteilnahme an der Studie hat keinerlei negative Folgen für Sie bzw. für den Patienten. Ebenso können Sie Ihre Einwilligung zur Teilnahme an der Studie jederzeit ohne eine Angabe von Gründen widerrufen, ohne dass Ihnen daraus irgendwelche Nachteile entstehen. Die Teilnahme an der Studie führt nicht zur Verlängerung des stationären Aufenthaltes des Patienten auf der Station 23B. Falls eine Entlassung oder Verlegung des Patienten aus medizinischen Gründen oder bei Ihrem Wünsch notwendig oder gewünscht ist, wird die eventuell noch laufende Studienteilnahme früher (zum Zeitpunkt der Entlassung oder der Verlegung) abgebrochen.

Einwilligungserklärung des gesetzlichen Vertreters

Hiermit willige ich

_____

Vorname, Name

_____

Geburtsdatum

_____

Straße, Hausnummer

_____

PLZ, Ort

_____

Telefonnummer

stellvertretend für Herrn/Frau

_____

Vorname, Name

_____

Geburtsdatum

_____

Straße, Hausnummer

_____

PLZ, Ort

in die Teilnahme an der Studie **„Untersuchung über die Effektivität der Benutzung einer Granulat-Decke (Firma Protac A/S, Dänemark) zur Verbesserung der Schlafqualität und der Tagesaktivität bei Patienten mit mittelschwerer bis schwerer Demenz mit Schlafstörungen“** ein, bei welcher Daten von dem Betreuten erhoben, gespeichert und verarbeitet werden.

Ich erkläre mich damit einverstanden, dass im Rahmen dieser Studie den Teilnehmer betreffende personenbezogene Daten/Angaben durch das Studienteam erhoben verschlüsselt (pseudonymisiert) auf elektronischen Datenträgern aufgezeichnet und verarbeitet werden dürfen. Ich bin auch damit einverstanden, dass die Studienergebnisse in nicht rück-entschlüsselbarer (anonymer) Form, die keinen Rückschluss auf den Teilnehmer zulassen, veröffentlicht werden. Mir ist bekannt, dass ich diese Einwilligung jederzeit ohne Angabe von Gründen und ohne nachteilige Folgen für den Betreuten zurückziehen und einer Weiterverarbeitung der Daten jederzeit widersprechen und ihre Löschung bzw. Vernichtung verlangen kann.

_____

Ort, Datum Unterschrift des gesetzlichen Vertreters/Vertreterin des Patienten

Universität Regensburg

medbo

Das Aufklärungsgespräch hat geführt:

_____

Name des Studienmitarbeiters

Hiermit erkläre ich, den/die o.g. gesetzlichen Vertreter am _____ über Wesen, Bedeutung, Tragweite und Risiken der o.g. Studie mündlich und schriftlich aufgeklärt und ihm/ihr eine Ausfertigung der Information sowie dieser Einwilligungserklärung übergeben zu haben.

_____

Ort, Datum Unterschrift des aufklärenden Studienmitarbeiters

Figure 23: Letter of consent

Mini-Mental Status Test (MMST)

Name _____ Datum _____ Score _____

A. Orientierung

Score

Zeit
(z. B. Welchen Tag haben wir heute?)

1. Jahr ①
2. Jahreszeit ①
3. Datum ①
4. Wochentag ①
5. Monat ①

Ort
(z. B. Wo sind wir?)

6. Land/Staat ①
7. Bundesland ①
8. Stadt/Ortschaft ①
9. Klinik/Praxis/Altersheim ①
10. Stockwerk ①

Summe (max. 10): ☐☐

B. Merkfähigkeit

Der Untersucher nennt folgende drei Gegenstände und fordert den Patienten auf, die Begriffe zu wiederholen (1 Punkt für jede richtige Antwort). Der Untersucher wiederholt die Wörter so lange, bis der Patient alle drei gelernt hat (höchstens 6 Wiederholungen).

1. >Auto< ①
2. >Blume< ①
3. >Kerze< ①

Summe (max. 3): ☐

C. Aufmerksamkeit und Rechenfähigkeit

Von 100 an sind jeweils 7 abzuziehen. Falls ein Rechenfehler gemacht wird und die darauf folgenden Ergebnisse „verschoben" sind, so wird nur ein Fehler gegeben.

1. >93< ①
2. >86< ①
3. >79< ①
4. >72< ①
5. >65< ①

ODER

Falls der Patient die Aufgabe nicht durchführen kann oder will, „RADIO" rückwärts buchstabieren lassen: O-I-D-A-R

1. O ①
2. I ①
3. D ①
4. A ①
5. R ①

Summe (max. 5): ☐

D. Erinnerungsfähigkeit

Der Untersucher fragt nach den drei zuvor genannten Wörtern.

1. >Auto< ①
2. >Blume< ①
3. >Kerze ①

Summe (max. 3): ☐

E. Sprache

Der Untersucher zeigt zwei Gegenstände und fordert den Patienten auf, sie zu benennen.

1. Armbanduhr ①
2. Bleistift ①

Der Untersucher fordert den Patienten auf, nachzusprechen

3. "Sie leiht ihm kein Geld mehr" ①

Der Untersucher läßt den Patienten folgendes Kommando befolgen.

4. „Nehmen Sie dieses Blatt in die rechte Hand" ①
5. „Falten Sie es in der Mitte" ①
6. „Legen Sie es auf den Boden" ①

Der Untersucher bittet den Patienten,

7. die Anweisung auf der Rückseite zu befolgen ①

Der Untersucher dreht das Blatt um und fordert den Patienten auf,

8. einen vollständigen Satz zu schreiben (Rückseite). ①

Der Untersucher läßt den Patienten die auf der Rückseite vorgegebene Figur malen (1 Punkt, wenn alle Seiten und Winkel stimmen und die sich überschneidenden Linien ein Viereck bilden).

9. Nachzeichnen (Rückseite) ①

Summe (max. 9): ☐

Gesamtsumme bitte oben eintragen

Bitte schließen Sie die Augen!

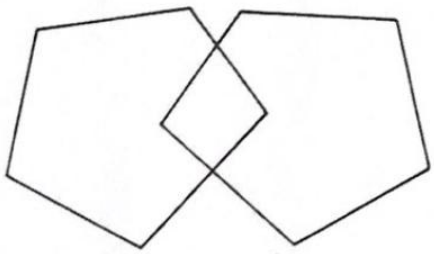


Figure 23: Mini-Mental State Exam

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