1.Title: In what way do music-based caregiving influence pain, daily activity, neuropsychiatric symptoms, and medication in patients with dementia?

Protocol approved by the Regional Comittees for Medical Research Ethics South East Norway, REK South East at **25.06.2019**

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2. Introduction

The main objective of this study is to evaluate the pain-relieving effect of a well-characterized non-pharmacological treatment program, music-based caregiving (MBC), to patients in nursing homes with dementia and pain. This intervention study will apply for one PhD candidate. Patients with dementia disease will be recruited from eight different nursing homes in Trondheim and Oslo, and each ward will be cluster randomized into intervention - or control wards. Then the health care personnel in the intervention wards will receive education in MBC and perform the intervention during eight weeks. The hypothesis is that this non-pharmacological intervention will reduce pain intensity and improve the activity of daily living (ADL), quality of life (QOL) and general activity, as well as reduce other symptoms in nursing home patients with dementia and pain compared to baseline.

Background

Pain is common in the elderly, and the prevalence of pain increase with age, co-morbidities and frailty 1,2. While the prevalence of pain in older adults in the general population is estimated to range from 25%-50% 2-4, the prevalence of pain in patients living in nursing homes and community care varies from 28% to 87% 5,6. Musculoskeletal pain disorders have been estimated to affect as many as 80% of those above 65 years 7,8. Although almost one fifth of the elderly have symptomatic osteoarthritis 9, most of the chronic pain disorders are of unknown cause 10. Thus opioids are not the best treatment with unclear effect over time and serious side effects (sedation, dizziness, falls, dysphoria, obstipation) in the elderly 11. This knowledge is in contrast to the practice today. In Denmark, 41% of nursing home residents and 28% of home-domiciled patients with dementia use opioids 12.

Previous studies demonstrate that more than 80% of patients in nursing homes in Norway had dementia disease 13,14. Dementia is a syndrome due to disease of the brain, usually of a chronic and progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, reasoning, orientation, comprehension, calculation, learning capacity, language, and judgement 15. Dementia has different stages; mild, moderate and sever dementia. In severe dementia (disease), most of the patients have lost verbal

language and are dependent on of nursing care 15. Patients with dementia also experience
many severe neuropsychiatric symptoms. SelbÃ¦k et al 16 followed 931 nursing home patients
with dementia over time. Agitation, irritability, disinhibition, and apathy were the most
prevalent and persistent symptoms during the study period. Depression and anxiety became
less severe over time, whereas the agitation subsyndrome (agitation /aggression, disinhibition,
and irritability) and apathy increased in severity during the follow-up period.

Pain is under-reported in the elderly since the elderly or the health care personnel do
not report pain, and because of failure of regular and systematic pain assessment in the health
care system 17. Pain assessment is challenging in the elderly because of impaired vision and
hearing, memory, verbal and cognitive functions, and neuropsychiatric symptoms. If not
adequately treated, chronic pain can cause depression, agitation, and aggression in patients
with dementia 18. Given the language loss in the most advanced stage of dementia and
sometimes after stroke, a cause of dementia, valid and reliable methods for pain assessment in
nonverbal older adults are needed 19. MOBID-2, an observation based pain assessment tool,
will be used in patients with dementia in the present study. MOBID-2 is validated in nursing
homes patients with dementia in Norway 6,20.

Based on current knowledge, non-pharmacological interventions should be the first-
line treatment approach for pain in most cases for patients with dementia 18. Since
pharmacological treatment for chronic pain is often inadequate and the elderly are prone to

side-effects, more evidence about non-pharmacological treatments is needed, especially for elderly with dementia. Many studies are conducted in this area today, but unstructured and non-evidence based interventions are commonly used 21 Based on current knowledge, non-pharmacological interventions should be the first-line treatment approach for pain in most cases for patients with dementia 18. Since pharmacological treatment for chronic pain is often inadequate and the elderly are prone to side-effects, more evidence about non-pharmacological treatments is needed, especially for elderly with dementia. Many studies are conducted in this area today, but unstructured and non-evidence based interventions are commonly used 21. One of the most common non-pharmacological approaches for treating behavioral and psychological symptoms of dementia is therapeutic use of music 22(. Many of the studies done have low methodological quality with small sample sizes 23, but there seems to be some evidence (for) that non-pharmacological interventions like activity and music can relieve pain 24, depression25 and increase QoL 23. However, more research is needed using controlled studies of high quality 23.

The most convincing evidence of effect when reviewing interventions addressing QOL, discomfort and behavior and psychiatric symptoms in person with dementia comes from functional analysis-based interventions 26. These rely on the nursing home staff to implement a care system, be involved in staff-education, protocol or systematic care planning. Examples of such interventions are the ABC dementia, Serial-trial intervention and (the) TIME 27-29.
These interventions prove to be powerful and important systems to structure care-work, deliverance and education, however they are comprehensive systems to implements and not designed to inform on one specific symptom like pain. That is also why there is a shortage of functional analysis-based interventions targeting pain intensity specifically.

The literature suggests that music may also provide effects for pain intensity for patients with dementia 30. However, so far the studies are small, underpowered or performed with less robust methods 31. A review that investigated whether interactive or receptive deliverance (i.e. listening to) of music are more effective to reduce agitation in persons with dementia found evidence that receptive deliverance does reduce agitation compared to

ordinary care, while interactive deliverance of music does not 32. In a recent review on non-
pharmacological treatments for individuals with dementia, sensory interventions like music
were most effective to reduce agitation followed by interventions targeting pain specifically
33. The evidence might suggest that music reduces stress due to sensory effects and by
activating reminiscing.

Physical activity and active training has been investigated in persons with dementia
and have been able to prevent falls, improve physical and mental function and also
neuropsychiatric symptoms 34. There is currently a dearth of studies to provide information on
what interventions have proved to benefit pain intensity, and also looking at effects by age,
gender, type and grade of dementia 21. The physiological and psychological effects of music
have been thoroughly researched in later years. Precise therapeutic use of music can aid
attention, regulate autonomic dysregulation and access latent functional mental resources 35.

Music-based caregiving (MBC) has been developed through a dialogue between
neuroscience and clinical research in dementia care since the early 1990s, inspired by the
work of Michael Thaut and Linda Gerdner 36,37. Thaut and Gerdnerâ€™s work has demonstrated
the clinical potential and efficacy of neurologic music therapy and individualized music 38.
MBC has (been) continually built on neuroscientific research in continuing dialogue with the
Center for Biomedical Research at Colorado State University, Berklee School of
Music/Harvard Medical School in Boston and the neuroscientific work of TÃ¶res Theorell and
associates at Karolinska Sjukhuset in Stockholm 39. The PhD project - Integrated music in
nursing homes, an approach to dementia care, developed song, music and dance into a
systematic approach to dementia care through the period 2000â€“2012 40.

MBC provides in-
depth training on how music, song and movement can be used in caregiving for people with dementia. The program has been developed on behalf of the Norwegian
Directorate of Health and is based on neurological music therapy with elements of music
therapy and music education, and added to KompetanselÃ¸ft 2020.

2.1 Need description

ï‚· Increased focus on pain and non-pharmacological pain management in a vulnerable group
of patients
ï‚· The non-pharmacological intervention can reduce pain intensity and strengthen ADL,
QOL and activity, reduce pharmacological side effects and reduce symptoms in nursing
home patients with dementia and pain without side effects.
ï‚· Reliving pain without side effects will also be valuable for the patientâ€™s family.
ï‚· This study will increase the focus on pain and pain management for health care
professionals in nursing homes and the community. The training of the staff in the
intervention nursing homes will enhance their clinical skills.
ï‚· This increased competence can strengthen the motivation for the staff in the care of the
patients with dementia, and may reduce the turnover of the staff. Hopefully it can also
stimulate their wish for knowledge update.
ï‚· The health professionals in the intervention group will receive education in a program
with music, song and dance with the intention to reduce pain, and strengthen ADL, QOL
and activity, reduce side effects and reduce symptoms in nursing home patients with
dementia and pain. If the intervention shows effect, the health care professionals in the
control nursing homes will retain and, hopefully use, the training after the study is ended.
ï‚· The research group is multi-professional from different research groups in Norway. All of
the nurses, physicians, experts in epidemiology, music therapy, and user participants work
together. This collaboration will strengthen the research competence for the group and for
the different members.

3.Aims and objectives

The overarching aim of the present study is to extend knowledge about pain in patients with
dementia and to evaluate if an intervention with music-based caregiving (MBC) will reduce

pain intensity and improve activity and QoL in nursing home patients with dementia and pain.

The baseline descriptions of pain and pain management in patients with dementia disease in
the included nursing homes will be published as a part of another study.

The research questions in the present study are:

1. Will music based caregiving reduce pain and the need for analgesics in patients with
dementia in nursing homes?
2. Will music-based caregiving impact on QoL, ADL function, and total daily physical
function?
3. Will implementation of music-based caregiving impact on neuropsychiatric symptoms
and psychopharmacological medication?

The primary aim is to give better and safer pain management to patients with pain and
dementia in nursing homes.

Secondary aims are:

- to increase total daily activity, ADL function, QoL, and reduce neuropsychiatric
symptoms, and

- to increase knowledge of pain in patients in nursing homes: the occurrence, intensity,
location, treatment, diagnoses, and comorbidities.

4. Project methodology

4.1. Design, method and analysis

This is a cluster-randomized controlled trial including patients with dementia and pain living
at different wards at eight nursing homes.

1) Eight nursing homes will be selected to participate, four in Trondheim and four in Oslo.
Both municipalities have accepted the collaboration, and contact has already been
established with randomly selected nursing homes.
2) Subsequently, all patients at the 8 nursing homes will be screened with respect to
dementia and pain (see screening tools later). If patients have dementia and report pain
(â‰¥3 on MOBID) they will be included in the study.
3) The included patients will then have a clinical examination of pain and pain management
by an expert physician (see below). Evaluation of the use of analgesics psychopharmacological medication will be performed. Inappropriate medication (both too
much and too little) will be corrected in collaboration with the nursing home doctor.
4) In addition to the clinical examination of pain, we will measure total daily physical
activity, ADL, QOL, and neuropsychiatric symptoms on all included patients (see below).
5) After the pre test - a randomization of the wards into intervention wards or control wards
will be performed.
6) About 5 staff members at each of the wards randomized to the intervention group will
receive education in the MBC before intervention (see below).
7) As a post-test three month after the intervention has ended, pain, total daily physical
activity, ADL, QOL, and neuropsychiatric symptoms will be measured.

This design facilitates the measurement of the outcome variables in nursing homes patients
before and after the intervention, and between the two groups. The results from the pre- and
post-tests will be compared between the groups to assess whether or not the intervention has
effects on the outcome variables when adjusting for baseline levels (pre-test). This approach
will allow us to evaluate whether changes in the outcome measure are caused by the
intervention or other elements.

Participants

In total, 240 patients with dementia and pain (120 from nursing homes in Trondheim and 120 from nursing homes in Oslo) will participate in the study. Contact is already established with nursing homes that will participate both places. Patients will be included if they report moderate pain or more (â‰¥3 on MOBID) and mild dementia or more (â‰¥1 on CDR). They will not be included if they have lived in the nursing home less than four weeks, have short (less than eight weeks) expected lifetime (judged by the nurses), and if they do not understand the Norwegian language. Anonymous data will be collected for comparing patients not included with those included, and the reasons for why they were not included will be described. Before inclusion in the study, patients or their relatives should give an informed consent.

Clinical examination

All the included patients will be clinically examined by expert physicians in the same way as performed in the HUNT3 study 10. Focal pain conditions will be diagnosed according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems 41, either as a disease diagnosis, or, if no cause of the pain can be identified, by a pain/symptom diagnosis. In addition, the physician will make a critical evaluation of their analgesic and other medications as mentioned above. If medications are inadequate, obviously give side effects, or are in violation with current guidelines, the recommendation for

correction will be given to the physician at the nursing home. This procedure will particularly
be the case for all patients having a pain state of known origin with documented effect of
specific medication (i.e. osteoarthritis or neuropathic pain).

Education of the health care professionals

After pre-test including clinical examination, a randomization of the wards into intervention
wards or control wards will be performed. About 5 staff members at each of the wards
randomized to the intervention group will receive education in the MBC. Approximately 60
employees will receive training in MBC by Myskja and HÃ¥pnes with a 5-day training course.
This training will facilitate the intervention in the way that the health professionals in the
intervention group will be competent in applying active (song, dance) and passive (music
listening) modalities in individualized music with groups and individuals as needed, mindful
of personal preference and dignity and aware of the sensory environment.

The MBC program

The MBC program has been developed as a hermeneutic circle (interpreted from the Vedic
scriptures) 42, expanding from literature reviews and teaching sites to observations of clinical
response, aided by video analyses. The Medical Research Council guidelines have been
followed in this process, using the cyclical stages of development, feasibility and piloting,
evaluation, and implementation 43. In the period from 2012, 490 health care workers have
been educated in this program in TrÃ¸ndelag.

Intervention

The intervention will be applied by the trained staff with daily individualized prerecorded
music integrated with activity with about 30 minutes duration, combined with a one hour
active session in groups twice weekly. The control group will receive regular treatment with
the same improved analgesic treatment as the intervention group, but without MBC. The
duration of the intervention and the control period will be eight weeks.

Measurements

As a part of the pre-test we will select data about the patientsâ€™ demographics, diagnoses and
medication use from the medical chart.

Stage of dementia disease

Clinical Dementia Rating Scale (CDR) is an assessment scale for the accurate clinical staging
of dementia in older subjects. The CDR includes six items assessing cognitive and functional
impairment. Based on an algorithm giving precedence to the item memory a CDR total score
is estimated. A score of 0, 0.5, 1, 2, 3 indicates no dementia, questionable dementia, mild,
moderate or severe dementia, respectively, and CDR score > 1, is cut-off score for dementia
disease. The scale has shown to be reliable and valid and is translated into Norwegian
language 44.

Pain

MOBID-2 pain scale will be used for pain assessment in elderly people with dementia 20,45.
The assessment of inferred pain intensity is observed based on patientâ€™s pain behaviors during
standardized, guided movements of different body parts (Part 1). In addition, MOBID-2
includes an observation of pain behavior related to internal organs, head and skin registered
on pain drawings and monitored over time (Part 2). MOBID-2 has shown to be sufficiently
reliable, valid and time-effective to assess pain in patients with severe dementia 46. We will
use MOBID-2 for assessment of pain in all the patients with dementia.

Quality of life and aids of daily living

Quality of Life in Late-Stage Dementia (QUALID) measures QOL in patients with severe dementia based on information and observations from nurses about the patientâ€™s emotions and behavior. The scale has been validated in a Norwegian nursing home population, showing satisfactory psychometric properties 47,48.

Dementia Quality of Life (DQoL). Because QUALID-scale is an observation scale, and there is a lack of studies comparing self-reported and observations QoL in those with dementia, we want to compare the observation estimate with self-report for patients with none, mild and moderate dementia (DQoL). DQoL consists of five domains: self-esteem, positive affect/ humor, feeling of belonging, and sense of aesthetics and negative affect. The instrument is evaluated in those with mild and moderate dementia and is used in nursing homes in Norway 49.

Barthelâ€™s Activities of Daily Living Index (ADL) is a screening instrument for patientsâ€™ daily life functioning. This 10-point scale measures patientsâ€™ degree of self-reliance with a total score ranging from 0 to 20. Lower scores indicate greater dependence on nursing care 50.

The total daily physical activity using two 3-axis accelerometers (Axivity, UK) attached to the skin on the right thigh and low back for 7 continuous days. By utilizing state-of-the-art machine-learning techniques, we have developed a preliminary activity recognition model for lying, sitting, standing, walking and other activities. This model is being used in the Nord-TrÃ¸ndelag health study (HUNT4). Specifically, the model captures walking velocity and transitions between postures and activities (e.g. sit-to-stand) and sleep quality/duration.

Neuropsychiatric symptoms and depression

The Neuropsychiatric Inventory (NPI-NH) measure 12 different psychiatric symptoms and behavioural disturbances in nursing home residents: delusions, hallucinations, dysphoria, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, aberrant motor activity, sleep and night-time behaviour disorders, appetite and eating disorders. The

screening question is asked to determine if the behavioural change is present. If a screening question is present, there will be sub-questions about frequency (score 1 to 4) and intensity (score 1 to 3) for each behavior. Total score for each behavior is from 1 to 12. The scale has been validated for patients in nursing homes in Norway 51.

Cornell scale for depression in dementia assesses signs and symptoms of major depression in patients with dementia in an interview with the health care providers. The scale consists of 19 items in five domains based on observation of behaviour 52. Each question is scored on a two-point scale: 0=absent; 1=mild or intermittent; 2=severe; n/a = unable to evaluate 2.

Sample size

A power calculation was performed on MOBID-2. Based on the literature review we assumed the mean difference to be 1.2 and the common standard deviation to be 3. To keep statistical power of 80% (beta = 0.2) and significance level of 5%, we would need 100 in each group to reveal the anticipated difference between the groups as statistically significant. Taking in consideration the possible cluster effect of 20% we aim to enrol 120 patients in both groups 20,53,54.

Statistical analyses

Participantsâ€™ background characteristics will be described as means and standard deviations (SD) for normally distributed continuous data or medians and range for continuous data with skewed distributions. Categorical data will be presented as counts and percentages. At the pre-test, possible between-group differences will be assessed using independent samples t-tests

when comparing pair of normally distributed continuous variables, chi-square test for
categorical variables and Mannâ€“Whitney test for continuous variables with skewed
distribution. Possible differences between the groups concerning the mean MOBID-2 Pain
Scale, QoL, ADL, total daily physical activity, and neuropsychiatric symptoms scores over
time and at given time points will be estimated with linear random intercept quantile mixed-
effect models. Mixed model regression modelled with linear random intercept permits
multiple measurements per person over time, irregular intervals between measurements and
allows for incomplete data on assumption that data are missing at random 55. A significance
level of 5 % will be considered statistically significant for all analyses. Data will be analyzed
using IBM Statistical Package for the Social Sciences (SPSS) version 23.

4.2. Participants, organization and collaboration

The multi-professional research group will unite clinical and scientific experience from four
different universities (for more details and contribution to the study, see e- application):

Petter Chr. Borchgrevink, MD, PhD (principal investigator, main supervisor). Leader of "Pain
research group". Head of "Dept of Pain and Complex Disorders" at St.OlavÂ´s Hospital and
Professor of Anesthesiology and Pain Management at NTNU. Leader of the Norwegian Dept
of Health-defined "Pilot Project for Joint Multidisciplinary Diagnosis Centers / Outpatient
Clinics for Patients With Chronic Pain and/or Fatigue Disorders of unknown cause". Has 118
scientific publications and supervised 9 candidates on their PhD.

Tone RustÃ¸en Professor, RN, PhD (co supervisor). She has 128 scientific publications, and
has been the main supervisor for 12 PhD candidates that have completed their PhD. RustÃ¸en
is a professor at University of Oslo and a researcher at Oslo University Hospital. She has a
long experience with pain research and is the leader of the Regional Research Network
NORSMAN funded by Helse SÃ¸r Ã˜st.

Karin Torvik RN, PhD. Associate professor, NTNU, Nord University, Faculty of Health and
Nursing, Levanger, Norway (co-supervisor). She has a long experience in guiding master and
bachelor students. Her research area is pain assessment and pain management in the elderly.

Geir SelbÃ¦k MD, PhD, professor (co supervisor): He has 134 scientific publications. He has supervised 7 candidates on their PhD, and is currently supervising 10 PhD candidates. He is the primary investigator for several large-scale clinical studies, nationally and internationally. His research experience spans a wide variety of fields including basic medicine, epidemiological studies, clinical trials. This year he was awarded the Norwegian dementia research prize by the Norwegian Health Association.

Audun Myskja MD, PhD. Advisor to The Norwegian National Resource Center for Arts and Health. He is a strong and important voice in the traditional academic setting, seeking to create simple practice-based methods to connect science and the fields of the common human experience, expanding the context of traditional Western medicine. He has long experience with innovative use of musical elements in rehabilitation of dementia and Parkinsonâ€™s patients, and for creating systematic tools for empowerment in persons with chronic illness.

Vegar Rangul PhD, Associate professor/Post.doc. HUNT Research Centre, Department of Public Health and Nursing, Faculty of Medicine, NTNU. Is a specialist in physical activity epidemiology and has extensive experience with the use of large epidemiological data sets to resolve issues relating the health effects of physical activity and their interaction with general health behavior and cardiovascular disease risk in particular. Has expertise in behavioral epidemiology, measurement of physical activity and epidemiological population studies.

Odd HÃ¥pnes, General manager of the Norwegian Resource Center for Arts and Health, NORD University. He holds a master of musicology, education-in-science and education and has been central in the development of MBC as a national program. He has been the head of the

national node for culture and health 2000-2003, and participates in international cooperation
and research networks in Arts and Health.

Reidun Sandvik RN, PhD. Associated professor, Western Norway University of Applied
Sciences and University of Bergen. She has experience with supervising master students. Her
PhD topic was pain in nursing home patients with dementia and she has continued with
research about pain management for this group of patients.

Milada C SmÃ¥stuen PhD, biostatistician. Will help with data management and statistical
analyses for the whole study and all three papers.

4.3. Budget

We will apply for one doctoral student. For details se the electronic application (esÃ¸knad).

4.4. Plan for activities, visibility and dissemination

Timeline - see electronic application

Publication plan The most important results to emerge from the project will be disseminated
through different channels. The PhD student will write 3 scientific papers:

a) The effect of music based caregiving on pain and the need for analgesics in patients with
dementia in nursing homes.

b) The effect of music-based caregiving on QoL, ADL function, and total daily physical
function.

c) The effect of music-based caregiving on neuropsychiatric symptoms and psychopharmacological medication.

Workshop, seminars and conferences: It is important that leaders in community health care
and individuals in charge of nursing homes have access to our results. To facilitate this, we
will arrange workshops and seminars to present our results. The PhD student will participate
in at least two international and one national conference during their study period, presenting
her/his work. â€œNasjonalforeningen for folkehelsenâ€ will assist in sharing our results to users
and to the general public.

4.5. Plan for implementation

As the study is an intervention study it can easily be implemented into practice if the results
are positive. The results from the present study will also be transferable to other patient
groups that cannot communicate their pain. The findings from the present study will be
relevant outside nursing homes as these patients also are in specialist hospitals and in the
community.

5. User involvement

Hans HÃ¸gh Henrichsen is user participant from Oslo Municipal. He has been informed about
the proposal in a meeting. The project was also discussed with â€œSykehjemsetatenâ€ , Oslo
Municipality (Torunn Vatne). From Trondheim, one patient with dementia and one relative of
one patient with dementia will be recruited from the Resource Center for Dementia Disease in
Trondheim and will be user participants. All participants will be involved in the detail
planning of all phases of the project. The National Association for Public Health, which has
given feedback on the application, will also recruit user participants from the local dementia
associations if the study should be funded.

6. Ethics

After permission to include the nursing homes, meetings will be arranged with the staff to
inform and motivate them for carrying out the study. The health care providers will collect

written or oral informed consent from the patients and/or their legal guardians or relatives. We
will use different inclusion procedures depending on the patientsâ€™ consent competence in
collaboration with the Ethical Committee.

Patients with consent competence will receive oral and written information prior to the study,
and the nurses will obtain written informed consent. If the patients cannot sign, they will give
oral consent to the nurse, and the nurse will sign the informed consent on behalf of the
patients. If the patients are cognitively impaired, guidelines from the Ministry of Health and
Care Service in Norway will be followed when recruiting these patients. Relatives of patients
or their legal guardians will receive written information prior to the study and consent on their
behalf. The cognitively impaired patients will receive oral information prior to the study and
will not be included if they decline to participate, even if their relatives/legal guardians had
consented on their behalf.

One can ask if it is unethical to not give music therapy to all included patients in the
nursing homes. However, we are not taking away anything from the patients, and all included
participants will receive pain assessment.

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