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Pain and its consequences in dementia: Observing the complex relationship between pain, behaviour and ADL in nursing home residents

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PAIN and its consequences in DEMENTIA

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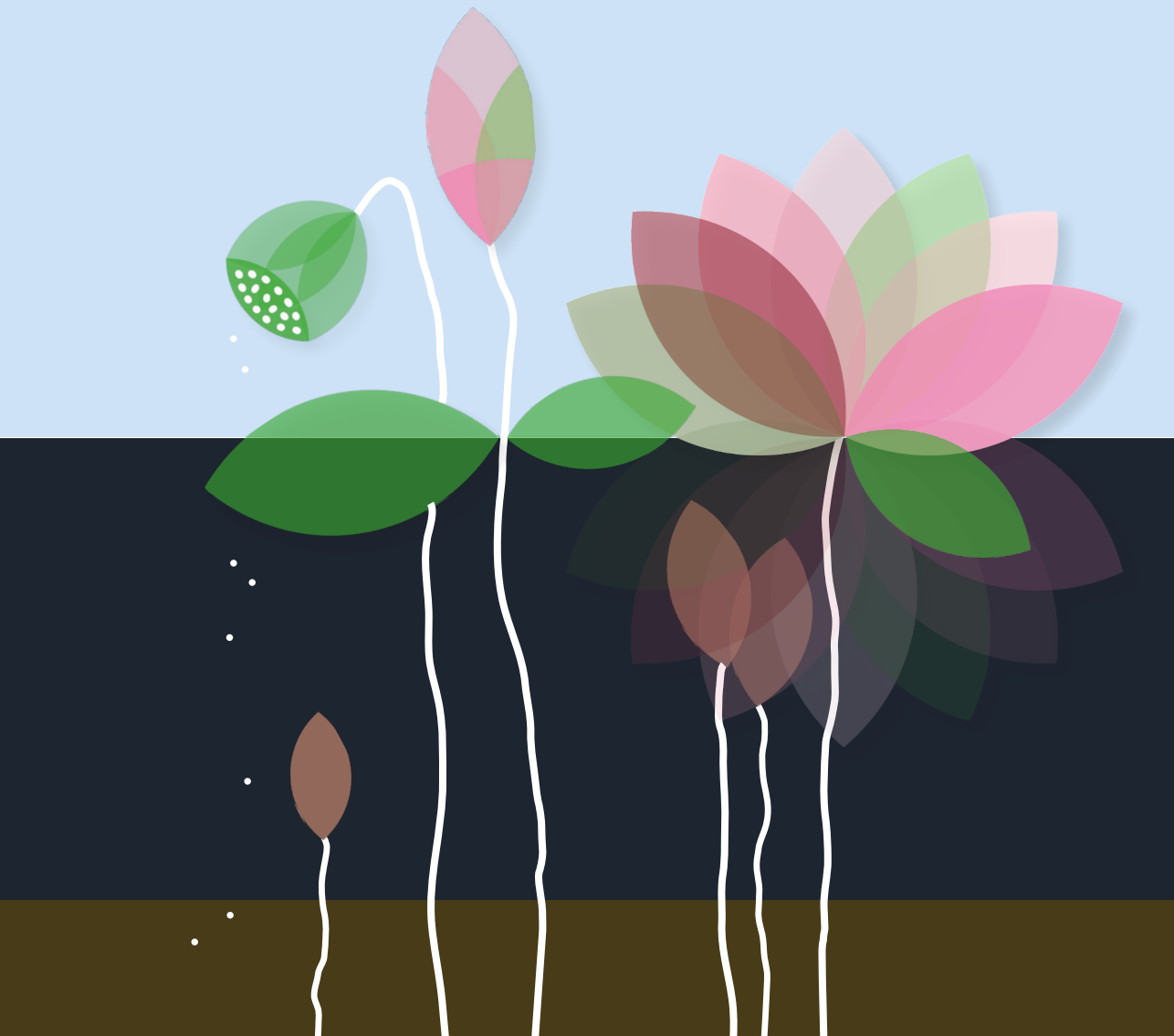
Annelore H. van Dalen - Kok



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Annelore H. van Dalen - Kok

Academic network for research in elderly care

The studies in this thesis took place in the University Network for the Care Sector South Holland (UNC-ZH). In this network, the Leiden University Medical Center (LUMC) collaborates structurally with 12 elderly care organisations in South Holland (Marente, Pieter van Foreest, Stichting Zorggroep Florence, Topaz, Argos Zorggroep, Saffier, Laurens, Zonnehuisgroep Vlaardingen, Woonzorgcentra Haaglanden, Aafje, ActiVite, Haagse Wijk- en Woonzorg).

Caregivers, policy makers, researchers, students, residents and relatives work together to improve the quality of care and quality of life for vulnerable older people. The UNC-ZH is a regional platform, inspirator and learning network for innovation in long-term care. Research, education and training, and practice are closely related.

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Cover illustration
"From the mud of adversity grows the lotus of hope".
The lotus flower symbolizes transformation, from unawareness to insight.
She is a symbol of hope for persons with dementia.

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Voor mijn ouders.

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CHAPTER 1

General introduction

A 65-year-old man named Hans has Lewy body dementia and Parkinson's disease. He lives on a psychogeriatric ward in a nursing home and suddenly started exhibiting agitated and even (physically) aggressive behaviour towards other residents. Nursing staff described several incidents where he, for example, physically assaulted another male resident by hitting him in the face without any provocation. He was also verbally aggressive towards nursing staff as well as to other residents. This new and unpredictable behaviour often caused interaction problems, leading to more aggressive incidents between him and other residents, and nursing staff. Nursing staff struggled to identify possible causes for the agitated and aggressive behaviour and were not successful in initiating effective interventions to counteract the behaviour. Furthermore, his wife also noticed a significant change in his behaviour and did not recognize her husband. She also noticed a change in his mobility; there were more OFF moments and he was limping with his right foot. It wasn't until his wife shared her concerns about his mobility that the nursing staff started to realize what might be the cause of his behaviour. Could it be pain?

This case illustrates a common situation on psychogeriatric wards in nursing homes. A combination of dementia, challenging behaviour, change in ADL functioning, and the possible presence of pain, all of which combined impact quality of life.

Dementia

Dementia is a major public health issue worldwide. It is associated with mortality and global economic costs. Dementia is not only overwhelming for the people who are diagnosed with the disease, but also for their relatives and caregivers.[1] Dementia is described as a clinical syndrome of a deterioration in memory, thinking, behaviour, and the ability to perform activities of daily living. Furthermore, it is characterized by its progressive nature. The most common cause of dementia is Alzheimer's disease, followed by vascular dementia, dementia with Lewy bodies, and frontotemporal dementia.[2]
Besides deterioration of cognition, the neuropathological changes of the brain are also responsible for numerous other symptoms, such as neuropsychiatric symptoms (e.g. agitation, hallucinations and restlessness), loss of communicative abilities, and they have an impact on the perception of pain. [3]

Pain

Ageing is a high risk for developing pain-related conditions, such as osteoporosis, arthrosis, and cardiovascular diseases.[4 5] Additionally, ageing is also the greatest risk for developing dementia. Therefore, it is to be expected that persons with dementia also experience pain. Previous research indicates that around 60% to 80% of people with dementia regularly experience pain. [6-8]

In order to understand the relationship between pain and dementia, the concept of pain needs to be addressed. The International Association for the Study of Pain (IASP) described pain in the following definition: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[9] However, this definition is difficult to use in persons with dementia because of terms like 'emotional experience'. Research on the emotional responsiveness to pain in persons with dementia is contradictory; both increased and decreased responsiveness were found. Furthermore, neuropathological changes in the brain, such as white matter lesions and atrophy, affect different parts of the brain: hippocampus, somatosensory cortex, and the amygdala, which all have a specific role in the nociception and experience of pain.[3] For example, the somatosensory cortex is important in localizing pain, the hippocampus is important in pain memory, and the amygdala is important in the emotional experience of pain.[3 10 11] One can imagine that, with these changes, the concept of pain in persons with dementia is different. Additionally, pain has several dimensions, i.e., biological, psychological, and social dimensions.[12-14] These are interconnected and result in a personal experience and expression of pain. Furthermore, the communicative abilities are also affected, which makes it difficult for them to verbalize their pain. All these changes combine to create a complex relationship between pain and dementia, causing various problems, for example with regard to recognizing that a person with dementia is in pain, and subsequently, providing adequate treatment of pain.

Recently, the IASP introduced a new definition of pain: *'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.* They also formulated accompanying notes, such as: pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors. Pain and nociception are different phenomena, and verbal description is only one of several behaviours to express pain.[15] Especially the latter is important in the recognition of pain in persons with dementia.

Neuropsychiatric symptoms

Neuropsychiatric symptoms (NPS), or challenging behaviour, such as agitation, aggression, but also depression and apathy, are common in persons with dementia. About 90% experience a form of challenging behaviour during the course of the disease.[16] Moreover, this is one of the most important reasons for institutionalization.[17] Over the years, several theoretical models were created which describe the aetiology of NPS.[18 19] One of the models is the Unmet Needs Model.[20]

Unmet needs are individual needs stemming from habits, personality, environmental conditions, and physical/mental state. Examples are hunger, thirst, lack of activities, and untreated pain. The Unmet Needs Model postulates a mismatch between the needs of the persons with dementia and care provided by environment and caregivers.[21] In dementia, especially the advanced stage, there is a decrease in the ability to meet one's needs, due to loss of communicative skills, and the ability to provide for oneself. Caregivers often do not interpret NPS as a sign of unmet needs, such as underlying distress or pain. Left untreated, pain becomes an unmet need that will not be dealt with correctly. NPS are often

treated with psychotropic drugs, like haloperidol and lorazepam.[22] Use of psychotropic drugs is associated with serious adverse events, such as increased cognitive decline, falls, extrapyramidal symptoms, cardiovascular events, and even death.[23-25]
To avoid inadequate treatment of an unmet need such as pain, neuropsychiatric symptoms/challenging behaviour like agitation or aggression should serve as a red flag and trigger further examination for pain as a potential cause. Next, a tailored (non)pharmacological treatment is possible.

Physical functioning

Physical functioning or Activities of Daily Living (ADL) refer to fundamental skills that are required to independently carry out self-care activities such as bathing, dressing, eating, and walking.[26 27] The inability to perform ADL activities results in dependence on others and an increasing need for support from care services.
In dementia, ADL functioning is subjected to the progressive nature of the neuropathological changes which cause the disease. Therefore, a decline in ADL functioning is to be expected, especially in the more advanced stages of dementia.[28 29] However, functional decline in dementia is a complex phenomenon. Apart from the dementia itself, various (indirect) causes can lead to functional impairment. For example, apathy or depression, medication use, such as psychotropic drugs, but also pain. Pain is known to interfere with ADL functions. [30-32]
However, it is unclear what the (added) effect of pain is on ADL functioning in persons with dementia.

Nursing home care setting in the Netherlands

Care for persons with advanced dementia is often centred in nursing homes, on special psychogeriatric wards. In 2021, approximately 290,000 people in the Netherlands are living with dementia.[33] An estimated 70,245 are living in a nursing home.[34]
The integrated medical and paramedical care in the nursing home is provided by a multidisciplinary team. This team consists of, at least, a psychologist, occupational therapist, physiotherapist, and an elderly care physician.[35] The Netherlands is the only country in the world which has a medical specialty called 'elderly care medicine'.[36-38]
Additionally, trained nursing staff provides day-to-day care, 7 days a week, 24 hours a day, and they are also part of the multidisciplinary team. This team formulates an individual care plan for the resident, including advance care planning and treatment of intercurrent medical issues.

Pain assessment

Due to the complex interplay between dementia, pain, NPS, and ADL functioning, recognizing pain is challenging, especially when verbalizing pain is hampered.
The American Geriatric Society (AGS) formulated several verbal and nonverbal pain-related behaviours and changes in normal functioning which could indicate the presence of pain.[39] For example, sighing, moaning, increased pacing, aggression, and changes in sleep. Additionally, the AGS published guidelines with recommendations for accurate pain assessment in persons with dementia.[39] The most important method is via direct observation of the residents and preferably using observational measurement instruments. Over time, many observational measurement instruments have been developed, such as the PACSLAC-D or PAINAD.[40-42] However, the psychometric properties, like validity and reliability, of many of these instruments were not thoroughly tested.[6 43] Furthermore, the existing tools are diverse and no universal tool is available. Although there is some agreement between the observational measurement instruments, there is great discrepancy in the way they are operationalized in clinical practice.[44]

Objectives of this thesis

The primary aim of this thesis is to investigate the complex relationship between pain, neuropsychiatric symptoms, and ADL functioning in people with dementia. (Figure 1). This is important, as it may help in targeting treatment options; should we treat pain, neuropsychiatric symptoms, or start interventions to prevent/stabilize functional loss?
The first part of this thesis focusses on unravelling this relationship, with specific attention to the effect of pain on ADL functioning.
The second part aims to investigate the psychometric properties of a new tool to measure pain in persons with dementia: Pain Assessment in Impaired Cognition (PAIC). This thesis focusses on the English as well as the Dutch research versions of the PAIC.

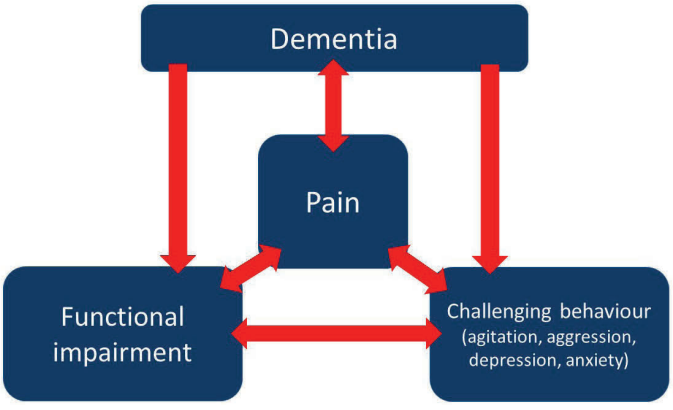

Figure 1. Interplay between dementia, pain, NPS, and ADL functioning

The main research questions in this thesis are:

Part I. Relationship between pain, neuropsychiatric symptoms, and ADL functioning

1. *What is the current state of evidence regarding the challenges of pain management in persons with dementia?*
2. *What is the strength of associations between pain, neuropsychiatric symptoms, and physical functioning in persons with dementia?*
3. *What is the relationship between the course of pain and change in ADL functioning, both generally and regarding specific ADL functions?*

Part II. Pain Assessment in Impaired Cognition: PAIC

4. *What is the content validity of the Dutch version of the Pain Assessment in Impaired Cognition scale?*
5. *What is the observer agreement on the individual 36 items of the Dutch version of the PAIC in a real-life nursing home setting?*
6. *What is the observer agreement and factor structure of each of the 36 items of the Pain Assessment in Impaired Cognition?*

Outline of this thesis

To address the objectives of this thesis, we performed both literature and clinical research. The first part of the thesis describes a literature review on the management of pain in persons with dementia (Ch. 2). It elaborates on four key perspectives: 1) effect of neuropathological changes on pain perception in dementia; 2) assessment of pain in dementia; 3) efficient treatment of pain; and 4) pain management.
In Chapter 3, a comprehensive systematic overview and meta-analysis of the strength of associations between pain, neuropsychiatric symptoms, and physical functioning is described, with special attention for the measurement of those three modalities.
Finally, in Chapter 4 the relationship between pain and ADL functioning in persons with dementia is investigated using a longitudinal study design.

In the second part of this thesis the psychometric properties of a new and improved observational measurement instrument (comprising 36 items) to measure pain in persons with dementia, Pain Assessment in Impaired Cognition (PAIC), is described. Observer agreement and factor structure, as well as the results of the validity and reliability study of all 36 items of the Dutch version of the PAIC are reported in Chapters 5, 6 and 7.
Finally, Chapter 8 presents a summary and a general discussion that reflects on the results presented in this thesis. General findings are put into context, methodological strengths and limitations are discussed, and implications for both clinical practice and research are described.
Last but not least, it reflects on the situation about Hans, the 67-year-old man with Lewy body dementia. We will indicate the steps that should be taken to reduce challenging behaviour, prevent loss of mobility, and ultimately improve his quality of life.

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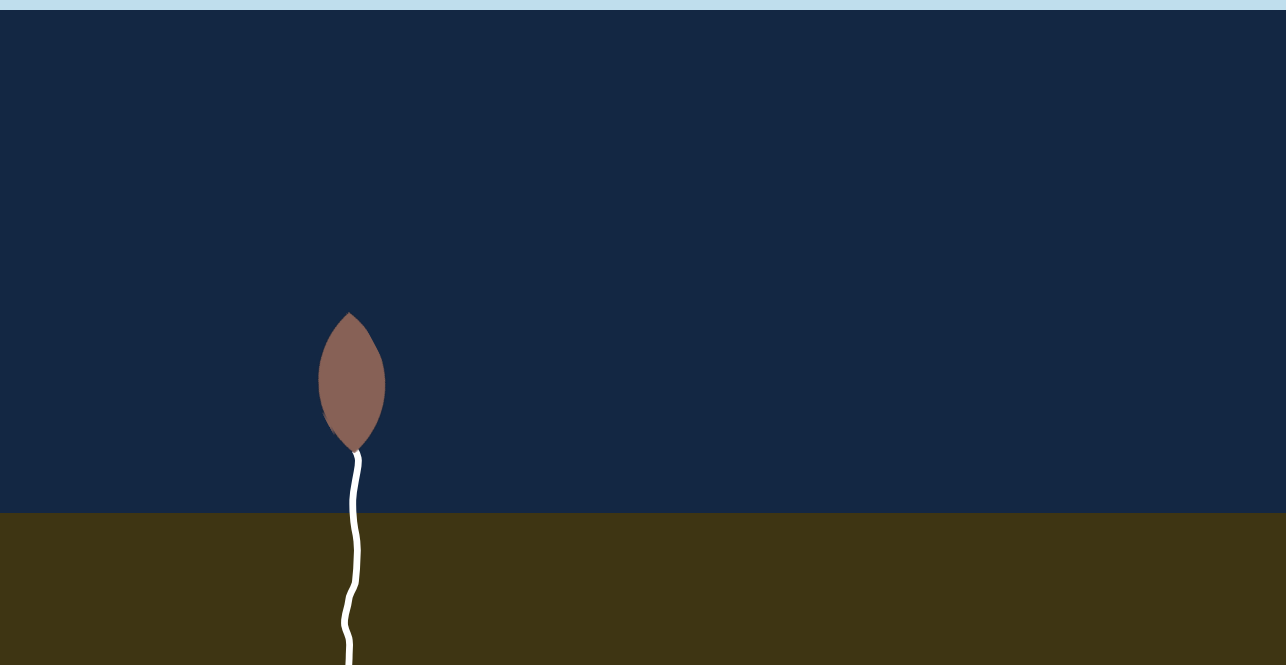
PART I

Relationship between pain, neuropsychiatric symptoms, and ADL functioning

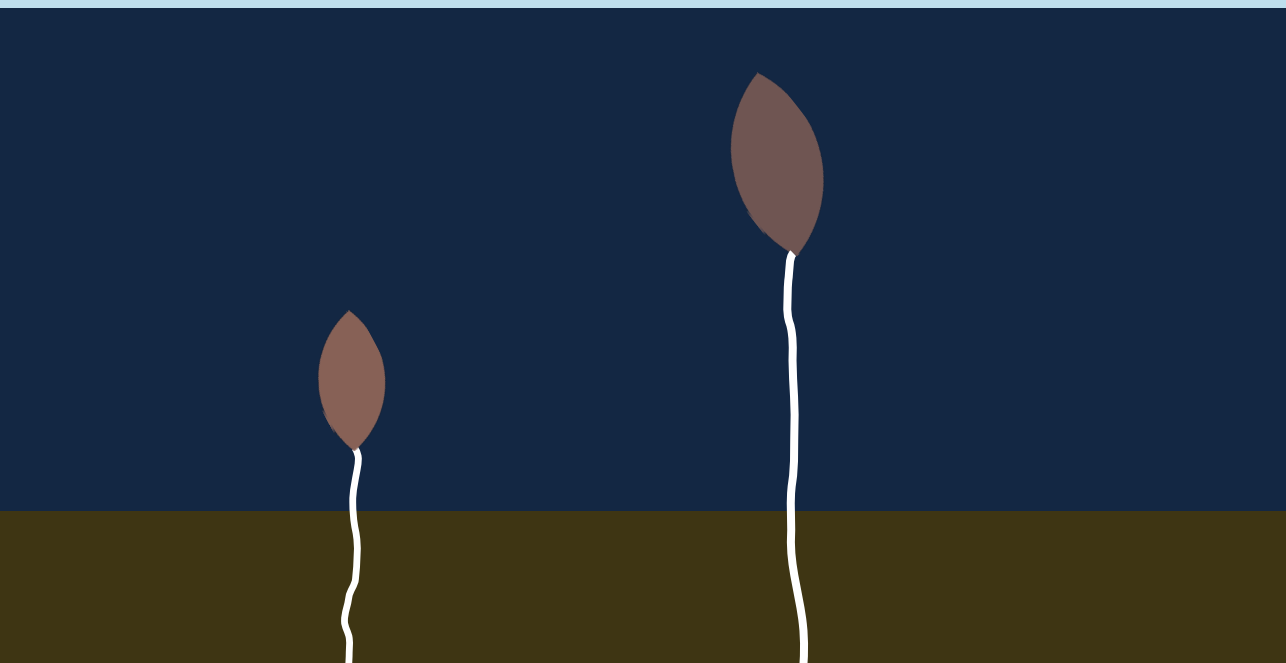


CHAPTER 2

Pain management in patients with dementia

Wilco P. Achterberg, Marjoleine J.C. Pieper, Annelore H. van Dalen-Kok, Margot W.M. de Waal, Bettina S. Husebo, Stefan Lautenbacher, Miriam Kunz, Erik J.A. Scherder, Anne Corbett.

Clin Interv Aging. 2013;8:1471-82. doi: 10.2147/CIA.S36739.



Abstract

There are an estimated 35 million people with dementia across the world, of whom 50% experience regular pain. Despite this, current assessment and treatment of pain in this patient group are inadequate. In addition to the discomfort and distress caused by pain, it is frequently the underlying cause of behavioural symptoms, which can lead to inappropriate treatment with antipsychotic medications. Pain also contributes to further complications in treatment and care. This review explores four key perspectives of pain management in dementia and makes recommendations for practice and research. The first perspective discussed is the considerable uncertainty within the literature on the impact of dementia neuropathology on pain perception and processing in Alzheimer's disease and other dementias, where white matter lesions and brain atrophy appear to influence the neurobiology of pain. The second perspective considers the assessment of pain in dementia. This is challenging, particularly because of the limited capacity of self-report by these individuals, which means that assessment relies in large part on observational methods. A number of tools are available but the psychometric quality and clinical utility of these are uncertain. The evidence for efficient treatment (the third perspective) with analgesics is also limited, with few statistically well-powered trials. The most promising evidence supports the use of stepped treatment approaches, and indicates the benefit of pain and behavioural interventions on both these important symptoms. The fourth perspective debates further difficulties in pain management due to the lack of sufficient training and education for health care professionals at all levels, where evidence-based guidance is urgently needed. To address the current inadequate management of pain in dementia, a comprehensive approach is needed. This would include an accurate, validated assessment tool that is sensitive to different types of pain and therapeutic effects, supported by better training and support for care staff across all settings.

Keywords:
pain assessment, Alzheimer's disease, cognitive impairment, behaviour

Introduction

There are an estimated 35 million people with dementia across the world. Currently, 5% of people over 65 years old have a diagnosis of dementia, rising to over 50% in those aged over 90 years.[1] Demographic changes in the coming decades and the increasingly aging population will lead to a substantial growth in the number of people affected and in the scale of the challenge associated with providing treatment and care. Pain presents a particular challenge in the treatment of dementia. The prevalence of pain, particularly chronic pain, is strongly related to age, hitting the oldest population the hardest, with prevalence rates of 72% above the age of 85 years.[2] Given these circumstances, it is clear that pain is probably very common among people with dementia; nevertheless, current knowledge is poor, which frequently leads to inappropriate treatment and care.

"Dementia" is defined as a "clinical syndrome due to disease of the brain, usually of a progressive nature, which leads to disturbances of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment."[3] The most common cause of dementia is Alzheimer's disease (AD), but vascular dementia (VaD), frontotemporal dementia (FTD), and Lewy body dementia, are also prevalent. In all subtypes of dementia, specific neuropathological changes are responsible for the decline in function. Besides the deleterious effects on cognition, the neuropathology of dementia is responsible for numerous other symptoms, such as behavioural disturbances, psychological problems, and the breakdown of language and communication. These problems have been summarized as "behavioural and psychological symptoms of dementia" (BPSD). Although memory dysfunction is the best-known symptom, BPSD, along with physical dysfunctions, have the highest impact on quality of life, and are one of the most important reasons for seeking help and institutionalization.[4]

Pain in dementia is also often expressed through behavioural disturbances. In fact, pain is thought to be one of the most important causal factors of BPSD.[5] However, this causal link is often difficult to identify due to the complexities of BPSD, which change over the stages of dementia and are more frequent in the later stages of the disease.[6] BPSD arising as a result of pain, such as agitation and aggression, can be extremely distressing for both the individual and their caregiver, and can lead to the inappropriate prescribing of antipsychotic medication instead of adequate pain treatment. While these medications do have their place in the treatment of severe or persistent psychiatric symptoms, they are associated with substantial side effects including increased mortality, cerebrovascular events, and falls.[7,8]

A further important and often forgotten issue is the impact of the neuropathological changes in dementia on pain perception.[9] The symptomology of dementia also means that assessment of pain is particularly challenging due to the loss of communication ability, which usually occurs during the condition. As a result, commonly used assessment tools are neither valid nor reliable and are difficult to use. To compound this, educational

and organizational shortcomings in dementia care settings often hamper the quality of care and treatment, including management of pain.

This narrative review discusses the evidence from relevant and recent literature regarding the challenges of pain management in dementia. The review focuses on four main perspectives that are critical to this discussion (Figure 1).
A literature search performed in PubMed (Medline) to supplement this review identified 1,669 publications relating to pain management in dementia. While the first mention of pain as a probable symptom in dementia appears in a publication in 1989,[10] the first review was not published until 1996,[11] which indicates that scientific interest in this theme is relatively new.

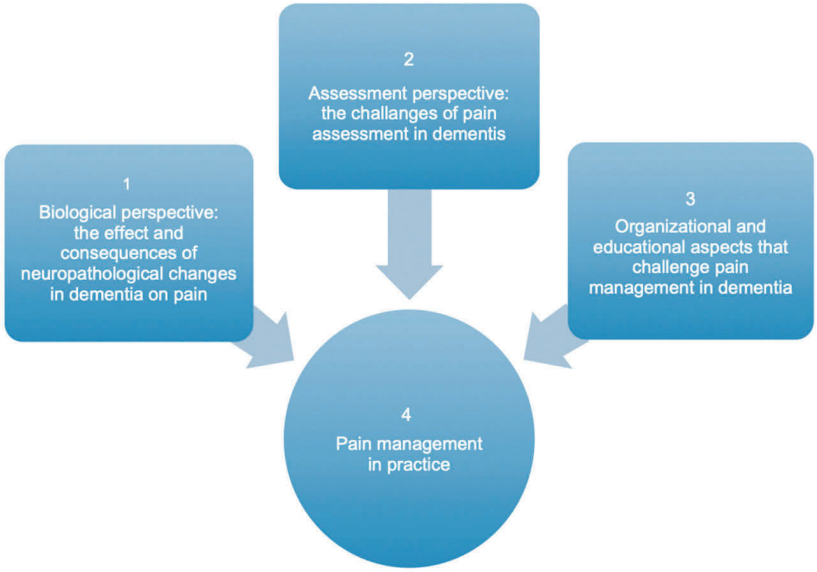


Figure 1. A model of challenges in pain management in patients with dementia

Biological perspective: the effect and consequences of neuropathological changes in dementia on pain

Both neuropathological and neuroimaging studies have described interconnected brain areas that are important in the mediation of pain processing.[9,11,12] Most studies describe two neuronal networks, the medial and lateral pain systems. The medial pain system – comprising the amygdala, medial thalamus, hippocampus, anterior cortex cinguli, and prefrontal cortex – is a pathway that mediates cognitive–evaluative and motivational-affective aspects of pain. In addition, autonomic–endocrine aspects are also mediated by the medial system.[9,13] The lateral pain system comprises, among others, the primary somato–sensoric areas and the lateral thalamic nuclei. The sensory–discriminative aspects

(localization, intensity, and quality of pain) are mediated by the lateral pain system.[9] Overlap of the two systems might occur in the insula. Recently, the existence of a third pathway mediating other critical aspects of pain has been proposed. This is thought to be a rostral, or limbic, pain system, which mediates behavioural aspects of pain – for example, agitated behaviour as a reaction to pain.[14]

Pain in AD

In AD, the distribution of neuropathological changes leads to a greater impact on the medial pain system than on the lateral system. This would imply that the cognitive-evaluative and motivational-affective aspects of pain are more greatly affected than the sensory-discriminative aspects.[9] The clinical consequences for people with AD would be an unchanged pain threshold but a higher pain tolerance. Some experimental studies have indeed confirmed this theory.[15,16] As would be expected following examination of the autonomic-endocrine aspects of the medial system and the changes in AD, blunted autonomic responses to pain have also been reported in experimental studies,[16] although these responses are thought to remain active in cases of intense pain.[17] Interestingly, however, more recent findings have shown that pain processing – as indicated by brain responses in electroencephalography and functional magnetic resonance imaging (fMRI) studies, pain reflexes, and facial responses to noxious stimuli – does not appear to be diminished in Alzheimer patients. Indeed, in some cases, it appears to be elevated.[12,18] These findings emphasize the caution that must be taken when extrapolating outcomes of animal studies to humans.

The rostral pain system overlaps with several components of the medial and lateral pathways, with the exception of the ventral striatum, which is generally not seen as a part of these other pathways. The striatum is severely affected in AD. Based on fMRI findings, it is hypothesized that people with mild to moderate AD have a relatively increased activation of the striatum in response to pain.[14] Conversely, this work indicates that there is a relatively decreased activation in severe AD. Behavioural changes in mild and moderate AD are therefore thought to be stronger, while in severe AD they might be normal or even blunted.[14] In fact, some clinical studies have found less pain-related behaviour in more severely cognitively impaired patients.[19,20] Relatively strong associations have been shown between pain and depression, as well as unspecified behavioural problems.[21,22] Associations of pain with agitation, aggression, delusions, wandering, and resistance to care have also been established, although the link is less consistent.[23–26]

In another fMRI study, a connectivity analysis was used to examine the impact of AD on the integrated functioning of brain regions mediating the sensory, emotional, and cognitive aspects of pain. Functional connectivity between the cortical and subcortical brain regions appeared enhanced in AD patients. Three functionally connected nodes were the right dorsolateral prefrontal cortex, hypothalamus, and periaqueductal gray, which tended to be constantly activated in the AD patients, who received repeated pain stimuli and could not reduce generalized brain activity.[27] Another important aspect of the neuropathological change that occurs in the prefrontal lobe in people with AD is the alteration of response to analgesic medication. An experimental study showed that

the endogenous expectation and placebo mechanism, an important aspect of pain management, is reduced in people with AD. This effect is particularly pronounced where damage in the connectivity between the prefrontal lobes and the rest of the brain is extensive, or where frontal neuropsychological function, as tested by the Frontal Assess ment Battery, is significantly reduced.[15] It is therefore likely that people with AD require a higher dosage of pain medication, to achieve the analgesic result that would normally be expected in a cognitively healthy adult. Further, there remains a great deal of uncertainty as to whether changes in the blood–brain barrier that occur during the dementia process might influence the effect of centrally acting pain medication such as morphine.[28]

Pain in other types of dementia

There have been few studies on pain in different subtypes of dementia such as VaD, FTD, or Lewy body dementia. In VaD, white matter lesions lead to several disconnections between areas of the brain in a process known as "deafferentiation." This is thought to be responsible for an increase in the motivational–affective aspects of pain. This type of pain, also called "central neuropathic pain," occurs frequently in patients who have had a stroke[29] and there is some clinical evidence that this type of deafferentiation pain might also occur in VaD.[17,30]

In people with FTD, it is plausible that the atrophy in the prefrontal cortex that characterizes the condition leads to a decrease in the motivational–affective aspects of pain, in a similar way to AD. In one study, patients with FTD reported less pain than patients with AD following the same experimental pain stimulus.[31] An underlying mechanism for this differential response may be due to the more extensive pathology in the pre- frontal cortex in FTD compared with in AD. Previous reviews and literature consistently highlight the lack of differential evidence around brain pathology and pain experience in different types of dementia.[32] However, while this criticism is valid, it is important to note that most people with dementia have mixed pathologies. It is particularly common to encounter combinations of gray matter atrophy and white matter lesions, and recent studies have shown that vascular damage, and, consequently, white matter lesions, is a prominent neuropathological characteristic in AD. It is therefore perhaps less useful to consider the specific pathologies of pain in different, yet overlapping, types of dementia, and more helpful to consider the locations within the brain that are affected.

Summary

There is conflicting evidence from neuropathological, neuroimaging, experimental, and clinical research regarding the impact of dementia neuropathology on pain processing and perception. One might speculate that atrophy of gray matter appears to lead to an increase in pain tolerance, while white matter lesions result in a decrease in tolerance. However, the consequences of the disturbed balance in excitatory and inhibitory processes in central nociception are still far from clear. These alterations in pain processing may have significant consequences for pain assessment and treatment, and should be considered when developing pain management approaches for use in dementia. Importantly, the

direction of the impact of neuropathology may differ in subtypes of dementia, and even within individuals. There thus remains a great deal of uncertainty regarding the effects of neuropathological changes in dementia. This lack of clarity likely contributes to indecision in practice and to inappropriate treatment choices.

Assessment perspective: the challenges of pain assessment in dementia

Accurate assessment of pain is a major prerequisite for adequate pain management and to assess the (positive) impact and potential adverse effects of analgesic medications. Assessment of pain in people with dementia is particularly challenging due to the loss of communication ability inherent in the symptomology of the condition, which limits the subjective reporting of pain that would normally be expected with cognitively healthy adults. The examination of a patient in pain aims to clarify the causal and maintaining factors leading to pain, which may be somatic or psychic, or an interaction of both. The outcome of an examination may therefore be the identification of dominating sources or mechanisms of pain, like nociceptive (i.e., musculoskeletal), visceral (i.e., internal organs), neuropathic (i.e., diabetic neuropathy), functional, or psychosomatic (i.e., fibromyalgia) pain. Evidence indicates that around 60%–80% of people with dementia in care homes regularly experience pain, most commonly related to musculoskeletal, gastrointestinal and cardiac conditions; genitourinary infections; and pressure ulcers.[5] Orofacial pain is also of frequent occurrence.[33] Different forms of pain present different challenges. Pain related to the internal organs, head, and skin is particularly challenging to detect compared with pain related to the musculoskeletal system, which can be identified through gentle guided movements.[34] Acute pain, such as that following a fall or acute heart attack is easier to assess than chronic pain, which often provokes pain avoidance through reduced movement or relieving posture.

Assessment through self-report

In the earlier stages of dementia, when cognitive impairment is limited and communication ability is mostly intact, self-report of pain is usually possible. There are several self-report scales, among which the Visual Analog Scale (VAS), the Numerical Rating Scale, and the Faces Pain Scale (FPS)[5] are the most frequently used. A study in 129 patients with severe dementia (mini-mental state examination score < 11), which aimed to assess the performance of self-assessment scales (the verbal-, visual-, and faces pain scales), found that 61% understood at least one scale[35] that is, they were able to explain the scale use and correctly indicate positions for no pain and extreme pain on two separate occasions. However, the study found that participants had difficulty using the FPS, which is perhaps less useful, even in earlier stages of dementia.[36] The “matching of a line length” to the intensity of pain, as required by the VAS, has also been shown to be challenging for people with cognitive impairment. Therefore, simple verbal or numerical categorical scales are recommended. As the neuropathological damage progresses, assessment by self- report becomes more difficult.

In more advanced stages of dementia, the majority of individuals are no longer able to give valid self-reports. In addition to their loss of communication, people are often no longer able to use introspection to gain knowledge about pain, are unable to report or anticipate its onset and duration, and are unable to understand questions related to the evaluation of their pain.[37] In these individuals, self-report is not an option, and a proxy rater, usually a primary caregiver, who knows the patient and their usual behaviour, should be included in pain assessment. However, it should be noted that one should always make an effort to obtain some sort of self-report within the limitations of the individual's symptoms and condition.

Assessment through observation of behaviour

Where self-report is not possible, observation and detection of pain-related behaviour is a valuable approach to identification of pain in dementia. An expert panel convened by the American Geriatrics Society (AGS) published guidance outlining the various behavioural expressions of pain in the elderly, including facial expressions, body movements and vocalizations, which are helpful when developing assessment tools for dementia (Table 1).[38] Facial expressions are particularly useful in detecting discomfort in AD.[39,40] Interestingly, sensory and affective components of pain can be differentially expressed in the face, with sensory aspects shown by movements around the eyes, and affective aspects depicted by movements of the eyebrows and the upper lip.[41] However, it should be noted that the accurate application of the method of reading facial expressions using the Facial Acting Coding System requires comprehensive training, which may make this approach unfeasible in clinical practice.[42]

Several observational scales have been developed based on the presence or alteration of the behaviours, emotions, interactions, and facial expressions described by the AGS Panel. Several review articles discuss the psychometric properties of these instruments and their use in clinical practice.[5,33,42–47] A common conclusion of the current body of literature is that there are a number of promising pain assessment instruments available but that most of these require further validation in people with dementia and assessment of their utility in clinical settings. Other weaknesses of many of the existing instruments are that the distinction between chronic and acute pain is rarely considered; validity studies in several situations where pain might arise, such as at rest, during day-to-day activities, and during guided movements, are often lacking; and it is unclear if different types of pain (nociceptive, neuropathic, visceral) can be addressed. Further, specific conditions such as orofacial pain have been almost completely overlooked.[33] Given the elevated level of facial response to pain stimuli in people with dementia compared with in cognitively healthy older adults, this is a key omission in the existing tools.[18]

Assessment of neuropathic pain

Neuropathic pain is often based on underlying diseases such as diabetic neuropathy, after stroke and amputation. Assessing this form of pain in dementia is extremely

Table 1. Common pain behaviours in cognitively impaired elderly persons according to the AGS Panel on persistent pain in older persons[38]

1. Facial expressions	Slight frown; sad, frightened face Grimacing, wrinkled forehead Closed or tightened eyes Any distorted expression Rapid blinking
2. Verbalizations, vocalizations	Sighing, moaning, groaning Grunting, chanting, calling out Noisy breathing Asking for help verbally abusive
3. Body movements	Rigid, tense body posture, guarding Fidgeting Increased pacing, rocking Restricted movement Gait or mobility changes
4. Changes in interpersonal interactions	Aggressive, combative, resisting care Decreased social interactions Socially inappropriate, disruptive withdrawn
5. Changes in activity patterns or routines	Refusing food, appetite change Increase in rest periods Sleep, rest pattern changes Sudden cessation of common routines Increased wandering
6. Mental status changes	Crying or tears Increased confusion Irritability or distress

challenging. The assessment of "central neuropathic pain," which is defined as pain caused by a lesion, or dysfunction of the central nervous system, is even more complex.[48] Approximately 35% of stroke patients suffer from post-stroke central neuropathic pain.[29] Because this deafferentiation also takes place in VaD, it has been suggested that central neuropathic pain is by far the most undertreated type of pain in patients with dementia.[49] The assessment and treatment of this type of pain is of high clinical relevance, but it has hardly been described in the literature, most likely because it requires assessment and treatment approaches that differ from those of other types of pain. In 2004, the European Federation of Neurological Societies (EFNS) Panel on Neuropathic Pain published guidelines on neuropathic pain assessment that included thorough sensory bedside testing in individuals with neuropathic pain.[50] This guidance would provide a useful basis for an assessment tool for neuropathic pain. However, as far as the authors are aware, no such instrument has been developed to date.

Organizational and educational aspects that challenge pain management in dementia

The challenges inherent in the assessment of pain in people with dementia, due to both symptomology and neuropathology, mean that health care workers are not sufficiently prepared to handle the difficulties in establishing good pain management practice for these patients. The literature suggests that a large proportion of these issues could be overcome through better education on specific aspects of pain management and through more effective facilitation of pain assessment within organizations. It has long been established that inaccurate beliefs and poor knowledge and training of staff and management in long-term care are important barriers to high quality care. Even experienced staff would be expected to benefit from specific education and training in pain assessment, pharmacological treatment, pain neurophysiology, and non-pharmacological treatments. A major educational goal is to improve their competency in distinguishing pain behaviours from other behavioural symptoms.[51] Managers in long-term care are often unaware of the best ways to manage pain in people with dementia. Many do not base decisions on evidence-based guidelines and often hold outdated beliefs regarding the use of treatment options (e.g., opioid analgesics).[52] Good-quality training is essential to address this. One recent study showed that after three interactive 3-hour sessions, gaps in staff knowledge of pain management were reduced and pain management strategies were put into practice four times more frequently than after the control intervention.[53] A controlled pre-post design trial studied the implementation of a pain protocol with a multifaceted approach. Next to skills training and education, this included a pain team and other quality improvement activities. Both quantitative and qualitative evaluation showed that this intervention was successful.[54]

Recommendations to improve pain assessment and management in nursing homes, including national guidelines, have stressed the importance of a well-trained, knowledgeable pain team.[55,56] In addition, implementation of treatment algorithms and consultation, continuous education, and team building within the care team are seen as the cornerstones of better pain management (Table 2).[56] A Canadian study that consulted frontline staff and administrators in long-term care revealed overall a general attitude that is open to change in which staff acknowledged the need for better implementation of pain management. Stakeholders identified a number of barriers including a lack of resources and lack of support from funding bodies. Free evidence-based tools and best practices for nurses, who work in nursing homes, are available through www.geriatricpain.org. However, it is clear that to elicit change in practice it will be key to position an accountable professional or onsite leader to champion implementation of better care standards.[57]

Use of evidence-based observational assessment instruments has often been advocated for regular practice.[44,55,58] Although there is considerable room for improvement in existing instruments, their use is certainly still recommended and can support better and more timely treatment of pain, particularly when self-report is not possible. A critical step in improving pain management is the promotion and implementation of these existing tools. Current uptake and use of instruments is low, and in some cases appears nonexistent. For example, a recent study in acute care settings in Finland showed very low use of pain instruments following hip fracture surgery. When an instrument was used, it was usually

the VAS, which is known to provide unreliable information in people with dementia.[59] Compliance in the use of these observational instruments in long-term care settings has also been disappointing. It is important to emphasize that while implementation of these observational scales is an important step to improve pain management, this alone will not necessarily mean that treatment will be improved. Key evidence and guidance are needed to support the decision-making process to translate a pain score to treatment. This is a complex process, as a recent Dutch study has shown,[60,61] and several studies emphasize that recognition of the pain does not necessarily lead to appropriate treatment.[62–66]

Table 2. Recommendations to improve pain assessment and management in nursing homes[56]

1.	Include an initial needs assessment of current pain care practices, formation of a pain quality improvement team guided by a systematic implementation process model, identification of clear quality indicators, and an ongoing educational component
2.	Use evidenced-based clinical decision-making algorithms for assessing and treating pain in persons with dementia
3.	Collaboratively engage all members of the care team, including residents, nurses at all levels within the organization, prescribers, medical directors, direct care workers, pharmacists, and families when considering pain care process changes
4.	Specifically target team-building with a goal of facilitating improvements in communication between prescribers and nurses about pain care in particular
5.	Incorporate a plan for regular periodic evaluation of pain management processes (eg, documentation of pain assessments and administration of analgesic medications on a scheduled basis) and resident outcomes, particularly pain severity and satisfaction, into efforts to ensure ongoing implementation of new practices
6.	Use consultants with expertise in pain management and process improvement strategies for on-site consultation

Pain management in practice

Some studies have suggested that pain is less prevalent in patients with dementia because they suffer from less comorbidity,[67] although several other studies have found that people with dementia do not have less painful conditions.[68,69] Taken together, the literature indicates that about 50% of patients with dementia are regularly in pain.[5] The largest study, which included over 5,000 home-care patients, also found no difference in pain prevalence in patients with or without dementia.[70]

Pain in people with VaD has received little attention in research. One of the few studies shows that, in line with the theory based on the neuropathological changes, more specifi-

cally white matter lesions, people with possible VaD may experience an increase in the experience of the motivational-affective aspects of pain.[71] Cross-sectional analyses in people with dementia living in nursing homes have demonstrated that there is a particular risk of severe pain in people with severe dementia and a mixed form of dementia (ADVaD) due to the restricted use of pain medication.[72] Those with ADVaD receiving opioids as pain treatment tended to have higher pain intensity than people without dementia receiving the same treatment. In addition, ADVaD patients have a significantly higher frequency of *International Statistical Classification of Diseases and Related Health Problems* 10th Revision (ICD-10) diagnoses and are therefore suggested to be more vulnerable.

As a consequence, they may have a lower tolerance for opioids. The evidence thus supports the importance of particular caution by physicians when prescribing opioids in people with ADVaD.

International epidemiological research has shown that the elderly in general, but especially those with dementia, receive less pain medication than their cognitively healthy counterparts, even in the same painful situations – for example, after a hip fracture.[73] The low dosage of pain medication seems to occur consistently in residential, nursing home, and hospital care.[63,74–77] Remarkably, recently, a few studies have reported a possible overuse of analgesics, particularly paracetamol, in patients with dementia,[68,78,79] stressing the clinical difficulties and uncertainties in the assessment of pain in these individuals (Figure 2). However, when people with dementia are prescribed pain medication, it is generally of low dosage and stronger pain medication such as opioids, are less likely to be considered.[5] For instance, patients with a hip fracture who have dementia receive significantly less opioids, both pre- and post-surgery. Where opioids are prescribed, they are used at a dosage that is one-third of that used in cognitively intact persons.[73]

The insufficient management of pain in patients with dementia can be explained by several factors. This uncertainty is partly due to the scarcity of pharmacological studies, which limits understanding of the pharmacodynamics of analgesic medication in this group of people.[80] The optimal treatment in these patients is therefore predominantly experience based. Clinicians must make decisions on type and dosage of analgesia without clear knowledge of the impact of the cognitive comorbidity of their patient. This lack of knowledge extends among the range of health professionals who work with people with dementia, including nurses and pharmacists.[81] It is likely that this results in both under- and overtreatment. Efficacy studies of analgesics in patients with dementia are challenging but feasible and there is an urgent need for more research in this area.[82]

The fact that pain is often expressed through challenging behaviour, particularly in advanced dementia, has led to several studies investigating the benefit of interventions for both pain and behaviour on reducing behavioural symptoms as a proxy measure for pain. Available evidence suggests that pain interventions targeting behavioural disturbances and behavioural interventions targeting pain are effective in reducing both pain and behavioural symptoms in dementia.[83] Since 2003, five randomized controlled trials (RCTs) have investigated the treatment effect on pain intensity or behavioural disturbances in these individuals. Manfredi et al evaluated the effect of opioid analgesics on behavioural disturbances in 25 patients with agitation assessed by Cohen-Mansfield Agitation Inventory.[84] Of the 25 subjects, 13 aged over 85 years showed significant reduction of agitation

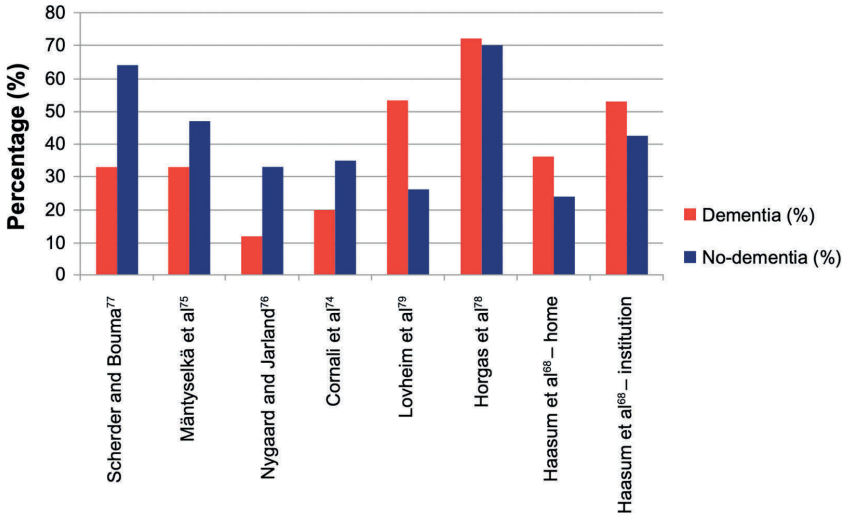


Figure 2. Studies on the prevalence (in %) of analgesic use in patients with dementia compared with in cognitively unimpaired patients (no dementia).

after 4 weeks. In another 4-week placebo-controlled crossover study, 39 patients with pain received regular paracetamol.[85] Pain was assessed using the Discomfort Scale for Dementia of the Alzheimer's Type. No significant differences in pain scores were found in the intervention group. However, the paracetamol dosage was low and might have been insufficient to have a therapeutic effect. In a placebo-controlled crossover trial with 25 patients, Chibnall et al investigated the efficacy of paracetamol on emotional well-being and behaviour assessed by Dementia Care Mapping and Cohen-Mansfield Agitation Inventory, respectively.[86] The study reported significant improvement in activities but found no effect on agitation. In the fourth study, 114 patients with behavioural disturbances were assigned randomly to either a serial trial intervention (STI) of stepped assessment and treatment or usual care. Patients randomized to the STI underwent non-pharmacological comfort intervention. Those still in pain after this treatment (n=26) received analgesics. Pain was assessed using the Discomfort Scale for Dementia of the Alzheimer's Type and behavioural disturbances by the Behavioural Pathology in Alzheimer's Disease Scale.[87] Results indicate that the STI approach improved behavioural symptoms significantly, but the effect of analgesics is not reported.

It is clear that most of these studies were underpowered with small sample sizes, were restricted to the use of paracetamol or opioids, and lacked validated outcome measures of pain.[83] The most striking study, an RCT in nursing home patients with dementia and high levels of behavioural symptoms, showed a significant relationship between improvement in agitation and improvement in pain, suggesting that better pain management was the main therapeutic factor. In addition, agitation worsened when the analgesia was discontinued, even though the study continued for only another 4 weeks.[88] The vast

majority of participants in the pain treatment group received only paracetamol, so it is unlikely that the effect was merely due to nonspecific sedation from stronger analgesics. Secondary analyses found that verbal agitation behaviours such as complaining, negativism, repetitious sentences and questions, constant request for attention, and cursing or verbal aggression responded to pain treatment. In addition, restlessness and pacing were sensitive to analgesics.[89]

Evaluation of pain management: responsiveness

The assessment of pain is the prerequisite for appropriate pain treatment. To provide effective treatment, it is also essential to identify when a treatment response is present. To enable this, there is an urgent need for a pain assessment instrument that can detect changes in pain intensity following treatment. As stated by Cohen-Mansfield and Jensen,[90] the utility of a pain assessment tool lies in its ability to identify persons whose manifestation of pain will decrease after receiving pain treatment. "Responsiveness" has recently been defined as "the ability of an instrument to detect change over time in the construct to be measured." [91] As pain is a subjective experience, this measurement requirement is difficult to document in patients with dementia and therefore merits particular attention during development of pain assessment tools. To date, as far as the authors are aware, only two studies have investigated the responsiveness of pain assessment instruments for patients with dementia and nonverbally communicating elderly people.[92,93] Cohen-Mansfield and Jensen compared the responsiveness of 12 self-report, informant rating, and observational instruments to pain treatment with non-opioids and opioids. Most sensitive to the effect of treatment were the Pain Assessment for the Dementing Elderly and Pain Assessment Instrument in Noncommunicative Elderly tools. Another subsequent trial of pain treatment in nonverbally communicating elderly reported very good responsiveness of the Elderly Pain Caring Assessment 2 tool after the pain treatment with non-opioids of 32 participants with dementia.[93]

To perform valid responsiveness studies, RCTs with appropriate sample sizes are a prerequisite, but most of the current controlled studies did not include a representative sample of elderly with dementia.[5] Further, it is vital that the final evaluation of the psychometric qualities of a scale considers the criterion of responsiveness against the criterion of reliability. Focusing only on the volatile and state-like aspects of pain (e.g., transient facial responses) in an instrument may increase its responsiveness, because every change is detected, but may neglect resistant and trait-like pain features (e.g., ongoing relieving posture). The result might be a premature "all-clear" when pain has not been fully addressed.

Discussion

The evidence presented in this review on pain management in people with dementia demonstrates the severe lack of effective assessment and treatment across the range of clinical settings. Pain is common among the elderly due to the increased prevalence of age-related conditions like osteoporosis, arthritis, and cardiovascular disease, and this is also true for people with dementia. These individuals appear to experience the intensity and affective component of pain differently than their cognitively intact counterparts do. In addition, the loss of communication ability leads to serious difficulties in detecting pain, particularly in more severe stages of dementia. In these individuals, pain is often also expressed in specific behaviours, such as agitation or withdrawal, that might mimic psychiatric conditions.

The etiology of these BPSD is multifactorial, and includes the neuropathological changes in the brain related to dementia, but also unmet physical and psychological needs, physical illnesses like urinary tract infections, and pain. In many cases, this results in the inappropriate treatment of behaviour with antipsychotic medication. Several studies have shown that treatment of pain might indeed decrease these behavioural symptoms. It is therefore of critical importance to improve the recognition and assessment of pain to ensure that patients receive the most appropriate treatment.

One of the main issues in this process is the development of an assessment toolkit that has good psychometric characteristics, can be used in different types of patients with cognitive impairment, is available in many languages, is sensitive to change, is easy to use in different settings, and is feasible and practical for nurses and other users. This task has been taken up in the European Cooperation in Science and Technology's (COST) action, "Pain assessment in patients with impaired cognition, especially dementia," which started in 2011. This 4-year initiative combines the knowledge of experimental and clinical researchers with that of clinical experts with the goal of reducing the fragmentation in international research and striving for international cooperation, bringing together leading researchers from a wide range of scientific disciplines. The major aim is the development of a comprehensive and internationally agreed-on assessment toolkit for older adults, targeting the various subtypes of dementia (see also COST).[94]

Alongside this work, it is essential that implementation and continuous education and training programs be developed, implemented, and evaluated to ensure the effective use of any new tool. These are prerogative steps for better management, but this will not follow automatically. There is a great need to provide support and clear guidance for clinicians and other health professionals, such as pharmacists and nurses who are involved in the treatment and care of people with dementia, to enable them to make informed decisions, and to remove the current reluctance to prescribe effective analgesia for people with dementia. The further introduction of established "pain teams" and opportunities for staff to consult with experts in all dementia care settings to come to collaborative decisions will also be potentially valuable in ensuring future improvements in the effective management of pain in dementia.

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CHAPTER 3

Association between pain, neuropsychiatric symptoms, and physical functioning in dementia: a systematic review and meta-analysis

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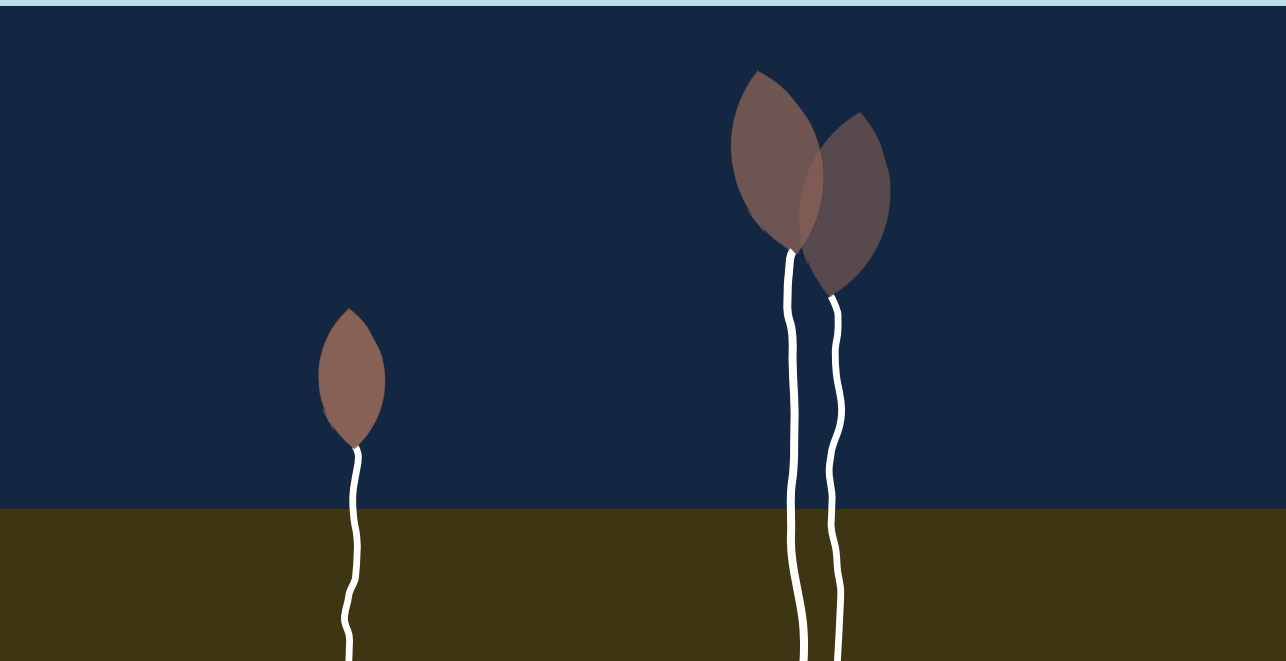
Awarded the 'Jan Stoop Prize' (2015) by the Interfacultair Overleg Specialisme Ouderengeneeskunde. This prize is an incentive price named after Jan Stoop, one of the pioneers of nursing home medicine in the Netherlands (1927-2009)



Abstract

Background

Pain, neuropsychiatric symptoms (NPS) and functional impairment are prevalent in patients with dementia and pain is hypothesized to be causal in both neuropsychiatric symptoms (NPS) and functional impairment. As the exact nature of the associations is unknown, this review examines the strength of associations between pain and NPS, and pain and physical function in patients with dementia. Special attention is paid to the description of measurement instruments and the methods used to detect pain, NPS and physical function.

Methods

A systematic search was made in the databases of PubMed (Medline), Embase, Cochrane, Cinahl, PsychINFO, and Web of Science. Studies were included that described associations between pain and NPS and/or physical function in patients with moderate to severe dementia.

Results

The search yielded 22 articles describing 18 studies, including two longitudinal studies. Most evidence was found for the association between pain and depression, followed by the association between pain and agitation/aggression. The longitudinal studies reported no direct effects between pain and NPS but some indirect effects, e.g., pain through depression. Although some association was established between pain and NPS, and pain and physical function, the strength of associations was relatively weak. Interestingly, only three studies used an observer rating scale for pain-related behaviour.

Conclusion

Available evidence does not support strong associations between pain, NPS and physical function. This might be due to inadequate use or lack of rating scales to detect pain-related behaviour. These results show that the relationship between pain and NPS, as well as with physical function, is complicated and warrants additional longitudinal evaluation.

Keywords:

pain; dementia; neuropsychiatric symptoms; physical function; associations

Background

Pain is common among older persons due to the increased prevalence of age-related diseases like osteoporosis and arthritis.[1] This also applies to patients with dementia living in nursing homes: around 50% is in pain[2 3].
Due to the changed perception of pain and loss of language skills in dementia, pain is often not communicated as such. In these patients, pain is often reported to be expressed as challenging behaviour (e.g., agitation or withdrawal) and is also known as neuropsychiatric symptoms (NPS)[4-6]. NPS includes depressive symptoms, agitated/aggressive behaviour, and psychotic symptoms like hallucinations and delusions[7].
NPS is highly prevalent: up to 80-85% of patients with dementia experience these symptoms[7-9] and they are one of the main reasons for institutionalisation[9 10]. The aetiology of NPS is multifactorial and includes neuropathological changes in the brain related to dementia and dementia severity, as well as unmet physical and psychological needs, physical illness (e.g., urinary tract infections), and pain[11].
Furthermore, pain influences the patient's physical function, including sleep, nutrition, and mobility[12-15]. Therefore, physical inactivity and disability in patients with dementia may be an expression of pain, but can also be the cause of pain[16 17]. This illustrates that, due to its diverse presentation, the interpretation of potential signs and symptoms of pain in dementia is difficult; moreover, to date, most studies still report a systematic under-recognition and under-treatment of pain[18-20]. There is evidence for specific pain-related behaviour, such as increased wandering or irritability, but facial expressions, body movements, and vocalizations are also common[21]. These behaviours can help in the clinical decision-making process[22]. Consequently, in the last decades, measurement and assessment of pain in patients with dementia by means of observations of these behaviours have received increasing attention. However, clinicians still have insufficient tools to face the challenges in the diagnostics and treatment of pain in this vulnerable group[22 23], and this may result in clinical indecisiveness. Nevertheless, there are validated measurement instruments available to detect pain in patients with dementia, such as the PACSLAC, DOLOPLUS-2, and the MOBID-2, based on observations[24 25]. Adequate use of these measurement instruments is of utmost importance in the management of pain.
Due to the challenges in the assessment and management of pain[26], people with dementia and NPS are more likely to receive antipsychotic drugs, despite the adverse side-effects like falls, somnolence and even death[27-29]. The latter underlines the importance of understanding the attributive effect of pain as a cause of NPS and decline in physical function. This would give healthcare workers more insight as to whether to target their treatment primarily on pain, NPS, disability, or on these conditions simultaneously.

Therefore, the aim of this systematic review is to assess the strength of associations between pain and NPS, and between pain and physical function, in patients with dementia. Special attention is paid to the description of measurement instruments and the method of detecting pain, NPS, and physical function to give clinical and scientific direction to the assessment and treatment of pain.

Methods

Study selection

This review was conducted following the PRISMA guidelines for systematic reviews[30]. A systematic search of the following databases was performed in March 2013: PubMed (Medline), Embase, Cochrane, Cinahl, PsychINFO, and Web of Science. In addition, the reference lists of the retrieved articles were screened. The following search terms (Additional file 1) were applied: Dementia AND Pain AND ((depression) OR (BPSD) OR (mobility) OR (sleep) OR (eating) OR (ADL)). Two reviewers, AvD and MP, independently, screened each title and abstract for suitability for inclusion; they decided independently on the eligibility of the article according to the predetermined selection criteria. Disagreement was resolved by consensus after review of the full article, or after the input of a third author (WA/MdW).

Articles that met the following criteria were included: patients with moderate to severe dementia (defined as a Mini Mental State Examination (MMSE) score of ≤ 18 or a Global Deterioration Scale (GDS) score of 5-7[31]), description of data on pain, description of NPS, and/or physical function (eating, sleep, activities of daily living (ADL) and mobility). For the purpose of this review, articles that described patients with mild to moderate dementia, but reported statistical data separately for the subgroup 'moderate dementia', were also included.
Eligible study designs included clinical trials, cohort, cross-sectional, observational, and longitudinal studies. Unless there was a clear description of the original data and baseline statistics, systematic reviews, qualitative studies, study protocols, (editorial) letters, case reports and randomised controlled trials (RCTs) were excluded. However, the reference lists of these articles were screened for eligible studies that were missed during the initial search. Only published data was included.
Excluded were articles that described patients who suffer from dementia resulting from Parkinson's disease and Huntington's disease, AIDS dementia complex, and Creutzfeldt-Jakob Syndrome. Furthermore, we excluded articles that did not report correlation coefficients or odds ratio's (OR), or when the articles did not provide sufficient information to calculate the OR ourselves. No time range or language restrictions were used.

Data extraction

Data were independently extracted by two reviewers (AvD and MP). A data extraction form was designed before extracting data from the included articles.
We recorded data on: study characteristics (design, country, setting, study population), pain and NPS measurement, prevalence of pain, and correlations of pain, NPS, and physical function. Where possible we present unadjusted associations, as these reflect the presence of co-occurrence as perceived by the caregivers. In addition, we calculated the OR ourselves if not reported. These ORs are reported as self-calculated odds ratio (SOR).

Furthermore, we recorded data on the use of rating scales to measure pain, NPS and physical function, as well as the method of detection. For example, if pain was measured with a rating scale for observational behaviours indicating pain and who performed the observation, i.e., a research nurse, a professional or patient's proxy.

Quality assessment

The methodological quality assessment of the included cross-sectional and longitudinal studies was based on previously developed checklists[32 33]. Two reviewers (AvD and MP) independently assessed the quality of each study. Disagreement was resolved by consensus or after input of a third author (MdW/WA). The maximum total score possible for cross-sectional studies was 12 points and for longitudinal studies 14 points. Cross-sectional studies that scored 0-4 points were considered to be of 'low quality', scores of 5-9 to be of 'moderate quality', and scores of ≥ 10 points were considered to be of 'high quality'. For longitudinal studies, scores of 0-5 points were considered to be of 'low quality', scores of 6-11 points to be of 'moderate quality', and scores of ≥ 12 points were considered to be of 'high quality'. See Additional file 3 for a more detailed overview of the awarded points and scores to the articles.

Scoring items

We selected items relevant for the assessment of observational studies, such as a description of a clearly stated objective, use of valid selection criteria, a response rate of ≥ 80%, valid/reproducible measurement of the outcome, adjusting for possible confounders, and the presentation of an association. One point was awarded for each question answered with 'yes' and 0 points for every 'no' or '?'. We added two questions concerning the study objective and population: i) was the selected objective similar to our objective, and ii) was the study population a selected population.
Furthermore, we wanted the quality assessment to reflect the ability to study our research objective. Therefore, we added a few items focusing on the measurement of pain, i.e., the use of specific rating scales, the method of detection, and information about the rater. Awarded points ranged from 0-2.
Additionally, two questions were added to the quality assessment for the longitudinal studies: i) was there major and selective loss to follow-up, and ii) was there a sufficiently long follow-up period. Again, 1 point was awarded for each question answered with 'yes' and 0 points for each 'no' or '?'.

Statistical analysis

To provide a more comprehensive overview of the association between pain, NPS and physical function, the available ORs are displayed in forest plots (using the program Review Manager 5.2) including the pooled ORs using a random effects model.

Results

Selected articles

The literature search yielded 1386 articles; 786 from PubMed (Medline), 304 from Embase, 77 from Cinahl, 57 from PsychINFO, 96 from Cochrane, and 66 from Web of Science. Additionally, 22 articles were retrieved from other sources (mainly through checking the reference lists). After removing duplicates, 1091 unique articles were identified. After carefully screening the titles, abstracts and full text, 22 publications met the inclusion criteria and were included in the present review (Figure 1).

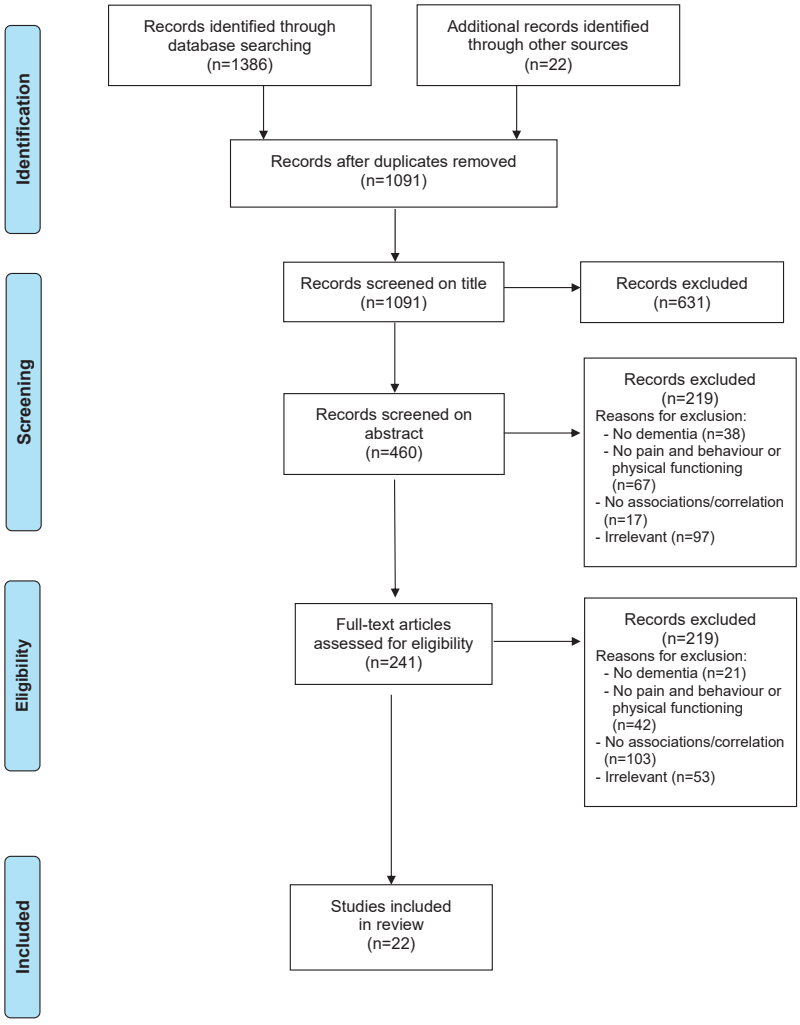


Figure 1. Flow diagram of the inclusion of studies

Description of included studies

All included articles were published between 2002 and 2013.
Of these 22 articles, eight articles illustrate correlates of pain with specified behavioural problems such as delusions/psychosis[3 34], anxiety[35], wandering[3 36], and resistance to care[3 37 38]. Furthermore, seven articles described associations between pain and unspecified behavioural problems, such as behavioural/psychiatric problems and dysfunctional behaviours[3 4 39-43]. It was not clarified which types of NPS were embedded in this term.
Eleven articles described the association between pain and depression[4 8 34 35 43-49] and eight articles between pain and aggression/agitation[8 34 36 38 47 48 50 51].
In addition, relationships between pain and physical function (e.g. ADL dependency and mobility) were described in ten articles[3 4 39 40 43 44 46 48 49 52].
The characteristics of these articles are presented in Table 1.

Table 1. Characteristics of the included studies

First author	*Country, setting*	*Dementia*	*Population: selection on pain, NPS or function?*	*Quality of study***
Ahn 2013 [36]	USA, nh	Moderate dementia, mean MDS cognitive performance scale 3.17 (SD 1.52)	Age ≥65 years, excluded when comatose	10
Bartels 2003 [8]	USA, ltc	Dementia, AD or signs of chronic stable cognitive impairment (in chart or MDS)	At risk for (or having) pressure ulcers	4
Black 2006 [39]	USA, nh	Advanced dementia, SIRS mean 10.3 (SD 6.7), AD 58%	Palliative care (life expectancy ≤6 months)	6.5
Brummel-Smith 2002 [40]	USA, nh	Moderate to severe dementia, MMSE mean 16.8 (SD 5.6) for 92 subjects	Age ≥ 55 years, had to have pain assessment, able to self-report on their level of pain	7
Cipher 2004 [4]	USA, ltc	Moderate dementia, mean NCSE 0.10 (SD 0.91)	Referral to clinical psychologist due to change in cognitive functioning, emotional distress, or behavioural dysfunction associated with dementia	7.5
Cipher 2006 [41]	USA, ltc	Dementia, mild 40%, moderate 41% and severe 19%, according to FAST (Reisberg) NCSE	Referral to clinical psychologist due to change in cognitive functioning, emotional distress, or behavioural dysfunction associated with dementia	7.5
D'Astolfo 2006 [44]	Canada, ltc	In 4% no dementia with MMSE>25, mild dementia 27%, moderate 44%, severe 25%	Admission in ltc at least 6 months to allow for patient charts to be completed	7
Gruber-Baldini 2005 [45]	USA, nh and residential care/ assisted living	Dementia, mild 14%, moderate 26% and severe 61%, according to MMSE or MDS-COGS.	Random sample aged ≥65 years (complete response 60%)	8.5
Kunik 2005 [34]	USA, va outpatients	Dementia, mild 46%, moderate 39%, severe 11%, according to DRS.	Veteran outpatients, not in LTC-facilities, with available caregiver	8.5
Leonard 2006 [50]	USA, nh	Dementia according to CPS-MDS dataset	At least one comprehensive MDS assessment, age ≥ 60 years	9

Table 1. Characteristics of the included studies *(continued)*

First author	*Country, setting*	*Dementia*	*Population: selection on pain, NPS or function?*	*Quality of study***
Leong 2007 [35]	Singapore, nh	Dementia with 33% mild (MIC) and 41% severe (SIC) cognitive impairment, according to AMT	No recent change in cognitive status, age ≥65 years. Here report of *communicative* subgroup *with dementia* (thus excluding 53 and including 125 of 358).	8.5
Lin 2011 [46]	Taiwan, nh	Dementia, 39% profound or end-stage dementia, according to CDR-C. Dementia, DemRS2 mean 4.12 (SD 2.79)	Admission at least 1 month	12
Morgan 2012 [47]	USA, Veterans Administration Medical Centre, longitudinal study		> 60 years, no aggressive behaviour in past year, no residence in nh and caregiver > 8 hrs a week, no onset of aggression before first follow-up (at 5 mo)	9.5
Norton 2010 [42]	USA, nh	Dementia, MMSE mean 6.4 (SD 6.7)	Verbal disruption (BEHAVE-AD >= 1.5), age ≥55 years, passed audiological assessment, and life expectancy >6 mo	9
Shega 2005 [48]	USA, outpatient geriatrics clinic	Dementia, MMSE mean 16.6 (SD 7.2)	Patient-caregiver dyad with pain-report on same day (77% of original sample)	9.5
Shega 2010 [49]	Canada, community dwelling	Cognitive impairment, 3 MS, mild to moderate dementia 18.5%	Community dwelling people aged ≥65 years, within one inclusion wave a pain self-assessment was incorporated	9
Torvik 2010 [52]	Norway, nh	No (13%), mild (46%) or moderate (41%) cognitive impairment, according to MMSE.	MMSE >11, aged ≥65 years (inclusion and response 35% of total sample). Communicative patients	6.5
Tosato 2012 [3]	EU and Israel, nh	Cognitive impairment, mild-moderate 55% and severe 45%, according to CPS	Several countries	11.5
Volicer 2009 [37]	Netherlands, nh/residential home	Dementia, according to MDS-CPS	Dependent in decision making, aged ≥65 years	11
Volicer 2011 [51]	Netherlands, nh, longitudinal study	Dementia, according to MDS	Availability of 4 quarterly MDS assessments within period of 15 months, aged ≥65 years	12
Williams 2005 [43]	USA, nh and residential care/assisted living	Dementia, with 29% MMSE>10 and MDS-COGS >2-4	Available pain data, aged ≥65 years	10
Zieber 2005 [38]	Canada, ltc	Moderate to severe cognitive impairment, according to FAST (Reisberg) score 6-7	Residents with continuous nursing care because of significant physical and/or cognitive impairments ('nh-level')	8

Abbreviations: nh, nursing home; MDS, Minimum Dataset; ltc, long term care facility; AD, Alzheimer's Disease; SIRS, The Severe Impairment Rating Scale; MMSE, Mini Mental State Examination; NCSE, Neurobehavioural Cognitive Status Examination; FAST, Functional Assessment Staging; MDS-COGS, Minimum Dataset Cognition Scale; va, veterans affairs; DRS, Dementia Rating Scale; CPS, Cognitive Performance Scale; AMT, Abbreviated Mental Test; CDR-C, Clinical Dementia Rating Scale-Chinese Version; Dem-RS2, Dementia Rating Scale 2; SD, Standard Deviation; BEHAVE-AD, Behavioural Pathology in Alzheimer's disease** Based on checklists from van der Windt et al.[52,53] Higher scores indicate higher quality (range observational studies 0-12, range longitudinal studie

Most of the studies described patients aged ≥ 65 years, who were mainly diagnosed with moderate to severe dementia and resided in long-term care facilities throughout the USA[4 8 34 36 39-43 45 47 48 50]. Three studies took place in Europe[3 51-53], three studies in Canada[38 44 49], and two studies took place in Asia[35 46].

Of the 20 cross-sectional studies, five studies were considered to be of high quality[3 36 37 43 46]. The remaining 15 studies were of low to moderate quality. Of the two longitudinal studies, that of Volicer et al. was considered to be of high quality[51] (Table 1).

Five studies described the use of selection criteria, mostly on NPS, and in eight other studies there might have been an indirect (unintentional) selection on pain, NPS or functioning. For instance, an indirect selection on pain by including patients with pressure ulcers[8].

Eight articles described the same study populations, sometimes with additional selection criteria, e.g. the two articles by Cipher et al[4 41]. Kunik et al. and Morgan et al. used data from a large longitudinal study on the causes and consequences of aggression in persons with dementia. Another two articles extracted data from the Dementia Care project of the Collaborative Studies of Long-Term Care[43 45] and two articles derived their data from the same Minimum Dataset 2.0 for nursing home care[37 51].

Overview of measurement instruments

Table 2 describes how pain, NPS, and physical function were measured.

Measurement of Pain

Three articles describe rating scales for observational behaviours indicating pain; both scales are validated for patients with moderate to severe dementia, i.e., the PAINAD[35 46] and DS-DAT[38]. The remaining articles describe other methods to measure pain (Additional file 2); some articles used the MDS dataset[3 36 37 50 51] and others used a variety of rating scales, e.g., the Faces Pain Scale[40], the Geriatric Multidimensional Pain and Illness Inventory[4 41], the Proxy Pain Questionnaire[52] and the Philadelphia Geriatric Center Pain Intensity Scale[34 43 45 47]. The Verbal Descriptive Scale and Verbal Rating Scale were also used to measure pain, sometimes combined with self-report[48 49 52]. Three articles used no rating scales to measure pain; they extracted data form patient's medical records[8 44] and interviewed patient's proxy and/or healthcare worker[39].

Additional file 2 provides a complete overview of the methods used.

Table 2. Measurements of pain, neuropsychiatric symptoms and physical function

	Measurement of pain		*Measurement of neuropsychiatric symptoms*		*Measurement of function*	
First author	***Rating scale***	***Method of detection***	***Rating scale***	***Method of detection***	***Rating scale***	***Method of detection***
Ahn 2013 [36]	MDS pain severity scale, combining pain frequency and pain intensity	Self-report, if not possible staff report based on proxy reports	MDS subscales; wandering-item, aggression behaviour scale (ABS), challenging behaviour profile (CBP) agitation subscale	Patient self-report, proxy and professional	MDS-ADL long form (7 items)	Staff observation
Bartels 2003 [8]	No use of rating scale	Data collection instrument (3-month period), raters unknown	MDS for depression	Medical records	MDS (number of ADLs)	Medical records
Black 2006 [39]	No use of rating scale	Medical records, preceding 6 months, interview surrogate and physician	No use of rating scales	Medical records, preceding 6 months, interview proxy and staff	No use of rating scale	Medical records, preceding 6 months, interview proxy and staff
Brummel-Smith 2002 [40]	1 out of 3 scales: faces or line scale, or word-based pain intensity scale	Self-report, assessed by trained research assistants	No use of rating scales	Trained research assistants	No use of rating scale	Trained research assistants
Cipher 2004 [4]	GMPI pain and suffering subscale	Part of neuropsychological evaluation by a licensed clinical geropsychologist	-GDS-15 -26 dysfunctional behaviours with scores 1-7	Part of neuropsychological evaluation by a licensed clinical geropsychologist	PRADLI	Part of neuropsychological evaluation by a licensed clinical geropsychologist
Cipher 2006[41]	GMPI	Part of neuropsychological evaluation by a licensed clinical geropsychologist and each instrument was administered after interviewing the resident, nursing staff and family members	GLDS, 19 categories with scores 1-7	Part of neuropsychological evaluation by a licensed clinical geropsychologist and each instrument was administered after interviewing the resident, nursing staff and family members Medical records, preceding 6 to max 26 months	GLDS	Part of neuropsychological evaluation by a licensed clinical geropsychologist and each instrument was administered after interviewing the resident, nursing staff and family members

D'Astolfo 2006[44]	No use of rating scale	Medical records, preceding 6 to max 26 months	No use of rating scales		No use of rating scale	Medical records Ambulatory status: independent, requires assistance, wheel chair (or bedridden n=1)
Gruber-Baldini 2005[45]	PGC-PIS, score ≥2	Rating by supervisory staff member	CSDD CMAI	Rating by supervisory staff member	MDS; activities of daily living scale, SMOI	Rating/observation by supervisory staff member
Kunik 2005[30]	PGC-PIS, item on level of pain in previous week, scores 1-6	Interview with patient and proxy by trained interviewer/research assistant	CMAI HAM-D NPI (subdomains delusion/ hallucinations)	Interview with patient and proxy by trained interviewer/research assistant	-	-
Leonard 2006[50]	MDS pain burden using a 4-level composite score based on pain frequency and intensity	-	MDS (Physical aggression: MDS item 'others were hit, shoved, scratched, sexually abused'; Depression: MDS score ≥3 on sum of 9 items, e.g. 'being sad', 'making negative statements', 'persistent anger with self or others', 'pained facial expressions'. (At least once in week before)	-	-	-
Leong 2007[35]	PAINAD for non-communicative patients	Interviews with patient and staff member by professionals for communicative patients	Depression with GDS-15 or STAI Anxiety with Cornell	Self-report or staff report	AAS	Not reported
Lin 2011[46]	PAINAD-Chinese version	Observation immediately following instances of routine care by principal investigator and research assistant	No use of rating scales	Medical records and observations by professional	No use of rating scale	Medical records and observation by professional

Table 2. Measurements of pain, neuropsychiatric symptoms and physical function *(continued)*

	Measurement of pain		*Measurement of neuropsychiatric symptoms*		*Measurement of function*	
First author	***Rating scale***	***Method of detection***	***Rating scale***	***Method of detection***	***Rating scale***	***Method of detection***
Morgan 2012[47]	PGC-PIS worst pain item	Not reported	CMAI aggression subscale CMAI non-aggressive physical agitation subscale HAM-D depression	Not reported	-	-
Norton 2010[42]	PPQ, intensity item, 10-14 day baseline	Primary CNA and data used from medical records	RMBPC-NH, selection of 3 need driven behaviours, BEHAVE-AD	Primary CNA and unit staff	PSMS	Nurses and trained research assistants
Shega 2005[48]	VDS, 1 item on presence and severity of pain 'right now'	Interviews with patients and caregivers by trained research assistant	GDS-15 CMAI	Interview patient and proxy	KATZ IADL	Interview patient and proxy
Shega 2010[49]	VDS, 5-point, 'pain past 4 weeks'	Interviews with patient by trained research assistant	Mental Health screening questionnaire; 5-item and 6-point scale	Interview with patient by trained research assistant	OARS/IADL; 3-point scale	Interview patient by trained research assistant
Torvik 2010[48]	VRS, 4-point, 'pain right now'	Patient self-report	DQoL, 29-items on 5 domains: self-esteem, aesthetics, positive affect, negative affect, belonging	Not reported	Barthel	Self-report and medical records
Tosato 2012[3]	InterRAI LTCF	InterRAI LTCF questions and observation of behaviour, any type of pain or discomfort of the body in previous 3 days by trained (research) staff	InterRAI LTCF 5 behavioural symptoms, previous 3 days	Not reported	MDS ADL Hierarchy Scale	Data recorded by study physicians

Volicer 2009 [37]	MDS-RAI pain frequency (item J2a)	Combination of physical examination, patient history, observation, consultation caregiver and medical records by staff	MDS Depression Rating Scale MDS item J1e for delusions MDS item J1i for hallucinations	Combination of physical examination, patient history, observation, consultation caregiver and medical records by staff	-	-
Volicer 2011 [51]	MDS	Combination of physical examination, patient history, observation, consultation caregiver and medical records by staff	MDS items I1ee, E1a, E1d, E1f, E1b, E1i, E1l, E1m for depression MDS for delusions and hallucinations MDS items B5b, E1b, E4aa, E4da for agitation	Combination of physical examination, patient history, observation, consultation caregiver and medical records by staff	-	-
Williams 2005 [43]	PGC-PIS, score ≥2, and 0-10 pain numeric rating scale	Registered nurses or licensed practical nurses and interview with overseeing supervisor	CSDD, score ≥7 CMAI, any behaviour at least weekly	Rating by care supervisors, registered nurses and licensed practical nurses	MDS-ADL, APAS SMOI	Rating by care supervisors, registered nurses and licensed practical nurses
Zieber 2005 [38]	DS-DAT, and a 7-point pain rating scale	Trained facility nurses, palliative care nurse consultants	PAS	Trained facility nurses	-	-

Abbreviation: MDS, Minimum Dataset; ADL, Activities of Daily Living; GMPI, Geriatric Multidimensional Pain and Illness Inventory; GDS-15, Geriatric Depression Scale-15 short version; PRADLI, Psychosocial Resistance to Activities of Daily Living Index; GLDS, Geriatric Level of Dysfunction Scale; PGC-PIS, Philadelphia Geriatric Centre Pain Intensity Scale; CSDD, Cornell Scale for Depression in Dementia; CMAI, Cohen-Mansfield Agitation Inventory; SMOI, Structured Meal Observational Instrument; HAM-D, Hamilton Rating Scale for Depression; NPI, Neuropsychiatric Inventory; PAINAD, Pain Assessment in Advanced Dementia; STAI, State-Trait Anxiety Inventory; AAS, Adjusted Activity Scale; PPQ, Proxy Pain Questionnaire; CNA, Certified Nursing Assistant; RMBPC-NH, Revised Memory and Behaviour Problems Checklist-Nursing Home; BEHAVE-AD, Behavioural Pathology in Alzheimer's disease; PSMS, Physical Self Maintenance Scale; VDS, Verbal Descriptor Scale; KATZ, Index of Independence in Activities of Daily Living; IADL, Instrumental Activities of Daily Living; OARS/IADL, Older Americans Recourses and Services/Instrumental Activities of Daily Living; VRS, Verbal Rating Scale; DQol, Dementia Quality of life; APAS, Albert Patient activity Scale; DS-DAT, Discomfort Scale - Dementia of Alzheimer Type; PAS, Pittsburgh Agitation Scale

Measurement of NPS

There was no uniform way of reporting NPS. The terms 'behavioural symptoms', 'psychiatric symptoms', and 'disruptive behaviour' were commonly used to describe any type of behavioural symptoms, e.g., agitation, depression, and anxiety[3 4 39-41].
The most common type of reported NPS was depression, followed by symptoms such as wandering, resistance to care, and verbal or physical abuse[36 37 42]. Four articles used no rating scales to measure NPS; they screened medical records instead[8 39 44 46]. Nine articles used more than one rating scale simultaneously to asses NPS[4 34 35 42 43 45 47 49 50]. Eight of those articles used rating scales to assess behaviour in patients with dementia; the Cornell Scale for Depression in Dementia[43 45], the Cohen-Mansfield Agitation Inventory[34 43 45 47 49], Behavioural Pathology in Alzheimer's disease[42], and the Neuropsychiatric Inventory[34] (Table 2). One article used the Mental Health screening questionnaire to assess depressed mood[49]. The MDS Dataset was also frequently used[8 36 37 50 51].

Measurement of Physical Function

Physical function was described in eleven articles[3 4 39 40 43-46 48 49 52]. Types of physical function that were reported in the articles are malnourishment[39 43 45], ADL dependency[3 4 40 43 49 52], and mobility[43 44 46].
Five articles used the MDS-ADL scale for measuring patient's physical function (Table 2). This was also the most frequently used measurement[3 8 36 43-45].

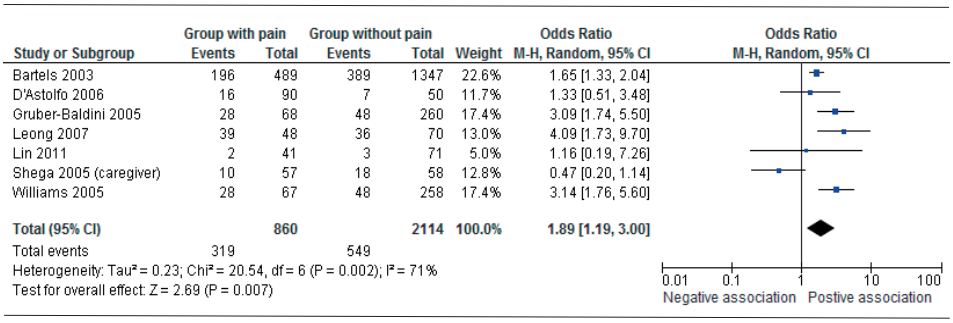
Associations between pain, NPS and physical function

Tables 3, 4, 5 and 6 describe the associations between pain, NPS, and physical function.
In total we found 81 associations expressed in either ORs or correlations. The prevalence rates of pain, NPS, and impairment of physical function ranged from 19-72%[3 4], 2-85%[37 39] and 12-92%, respectively[40 43 45]. Of the 22 included articles, the ORs could be extracted in six and the correlation coefficient in nine articles; in addition, we could calculate the SOR for the associations in ten articles.

Pain and neuropsychiatric symptoms

The most commonly described associations were between pain and depression (Table 3), pain and agitation (Table 4), and pain and specified NPS (Table 5), such as a negative association between pain and wandering, resistance to care, physical and verbal abuse, and aberrant vocalizations[3 36-38].
Eleven articles described associations between pain and depression (Table 3); in seven of these there was a positive association, with three articles reporting a strong association with an OR > 3 or r=0.5. In four articles the association was not significant: one article did not use a rating scale but examined medical records, one article used the rating scale PAINAD to measure pain, one article measured pain by observations, and another article used self-report. Remarkably, in the study by Shega et al. the OR for pain and depression was lower when pain was rated by the caregiver compared to the self-report of pain:

OR 0.47 (95% CI: 0.20-1.14) and OR 1.52 (95% CI: 0.63-3.68), respectively[48]. We could include seven articles in the meta-analysis (see Figure 2) and the pooled OR for pain and depression was 1.84 (95% CI 1.23-2.80).



Note: Studies with a large sample size (e.g., studies using the MDS dataset) were awarded more weight in the meta-analysis. However, this is not necessarily correct because, in observational studies, a larger sample size does not necessarily mean that these studies are of good methodological quality.

Figure 2. Forest plot: Pain and Depression

Eight articles described cross-sectional associations between pain and agitation/aggression (Table 4): four found positive associations, one found a negative association, two found no association, and one study found no association with pain self-report but a positive association with caregiver pain report. The strongest correlation found was in the study by Zieber et al., i.e., r=0.51 ($p<0.01$) between the DS-DAT scores and agitation.
Interestingly, two articles reported on longitudinal changes with follow-up data. In veterans living at home without aggressive behaviour in the preceding year or in the first five months of follow-up, Morgan et al. found that depression indirectly predicted the onset of aggression through pain[47]. In an unselected population Volicer et al. found that changes in agitation scores were related to changes in depression score but not to pain[51].

Table 3. Correlates of Pain with Depression

First author	*N*	*Pain: prevalence*	*Depression: prevalence*	*Correlates of pain with depression*	*Quality of study*
Bartels 2003 [8]	1836	Pain 27%	Depression 32%	**SOR 1.6 (95% CI: 1.3-2.0)**	4
Cipher 2004 [4]	234	Persistent pain 72%	Depression (GDS-15) mean 7.8 (SD 3.12)	Correlations with GMPI 'pain and suffering' **r=0.13 (p<0.05)** with GDS-15 depression	7.5
D'Astolfo 2006[44]	140	Pain 64% (musculoskeletal pain 40%)	Depression 16%	SOR 1.3 (95% CI: 0.5-3.5) (analyses in sample of no dementia-severe dementia)	7
Gruber-Baldini 2005 [45]	328	High pain 21%	Depression 23%	**SOR 3.1 (95% CI: 1.7-5.5)** (n=328)	8.5
Kunik 2005 [34]	99	Pain mean (PGC-PIS) 2.4 (SD 1.2)	Depression (HAM-D) mean 7.7 (SD 6.1)	**r=0.49 (p ≤ 0.01)**	8.5
Leong 2007 [35]	225	Pain 44%; chronic pain 34%	Depression 61%	**SOR 3.2 (95% CI: 1.8-5.9)**	8.5
Lin 2011 [46]	112	Observed pain 37% (PAINAD >= 2)	Depression 5%	OR=1.2 (95% CI: 0.19-7.26)	12
Morgan 2012 [47]	171	Worst pain mean 1.91 (SD 1.53)	Depression (HAM-D) mean 6.16 (SD 5.28)	Baseline: r = 0.30 (n.s.)	9.5
Shega 2005 [48]	115	Any current pain self-report 32%, caregiver report 53%	Depression (GDS-15) mean 3.1 (SD 2.7)	*For self-report pain* SOR 1.5 (95% CI: 0.6-3.7) *For caregiver pain report:* SOR 0.5 (95% CI: 0.2-1.1) with patient depression	9.5
Shega 2010 [49]	5549	Moderate or greater pain: 35.8%	Depressed mood 37.3%	**OR=1.69 (95% CI: 1.18-2.44)** with depressed mood (Adjusted for demographics)	9
Williams 2005[43]	331	Pain 21%, in nh 23%, in rc/al 20% *(self-report for subgroup mmse>10 was: 39% and 25%)*	Depressed 23%	**OR=2.3 (1.1-4.8)** and **AOR=2.9 (1.2-7.2)** (Adjusted for: sex, race, age, cognitive status, number of 10 comorbidities, impairments of 7 activities of daily living)	10

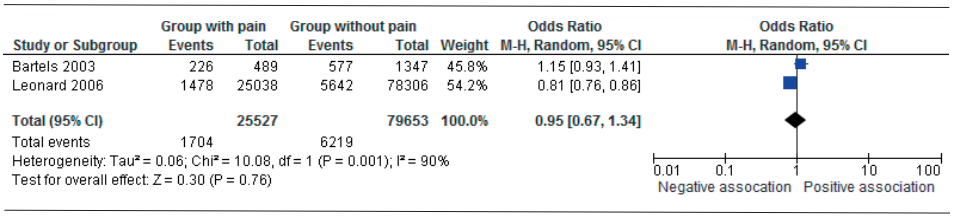
Abbreviations: SOR, Self-Calculated Odds Ratio; SD, Standard Deviation; r, correlation coefficient; AOR, Adjusted Odds Ratio; OR, Odds Ratio; n.s., not significant; GMPI, Geriatric Multidimensional Pain and Illness Inventory; PGC-PIS, Philadelphia Geriatric Centre Pain Intensity Scale

Table 4. Correlates of Pain with Agitation/aggression

First author	*N*	*Pain: prevalence*	*Agitation/ aggression: prevalence*	*Correlates of pain with agitation/aggression*	*Quality of study*
Ahn 2013 [36]	56577	Not reported	Aggression 24% Agitation 24%	**AOR 1.04 (95% CI: 1.01-1.08)** with aggression **AOR 1.17 (95% CI: 1.13-1.20)** with agitation *Subsample without use of psychotropic medication* **AOR 1.07 (95% CI: 1.01-1.15)** with aggression **AOR 1.16 (95% CI: 1.08-1.25)** with agitation (Adjusted for cognition, ADL, sociodemographics)	10
Bartels 2003 [8]	1836	Pain 27%	Agitation 44%,	SOR 1.1 (95% CI: 0.9-1.4) with agitation	4
Kunik 2005 [34]	99	Pain mean 2.4 (SD 1.2)	Agitation (CMAI) mean 14.3 (SD 4.1)	**r=0.20 (p≤0.05)** with aggression	8.5
Leonard 2006[50]	103344	Pain 24%; mild pain 15%, moderate to severe pain 9%	Physical aggression 7%	**SOR 0.8 (95% CI: 0.8-0.9)** for pain burden and physical aggression	9
Morgan 2012[47]	171	Worst pain mean 1.91 (SD 1.53)	Non agressive physical agitation (CMAI) mean 12.14 (SD 4.50)	Baseline: r = 0.06 (n.s.) with aggression *Follow-up:* depression indirectly predicted onset of aggression, through pain	9.5
Shega 2005 [48]	115	Any current pain self-report 32%, caregiver report 53%	Agitation (CMAI) mean 46.9 (SD 18.9),	*For self-report pain* no association with agitation (p>0.05) *For caregiver pain report* p=0.04 with agitation	9.5
Volicer 2011 [51]	1101	Any pain 49%	Agitation (score>0, range 0-5) 76%	**r=0.22 to 0.26 (p<0.001)** with agitation (Range of correlations scores over 4 periods.) *Follow-up:* Longitudinal changes in agitation scores are related to changes in depression score but not to pain.	12
Zieber 2005 [38]	58	Not reported	Not reported	**r=0.51 (p<0.01)** for DS-DAT scores and agitation (PAS-total) <u>Pain rating by palliative care nurse consultants:</u> **r=0.49 (p<0.01)** with agitation (PAS-total) <u>Pain rating by facility nurse:</u> **r=0.28 (p<0.05)** with agitation (PAS-total)	8

Abbreviations: AOR, Adjusted Odds Ratio; ADL, Activities of Daily Living; SOR, Self-Calculated Odds Ratio; SD, Standard Deviation; r, correlation coefficient; n.s, not significant; CMAI, Cohen Mansfield Agitation Inventory; DS-DAT, Discomfort Scale- Dementia of Alzheimer Type; PAS, Pittsburgh Agitation Scale

Furthermore, in a subsample of patients with moderate dementia without the use of psychotropic medication, the association between pain and agitation/aggression was similar compared to residents who used psychotropic drugs[36]. Only two articles could be incorporated in the meta-analysis (see Figure 3) resulting in a pooled OR of 0.95 (95% CI 0.67-1.34).



Note: Studies with a large sample size (e.g., studies using the MDS dataset) were awarded more weight in the meta-analysis. However, this is not necessarily correct because, in observational studies, a larger sample size does not necessarily mean that these studies are of good methodological quality.

Figure 3. Forest plot: Pain and Agitation/Aggression

Table 5 describes NPS, other than depression and agitation/aggression. Relations between pain and anxiety, hallucinations and delusions, were rarely studied. Only one article described an association between pain and anxiety, which was positive: SOR 1.8 (95% CI 1.0-3.0)[35]. Two articles described psychosis and delusions as being related to pain[3 34]. Kunik et al. found a small but non-significant association (r=0.15; p>0.05) with psychosis and Tosato et al. found an OR of 1.5 (95% CI 1.07-2.03) between pain and delusions.
Furthermore, terms like 'behavioural/psychiatric problems' and 'disruptive behaviour' were also frequently used to describe unspecified NPS (Table 5). Two out of seven articles reported moderate positive associations, with r=0.22 (p<0.05) as the strongest correlation between pain and dysfunctional behaviour[4].

Table 5. Correlates of Pain and Neuropsychiatric symptoms

Correlates of pain and specified NPS					
First author	***N***	***Pain: prevalence***	***Neuropsychiatric symptoms: prevalence***	***Correlates of pain with NPS***	***Quality of study***
Ahn 2013 [36]	56577	Not reported	Wandering 9%	**AOR 0.77 (95% CI: 0.73-0.81)** with wandering Subsample without psychotropic medication: **AOR 0.72 (95% CI: 0.63-0.83)** with wandering (Adjusted for cognition, ADL, sociodemographics)	10
Kunik 2005 [34]	99	Pain mean 2.4 (SD 1.2)	Delusions/ hallucinations mean 0.35 (SD 0.48)	**r=0.15 (p>0.05)** with psychosis	8.5

Table 5. Correlates of Pain and Neuropsychiatric symptoms *(continued)*

Correlates of pain and specified NPS					
First author	***N***	***Pain: prevalence***	***Neuropsychiatric symptoms: prevalence***	***Correlates of pain with NPS***	***Quality of study***
Leong 2007 [35]	225	Pain 44%, chronic pain 34%	Anxiety 48%	**SOR 1.8 (95% CI: 1.0-3.0)** with anxiety	8.5
Norton 2010 [42]	161	Not reported	BEHAVE-AD mean 6.4 (SD 29.2) RMBPC-NH mean 1.45 (SD 0.64)	r=0.15 (p=0.08) for pain intensity and emotional behaviour problems r=0.05 (p=0.58) for pain intensity and resistiveness to care	9
Torvik 2010 [52]	106	Current pain in total group 55%, in cognitive impaired group 52%	Negative affect index (DQoL) mean 2.0 (SD 0.75), positive affect/humour index (DQoL) mean 3.4 (SD 0.9)	**p<0.01** for current pain and negative affect p=0.11 for current pain and with positive affect/humour	6.5
Tosato 2012 [3]	2822	Any pain 19% (moderate/ severe/ excruciating pain 13%)	Behavioural symptoms 37% Psychiatric symptoms 21%	**AOR=0.74 (95% CI: 0.55-1.0)** with wandering **AOR=1.4 (95% CI: 1.08-1.8)** with resistance to care **AOR 1.5 (95% CI: 1.07-2.03)** with delusions AOR 1.06 (95% CI: 0.80-1.41) with verbal abuse AOR 1.08 (95% CI: 0.75-1.55) with physical abuse (Adjusted for age, gender, country, cognitive impairment, number of diseases, ischemic heart disease, stroke, falls, communication problems, and a flare-up of a chronic or recurrent condition)	11.5
Volicer 2009 [37]	929	Daily pain 29%, less than daily pain 19%	Verbally abusive not easily altered 2%, physically abusive not easily altered 12% Delusions 8% Hallucinations 9%	r=0.07 (p=0.03) for pain frequency and verbal abuse AOR=0.9(p=0.53) with resisting care AOR=0.7 (p=1.2) with verbal abuse AOR=0.7 (p=0.16) with physical abuse (Both multivariate models among others controlled for resisting care)	11
Zieber 2005 [38]	58	Not reported	Not reported	**r=0.46 (p<0.01)** for DS-DAT scores and resisting care **r=0.42 (p<0.01)** for DS-DAT scores and aberrant vocalization *Pain rating by palliative care nurse consultants:* **r=0.51 (p<0.01)** with resisting care **r=0.40 (p<0.01)** with aberrant vocalizations *Pain rating by facility nurse:* **r=0.48 (p<0.01)** with resisting care **r=0.065 (p<0.63)** with aberrant vocalizations	8

Table 5. Correlates of Pain and Neuropsychiatric symptoms *(continued)*

Correlates of pain and specified NPS					
First author	***N***	***Pain: prevalence***	***Neuropsychiatric symptoms: prevalence***	***Correlates of pain with NPS***	***Quality of study***
Black 2006 [39]	123	Pain 63%	Psychiatric disorders or behaviour problems 85%, behaviour problems 67%	SOR 1.9 (95% CI: 0.7-5.3) with psychiatric/ behaviour problems SOR 1.2 (95% CI: 0.5-2.5) with behaviour problems	6.5
Brummel-Smith 2002 [40]	104 (excluding those unable to self-report pain)	Moderate-severe pain 60% No-mild pain 40% 50 subject unable to answer	≥1 disruptive behaviours (wandering, verbal disruption, physical aggression, regressive behaviour, hallucinations) 70% in dementia sample n=154	SOR 1.8 (95% CI: 0.8-4.0) with ≥1 disruptive behaviour	7
Cipher 2004 [4]	234	Persistent pain 72%	Dysfunctional behaviours mean 4.4 (SD 0.76)	**r=0.22 (p<0.05)** with dysfunctional behaviours	7.5
Cipher 2006 [41]	277	Acute pain 29% Chronic pain 59%	-	**r=0.18 (p<0.05)** with GLDS mean behavioural intensity	7.5
Norton 2010 [42]	161	Not reported	BEHAVE-AD mean 61.4 (SD 29.2) RMBPC-NH mean 1.45 (SD 0.64)	r=0.18 (p=0.03) for pain intensity and disruptive behaviour problems r=0.05 (p=0.53) for pain intensity and global need driven behaviours	9
Tosato 2012 [3]	2822	Any pain 19% (moderate/ severe/ excruciating pain 13%)	Behavioural symptoms 37% Psychiatric symptoms 21%	**AOR=1.4 (95% CI: 1.04-1.8)** with socially inappropriate behaviour (Adjusted for age, gender, country, cognitive impairment, number of diseases, ischemic heart disease, stroke, falls, communication problems, and a flare-up of a chronic or recurrent condition)	11.5
Williams 2005 39	331	Pain 21%, in nh 23%, in rc/al 20% (self-report for subgroup mmse>10 was higher: 39% and 25%)	Behavioural symptoms 58%	OR=1.1 (95% CI: 0.49-2.29) and AOR=1.2 (95% CI: 0.57-2.36) with behavioural symptoms (Adjusted for: sex, race, age, cognitive status, number of 10 comorbidities, impairments of 7 activities of daily living)	10

Abbreviations: AOR, Adjusted Odds Ratio; ADL, Activities of Daily Living; SD, Standard Deviation; r, correlation coefficient; SOR, Self-Calculated Odds Ratio; BEHAVE-AD, Behavioural Pathology in Alzheimer's disease RMBPC-NH, Revised Memory and Behaviour Problems Checklist-Nursing Home; DQoL, Dementia Quality of life; DS-DAT, Discomfort Scale- Dementia of Alzheimer Type; GLDS, Geriatric Level of Dysfunction Scale; rc/al, residential care/assisted living; MMSE, Mini Mental State Examination; OR, Odds Ratio

Pain and physical function

Eleven articles reported associations between pain and physical function, although in most cases this was not the main topic of the study (Table 6). We found associations between pain and ADL or iADL impairment[3 4 40 48 49 52]. One article reported a positive association between pain and iADL impairment: OR 1.74 (95% CI 1.15-2.62). Other associations (although not significant) with physical impairment described in the articles were immobility[44 46] and malnourishment[43].

Only two articles described a positive association: one study used the PAINAD to objectify pain and one study used a five-point verbal descriptive scale to measure pain and a three-point scale (OARS/IADL) to measure functional impairment[46 49].

Table 6. Correlates of Pain with Physical Function

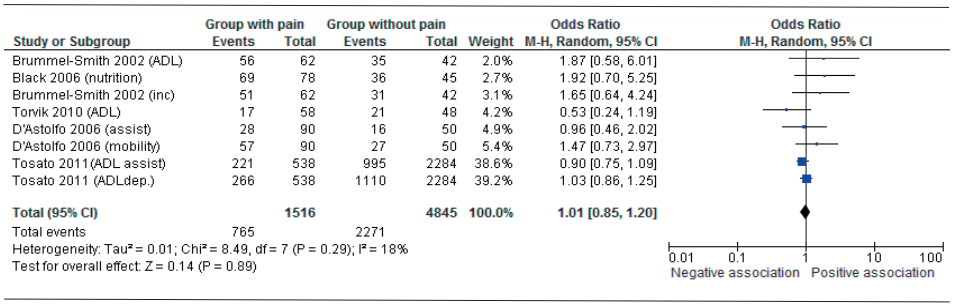
Correlates of pain and ADL or IADL					
First author	***N***	***Pain: prevalence***	***Physical function: prevalence***	***Correlates of pain with ADL or IADL***	***Quality of study***
Brummel-Smith 2002[36]	104 (excluding those unable to self-report pain)	Moderate-severe pain 60%, no-mild pain 40% (50 subject unable to answer)	≥ 1 ADL limitations 92% in dementia sample (n=154)	SOR 1.9 (95% CI: 0.6-6.0) with ≥ 1 ADL limitation	7
Cipher 2004[4]	234	Persistent pain 72%	ADL independency mean 0.09 (SD 0.99)	*Correlations with GMPI 'pain and suffering'* r=-0.04 (α>0.05) with ADL independency	7.5
Shega 2005[44]	115	Any current pain self-report 32%, caregiver report 53%	KATZ mean 8.5 (SD 2.7), IADL mean 15.3 (SD 3.9)	*For self-report pain* No association ADL and IADL (p> 0.05) *For caregiver pain report* No association with ADL or IADL (p> 0.05)	9.5
Shega 2010[45]	5549	Moderate or greater pain: 35.8%	Any IADL impairment: 66.5%	**OR=1.74 (95% CI: 1.15-2.62)** with any iADL impairment (Adjusted for demographics)	9
Torvik 2010[48]	106	Current pain in total group 55%, in cognitive impaired group 52%	Highly or moderate ADL dependent 36%	p=0.20 for current pain and ADL SOR=0.5 (95% CI: 0.2-1.2) for current pain and ADL high/medium v.s. low.	6.5
Tosato 2012[3]	2822	Any pain 19% (moderate/ severe/ excruciating pain 13%)	No disability 8%, assistance required 43%, dependent 49%	SOR 1.0 (95% CI: 0.9-1.2) with ADL-dependent SOR 0.9 (95% CI: 0.75-1.09) with ADL assistance required (Adjusted for age, gender, country, cognitive impairment, number of diseases, ischemic heart disease, stroke, falls, communication problems, and a flare-up of a chronic or recurrent condition)	11.5

Table 6. Correlates of Pain with Physical Function *(continued)*

Correlates of pain and other functional impairment					
First author	***N***	***Pain: prevalence***	***Physical function: prevalence***	***Correlates of pain with other functional impairments***	***Quality of study***
Black 2006 [39]	123	Pain 63%	Nutrition/hydration problems total sample 85%	SOR 1.9 (95% CI: 0.7-5.3) with nutrition/hydration problems	6.5
Brummel-Smith 2002 [40]	104 (excluding those unable to self-report pain)	Moderate-severe pain 60%, no-mild pain 40% (50 subject unable to answer)	≥1 ADL limitations 92% in dementia sample (n=154)	SOR 1.6 (95% CI: 0.6-4.2) with bladder incontinence	7
D'Astolfo 2006 [44]	140	Pain 64% (musculoskeletal pain 40%)	Use of wheel chair 60% Requires assistance 34%	SOR 1.5 (95% CI: 0.7-3.0) with use of wheel chair or bedridden SOR 1.0 (95% CI: 0.5-2.0) with requires assistance (Analyses in sample of no dementia-severe dementia)	7
Lin 2011 [46]	112	Observed pain 37% (PAINAD >=2)	Being restrained 46%; observed care activities: bathing 43%, assisted transfer 31%, self-transfer 26%	**OR=5.4 (95% CI: 2.3-12.5)** and **AOR=3.0 (95% CI: 1.0-8.7)** with being restrained **OR=23.4 (95% CI: 3.0-188)** and **AOR=19.2 (95% CI: 2.3-162)** with bathing **OR=29.7 (95% CI: 3.6-242**) and **AOR=11.3 (95% CI: 1.2-102)** with assisted transfer, both compared to self-transfer (Adjusted for gender, age, wound, restraint, tube present in body, recent fall, severity of dementia and type of activity)	12
Williams 2005[43]	331	Pain 21%, in nh 23%, in rc/al 20% (self-report for subgroup MMSE>10 was higher: 39% and 25%)	Low activity 47%, immobile 12% Low food intake 53% Low fluid intake 51%	OR=0.65 (95% CI: 0.38-1.11) and AOR=0.64 (95% CI: 0.37-1.10) with low activity OR=1.1 (95% CI: 0.49-2.29) and AOR=0.8 (95% CI: 0.37-1.69) with immobility OR=1.18 (95% CI: 0.64-2.17) and AOR=1.03 (95% CI: 0.56-1.87) with low food intake OR=1.20 (95% CI: 0.67-2.15) and AOR 1.14 (95% CI: 0.66-1.99) with low fluid intake (Adjusted for: sex, race, age, cognitive status, number of 10 comorbidities, impairments of 7 activities of daily living)	10

Abbreviations: SOR, Self-Calculated Odds Ratio; ADL, Activities of Daily Living; SD, Standard Deviation; r, correlation coefficient; GMPI, Geriatric Multidimensional Pain and Illness Inventory; PAINAD, Pain Assessment in Advanced Dementia; OR, Odds Ratio; AOR, Adjusted Odds Ratio; KATZ, Index of Independence in Activities of Daily Living; IADL, Instrumental Activities of Daily Living; nh, nursing home; rc/al, residential care/assisted living; MMSE, Mini Mental State Examination

The strongest reported association was with assisted transfer compared to self-transfer; however, this had a very broad confidence interval: OR 29.7 (95% CI 3.6-242)[46]. The remaining eight articles reported associations which were not significant. Based on five articles, the pooled OR (see Figure 4) for pain and overall physical function was 1.01 (95% CI 0.85-1.20).



Note: Studies with a large sample size (e.g., studies using the MDS dataset) were awarded more weight in the meta-analysis. However, this is not necessarily correct because, in observational studies, a larger sample size does not necessarily mean that these studies are of good methodological quality.

Figure 4. Forest plot: Pain and Physical Function (with reports of 5 out of 10 included studies)

Discussion

Despite the increased attention for pain in dementia, relatively few studies have explored associations between pain and NPS, and pain and physical function. We found 22 articles reporting the strength of associations between these three modalities, including only two longitudinal studies.

We found most evidence for the association between pain and depression (in 7 of 11 articles), followed by the association between pain and agitation/aggression (in 5 of 8 articles). The two longitudinal studies reported no direct effects between pain and NPS but only some indirect effects, e.g., of pain through depression. Interestingly, articles reporting a significant positive association between pain and NPS, and between pain and physical function, were mainly of low methodological quality. One article with high methodological quality reported a non-significant correlation between pain frequency and verbal abuse[37]. Four high-quality articles reported a positive association between pain, aggression/agitation and wandering[36 51], between pain and functional impairment[46], and between pain and behavioural symptoms[43].

Due to the hypothesized effect of pain on NPS and physical function, and some overlap of items in the measurement instruments, we expected to find stronger associations; particularly since pain interventions targeting NPS and behavioural interventions targeting pain are reported to reduce both pain and NPS (such as depression and agitation/aggression)[54]. In addition, a cluster RCT by Husebo et al., investigating a sample of moderate to severe dementia patients with challenging behaviour, showed that treating pain led to a significant improvement in mood symptoms such as depression, apathy, and eating

disorders, and improvements in ADL function were also found[12]. Furthermore, research among elderly without cognitive impairment shows an association between pain and depression; there is also evidence that treatment of depression in cognitively intact older patients improves pain and physical function[46 55 56]. It is plausible that this also applies to patients with dementia.

However, the associations found in the present systematic review were rather weak. This may be the result of inadequate assessment of both pain and NPS in the included studies. Most studies did not use measurement instruments developed for the assessment of pain in people with dementia. For example, D'Astolfo et al. did not use a measurement instrument for pain or for NPS, but only screened medical records and found relatively weak and non-significant associations. Also, it is possible that healthcare workers interpret NPS as symptoms of either pain *or* challenging behaviour; if this is the case, then only pain *or* NPS is reported in the medical records and no association will be found.

Five articles used the MDS-RAI Dataset to measure pain and also reported weak associations[3 36 37 50 51]. These articles also report weak associations. This might be due to the doubt about the accuracy of measuring pain in people suffering from dementia with the MDS-RAI Dataset[57 58].

We hypothesize that validated rating scales, used by a professional, will provide a more accurate reflection of the relationship between pain and NPS. This is illustrated by the study of Zieber et al. in which a clear distinction is seen in the strength of the correlations between pain and agitation when rated by a palliative nurse consultant or when rated by the facility nurse[38]. When rated by the palliative nurse consultant the correlation was stronger: $r=0.49$ ($p<0.01$) compared with the rating by the facility nurse: $r=0.28$ ($p<0.05$). This also applied to the correlation between pain and aberrant vocalizations: $r=0.40$ ($p<0.01$) and $r=0.065$ ($p<0.63$), respectively, but not between pain and resisting care: $r=0.51$ ($p<0.01$) and $r=0.48$ ($p<0.01$), respectively. In addition, in a study by Leong et al. a professional used the PAINAD to assess pain and found a SOR of 3.2 (95% CI 1.8-5.9) between pain and depression[35]. However, other studies with a relative strong association between pain and depression did not use professionals or validated rating scales to assess pain in patients with dementia[43 45]. Therefore, the results of the present review cannot fully support the hypothesis of a better reflection of the relationship between pain and NPS when validated rating scales are used by professionals.

Another explanation for the rather weak associations found in this review could be the inclusion of six articles which described individuals with predominantly severe dementia. Together with the progression of dementia, the assessment of pain becomes even more difficult due to diminished pain behaviours[59], but facial expressions tend to increase in the course of dementia[60]. Of the measurement instruments used in the included studies, only the PAINAD and DS-DAT include facial expressions of pain. In addition, in the included studies, the use of antipsychotic drugs could also explain the weak associations. Antipsychotic drugs may distort and diminish the expression of NPS while a possible cause of NPS, for instance pain, is not treated. This may have resulted in the under-recognition and poor report of NPS. However, the study by Ahn et al. shows that, in a subsample of patients without psychotropic drugs, the association between pain and agitation/aggression, and between pain and wandering, was similar to that in residents who used psychotropic drugs[36].

Moreover, we could have anticipated finding rather weak associations, because most of the included studies were cross-sectional in design. This is illustrated by studies that found that a change in pain after an intervention is related to a decrease in NPS or function[61 62]. To some extent the included articles measured overall functional impairment with, for example, total ADL scores. Some articles focused on specific components of physical function, like nutritional status and mobility, which are often hampered in patients with dementia. However, because the focus of these articles was not on the association between pain and physical function, in most cases we had to calculate the association between pain and physical function (SOR) ourselves. This raises the question as to whether physical function is receiving the attention it deserves and, possibly, may even lead to publication bias. Physical inactivity or impairment is an important sign that a patient with dementia could be in pain; this is illustrated by a study in which patients with moderate to severe dementia (treated with acetaminophen) tend to spend more time in social interaction and engage with the environment more actively, than patients who received placebo[62]. Unfortunately, until now, no longitudinal studies are available that describe the course of physical function in patients with dementia in relation to pain.

Strengths and limitations

This study is the first to give a comprehensive and systematic analysis of the associations between pain and NPS, and pain and physical function, in patients with dementia. One of the strengths of this study is that we not only included publications that presented associations between pain and NPS and pain and physical function, but also publications that provide enough information to compute ORs, thus taking full advantage of the available evidence. In addition, when possible, we present the crude OR as this reflects the presence of co-occurrence as perceived by the caregivers. Furthermore, we used a methodological quality assessment based on previously developed checklists[32 33]. By adding extra items focusing on the measurement of pain, study objective and population, we tailored the quality assessment to the purpose of this review. We believe that this strategy has led to a better reflection of the challenges in the assessment of pain and NPS. A possible limitation could be some publication bias, e.g., if some studies do not report the associations because they were negative. Also, we explicitly searched for publications about pain and not for terms like 'distress' or 'discomfort'. However, we believe that this approach provides the best reflection of the complex relation between pain, NPS and physical function. Furthermore, we were unable to include every study in the meta-analysis due to missing data. In addition, the forest plots should be interpreted with caution, since the included studies are heterogeneous and studies with a large sample size (e.g., studies using the MDS Dataset) were awarded more weight in the meta-analysis; however, this weighting is not necessarily justified because, in observational studies, a larger sample size does not necessarily mean that these studies are of good methodological quality. Another possible limitation is that we did not include delirium as a separate search term in our search strategy. However, as delirium is a syndrome with specific neuropsychiatric symptoms, we looked at the clinical features of a delirium by including these symptoms, such as hallucinations and delusions, in our search strategy.

Clinical implications

The American Geriatrics Society (AGS) published clinical guidance on persistent pain, outlining 26 behavioural expressions of pain in the elderly[21]. The AGS panel advises clinicians to assess pain in older persons with moderate to severe dementia via direct observation of this pain-related behaviour, or via history from caregivers. Several observational scales are available based on the presence of or alterations in behaviours, emotions, interactions, and facial expressions. However, there is little empirical evidence that these 26 behavioural expressions are indeed related to pain. In our review, only depression and agitation/aggression seem to be associated with pain.

The advice of direct observation of pain-related behaviour seems to be poorly implemented, as illustrated by this review, in which only three studies used rating scales based on behavioural observations[35 38 46]. It can be assumed that, when this non-optimal situation exists in a research setting, then routine implementation of rating scales based on behavioural observation in clinical practice will be even less optimal.

The results presented in this review do not fully support the association between pain, NPS and functional impairment in dementia. However, they do highlight the presence of difficulties in the management of pain in dementia. This is illustrated by the frequent use of terms like 'behavioural symptoms', 'disruptive behaviour', and 'psychiatric symptoms'. There is no uniform way of reporting neuropsychiatric symptoms; this could complicate the comparison between behavioural symptoms and also reveals the challenges in differentiating between the different, but often very similar, types of challenging behaviour. This also applies to the description of physical function; the specific functions and activities should be properly described (e.g., malnutrition, sleep disturbances, and immobility) and not merely presented as a total ADL score.

Clearly, co-occurrence will not (and can not) be easily observed, probably leading to clinical indecisiveness. However, regardless of co-occurrence, we want to stress the importance of pain detection in patients with dementia because pain can be the cause of other disorders, such as NPS. Moreover, it has been proven that pain treatment significantly reduces behavioural disturbances, such as agitation[12 54 61]. Pain and its consequences have an impact on the quality of life and therefore should be recognized, measured and treated.

Conclusion

This review shows, unexpectedly, rather weak associations between pain and NPS, and between pain and physical function. Nevertheless, the relationship between pain and the onset of NPS, as well as the effect on physical function, remains unclear and should be further explored. To unravel this complex relationship, the course of pain, NPS and physical function should be examined longitudinally, using valid measurement instruments. A longitudinal study design will provide more information on causality and the sequence of these modalities, providing evidence that can be incorporated in clinical practice to improve the management of pain for people with dementia.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

AvD performed the literature searches and selected eligible articles, extracted data from these articles, did the analyses and prepared the first draft of the review. MP contributed to the selection of articles, data extraction and methodological quality assessment of the systematic review. MdW and WA helped to determine the concept of the review and contributed to the writing. All authors reviewed and commented on the report.

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Appendix 1 Search terms

Dementia	"Dementia"[mesh:noexp] OR "Alzheimer Disease"[mesh] OR "Frontotemporal Lobar Degeneration"[mesh:noexp] OR "Lewy Body Disease"[mesh] OR dementia[tw] OR dement*[tw] OR alzheimer*[tw] OR "Frontotemporal Lobar Degeneration" OR "Lewy Body Disease" OR "Delirium, Dementia, Amnestic, Cognitive Disorders"[Mesh:NoExp]
Pain	pain OR pain* OR "Analgesics"[mesh] OR Analgesic[tw] OR Analgesics[tw] OR discomfort[tw] OR discomfort*
Depression	"Depressive Disorder"[mesh] OR depression[tw] OR depressive[tw] OR "Depression"[mesh]
BPSD	agitation OR agitated OR "Psychomotor Agitation"[mesh] OR "Psychomotor Hyperactivity" OR Restlessness OR "Psychomotor Excitement" OR "Psychomotor Disorders"[mesh:noexp] OR "behavioural disturbance" OR "behavioural disturbances" OR "behavioural disturbance" OR "behavioural disturbances" OR "Social Behaviour Disorders"[mesh] OR "dysfunctional behaviour" OR "dysfunctional behaviours" OR "dysfunctional behaviour" OR "dysfunctional behaviours" OR "challenging behaviour" OR "challenging behaviours" OR "challenging behaviour" OR "challenging behaviours" OR BPSD[tw] OR "behavioural and psychological symptoms of dementia" OR "behavioural and psychological symptoms of dementia" OR hallucination OR hallucinations OR aggression OR aggressive behaviour OR aggressive behaviour OR apathy OR delusion OR delusions OR delusional OR resistiveness OR "Behavioural Symptoms"[mesh:noexp] OR "psychological symptoms"[tiab] OR "psychological symptom"[tiab] OR "Behavioural Symptoms"[tiab] OR "Behavioural Symptom"[tiab] OR "Behavioural Symptoms"[tiab] OR "Behavioural Symptom"[tiab] OR "neuropsychiatric symptom"[tiab] OR "neuropsychiatric symptoms"[tiab] OR irritability OR irritabilities OR "anxiety"[mesh:noexp] OR "anxiety disorders"[mesh] OR "anxiety disorder" OR "anxiety disorders" OR anxiety[ti]
Mobility	"mobility" OR "Mobility Limitation"[mesh] OR "Range of Motion, Articular"[Mesh] OR "Motor Activity"[Mesh]
Sleep	"sleep"[Mesh] OR "sleep disorder" OR "sleep disorders" OR "Sleep Disorders"[Mesh] OR "sleep deprivation" OR "Sleep Deprivation"[Mesh] OR "circadian rhythm" OR "Circadian Rhythm"[Mesh] OR "Circadian Clocks"[Mesh] OR "sleeping"
Eating	"eating"[Mesh] OR "eating disorder" OR "eating disorders" OR "eating disorders"[Mesh] OR eating[ti]
ADL	"ADL" OR "activities of daily living"[Mesh] OR "activities of daily living" OR "functional impairment" OR "functional status" OR "functional ability" OR "functional abilities" OR "functional outcome" OR "functional outcomes" OR functional[ti] OR "physical functioning" OR "physical function" OR "physical functions" OR functioning[ti] OR barthel[tiab] OR katz[tiab]

Appendix 1.2 Prisma 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Not applicable
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Additional file 1 and page 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4-5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Appendix 1.2 Prisma 2009 checklist *(continued)*

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 and figure 1 on page 8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1, page 9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Additional file 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 3-6, additional file 'Figures'
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Additional file 'Figures' and pages 12-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-14-15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17-18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097
For more information, visit: www.prisma-statement.org.

Appendix 2 Rating scales for pain that were used in the reported studies

Pain rating scale	Type of measurement	Reason for development	Studies (first author)	
Rating of observations				
PAINAD	Pain Assessment in Advanced Dementia Scale (Warden 2003)	5-item scale (nonverbal behaviours) Each item rated on a 3-point scale (0-2)	Developed to provide a clinically relevant and easy to use pain assessment tool for individuals with advanced dementia	Leong 2007, Lin 2011
DS-DAT	Discomfort Scale-Dementia Alzheimer Type (Hurley 1992)	9-item scale (nonverbal behaviours) Each item is measured for absence or presence of indicators of *discomfort* which, if present, are scored for frequency, duration and intensity·	Developed to measure *discomfort* in elders with dementia of the Alzheimer's type·	Zieber 2005
Rating of pain based on interview or observation				
GMPI	Geriatric Multidimensional Pain and Illness Inventory (Clifford 2005)	12-items in 3 subscales: pain and suffering (3), interference (5), emotional distress (4) Each item rated on a 10-point scale	Designed to assess pain and its functional, social and emotional consequences, in residents in long term care	Cipher 2004/2006
PPQ	Proxy Pain Questionnaire (Fisher 2002)	3 items: presence Y/N, frequency, and intensity of pain on 13-point scale	To assess pain in cognitively impaired older people	Norton 2010 (1 item)
PGC-PIS	Philadelphia Geriatric Centre–Pain Intensity Scale (Parmelee 1991)	"worst pain" item: highest level of pain experienced over preceding 4 weeks on a 5-point scale		Gruber-Baldini 2005, Kunik 2005/ Morgan 2012, Williams 2005
InterRAI LCTF	InterRAI instrument for Long-Term Care Facilities	Any type of pain or discomfort in 3 days before assessment, based on extensive evaluation Items on pain frequency, and severity (0-4)		Tosato 2011

Appendix 2 Rating scales for pain that were used in the reported studies *(continued)*

Pain rating scale	Type of measurement	Reason for development	Studies (first author)
MDS **Self-report of pain***	Minimum Data Set	Items: pain intensity and frequency Each item rated on a 3-point scale (0-3)	Ahn 2013, Leonard 2006, Volicer 2009/2011
- VDS VRS	Non-verbal visual analogue scale Verbal Descriptor Scale Verbal Rating Scale	7-point scale 7-point scale, pain right now 4-point scale, pain right now	Brummel-Smith 2002 Shega 2005/2010 Torvik 2010

* Developed for self-report, but sometimes used in interview

References

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3 Hurley, A.C., Volicer, B.J., Hanrahan, P.A., Houde, S., and Volicer, L., 1992. Assessment of discomfort in advanced Alzheimer patients. Res.Nurs.Health 15, 369-377.

4 Parmelee, P.A., Katz, I.R., and Lawton, M.P., 1991. The relation of pain to depression among institutionalized aged. J.Gerontol. 46, 15-21.

5 Warden, V., Hurley, A.C., and Volicer, L., 2003. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. J.Am.Med.Dir.Assoc. 4, 9-15.

Appendix 3 Quality assessment of included studies

Author	Morgan[43]	Volicer[47]	Ahn[32]	Bartels[8]	Black[35]	Brummel-Smith[36]
Year	2021	2011	2003	2003	2006	2002
Journal	Gerontologist	Int J Geriatr Psychiatry	BMC Geriatrics	Am J Geriatr Psychiatry	Alzheimer Dis&Ass Dis	J Am Geriatr Soc
Study population						
Is there a specific, clearly stated objective described?	1	1	1	1	1	1
Is the stated objective similar to our objective?	0	1	1	0	1	0
Study population						
Were valid selection criteria used for the study population? (sampling frame and distribution of the population by age and sex)	1	1	1	1	1	1
Is there a specified selected population? (other than severity of dementia and age) For example, a population selected on pain (e.g., pressure ulcers), behaviour or function. (yes=o, no=1)	0	1	1	0	0	0
Did more than 80% of the eligible subjects participate in the study? Or did 60-80% participate and non-responders were not selective? (data presented)	1	1	1	1	0	1
Is there major and selective loss during follow-up? (yes=0, no=1)	1	1				
Measurement of pain			1	0	0	0.5
Was pain measured with a valid measurement instrument? (rating of observations (2), rating based on observations (1), self-report instruments (0,5) no measurement instrument (0))	1	1	0.5	0	0.5	0.5
Was the method of detection by direct observation (1), interview staff/ proxy/self-report (0,5) or screening medical records (0)?	0.5	1.5	0.5	0	0	1
Was the measurement performed by a trained professional/research assistant (1), staff member (0,5) or a proxy/self-report (0)?	0	0.5				
Outcome measure (behaviour, physical function)			1	1	1	1
Was the outcome measured with a valid and reproducible method?	1	1				
Was the follow-up period sufficient enough?	1	1	1	0	1	1
Analysis			1	0	1	0
Were the results adjusted for possible confounders?	1	0	10	4	6.5	7
Is there an association presented (OR/RR/correlation coefficient), including 95% CIs and numbers in the analyses?	1	1				
Total score	9.5	12				

Appendix 3 Quality assessment of included studies *(continued)*

Author	Cipher[4]	Cipher[37]	D'Astolfo[40]	Gruber-Baldini[41]	Kunik[30]	Leonard[46]
Year	2004	2006	2006	2006	2005	2006
Journal	Int J Geriatr Psychiatry	J Am Med Dir Assoc	BMC Geriatrics	Gerontologist	Psychiatr Serv	Arch Intern Med
Study population						
Is there a specific, clearly stated objective described?	1	1	1	1	1	1
Is the stated objective similar to our objective?	0	1	1	0	1	1
Study population						
Were valid selection criteria used for the study population? (sampling frame and distribution of the population by age and sex)	1	1	1	1	1	1
Is there a specified selected population? (other than severity of dementia and age) For example, a population selected on pain (e.g. pressure ulcers), behaviour or function. (yes=o, no=1)	0	0	1	1	1	1
Did more than 80% of the eligible subjects participate in the study? Or did 60-80% participate and non-responders were not selective? (data presented)	1	0	1	1	0	1
Measurement of pain						
Was pain measured with a valid measurement instrument? (rating of observations (2), rating based on observations (1), self-report instruments (0,5) no measurement instrument (0))	1	1	0	1	1	1
Was the method of detection by direct observation (1), interview staff/proxy/self-report (0,5) or screening medical records (0)?	0.5	0.5	0	0	0.5	0
Was the measurement performed by a trained professional/research assistant (1), staff member (0,5) or a proxy/self-report (0)?	1	1	0	0.5	1	0
Outcome measure (behaviour, physical function)						
Was the outcome measured with a valid and reproducible method?	1	1	1	1	1	1
Analysis						
Were the results adjusted for possible confounders?	0	0	1	1	0	1
Is there an association presented (OR/RR/correlation coefficient), including 95% CIs and numbers in the analyses?	1	1	0	1	1	1
Total score	7.5	7.5	7	8.5	8.5	9

Appendix 3 Quality assessment of included studies *(continued)*

Author	Leong[31]	Lin[42]	Norton[43]	Shega[44]	Shega[45]	Torvik[48]
Year	2007	2011	2010	2005	2010	2010
Journal	Clin J Pain	Journal of Clinical Nurs	Gerontologist	J Palliat Med	Pain Med	Pain Manag Nurs
Study population						
Is there a specific, clearly stated objective described?	1	1	1	1	1	1
Is the stated objective similar to our objective?	0	1	1	1	0	0
Study population						
Were valid selection criteria used for the study population? (sampling frame and distribution of the population by age and sex)	1	1	1	1	1	1
Is there a specified selected population? (other than severity of dementia and age) For example, a population selected on pain (e.g., pressure ulcers), behaviour or function. (yes=o, no=1)	1	1	0	1	1	0
Did more than 80% of the eligible subjects participate in the study? Or did 60-80% participate and non-responders were not selective? (data presented)	1	1	1	1	1	0
Measurement of pain						
Was pain measured with a valid measurement instrument? (rating of observations (2), rating based on observations (1), self-report instruments (0,5) no measurement instrument (0))	2	2	1	1	0.5	1
Was the method of detection by direct observation (1), interview staff/ proxy/self-report (0,5) or screening medical records (0)?	0.5	1	0.5	0.5	0.5	0.5
Was the measurement performed by a trained professional/research assistant (1), staff member (0,5) or a proxy/self-report (0)?	1	1	0.5	1	1	1
Outcome measure (behaviour, physical function)						
Was the outcome measured with a valid and reproducible method?	1	1	1	1	1	1
Analysis						
Were the results adjusted for possible confounders?	0	1	1	0	1	0
Is there an association presented (OR/RR/correlation coefficient), including 95% CIs and numbers in the analyses?	0	1	1	1	1	1
Total score	8.5	12	9	9.5	9	6.5

Appendix 3 Quality assessment of included studies *(continued)*

Author	Tosato[3]	Volicer[33]	Williams[39]	Zieber[34]
Year	2012	2009	2005	2005
Journal	Pain	J Am Med Dir Assoc	Gerontologist	Int J Palliat Nurs
Study population				
Is there a specific, clearly stated objective described?	1	1	1	1
Is the stated objective similar to our objective?	1	1	1	1
Study population				
Were valid selection criteria used for the study population? (sampling frame and distribution of the population by age and sex)	1	1	1	1
Is there a specified selected population? (other than severity of dementia and age) For example, a population selected on pain (e.g. pressure ulcers), behaviour or function.(yes=o, no=1)	1	1	1	0
Did more than 80% of the eligible subjects participate in the study? Or did 60-80% participate and non-responders were not selective? (data presented)	1	1	1	0
Measurement of pain				
Was pain measured with a valid measurement instrument? (rating of observations (2), rating based on observations (1), self-report instruments (0,5) no measurement instrument (0))	1	1	1	2
Was the method of detection by direct observation (1), interview staff/ proxy/self-report (0,5) or screening medical records (0)?	0.5	1	0.5	1
Was the measurement performed by a trained professional/research assistant (1), staff member (0,5) or a proxy/self-report (0)?	1	0	0.5	1
Outcome measure (behaviour, physical function)				
Was the outcome measured with a valid and reproducible method?	1	1	1	0
Analysis				
Were the results adjusted for possible confounders?	1	1	1	0
Is there an association presented (OR/RR/correlation coefficient), including 95% CIs and numbers in the analyses?	1	1	1	1
Total score	11.5	11	10	8

CHAPTER 4

The impact of pain on the course of ADL functioning in patients with dementia

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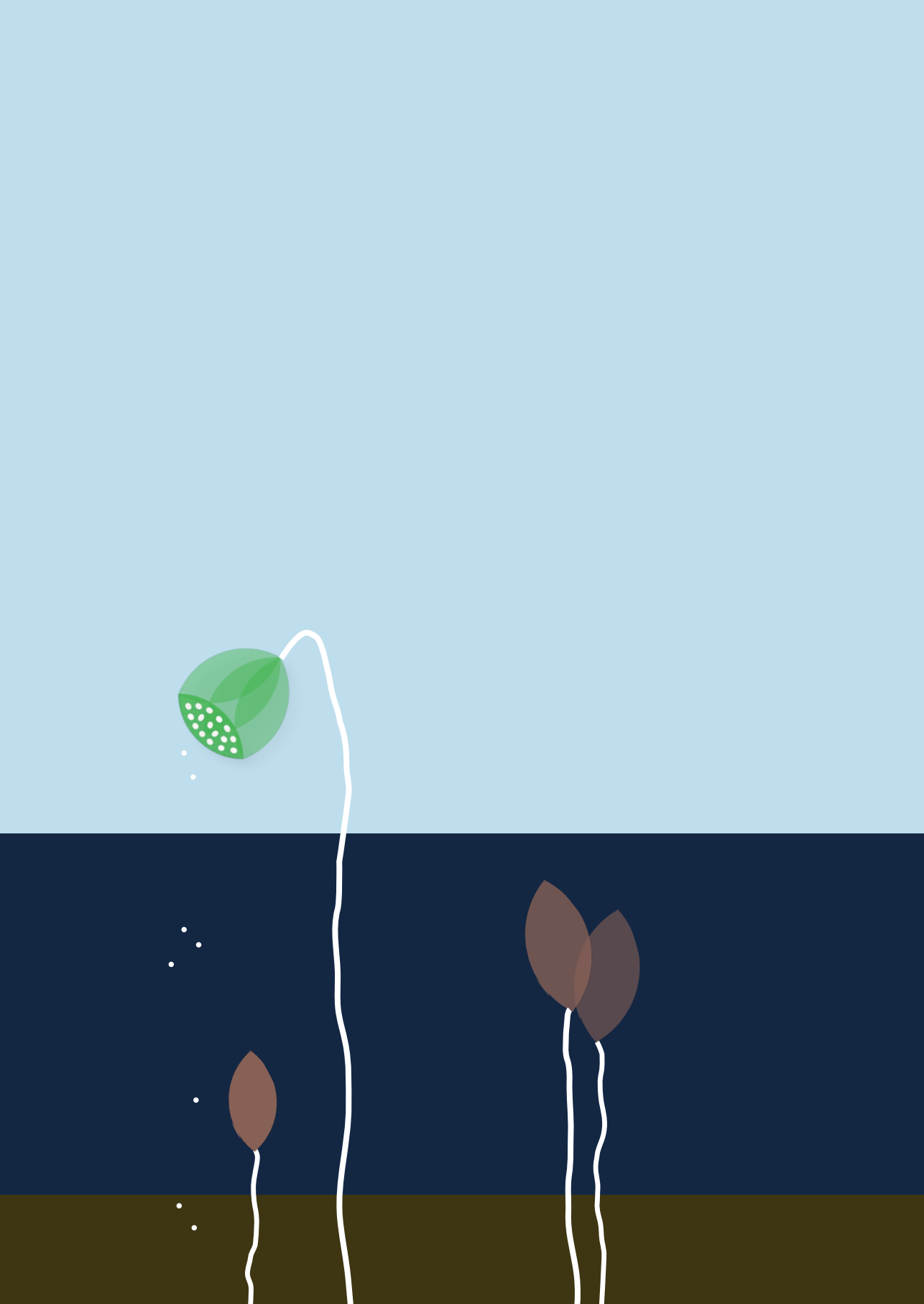

Abstract

Background

Understanding if and how pain influences activities of daily living (ADL) in dementia is essential to improving pain management and ADL functioning. This study examined the relationship between the course of pain and change in ADL functioning, both generally and regarding specific ADL functions.

Methods

Participants were Dutch nursing home residents (n=229) with advanced dementia. ADL functioning was assessed with the Katz ADL scale, and pain with the Dutch version of the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC-D). Changes of PACSLAC-D and Katz ADL scores were computed based on the difference in scores between baseline, 3-month and 6-month follow-up. Multivariate linear regression models were used to assess the relationships between change in pain score, change in total ADL score and specific ADL item scores during follow-up.

Results

At baseline, residents had a median ADL score of 18 (interquartile range 13-22, range 6-24) and 48% of the residents were in pain (PACSLAC-D ≥4). Residents with pain were more ADL dependent than residents without pain. A change in pain score within the first 3 months was a significant predictor for a decline in ADL functioning over the 6-month follow-up (B=0.10, SE=0.05, *P*=0.045), and specifically, a decline on the items 'transferring' over the 6-month follow-up and 'feeding' during the first 3 months of follow-up.

Conclusions

Pain is associated with ADL functioning cross-sectionally, and a change in pain score predicts a decline in ADL functioning, independent of dementia severity. Awareness of (changes in) ADL activities is clearly important and might result in both improved recognition of pain and improved pain management.

Keywords:

dementia, pain, activities of daily living, nursing home, longitudinal study, older people

Key points:

- Recognition of pain in dementia is challenging and often leads to undertreatment, with negative consequences for quality of life
- Persons with dementia and pain were more ADL dependent compared with residents without pain
- Pain and change in pain affect ADL functioning in dementia, independent of dementia severity
- Pain affects overall ADL functioning as well as specific ADL activities such as transferring and feeding
- Changes in ADL functioning could serve as a red flag for the presence of pain

Introduction

In dementia, activities of daily living (ADL) are challenged by the progressive nature of the neuropathological changes that cause dementia. Consequently, a decline in ADL is to be expected, especially in the more advanced stages of dementia [1]. However, functional decline in dementia is a complex phenomenon and besides dementia itself, various (indirect) causes can lead to functional impairment. Examples include age-related diseases, such as osteoporosis and arthritis, depression, apathy, and the use of medication such as psychotropic drugs [2-4]. Furthermore, pain might even be an independent cause of decline in ADL [5 6], although few studies have described a relationship between pain and ADL functioning in persons with moderate to severe dementia [7]. Some studies have described positive associations between pain and instrumental ADL impairment, and between pain and specific ADL functions such as bathing and transfers [8 9], but ADL functioning was often not the main topic of these studies, and use of valid measurement instruments to measure pain and ADL functioning was frequently lacking [7]. Despite the paucity of studies investigating this relationship, understanding the impact of pain on ADL functioning is of the utmost importance. Impairment of ADL has a significant impact on the quality of life of persons with dementia and hampers social interactions and wellbeing [10], representing a burden not only for patients but also for caregivers and society as a whole [11 12].

In order to study the relationship between pain, a change in pain score, and change in ADL functioning in general and in specific ADL activities, prospectively collected data were used in addition to cross-sectional data. Our hypothesis was that pain, and especially a change in pain, predicts a general decline in ADL functioning and a decline in specific ADL functions in persons with moderate to severe dementia.

Methods

Setting and study population

The present study was conducted within the framework of the STA-OP! trial, a single-blinded, cluster-randomised controlled trial in Dutch nursing homes [13].
The STA-OP! trial has been approved by the Medical Ethics Review Committee of the VU University Medical Center, Amsterdam (registration number 2009/119).
Within 12 nursing homes (with 21 units), residents were included with moderate to severe cognitive impairment (Reisberg Global Deterioration Scale (GDS) stage 5, 6, 7), and no chronic psychiatric diagnosis other than a dementia-related diagnosis[13].
A total of 288 residents were included and randomly assigned to the intervention (n=148) or to usual care (n=140). For the purposes of the longitudinal analyses in this study, we included 229 residents, excluding residents who died (n=58) or were transferred to another facility (n=1) during the 6-month follow-up period.

Assessments

Demographic characteristics (age, gender, marital status and length of stay), dementia severity, ADL functioning and pain were collected by trained research assistants (psychologists) through face-to-face interviews with healthcare professionals familiar with the patient. Medication use was derived from daily logs of registered nurses and from pharmacists' electronic patient records. The MDS-RAI comorbidity index was used to collect data on comorbidity and was completed by the attending elderly care physician.

ADL functioning

The primary outcome measure for this study was ADL functioning measured with the Katz ADL scale [14]. This version of the Katz ADL scale is commonly used in Belgian nursing home care [15], and the scale consists of six items: 1) bathing, 2) dressing, 3) transferring, 4) going to the toilet, 5) continence, and 6) feeding. The range of the total score per item level is 1-4, with higher scores indicating a higher level of dependency: 1) independent, 2) requires some assistance, 3) requires full assistance, and 4) completely dependent. The total Katz-ADL score indicates the degree of dependency, with higher scores indicating a higher level of dependency.

Pain

Pain was assessed using the Dutch version of the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC-D) [16 17]. This is an observational pain assessment instrument consisting of 24 items. Reliability and validity have been established [16 18].
A score of ≥ 4 is considered indicative of the presence of pain [18].
The PACSLAC-D was based on the most recent care moment with the resident, with a maximum time span of 24h.

Dementia severity

The Reisberg GDS was used to assess dementia severity [19]. The GDS rates the clinically identifiable stages of cognitive decline on a 7-point rating scale. Scores range from 1) 'no cognitive decline' to 7) 'very severe cognitive decline'. The scores reflect both cognitive and functional performance testing. Interrater reliability was high (r=.82), as was validity (r=.62) [20 21]. The GDS was completed by the attending elderly care physician.

Statistical analyses

Descriptive statistics were used to examine the demographics and clinical characteristics of the study population. Data were expressed as means with standard deviations (SD) or medians with interquartile range (IQR), as appropriate. For the non-normally distributed variables, differences between groups were analyzed using the Mann-Whitney U-test.

To assess the course of ADL functioning, differences in Katz ADL scores between 6-month follow-up and baseline (T2-T0), between 3-month follow-up and baseline (T1-T0), and between 6-month follow-up and 3-month follow-up (T2-T1) were computed. A change of PACSLAC-D scores was also computed as the difference in score between 3-month follow-up and baseline (T1-T0).
Multivariate linear regression models were used to analyse whether a change in pain score in the first 3 months (independent variable) was a predictor for: 1) a decline in ADL functioning during the 6-month follow-up period, 2) decline in ADL functioning in the first 3 months of follow-up, and 3) decline in ADL functioning in the last 3 months of follow-up (dependent variables). These models also included baseline ADL score, pain at baseline (PACSLAC-D ≥ 4 yes/no), and dementia severity (GDS ≥ 7 yes/no) as independent predictors. Consequently, B-values can be interpreted as the independent contribution of each variable, with a value of 1 representing 1-point change in Katz ADL score per unit of the independent variable. R^2 represents the percentage of the variation of the dependent variable that a linear model (all variables together) explains. We further adjusted for intervention assignment, marital status, length of stay, co-morbidity, and use of medication known to have an impact on ADL functioning and/or pain (opioids, paracetamol, antipsychotics, anxiolytics, sedative/hypnotics, antidepressants, and anti-dementia drugs).
Analyses were performed with IBM SPSS statistics for Windows version 25.0.

Results

Resident characteristics

The majority of residents were female (72.5%), the mean age was 83.1 (range 59-103 years), and almost 90% had advanced dementia (Reisberg GDS score 6-7) (Table 1, Figure 1). At baseline, the median length of stay in the nursing home was 22.9 months. Almost half (48%) of the residents were experiencing pain (PACSLAC-D score ≥4).

Table 1. Characteristics of the study population (n=229) at baseline

Age (years), mean	83.1 (SD 7. 2)
Gender	
Male	63 (27.5%)
Female	166 (72.5%)
Marital status	
Single	157 (68.6%)
Significant other	72 (31.4%)
Length of stay (months), median	22.9 (IQR 11-43)
Dementia severity (GDS), mean	6.2 (SD 0.6)
GDS 5 (moderate-severe)	28 (12.2%)
GDS 6 (severe)	134 (58.5%)
GDS 7 (very severe)	67 (29.3%)
Pain (PACSLAC-D), mean	4.4 (SD 4.41)
Pain No (PACSLAC-D <4)	119 (52.0%)
Pain Yes (PACSLAC-D ≥4)	110 (48.0%)
Physical function (Katz ADL score), median	18.0 (IQR 13-22)
Co-morbidity	
Diseases of circulatory system	115 (50.2%)
Diseases of musculoskeletal system	58 (25.3%)
Diseases of nervous system	35 (15.3%)
Diseases of respiratory system	23 (10.0%)
Clinical diagnosis depression	22 (9.6%)
Cancer	8 (3.5%)
Medication (missing, n=3)	
Paracetamol	92 (40.7%)
Anxiolytics	81 (35.8%)
Antipsychotics	76 (33.6%)
Antidepressants	53 (23.5%)
Sedatives/hypnotics	46 (20.4%)
Anti-dementia	20 (8.8%)
Opioids	11 (4.9%)

SD: Standard Deviation; GDS: Global Deterioration Scale; IQR: Inter Quartile Range

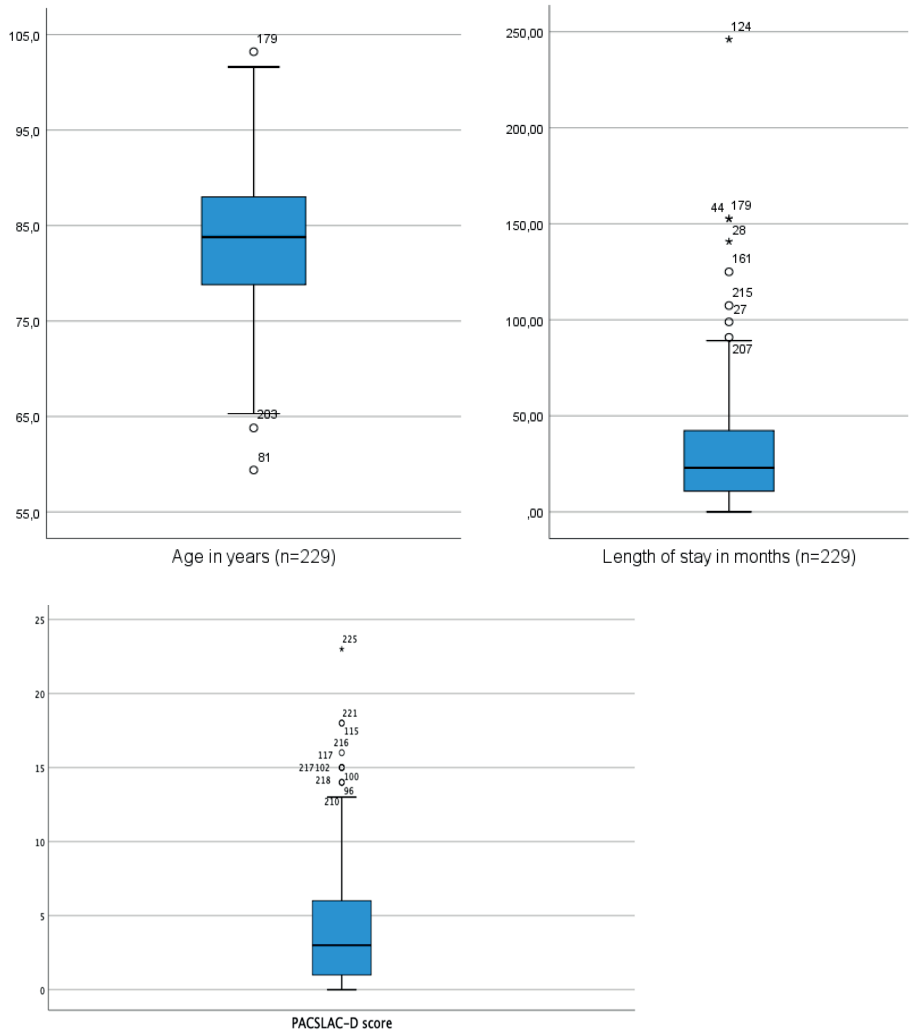

Figure 1. Boxplots baseline characteristics

Cross-sectional relationships between ADL functioning and presence of pain at baseline showed that the median ADL score was higher in residents with pain compared to residents without pain: 20 (IQR 16-23) and 16 (IQR 11-19), respectively (p<0.001), indicating higher levels of dependency in those with pain (Table 2). This was also true for median scores on the ADL items; in residents with pain all items were scored significantly higher compared to residents without pain. In residents with pain, the items 'bathing', 'dressing' and 'continence' had the highest scores, again indicating higher levels of dependency.

Table 2. ADL functioning at baseline in residents without and with pain

	Pain: No (n=119) (PACSLAC-D <4)	Pain: Yes (n=110) (PACSLAC-D ≥4)	*P*-value
Baseline Katz ADL total score	16.0 (11-19)	20.0 (16-23)	< 0.001
Katz ADL score on item level			
- Bathing	3.0 (2-4)	4.0 (3.8-4)	< 0.001
*% Independent**	6.7	1.8	
- Dressing	3.0 (2-4)	4.0 (3.8-4)	< 0.001
% Independent	10.1	2.7	
- Transferring	2.0 (1-2)	3.0 (1.8-4)	< 0.001
% Independent	47.1	24.5	
- Going to the toilet	3.0 (1-3)	3.0 (3-4)	< 0.001
% Independent	25.2	13.6	
- Continence	3.0 (2-4)	4.0 (2-4)	< 0.001
% Independent	21.8	10.9	
- Feeding	2.0 (1-3)	2.5 (2-4)	< 0.001
% Independent	45.4	23.6	

Numbers represent median (IQR). *Indicates the number of residents who are completely independent on that specific item.

Predictors of the course of ADL functioning: total ADL score

Multivariate linear regression analyses (Table 3) showed that a change in pain score within the first 3 months was a significant predictor of a decline in ADL functioning over the 6-month follow-up period (B=0.10, SE=0.05, *P*=0.045), and especially during the first 3 months of follow-up (B=0.09, SE=0.4, *P*=0.02). Pain at baseline was not a significant predictor of a decline in the ADL total score throughout the 6-month follow-up period (B=-0.14, SE=0.46, *P*=0.76), during the first 3 months of follow-up (B=-0.08, SE=0.36, *P*=0.82) or during the last 3 months of follow-up (B=-0.06, SE=0.43, *P*=0.88). A higher score on the GDS, indicating more advanced dementia, was a significant predictor of a decline in ADL functioning over the 6-month follow-up period (B=1.16, SE=0.51, *P*=0.02).

Table 3. Predictors of change in the Katz ADL score over 6 months of follow-up (multivariate analyses, n=229)

	6-month follow-up			First 3-month follow-up			Last 3-month follow-up		
Patient characteristics	**B**	**SE**	***P*-value**	**B**	**SE**	***P*-value**	**B**	**SE**	***P*-value**
Age	0.02	0.03	0.54	0.01	0.02	0.68	0.01	0.03	0.75
Gender, female	0.78	0.48	0.10	0.43	0.37	0.24	0.35	0.44	0.42
Dementia severity, GDS 7	**1.16**	**0.51**	**0.02**	0.44	0.39	0.26	0.72	0.47	0.12
Baseline Katz ADL score*	**-0.23**	**0.05**	**<0.001**	-0.10	0.04	0.09	**-0.13**	**0.04**	**0.003**
Pain at baseline	-0.14	0.46	0.76	-0.08	0.36	0.82	-0.06	0.43	0.88
Change in pain score in first 3 months	**0.10**	**0.05**	**0.045**	**0.09**	**0.40**	**0.02**	0.01	0.05	0.77

Adjusted for intervention assignment, marital status, length of stay, co-morbidity, and medication use. R^2 6-month follow-up: 0.22, R^2 first 3-month follow-up: 0.18, R^2 last 3-month follow-up: 0.11. * Higher scores indicate higher level of dependency. Bold values represent significant values.

Predictors of the course of ADL functioning at the item level

A change in pain score within the first 3 months was a significant predictor for a decline in the ADL item 'transferring' over 6 months of follow-up (B=0.03, SE=0.01, *P*=0.04) , but it did not reach significance during the first 3 months of follow-up (B=0.02, SE=0.01, *P*=0.12) or during the last 3 months of follow-up (B=0.01, SE=0.01, *P*=0.32) (Table 4). Furthermore, a change in pain score within the first 3 months was a significant predictor for a decline in the ADL item 'feeding' during the first 3 months of follow-up (B=0.02, SE=0.01, *P*=0.04) None of the other ADL items were significantly affected by a change in pain score within the first 3 months. In addition, pain at baseline was not a predictor for a decline in ADL scores for any item after 6 months of follow-up, although pain at baseline was a significant predictor for a decline in the item 'bathing' at 3- month follow-up (B=0.18, SE=0.09, *P*=0.04). All items were significantly affected by baseline ADL score on item level over 6 months of follow-up.

Table 4. Predictors of change in the Katz ADL score on item level over 6 months of follow-up (multivariate analysis, n=229)

Patient characteristics	**Bathing**			**Dressing**		
6-month follow-up	**B**	**SE**	***p*-value**	**B**	**SE**	***p*-value**
Age	**0.01**	**0.01**	**0.03**	0.01	0.01	0.24
Gender, female (reference=male)	0.10	0.10	0.34	0.05	0.11	0.65
Dementia severity, GDS 7 (reference=GDS 5/6)	**0.29**	**0.10**	**0.004**	**0.32**	**0.11**	**0.01**
Baseline Katz ADL score item level	**-0.37**	**0.05**	**<0.001**	**-0.48**	**0.06**	**<0.001**
Pain at baseline	0.06	0.10	0.54	0.09	0.11	0.41
Change in pain score in first 3 months	0.01	0.01	0.17	0.02	0.01	0.07
First 3-month follow-up						
Age	0.002	0.01	0.76	0.01	0.01	0.28
Gender, female (reference=male)	0.03	0.09	0.75	0.05	0.10	0.62
Dementia severity, GDS 7 (reference=GDS 5/6)	0.13	0.09	0.13	0.14	0.10	0.15
Baseline Katz ADL score item level	**-0.30**	**0.05**	**<0.001**	**-0.24**	**0.05**	**<0.001**
Pain at baseline	**0.18**	**0.09**	**0.04**	0.05	0.09	0.60
Change in pain score in first 3 months	0.02	0.01	0.10	0.01	0.01	0.22
Last 3-month follow-up						
Age	0.01	0.01	0.07	0.002	0.01	0.80
Gender, female (reference=male)	0.07	0.11	0.53	0.004	0.12	0.97
Dementia severity, GDS 7 (reference=GDS 5/6)	0.16	0.11	0.15	0.18	0.12	0.13
Baseline Katz ADL score item level	-0.07	0.06	0.20	**-0.24**	**0.06**	**<0.001**
Pain at baseline	-0.12	0.11	0.27	0.04	0.11	0.70
Change in pain score in first 3 months	-0.001	0.01	0.96	0.01	0.01	0.46

Adjusted for, intervention assignment, marital status, length of stay, co-morbidity, and medication use. R^2 6-months follow-up: bathing: 0.30, dressing: 0.34, transferring: 0.19, going to toilet: 0.29, continence: 0.28, feeding: 0.29. R^2 first 3 months follow-up: bathing: 0.24, dressing: 0.22, transferring: 0.19, going to toilet: 0.16, continence: 0.20, feeding: 0.29. R^2 last 3 months follow-up: bathing: 0.10, dressing: 0.12, transferring: 0.12, going to toilet: 0.12, continence: 0.12, feeding: 0.11. * Higher scores indicate higher level of dependence. Bold values represent significant values.

Transferring			Going to toilet			Continence			Feeding		
B	**SE**	***p*-value**	**B**	**SE**	***p*-value**	**B**	**SE**	***p*-value**	**B**	**SE**	***p*-value**
-0.01	0.01	0.53	**-0.01**	**0.01**	**0.03**	0.01	0.01	0.58	0.01	0.01	0.45
0.19	0.14	0.17	0.17	0.10	0.08	0.22	0.13	0.10	0.09	0.13	0.50
0.37	**0.13**	**0.01**	**0.19**	**0.10**	**0.05**	0.22	0.13	0.09	**0.39**	**0.15**	**0.01**
-0.23	**0.05**	**<0.001**	**-0.32**	**0.05**	**<0.001**	**-0.35**	**0.05**	**<0.001**	**-0.38**	**0.06**	**<0.001**
-0.05	0.13	0.69	0.06	0.09	0.50	0.12	0.71	0.62	-0.04	0.12	0.75
0.03	**0.01**	**0.04**	0.02	0.01	0.09	-0.001	0.01	0.93	0.01	0.01	0.55
-0.002	0.01	0.75	-0.003	0.01	0.62	0.01	0.01	0.36	-0.004	0.01	0.59
0.02	0.11	0.88	0.03	0.09	0.73	**0.24**	**0.12**	**0.05**	0.11	0.12	0.32
0.32	**0.10**	**0.002**	0.15	0.09	0.10	0.11	0.12	0.39	**0.31**	**0.14**	**0.02**
-0.16	**0.04**	**<0.001**	**-0.17**	**0.04**	**<0.001**	**-0.25**	**0.05**	**<0.001**	**-0.30**	**0.06**	**<0.001**
-0.08	0.10	0.42	-0.04	0.09	0.68	0.15	0.12	0.19	0.09	0.11	0.42
0.02	0.01	0.12	0.001	0.01	0.91	0.01	0.01	0.70	**0.02**	**0.01**	**0.045**
-0.003	0.01	0.67	-0.01	0.01	0.07	-0.002	0.01	0.75	0.01	0.01	0.25
0.17	0.12	0.15	0.14	0.09	0.15	-0.02	0.12	0.88	-0.03	0.14	0.84
0.05	0.12	0.67	0.04	0.10	0.68	0.11	0.13	0.36	0.08	0.16	0.61
-0.07	0.05	0.11	**-0.14**	**0.04**	**0.001**	**-0.10**	**0.05**	**0.04**	-0.08	0.07	0.26
0.03	0.12	0.79	0.10	0.09	0.28	-0.03	0.12	0.77	-0.13	0.13	0.33
0.01	0.01	0.32	0.02	0.01	0.10	-0.01	0.01	0.64	-0.02	0.01	0.28

Discussion

To the best of our knowledge, this is the first study to examine the longitudinal relationship between pain and ADL functioning in persons with moderate to severe dementia.
A change in pain score predicted a decline in ADL functioning during the 6-month follow-up period, as well as during the first 3 months of follow-up, independent of dementia severity. In particular, the items 'transferring' (6-month follow-up) and 'feeding' (first 3 months) were affected by a change in pain score during the first 3 months. A change in pain score within the first 3 months did not affect any ADL item during the last 3 months of follow-up. This remained true after controlling for co-morbidity, length of stay in the nursing home, and medication use.

The cross-sectional findings were in line with the few similar studies available, which reported that pain is related to poorer ADL function in persons with dementia [8 9 22].
Interestingly, this longitudinal study suggests that it is not so much the presence of pain, but rather the change in pain score that is related to a decline in ADL functioning. Labus et al. showed that the relation between pain behaviour, such as the slower performance of certain activities, and the experience of pain is stronger in acute pain compared to persistent pain [23]. In the present study, pain was measured using the PACSLAC-D and was based on the most recent care moment with the resident. This implies that the PACSLAC-D may have captured both acute and chronic pain. In theory, a change in pain score might represent either worsening or improvement. However, in this study a change in pain score is more likely to represent acute pain, and the largest effect on ADL functioning may be during the acute phase of pain. Furthermore, the PACSLAC-D does not provide information on pain location. Although this might be important knowledge, persons with dementia are often non-verbal, which hampers them to identify pain locations. Observation of pain related behaviour/pain severity is the key.
Additionally, this study shows that ADL functions deteriorate with the progression of dementia [2 10 24 25]. This was to be expected, especially as the GDS also includes ADL (feeding, toileting) and psychomotor skills (e.g., ability to walk) that measure dementia severity. Nevertheless, the present study shows that a change in pain score within the first 3 months significantly predicts a decline in ADL functioning, regardless of dementia severity. This is an important finding that can be applied in daily practice, as a decline in ADL functioning may serve as a red flag for the presence of pain.

This study had several strengths, including the longitudinal study design, ADL functioning as a primary outcome measure and a focus on individual ADL items instead of solely focussing on the total ADL score. This is important because it is possible that the way ADL scores are interpreted might aid understanding of the complexity of the relationship between pain and ADL functioning. Whereas a total ADL score provides information on the degree of overall ADL dependency, scores on item level tell us which ADL functions are most affected. An example is the cross-sectional study by Lin et al., in which pain was observed immediately following routine care and a higher prevalence of pain was noted in patients during bathing (46%) and during assisted transfer (51%) compared to patients in self-transfer situations (3%) [8]. The present study also provides insight into which ADL functions are most affected by pain, i.e., transferring and feeding (rather than bathing,

dressing, going to toilet, and continence). However, B-values for both transferring and feeding were small (transferring: B=0.03; bathing: B=0.02), and one could question the clinical significance of these results. Furthermore, the item feeding might also capture appetite, as a resident with a loss of appetite might be reluctant to eat, behaviour that could be interpreted by the nurse as a need for assistance during dinner. Nevertheless, this information is important to health care workers as it may assist in clinical management and raise awareness of pain as a potential cause. Possible limitations of this study should also be considered. The 6-month follow-up period might appear brief, but appears less so when one considers that the median length of stay after admission to a psychogeriatric ward is only two years [26]. Furthermore, the fluctuation of ADL functioning and pain over time makes it difficult to capture all changes in these items, and although longitudinal analysis facilitated examination of time-related changes in ADL functioning, we did not include the onset of ADL decline or disability, unlike (for example) Eggermont et al. [5]. One could also argue that an ADL scale might not be the best instrument to measure ADL functioning and explore the complex relationship between pain and ADL functioning. Measuring care dependency with, for example the Care Dependency Scale (CDS) [27] might better reflect ADL functioning and especially ADL dependency. The CDS consists of 15 items, including items on ADL functioning (eating, drinking and getting (un)dressed), social activities, communication, and mobility [28]. Together these 15 items capture a much broader view of ADL functioning because they are not restricted to only the basic ADL activities. Finally, it would be most interesting to investigate the causal relationship between pain and ADL functioning in dementia. However, the present study was nested in the STA-OP! trial [29] and therefore not designed to test for causality between pain and ADL functioning. This is also true for investigating the effect of pain medication on ADL impairment. Interestingly, a randomised double-blind, placebo-controlled crossover trial by van Dam et al, aims to evaluate the scheduled effect of pain medication on ADL functioning and care dependency [30].

Conclusion

The results of this study suggest that pain, and change in pain, in nursing home residents with dementia is related to a decline in ADL functions, independent of dementia severity. Recognizing a decline in ADL functioning, both in general and in specific ADL activities, may serve as an important cue for the presence of pain. Consequently, we urge health-care workers to focus on regular assessment of pain and ADL functions, for example every 3 months. When assessing ADL functioning it is important that the separate items of the Katz ADL scale or other measurement tools, such as the Barthel Index or the CDS, should be considered [27 31]. This approach might facilitate tailored (non)pharmacological interventions [25 32]. In addition, regular assessment of both pain and ADL functions should assist in improving pain management in persons with dementia and help to decelerate, or even avoid, functional loss.

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Conflict of interest

None of the authors have conflicts of interest or dual commitments.

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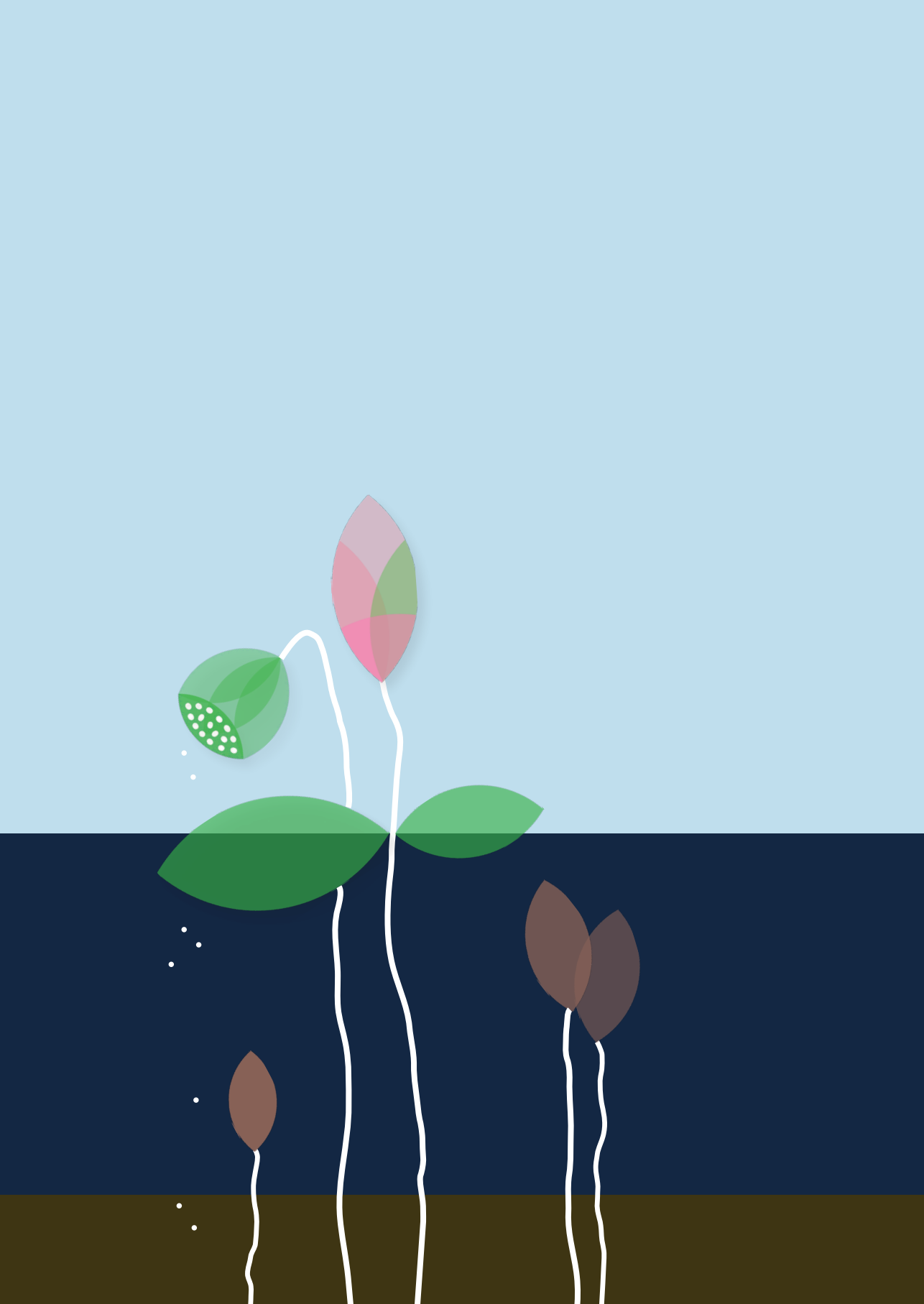
PART II

Pain Assessment in Impaired Cognition: PAIC



CHAPTER 5

Pain assessment in impaired cognition (PAIC): content validity of the Dutch version of a new and universal tool to measure pain in dementia

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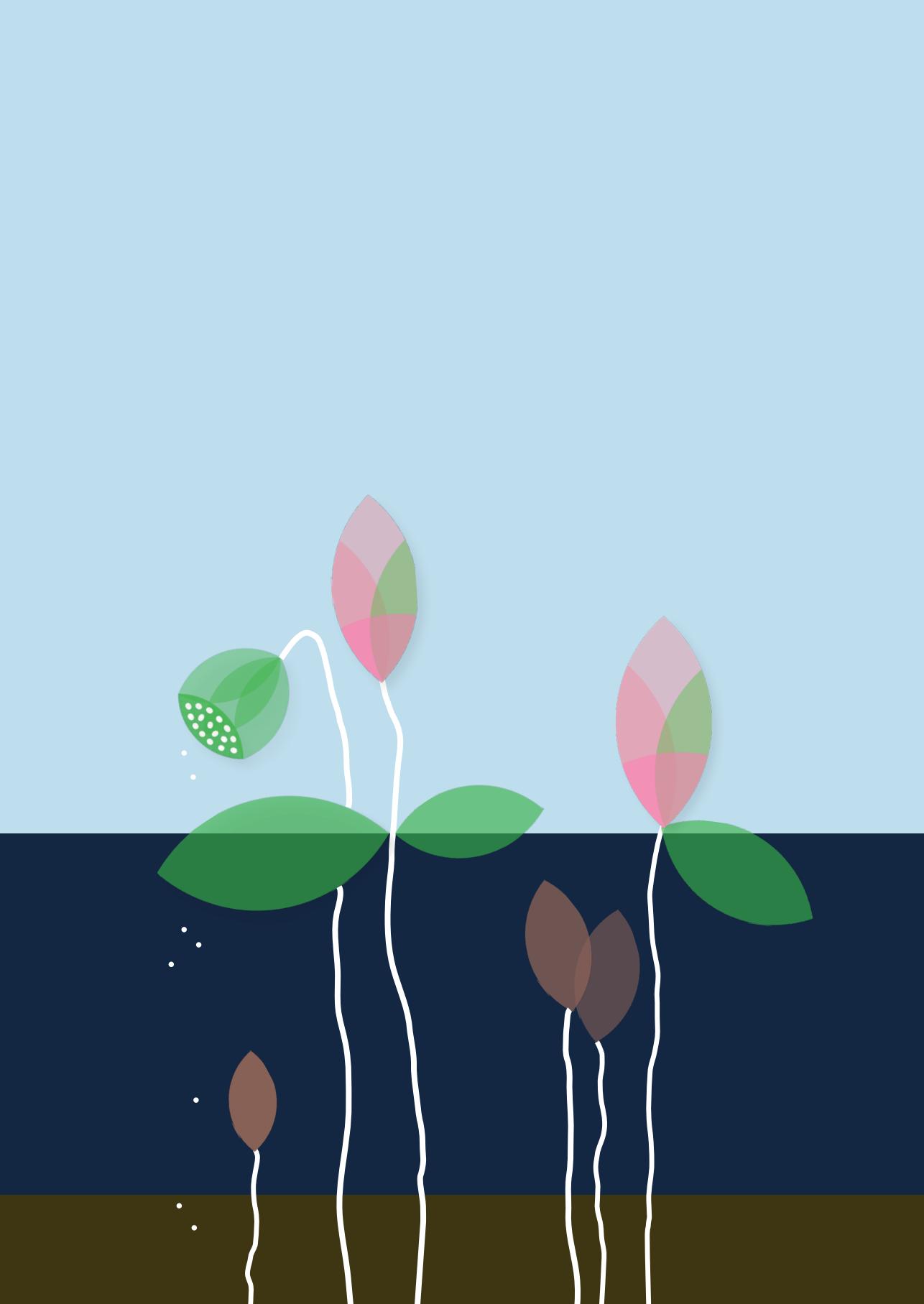

Abstract

Objectives

Detection and measurement of pain in persons with dementia by using observational pain measurement tools is essential. However, the evidence for the psychometric properties of existing observational tools remains limited. Therefore, a new meta-tool has been developed: Pain Assessment in Impaired Cognition (PAIC), as a collaborative EU action. The aim is to describe the translation procedure and content validity of the Dutch version of the PAIC.

Methods

Translation of the PAIC into Dutch followed the forward-backward approach of the Guidelines for Establishing Cultural Equivalence of Instruments. A questionnaire survey was administered to clinical nursing home experts (20 physicians and 20 nurses) to determine whether the PAIC items are indicative of pain and whether items are specific for pain, or for other disorders (anxiety disorder, delirium, dementia, or depression). To quantify content validity, mean scores per item were calculated.

Results

Eleven items were indicative of pain, for example: 'frowning', 'freezing', and 'groaning'. Fifteen items were considered to be pain-specific, for example, 'frowning', 'curling up', and 'complaining'. There were discrepancies between the notion of pain characteristics according to nurses and physicians, especially in the facial expressions domain.

Discussion

Within the body movement domain, PAIC items correspond well with the clinical experience of the physicians and nurses. However, items in the facial expressions and vocalizations domain need further study with respect to item reduction. Also, differences were revealed in the notion of pain characteristics between physicians and nurses, suggesting the need for more interdisciplinary education on pain in dementia.

Keywords:

content validity, dementia, education, nursing home, observational pain measurement tool, pain

Introduction

Detection of pain in persons with dementia is challenging due to loss of ability to communicate and to the diverse presentation of pain. [1] Therefore, in these individuals, observational pain measurement tools play an important role in the detection and measurement of pain. However, in clinical practice, it is often difficult to distinguish pain-related behaviour from behavioural symptoms related to other disorders, such as anxiety disorder, delirium, depression, or to dementia-related behaviours.

Over the years, many observational pain measurement tools have been developed, including: PAINAD [2], PACSLAC [3], and MOBID-2 [4]. However, a systematic review of systematic reviews showed that there is limited evidence for the reliability, validity, feasibility, or clinical utility of these tools; the authors concluded that no specific available tool can be recommended for use in clinical practice. [5] Moreover, nurses do not always use observational pain tools [6] and often prefer to rely on their intuition and feelings. [7] However, the non-use of observational pain measurement tools is a barrier to adequate pain management in persons with dementia. [8] Therefore, observational pain measurement tools are an essential addition to pain assessment, especially in persons with dementia living in a nursing home. Consequently, there is a need for more evidence-based observational pain measurement.

In light of these findings, the EU-COST action TD 1005 program Pain Assessment in Patients with Impaired Cognition, especially Dementia, developed a meta-tool: Pain Assessment in Impaired Cognition (PAIC). [9] The EU-COST action TD 1005 was a 4-year EU initiative (2010-2014), which combined knowledge of experimental and clinical researchers with that of clinical experts, including developers of (some of the) other observational pain measurement tools. One of the aims of the EU-COST action was for the PAIC to become a universal meta-tool, which 1) comprises the best elements of existing observational instruments, and 2) can be used in both daily practice and research.

The PAIC consists of three domains of possible indicators for pain: 'facial expressions', 'body movements', and 'vocalizations' (Appendix 1). These carefully chosen domains were based on research by the American Geriatric Society (AGS). [9 10] The 36 PAIC items were systematically selected based on 12 existing assessment tools, expert opinion, previous research, and the AGS criteria. [9] These 36 individual items are the main focus of the present study.

In the Netherlands, healthcare workers in nursing homes, such as elderly care physicians (ECPs) and nurses, are likely to be target users of the PAIC. Therefore, the PAIC items should represent/reflect the notion of pain in persons with dementia as perceived by ECPs and nurses. Different notions of pain characteristics might lead to suboptimal communication between physicians and nurses [11] and hinder adequate pain assessment and treatment.

The aim of this study was to describe the translation and evaluation of the content validity of all individual items of the Dutch version of the meta-tool PAIC. It is important to investigate whether all items are indicative of pain [12] and whether potential users of the PAIC (ECPs and nurses) consider the different items to be pain-specific, or more specific for other disorders (e.g., delirium, dementia, depression, or anxiety disorder).

Material and Methods

Translation

Dutch version of the PAIC

Translation into Dutch followed the forward-backward approach of the Guidelines for Establishing Cultural Equivalence of Instruments.[13] Forward translation from English into Dutch was performed by two independent translators whose native language is Dutch. The professional translator had no medical background and the second translator was a general practitioner with English as a second language. Both forward translations were compared and combined into one common version. The common forward translation was translated back into English by an independent professional translator whose native language is English and who was experienced in translating measurement instruments. The second back translator was a pediatric nursing oncology consultant, familiar with the development and translation of measurement instruments. Both back translations were compared and combined, and the final English version was then compared with the original English version. Discrepancies were discussed until consensus was achieved. Finally, the resulting Dutch version was tested during a 'think aloud' test[12] among nurses working in nursing homes. In this 'think aloud' test three nurses (experienced in the care for persons with dementia) were asked to think out loud while filling out the PAIC. Each nurse rated five video-recordings of persons with dementia. All these persons were admitted to a psychogeriatric ward and filmed during their morning care and mealtime. The goal of this test was to look for cues that indicated where the clarity or translation of the items was inadequate, whether the scoring system used was understandable, and whether there were situations in which rating was not possible.

Content validity

Participants

A questionnaire to assess content validity of the PAIC was administered to potential users, that is, nursing home staff who comprised ECPs (n=20) and nurses (n=20) working in seven different nursing home organizations in the Netherlands. All participants had experience in working with persons with dementia at psychogeriatric wards of a nursing home; henceforth, these ECPs and nurses are referred to as 'clinical experts'.

Questionnaire

The questionnaire consisted of five general questions: 1) What is your profession? 2) What is your age? 3) Do you feel competent to estimate if a person with dementia is in pain? 4) Are pain measurement tools used in your organization? and 5) How often do you use a pain measurement tool?

Next, the clinical experts were asked their opinion about the different items per domain of the PAIC. They were asked whether they considered an item to be indicative of pain, responding on a 4-point Likert scale, that is, 1) no, definitely not; 2) no, probably not; 3) yes, probably; and 4) yes, definitely.
They were also asked to indicate whether the different items were most specific for pain or for one of the other disorders such as anxiety disorder, delirium, dementia, or depression. The clinical experts were explicitly asked to indicate only one disorder per item.

Statistical analyses

Descriptive statistics were used to describe the demographic characteristics of the participants. Data were expressed as means with standard deviation (SD), or medians with interquartile range (IQR), as appropriate.
For the interpretation of content validity of the different items, the sum score was calculated. The 4-point scale was recoded into the following scores: 'No, definitely not': -1, 'No, probably not':-0.5, 'Yes, probably': 0.5, and 'Yes, definitely': 1.
An item was considered indicative for pain if the mean score was >0.50. To visualize disorder specificity, the items were displayed in three different bar charts, representing each domain of the PAIC. An item was considered pain-specific, or specific for another disorder, if at least 50% of the clinical experts indicated the item to be pain-specific.

The analyses were first conducted for all clinical experts together and then for the ECPs and nurses separately.
Analyses were performed with IBM SPSS Statistics version 20.0 for Windows.

Results

Translation

The PAIC has been translated and culturally adapted for the Netherlands (Appendix 2). In the 'think aloud' test, all items of the Dutch version of the PAIC were found useful in detecting pain and also relatively easy to score in the clinical setting. The few criticisms made were related to semantics and to the interpretation of some items. For example, nurses questioned whether the item 'opened mouth' referred to the active movement of opening the mouth, or whether the item referred to the static state in which the mouth was already open.

Clinical experts

The clinical experts consisted of 20 ECPs and 20 nurses (Table 1). The majority was female (80%), and the total mean score on 'feeling competent to assess pain in persons with dementia' was 7.5 (SD 1.3) on a 1-10 Likert scale, on which higher scores indicate a higher level of competence. ECPs and nurses felt equally competent to estimate pain in persons with dementia, that is, median 7.0 (IQR 6.5-8.1) and 7.6 (IQR 7.0-9.4), respectively.

Of the clinical experts, 72% indicated that some form of pain measurement tool was implemented in their organization but was hardly used; only 14% used such a tool once or twice a month.
Compared to ECPs, nurses less often used a pain measurement tool. For example, no nurse used a tool monthly (or more) compared with 45% of the ECPs.

Table 1. Characteristics of the clinical experts

Characteristics	Elderly care physicians	Nurses	Total
Gender, female	(n=20) 12 (60%)	(n=20) 20 (100%)	(n=40) 32 (80%)
	(n=20)	(n=16)*	(n=36)*
Feeling competent to assess pain in patients with dementia (Likert scale 0-10)	7.0 (IQR 6.5-8.1)	7.6 (IQR 7.0-9.4)	7.5 (SD 1.3)
Implementation of pain measurement instrument in nursing home			
o Yes	17 (85%)	9 (56 %)	26 (72%)
o No	3 (15%)	7 (44 %)	10 (28%)
How often do you use pain measurement instruments in daily practice?			
o Never	3 (15%)	8 (50%)	11 (31%)
o < 1 x month	8 (40%)	8 (50%	16 (44%)
o 1-2 x month	5 (25%)	-	5 (14%)
o 1 x week	3 (15%)	-	3 (8%)
o Almost daily	1 (5%)	-	1 (3%)

Note: *Lower n due to missing items. Abbreviations: IQR, interquartile range.

PAIC items indicative of pain

Table 2 presents the scores of all the clinical experts together, and ECPs and nurses separately, on how indicative the PAIC items are to detect pain. For each item the mean (SD) of sumscores is presented.

Facial expressions

Of the 15 facial expression items, 'pained expression' and 'frowning' had the highest mean score: 0.90 (SD 0.20) and 0.54 (SD 0.41), respectively (Table 2). Five items had a mean score below zero, with the lowest mean scores of-0.45 (SD 0.54) and
-0.50 (SD 0.56) for 'empty gaze' and 'seeming disinterested', respectively, indicating that these items were considered less indicative of pain.

In the subgroup of ECPs, the items 'pained expression' and 'frowning' were also considered indicative of pain. This was also true for the subgroup of nurses, although the item 'frowning' did not reach the level of >0.50. Additionally, nurses also considered 'tightened lips' 0.53 (SD 0.61), 'looking tense' 0.53 (SD 0.50) and 'looking frightened' 0.55 (SD 0.58) to be indicative of pain.

Body movements

In the body movements domain, as none of the items scored below zero, all items were considered indicative of pain. Five items had a mean score >0.50: 'freezing' (0.65, SD 0.36), 'curling up' (0.69, SD 0.37), 'guarding' (0.65, SD 0.41), 'rubbing' (0.54, SD 0.42), and 'limping' (0.68, SD 0.42).
Subgroup analyses showed no difference between ECPs and nurses compared to the whole sample, with the exception of the item 'pacing'. On average, nurses considered 'pacing' to be probably indicative of pain, as opposed to ECPs who considered the item to be probably not indicative of pain.

Vocalizations

Four items of the vocalizations domain had mean scores >0.50: 'complaining', 'groaning', and 'crying', with the highest mean score of 0.90 (SD 0.29) for the item 'using pain-related words'. This applied to both subgroups of the clinical experts.
Two items were considered not indicative of pain: 'repeating words' -0.26 (SD 0.53) and 'mumbling' -0.18 (SD 0.55). The only item with low mean scores assigned by both ECPs and nurses was 'repeating words': -0.33 (SD 0.52) and -0.20 (SD 0.55), respectively.

Table 2. Scoring of PAIC items on question indicative of pain and on question specific for pain

	Clinical experts (n=40)		ECPs (n=20)		Nurses (n=20)	
	Indicative of pain (mean, SD)*	**Specific for pain§**	**Indicative of pain (mean, SD)***	**Specific for pain§**	**Indicative of pain (mean, SD)***	**Specific for pain§**
Facial expressions						
Pained expression	**0.90 (0.20)**	**X**	**0.88 (0.22)**	**X**	**0.93 (0.18)**	**X**
Frowning	**0.54 (0.41)**	**X**	**0.58 (0.18)**	**X**	0.50 (0.56)	
Narrowing eyes	0.27 (0.52)	X	0.45 (0.36)	X	0.13 (0.60)	X
Closing eyes	-0.05 (0.61)		-0.20 (0.55)		0.10 (0.64)	
Raising upper lip	0.15 (0.58)	X	0.11 (0.54)	X	0.20 (0.62)	X
Opened mouth	-0.23 (0.62)		-0.40 (0.50)		-0.05 (0.69)	
Tightened lips	0.41 (0.52)	X	0.30 (0.41)	X	**0.53 (0.61)**	**X**
Clenched teeth	0.41 (0.52)	X	0.45 (0.36)	X	0.36 (0.66)	X
Empty gaze	-0.45 (0.54)		-0.60 (0.35)		-0.29 (0.65)	
Seeming disinterested	-0.50 (0.56)		-0.75 (0.26)		-0.24 (0.67)	
Pale face	-0.27 (0.61)		-0.50 (0.41)		-0.02 (0.70)	X
Teary eyed	0.13 (0.63)		0.00 (0.58)		0.25 (0.66)	X
Looking tense	0.44 (0.48)		0.35 (0.46)		**0.53 (0.50)**	
Looking sad	0.10 (0.68)		-0.08 (0.54)		0.29 (0.77)	
Looking frightened	0.49 (0.58)		0.41 (0.58)		**0.55 (0.58)**	
Body movements						
Freezing	**0.65 (0.36)**	**X**	**0.70 (0.25)**		**0.60 (0.45)**	**X**
Curling up	**0.69 (0.37)**	**X**	**0.78 (0.26)**	**X**	**0.60 (0.44)**	
Clenching hands	0.41 (0.47)		0.45 (0.36)		0.38 (0.56)	
Resisting care	0.19 (0.49)		0.17 (0.49)		0.23 (0.53)	
Pushing	0.33 (0.58)		0.20 (0.55)		0.45 (0.60)	
Guarding	**0.65 (0.41)**	**X**	0.68 (0.37)	**X**	**0.63 (0.46)**	**X**
Rubbing	**0.54 (0.42)**	**X**	**0.53 (0.41)**	**X**	**0.55 (0.44)**	**X**
Limping	**0.68 (0.42)**	**X**	**0.63 (0.46)**	**X**	**0.73 (0.38)**	**X**
Restlessness	0.23 (0.57)		0.08 (0.46)		0.38 (0.56)	
Pacing	0.09 (0.62)		-0.05 (0.58)		0.23 (0.64)	

Table 2. Scoring of PAIC items on question indicative of pain and on question specific for pain *(continued)*

	Clinical experts (n=40)		ECPs (n=20)		Nurses (n=20)	
	Indicative of pain (mean, SD)*	Specific for pain§	Indicative of pain (mean, SD)*	Specific for pain§	Indicative of pain (mean, SD)*	Specific for pain§
Vocalizations						
Using offensive words	0.23 (0.55)		0.13 (0.54)		0.34 (0.55)	
Using pain-related words	**0.90 (0.29)**	**X**	**0.89 (0.21)**	**X**	**0.90 (0.35)**	**X**
Repeating words	-0.26 (0.53)		-0.33 (0.52)		-0.20 (0.55)	
Complaining	**0.64 (0.36)**	**X**	**0.65 (0.24)**	**X**	**0.63 (0.46)**	
Shouting	0.03 (0.58)		-0.05 (0.58)		0.10 (0.58)	
Mumbling	-0.18 (0.55)		-0.35 (0.46)		0.00 (0.58)	
Screaming	0.26 (0.53)		0.15 (0.56)		0.38 (0.48)	
Groaning	**0.71 (0.32)**	**X**	**0.66 (0.37)**	**X**	**0.75 (0.26)**	**X**
Crying	**0.60 (0.40)**		**0.53 (0.41)**		**0.68 (0.37)**	**X**
Gasping	0.35 (0.57)	X	0.35 (0.54)		0.35 (0.61)	X
Sighing	0.14 (0.58)		0.10 (0.58)		0.18 (0.59)	X

Notes: *Mean score >0.50 considered content valid. §When marked with an 'X', at least 50% of clinical experts rated the item as specific for pain. Bold entries indicate PAIC items indicative of pain as well as specific for pain.
Abbreviations: PAIC, Pain Assessment in Impaired Cognition, ECP, elderly care physician.

PAIC items specific for pain

Figures 1-3 show whether the clinical experts considered the different items of the PAIC to be pain-specific, or more specific for other disorders. An item was considered specific for a disorder when (at least) 20 out of 40 clinical experts rated it as such. Furthermore, Table 2 also shows which items were considered specific for pain. An item was considered specific for a disorder when (at least) 50% of the clinical experts and (at least) 50% of the ECPs and nurses rated it as such (marked with 'x').

Facial expressions

The clinical experts indicated six items to be pain-specific: 'pained expression', 'frowning', 'narrowing eyes', 'raising upper lip', 'tightened lips', and 'clenched teeth' (Figure 1). The remaining items were indicated to be more specific for one of the other disorders: anxiety disorder, depression, and dementia. For example, the items 'looking tense' and 'looking frightened' were indicated to be most specific for anxiety disorder, the items 'opened mouth' and 'empty gaze' for dementia, and the item 'looking sad' for depression. Facial expressions were seldom found to be specific for delirium.
Subgroup analyses showed that ECPs rated some items to be more specific for depression (Appendix 3 and 4). Especially, the items 'closing eyes', 'seeming disinterested', 'teary

eyed', and 'looking sad' were considered to be most specific for depression. On the other hand, nurses only indicated 'looking sad' to be most specific for depression. Additionally, nurses indicated the item 'pale face' to be pain-specific, whereas ECPs indicated the item to be most specific for anxiety disorder. Both ECPs and nurses considered the item 'empty gaze' not to be pain-specific at all; this item was found to be most specific for dementia.

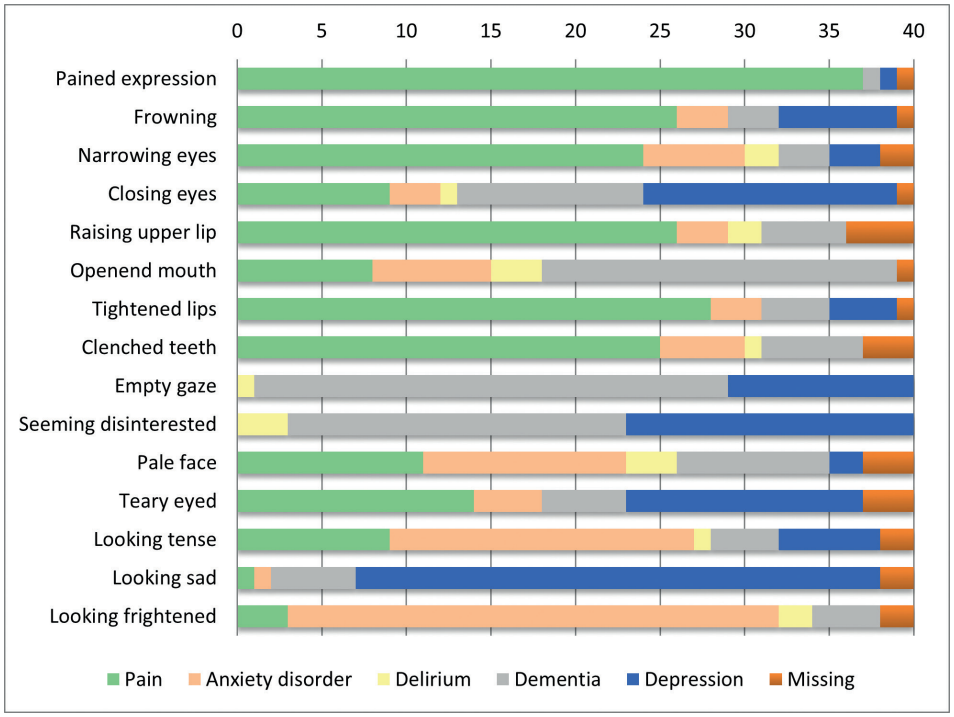

Figure 1. Facial expressions considered pain-specific or specific for other disorders by the clinical experts (n=40).

Body movements

Of the 10 items in the body movements domain, half were indicated to be pain-specific: 'freezing', 'curling up', 'guarding', 'rubbing', and 'limping' (Figure 2). The item 'pacing' was indicated to be most specific for dementia itself, as was the item 'restlessness'. The items of the body movements domain were often considered not to be specific for the disorders delirium and depression.

There was a substantial agreement between ECPs and nurses. They indicated most of the body movements to be most specific for pain and dementia (Appendix 3). Furthermore, both ECPs and nurses indicated that some items were specific for an anxiety disorder, for example, 'resisting care' and 'clenching hands'. According to ECPs and nurses, depression was almost never related to the items of the body movements domain.

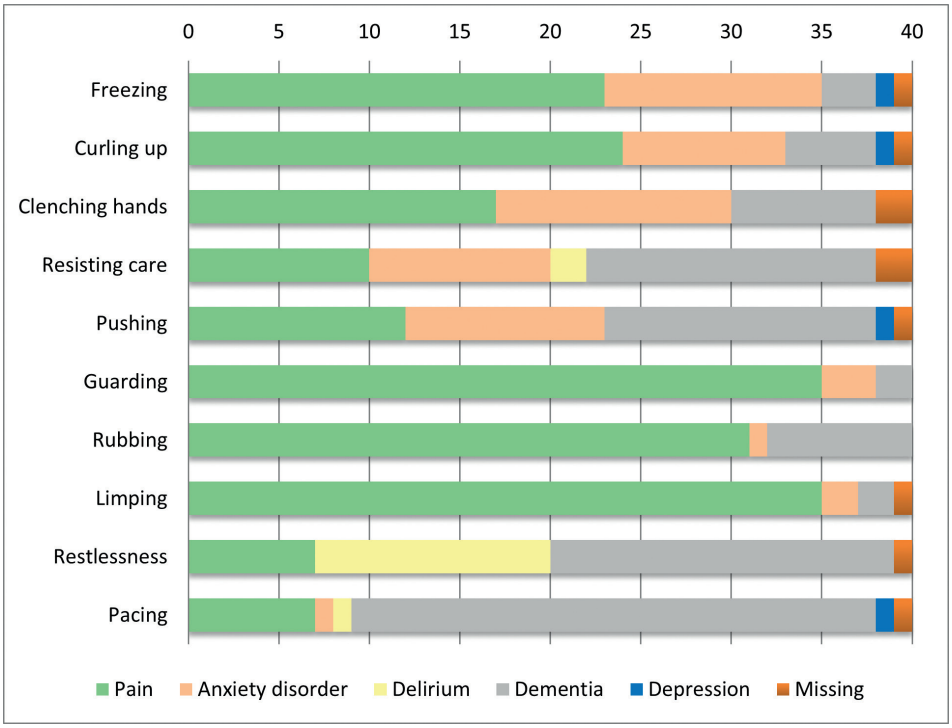

Figure 2. Body movements considered pain-specific or specific for other disorders by the clinical experts (n=40)

Vocalizations

The items 'using pain-related words', 'complaining', 'groaning', and 'gasping' were indicated to be most pain-specific (Figure 3); however, the item 'complaining' was also considered specific for depression. The clinical experts indicated five items to be most specific for dementia: using offensive words', 'repeating words', 'shouting', 'mumbling', and 'screaming'.

'Crying' and 'sighing' were found to be specific for depression, but were also considered pain-specific. Overall, the items of the vocalizations domain were not often found to be specific for the disorder delirium

The item 'pain-related words' was considered to be definitely pain-specific and not specific for one of the other disorders. This also applied on the subgroup level (Appendix 3).

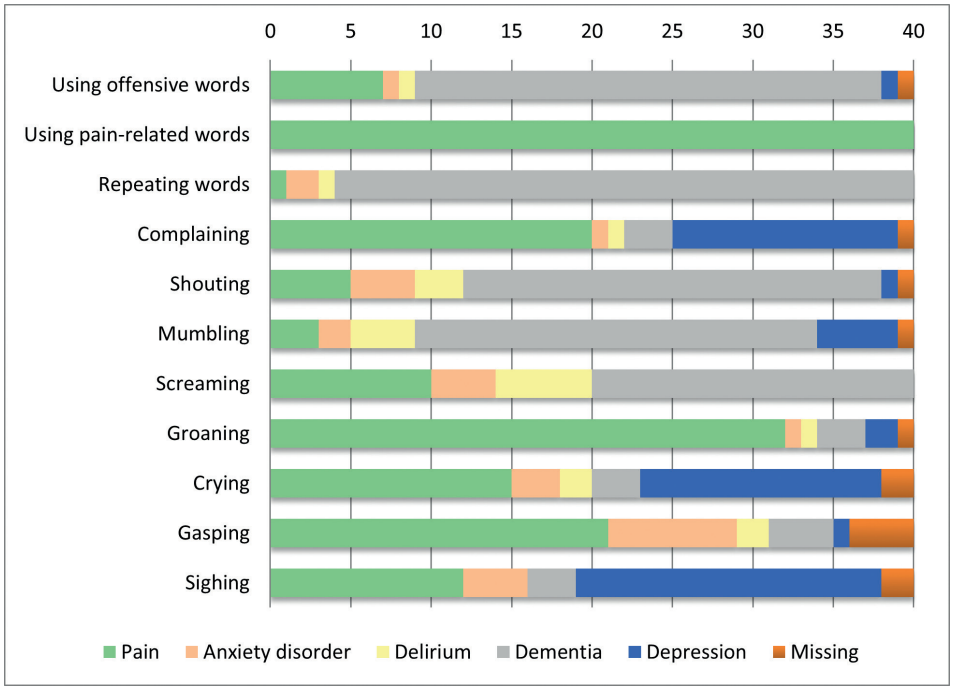

Figure 3. Vocalizations considered pain-specific or specific for other disorders by the clinical experts (n=40)

Discussion

In this study, the PAIC was translated into Dutch and content validity was examined. Overall, the study suggests that especially the items of the body movements domain correspond well with the clinical experience of the ECPs and nurses in Dutch nursing homes and showed good content validity. Compared with the body movements domain, lower content validity was shown for a number of items of the facial expressions domain and, to a lesser extent, for items of the vocalizations domain.

In total, 11 items (30.6%) had mean scores of >0.50 and were considered most definitely indicative of pain: 'pained expression', 'frowning', 'freezing', 'curling up', 'guarding', 'rubbing', 'limping', 'using pain-related words', 'complaining', 'groaning', and 'crying'.

However, six items with lower scores may still be promising, as they were found to be most pain-specific: 'clenched teeth', 'tightened lips', 'raising upper lip', 'narrowing eyes', 'gasping', and 'complaining'. The remaining items were found to be most specific for one of the other disorders, that is, anxiety disorder, delirium, depression, or dementia. More importantly, 10 items were considered indicative of pain as well as specific for pain: 'pained expression', 'frowning', 'freezing', 'curling up', 'guarding', 'rubbing', 'limping', 'using pain related words', 'complaining', and 'groaning'. This suggests that these items fit most with the opinion of the clinical experts and are, therefore, promising items in the measurement of pain.

Surprisingly, of the 11 items considered indicative of pain by ECPs and nurses, only two belonged to the facial expressions domain. Also, according to ECPs, several items of the facial expressions domain are more specific for depression or an anxiety disorder. This is remarkable because the items included in the PAIC were carefully selected by an expert panel from existing observational pain measurement instruments [9]. Based on that selection procedure, one would expect more items of the facial expressions domain to have good content validity. Even more striking is that, in an experimental setting, facial expressions are found to be most specific for pain, especially in persons with dementia. [14-16] Thus, this might suggest that the translation from bench to bedside does not fit the clinical notion of expressions of pain.

Additionally, there was a discrepancy between items considered indicative of pain and items considered pain-specific. For example, the items 'narrowing eyes', 'raising upper lip', 'clenched teeth', and 'tightening lips' had mean scores below 0.50; although they were considered less indicative of pain, they were considered more pain-specific compared to the other disorders (Table 2 and Figure 1). Interestingly, compared to ECPs, nurses found more items indicative of pain and also more items specific for pain.

These findings reveal not only a discrepancy between items being indicative of pain, but also a discrepancy between the notion of pain characteristics in dementia according to nurses and ECPs. This might be due to a lack of education of healthcare workers in the nursing home on pain assessment and management of persons with dementia. [17] Moreover, a lack of training and education can present a barrier to adequate pain management. [8] A lack of empirical evidence regarding which symptoms and behaviours are really related to pain might also play a role in this discrepancy. Since pain is an individual and personal experience, which is influenced by training and experience, healthcare workers may not think alike when identifying signs and symptoms of pain in persons with dementia. [18] This discrepancy adds to the already difficult challenge of identifying pain in persons with dementia.

It is most important that nurses and physicians speak the same language and recognize the same items as pain indicators to achieve adequate pain management, especially since nurses play a key role in the care for and monitoring of symptoms in persons with dementia.

Interestingly, such discrepancies did not exist for the items of the body movements domain. First, there were no major discrepancies between items being indicative of pain versus items being pain-specific. In other words, all those items considered most definitely indicative of pain were also considered most pain-specific. Second, this domain showed hardly any differences between the nurses' and ECPs' notion of pain characteristics. The mean scores of nurses and ECPs separately did not differ, except for the item 'pacing' which ECPs rated with a mean score of -0.05 (SD 0.58) compared to 0.23 (SD 0.64) by nurses. In both groups, 'pacing' was found most specific for dementia.

Regarding the items of the vocalizations domain, the clinical experts indicated four items most definitely indicative of pain: 'crying', 'groaning', 'complaining', and 'using pain-related words'. Of those items, 'groaning', 'complaining', and 'using pain-related words' were also found to be most pain-specific. No major discrepancies were found between nurses and ECPs on items of the vocalizations domain. Surprisingly, despite the high mean score of the item 'crying' (0.60, SD 0.40), the clinical experts indicated 'crying' to be less pain-specific compared to the other disorders. In fact, the item 'crying' was also found to be

specific for depression. Furthermore, the item 'gasping' had a low mean score on being indicative of pain (0.35, SD 0.57), but was indeed considered pain-specific. Moreover, more than half of the items were found to be less indicative of pain and, remarkably, several items of the vocalizations domain were indicated to be also specific for dementia. This might suggest that nurses and ECPs do not interpret most of the vocalization items as an evident expression of pain.

A possible explanation for the overall agreement between nurses and ECPs on the items of the body movements and vocalizations domain, might be that pain-related body movements and vocalizations are more easily recognized than facial expressions of pain, [19 20] which require more specific training and education. [21] However, a recent study by Lautenbacher et al., showed that nurses caring for persons with dementia already focus on certain facial expressions like 'narrowed eyes' and 'frowning', without specific training. [22] Again, this emphasizes the need for additional, improved, and interdisciplinary education on pain recognition in dementia.[23]

Strengths and limitations

The strength of the present study is that the content validity was examined separately among ECPs and nurses. It is important that the content of a measurement instrument contains the views and beliefs of the potential users. This is also called 'user-centeredness' and is considered an important part of developing and testing a new measurement instrument. [24] Ultimately, this will contribute to better psychometric properties and feasibility of implementation of observational instruments, such as the PAIC.

Furthermore, our sample size was larger compared to other studies investigating psychometric properties of observational pain measurement tools. [5] A larger sample size provides more solid results in terms of content validity.

A possible limitation is that content validity is a subjective assessment and no standardized procedures are available to investigate this. Moreover, most studies investigating observational pain tools do not report on content validity, despite that this is an important part of psychometrics, also with respect to feasibility of implementation. [5 25] When content and face validity are missing, this might be a good reason not to use that specific measurement instrument. [12]

Additionally, in this study, the clinical experts were asked to indicate whether the items of the PAIC were most specific for pain, or for one of the other (fixed) disorders. They could indicate only one disorder per item, for example, anxiety disorder, delirium, dementia, depression, or pain. However, because these preselected disorders may not fully represent the opinion of the experts, some crucial information could have been missed. For example, one could suggest that the item 'pale face' is specific for Parkinson's disease, whereas this could not be indicated as such.

Furthermore, the items of the PAIC in this study were not assessed on prevalence in persons with dementia who experience pain; rather, the potential users of the PAIC were asked their clinical opinion about the items. However, the potential users of this study were considered clinical experts with considerable experience in the care for persons with dementia. Furthermore, we did not ask the clinical opinion of health care assistants or

nursing auxiliaries as they could play an important role in the recognition of a change in behaviour. They could provide additional information on possible cues for pain.
Finally, since this study concerns validating the Dutch version of the PAIC, it is possible that, due to differences in culture and training, the results may not be generalizable to other countries.

Clinical implications

Besides establishing the content validity of the PAIC, this study also has clinical implications. For example, the study sheds light on the opinion of physicians and nurses regarding the cues used to decide whether a person with dementia is in pain. The study also reveals important differences of opinion between physicians and nurses. This information suggests that educational shortcomings may exist (especially interdisciplinary education) among healthcare workers in nursing homes. The study also provides insight into the empirical performance of the PAIC.
Due to its solid scientific basis, the PAIC seems a promising assessment tool. [9] However, a lack of empirical evidence and of interdisciplinary education on pain in dementia could be a barrier to adequate pain management and treatment. Therefore, in addition to aiming to create the most valid/reliable assessment tool to measure pain in persons with dementia, it is also important to provide education on pain in dementia and training in the use of observational pain measurement tools. Also, considering that implementation of an observational pain measurement tool does not necessarily lead to better care [26], a constant flow of education should be available to maintain a certain level of awareness to ensure adequate management of pain. [27-29] This validity study reveals, in particular, the need for more education in facial expressions.

Future directions PAIC

The first step in testing the Dutch version of the new, universal, meta-tool PAIC, was to examine the content validity of a wide range of individual items. To improve and refine the PAIC, item reduction is needed. For this, especially the facial expressions domain and (to a lesser extent) the vocalizations domain need additional study. The next important step is to examine content validity in other countries, so that the PAIC can become an internationally agreed upon observational measurement tool. Also, by investigating content validity in a larger population, factor analyses can be used to determine which items correlate with each other.[12] For example, if the different domains of the PAIC cluster together, a decision could be made to measure pain using the domain that corresponds most with the clinical experience and, therefore, is the easiest to score. Based on the present study, the body movements domain would be the most suitable to measure pain in persons with dementia. It might also be worthwhile to investigate if solely those items with good content validity (e.g., both indicative of pain and specific for pain) are sufficient for the measurement of pain in persons with dementia. In that case, this study suggests that the PAIC could be reduced from 36 items to only 10 items. However, although a shorter measurement tool might offer more advantages (e.g., easier to use, less time-consuming) with regard to

feasibility, clinical utility, and implementation in clinical/research settings, further testing using, for example factor analyses is needed.

Conclusion

This study shows that the Dutch version of the PAIC has overall good content validity but that differences exist in the notion of pain characteristics between nurses and physicians working in nursing homes. This important information indicates a need for more, interdisciplinary, education on pain in dementia. However, before implementing the PAIC in clinical and research settings, it is necessary to further test the reliability, clinical utility, and feasibility. Additionally, investment in more education of physicians and nurses might be required to accomplish more successful management of pain in persons with dementia.

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Disclosure

The authors report no conflicts of interest in this work.

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Appendix 1. PAIC-36 – English version

Facial Expressions

Please record the appearance of the facial expressions described in the table below according to **how visible** they are in the person you are observing

FACIAL EXPRESSIONS	Meaning of items	Not at all	Slight degree	Moderate degree	Great degree	Not scored A. Item is not clear B. Situation is unsuitable C. Physical status of person not suitable forscoring D. Other [describe]
Pained expression	facial display of pain	**0**	**1**	**2**	**3**	
Frowning	lowering and drawing brows together	**0**	**1**	**2**	**3**	
Narrowing eyes	narrowed eyes with tension around the eyes	**0**	**1**	**2**	**3**	
Closing eyes	not just blinking	**0**	**1**	**2**	**3**	
Raising upper lip	upper lip raised, nose may be wrinkled	**0**	**1**	**2**	**3**	
Opened mouth	the lips are parted, jaw is dropped	**0**	**1**	**2**	**3**	
Tightened lips	lips are pressed together and appear more narrow	**0**	**1**	**2**	**3**	
Clenched teeth	teeth are pressed together with tension	**0**	**1**	**2**	**3**	
Empty gaze	Eyes do not reflect any emotion or thinking activity ("blank expression")	**0**	**1**	**2**	**3**	
Seeming disinterested	face does not reflect any interest in the environment	**0**	**1**	**2**	**3**	
Pale face	pale skin colour	**0**	**1**	**2**	**3**	
Teary eyed	watery eyes	**0**	**1**	**2**	**3**	
Looking tense	facial display of strain or worry	**0**	**1**	**2**	**3**	
Looking sad	facial display of unhappiness, sorrow or low mood	**0**	**1**	**2**	**3**	
Looking frightened	facial display of fear, alarm or heightened anxiety	**0**	**1**	**2**	**3**	

Appendix 1. PAIC-36 – English version

Body movements

Please record the occurrence of the body movements described in the table below according to **how visible** they are in the person you are observing

BODY MOVEMENTS	Meaning of items	Not at all	Slight degree	Moderate degree	Great degree	Not scored A. Item is not clear B. Situation is unsuitable C. Physical status of person not suitable for scoring D. Other [describe]
Freezing	sudden stiffening, avoiding movement, holding breath	**0**	**1**	**2**	**3**	
Curling up	curling up the body tightly, pulling in arms and legs	**0**	**1**	**2**	**3**	
Clenching hands	tensing hands, making fists, grabbing objects tightly	**0**	**1**	**2**	**3**	
Resisting care	resisting being moved or resisting care, being uncooperative	**0**	**1**	**2**	**3**	
Pushing	actively pushing somebody or something away	**0**	**1**	**2**	**3**	
Guarding	protecting affected body part, holding body part, avoiding touch, moving away	**0**	**1**	**2**	**3**	
Rubbing	tugging or massaging affected body part	**0**	**1**	**2**	**3**	
Limping	avoiding pain while walking in an unbalanced way	**0**	**1**	**2**	**3**	
Restlessness	fidgeting, wringing hands, rocking back and forth	**0**	**1**	**2**	**3**	
Pacing	wandering restlessly back and forth (might also be in a wheelchair)	**0**	**1**	**2**	**3**	

Appendix 1. PAIC-36 – English version

Vocalizations

Please record the vocalizations described in the table below according to **how audible** they are in the person you are observing

VOCALIZATION	Meaning of items	Not at all	Slight degree	Moderate degree	Great degree	Not scored A. Item is not clear B. Situation is unsuitable C. Physical status of person not suitable for scoring D. Other [describe]
Using offensive words	cursing, swearing, or using foul language	**0**	**1**	**2**	**3**	
Using pain-related words	using pain words, like "ouch", "ow", or "that hurts"	**0**	**1**	**2**	**3**	
Repeating words	repeating words or phrases again and again (not stuttering)	**0**	**1**	**2**	**3**	
Complaining	expressing being unhappy, sick, uncomfortable, and/or in pain	**0**	**1**	**2**	**3**	
Shouting	using a loud voice to express words	**0**	**1**	**2**	**3**	
Mumbling	uttering words and/or sounds indistinctly	**0**	**1**	**2**	**3**	
Screaming	using a loud and/or high-pitched voice to express sounds	**0**	**1**	**2**	**3**	
Groaning	making a deep, inarticulate sound	**0**	**1**	**2**	**3**	
Crying	whimpering, sobbing, wailing, or weeping	**0**	**1**	**2**	**3**	
Gasping	breathing sharply, laboriously, and/or loudly	**0**	**1**	**2**	**3**	
Sighing	taking in and letting out a long, loud breath	**0**	**1**	**2**	**3**	

Appendix 2: PAIC – Dutch version

Gezichtsuitdrukkingen

Noteer het voorkomen van de gezichtsuitdrukkingen beschreven in de onderstaande tabel op basis van **hoe duidelijk** ze aanwezig zijn bij de persoon die u observeert.

GEZICHTS-UITDRUKKINGEN	Betekenis items	Helemaal niet	Geringe mate	Gemiddelde mate	Hoge mate	Niet gescoord a = Item is onduidelijk b = Situatie is ongeschikt c = Fysieke toestand cliënt is niet geschikt om te scoren d = Anders:.....
Gepijnigde uitdrukking	Gezichtsuitdrukking van pijn	**0**	**1**	**2**	**3**	
Fronsen	Wenkbrauwen omlaag bewegen en samentrekken	**0**	**1**	**2**	**3**	
Ogen vernauwen	Oogleden samenknijpen, met spanning rond de ogen	**0**	**1**	**2**	**3**	
Ogen sluiten	Ogen actief sluiten, niet alleen knipperen	**0**	**1**	**2**	**3**	
Bovenlip omhoog trekken	Bovenlip omhoog omhoog getrokken, huid rond neus kan plooien	**0**	**1**	**2**	**3**	
Geopende mond	Lippen en kaken van elkaar	**0**	**1**	**2**	**3**	
Samengeperste lippen	Lippen zijn samengeperst en lijken smaller	**0**	**1**	**2**	**3**	
Op elkaar geklemde tanden	Tanden en kiezen zijn op elkaar geklemd met spanning in de kaken	**0**	**1**	**2**	**3**	
Lege blik	Ogen laten geen enkele emotie of actieve gedachtegang zien, “uitdrukkingsloos”	**0**	**1**	**2**	**3**	
Ongeïnteresseerde blik	Gezicht laat geen enkele interesse in de omgeving zien	**0**	**1**	**2**	**3**	
Bleek gezicht	Bleke huidskleur	**0**	**1**	**2**	**3**	
Betraande ogen	Waterige ogen (meer dan normaal)	**0**	**1**	**2**	**3**	
Gespannen uitdrukking	Gezichtsuitdrukking is gespannen, bezorgd	**0**	**1**	**2**	**3**	
Verdrietige uitdrukking	Gezichtsuitdrukking is droevig, neerslachtig of niet gelukkig	**0**	**1**	**2**	**3**	
Er angstig uitzien	Gezichtsuitdrukking is angstig, gealarmeerd, of geeft verhoogde ongerustheid weer	**0**	**1**	**2**	**3**	

Appendix 2: PAIC – Dutch version

Lichaamsbewegingen

Noteer het voorkomen van de lichaamsbewegingen beschreven in de onderstaande tabel op basis van **hoe duidelijk** ze aanwezig zijn bij de persoon die u observeert.

LICHAAMS BEWEGINGEN	Betekenis items	Helemaal niet	Geringe mate	Gemiddelde mate	Hoge mate	Niet gescoord a = Item is onduidelijk b = Situatie is ongeschikt c = Fysieke toestand cliënt is niet geschikt om te scoren d = Anders:.....
Verstarren	Plotselinge verstijving, vermijden van beweging, adem inhouden	**0**	**1**	**2**	**3**	
Ineenkrimpen	Lichaam stevig opkrullen, armen en benen intrekken	**0**	**1**	**2**	**3**	
Gebalde handen	Handen gespannen, vuisten maken, voorwerpen stevig vastgrijpen	**0**	**1**	**2**	**3**	
Verzetten tegen zorg	Verzetten tegen verplaatsing of zorg, niet meewerken	**0**	**1**	**2**	**3**	
Duwen	Actief iemand of iets wegduwen	**0**	**1**	**2**	**3**	
Beschermen	Aangedaan lichaamsdeel beschermen, lichaamsdeel vasthouden, aanraking vermijden, afwenden	**0**	**1**	**2**	**3**	
Wrijven	Aanraken of masseren van het aangedane lichaamsdeel	**0**	**1**	**2**	**3**	
Strompelen	Pijn vermijden door op een ongebalanceerde manier te lopen	**0**	**1**	**2**	**3**	
Rusteloosheid	Friemelen, in de handen knijpen, heen en weer wiegen	**0**	**1**	**2**	**3**	
IJsberen	Rusteloos heen en weer lopen; kan ook in een trippelrolstoel zijn	**0**	**1**	**2**	**3**	

Appendix 2: PAIC – Dutch version

Stemgeluiden

Noteer het voorkomen van de stemgeluiden beschreven in de onderstaande tabel op basis van **hoe hoorbaar** ze zijn bij de persoon die u observeert.

STEMGELUIDEN	Betekenis items	Helemaal niet	Geringe mate	Gemiddelde mate	Hoge mate	Niet gescoord a = Item is onduidelijk b = Situatie is ongeschikt c = Fysieke toestand cliënt is niet geschikt om te scoren d = Anders:.....
Beledigende taal gebruiken	Vloeken, schelden, onbehoorlijke taal gebruiken	**0**	**1**	**2**	**3**	
Pijngerelateerde woorden gebruiken	Pijnwoorden gebruiken zoals 'auw', 'ahh' of 'dat doet pijn'	**0**	**1**	**2**	**3**	
Herhalen van woorden	Keer op keer herhalen van woorden of zinnen (niet stotteren)	**0**	**1**	**2**	**3**	
Klagen	Aangeven/zeggen ongelukkig, ziek oncomfortabel te zijn en/ of pijn te hebben	**0**	**1**	**2**	**3**	
Roepen	Hard stemgeluid gebruiken om iets te zeggen	**0**	**1**	**2**	**3**	
Mompelen	Woorden en/of geluiden onduidelijk uitspreken	**0**	**1**	**2**	**3**	
Schreeuwen	Hard en/of hoog stemgeluid gebruiken om geluiden te uiten	**0**	**1**	**2**	**3**	
Kreunen	Een laag, onsamenhangend geluid maken	**0**	**1**	**2**	**3**	
Huilen	Jammeren, snikken, weeklagen of wenen	**0**	**1**	**2**	**3**	
Naar lucht happen	Scherp, moeizaam en/of luid ademhalen	**0**	**1**	**2**	**3**	
Zuchten	Inademen en lang, nadrukkelijk uitademen	**0**	**1**	**2**	**3**	

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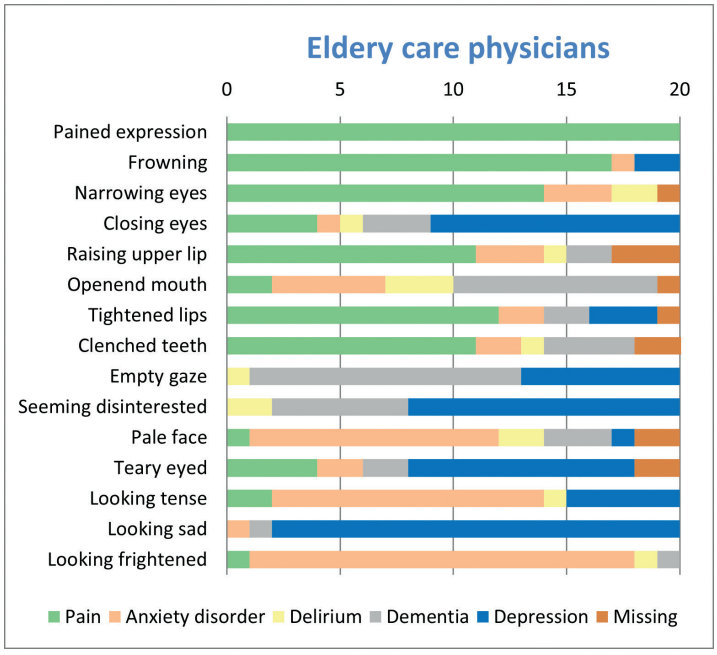
Appendix 3: Figures doctors vs. nurses



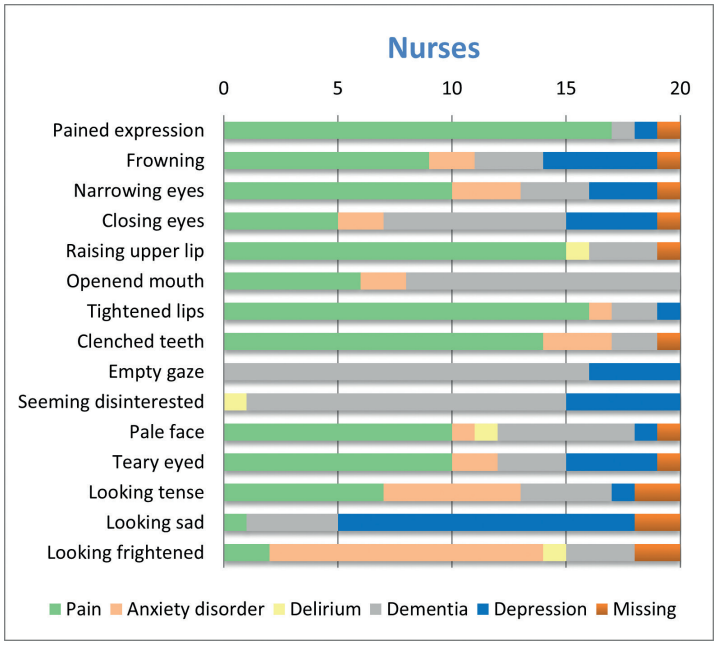
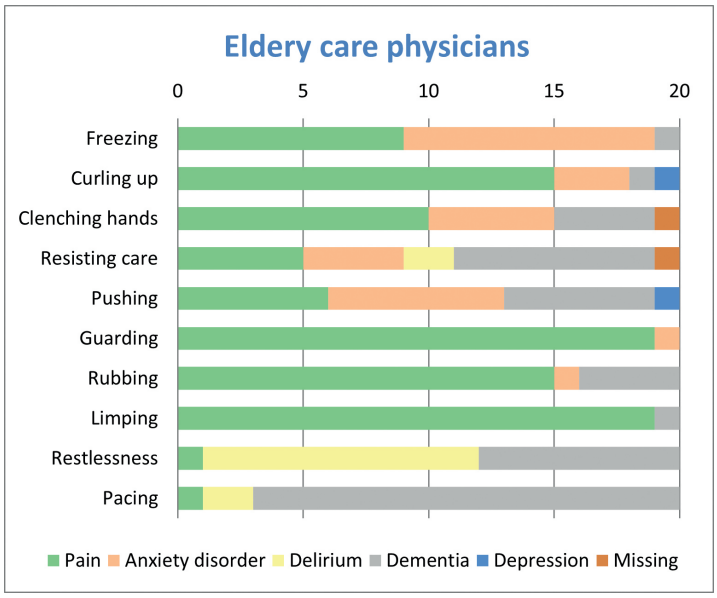


Figure 4. Facial expression specific for pain or other disorders: Elderly care physicians & nurses

Appendix 3: Figures doctors vs. nurses



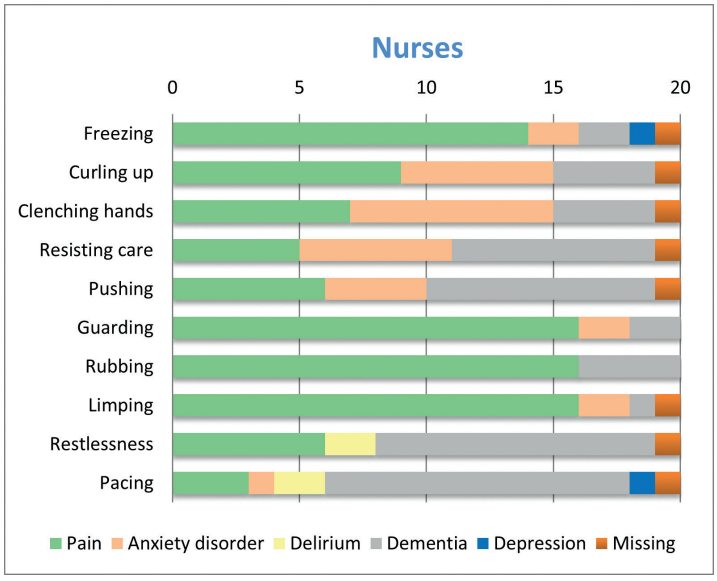
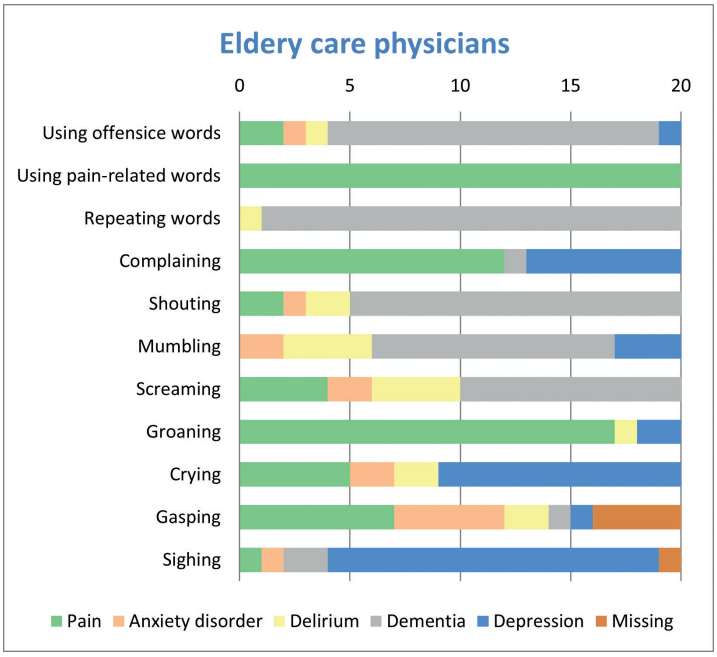


Figure 5. Body movements specific for pain or other disorders: Elderly care physicians & nurses

Appendix 3: Figures doctors vs. nurses



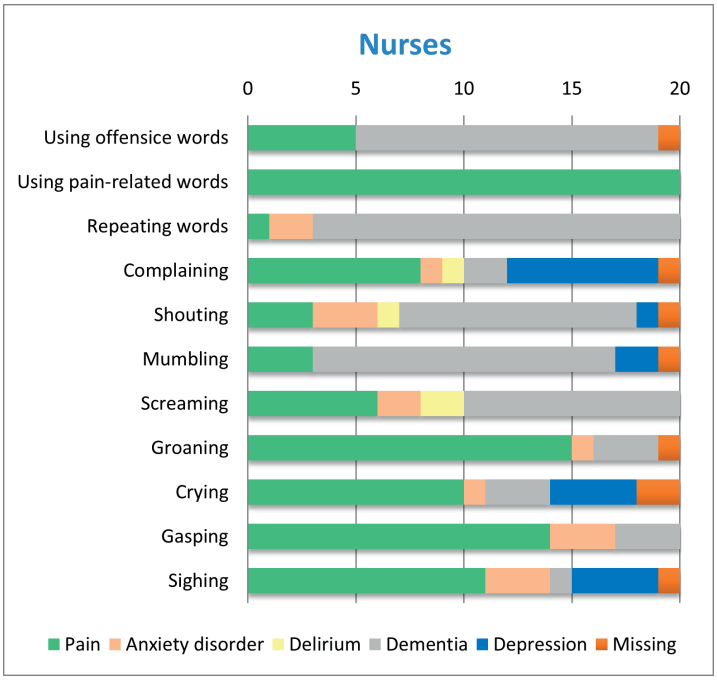


Figure 6. Vocalizations specific for pain or other disorders: Elderly care physicians & nurses

Appendix 4: Table 3-5

Table 3. Scoring of PAIC-items on question indicative of pain: Clinical experts

	Clinical experts (n=40)					
	No (n)		*Yes (n)*			
	Definitely not (=-1.0)	*Probably not (=-0.5)*	*Probably (=0.5)*	*Definitely (=1.0)*	*Missing*	*Mean (SD)**
Facial expressions						
Pained expression	-	-	8	32		**0.90 (0.20)**
Frowning	-	4	25	11		**0.54 (0.41)**
Narrowing eyes	1	9	26	4		0.27 (0.52)
Closing eyes	2	21	13	4		-0.05 (0.61)
Raising upper lip	1	14	20	4	1	0.15 (0.58)
Opened mouth	4	25	5	5	1	-0.23 (0.62)
Tightened lips	1	6	23	8	2	0.41 (0.52)
Clenched teeth	2	4	25	7	2	0.41 (0.52)
Empty gaze	10	23	4	2	1	-0.45 (0.54)
Seeming disinterested	14	19	4	2	1	-0.50 (0.56)
Pale face	7	19	9	2	3	-0.27 (0.61)
Teary eyed	4	11	21	4		0.13 (0.63)
Looking tense	-	7	24	9		0.44 (0.48)
Looking sad	4	13	15	7	1	0.10 (0.68)
Looking frightened						0.49 (0.58)
Body movements						
Freezing	1	6	15	14	4	**0.65 (0.36)**
Curling up	-	2	19	19		**0.69 (0.37)**
Clenching hands	1	5	28	6		0.41 (0.47)
Resisting care	1	8	22	-	9	0.19 (0.49)
Pushing	1	10	20	9		0.33 (0.58)
Guarding	-	3	19	18		**0.65 (0.41)**
Rubbing	-	4	24	11	1	**0.54 (0.42)**
Limping	-	3	17	20		**0.68 (0.42)**
Restlessness	-	14	20	6		0.23 (0.57)
Pacing	1	18	15	6		0.09 (0.62)

Table 3. Scoring of PAIC-items on question indicative of pain: Clinical experts *(continued)*

	Clinical experts (n=40)					
	No (n)		*Yes (n)*			
	Definitely not (=-1.0)	***Probably not (=-0.5)***	***Probably (=0.5)***	***Definitely (=1.0)***	***Missing***	***Mean (SD)****
Vocalizations						
Using offensive words	-	13	21	5	1	0.23 (0.55)
Using pain-related words	-	1	5	33	1	**0.90 (0.29)**
Repeating words	3	27	8	2		-0.26 (0.53)
Complaining	-	2	23	15		**0.64 (0.36)**
Shouting	2	17	19	2		0.03 (0.58)
Mumbling	3	23	13	1		-0.18 (0.55)
Screaming	1	10	25	4		0.26 (0.53)
Groaning	-	1	20	18	1	**0.71 (0.32)**
Crying	-	3	23	14		**0.60 (0.40)**
Gasping	2	7	23	8		0.35 (0.57)
Sighing	-	17	18	5		0.14 (0.58)

Table 4. Scoring of PAIC-items on question indicative of pain: Elderly care physicians versus nurses

	Elderly care Physician (n= 20)						Nurses (n= 20)						
	No		*Yes*				*No*		*Yes*				
	Def. not	*Prob. not*	*Prob.*	*Def.*	*Mean (SD)*	*Missing*	*Def. not*	*Prob. not*	*Prob.*	*Def.*	*Mean (SD)*	*Missing*	*p-value*
Facial expressions													
Pained expression	-	-	5	15	**0.88 (0.22)**		-	-	3	17	**0.93 (0.18)**		0.44
Frowning	-	-	17	3	**0.58 (0.18)**		-	4	8	8	0.50 (0.56)		0.57
Narrowing eyes	-	2	16	2	0.45 (0.36)		1	7	10	2	0.13 (0.60)		**0.05**
Closing eyes	1	13	5	1	-0.20 (0.55)		1	8	8	3	0.10 (0.64)		0.12
Raising upper lip	-	8	10	1	0.11 (0.54)		1	6	10	3	0.20 (0.62)		0.61
Opened mouth	3	14	2	1	-0.40 (0.50)		1	11	3	4	-0.05 (0.69)	1	0.06
Tightened lips	-	4	16	-	0.30 (0.41)		1	2	7	8	**0.53 (0.61)**	2	0.19
Clenched teeth	-	2	16	2	0.45 (0.36)		2	2	9	5	0.36 (0.66)	2	0.60
Empty gaze	6	13	1	-	-0.60 (0.35)		4	10	3	2	-0.29 (0.65)	1	0.07
Seeming disinterested	10	10	-	-	-0.75 (0.26)		4	9	4	2	-0.24 (0.67)	1	**0.003**
Pale face	4	13	2	-	-0.50 (0.41)	1	3	6	7	2	-0.02 (0.70)	2	**0.02**
Teary eyed	1	9	9	1	0.00 (0.58)		3	2	12	3	0.25 (0.66)		0.21
Looking tense	-	4	14	2	0.35 (0.46)		-	3	10	7	**0.53 (0.50)**		0.26
Looking sad	1	10	9	-	-0.08 (0.54)		3	3	6	7	0.29 (0.77)	1	0.10
Looking frightened	-	4	7	5	0.41 (0.58)	4	1	2	8	9	**0.55 (0.58)**		0.47
Body movements													
Freezing	-	-	12	8	**0.70 (0.25)**		-	2	10	8	**0.60 (0.45)**		0.39
Curling up	-	-	9	11	**0.78 (0.26)**		-	2	10	8	**0.60 (0.44)**		0.14
Clenching hands	-	2	16	2	0.45 (0.36)		1	3	12	4	0.38 (0.56)		0.62
Resisting care	-	6	12	2	0.17 (0.49)		1	2	10	7	0.23 (0.53)		0.73

	Elderly care Physician (n= 20)						Nurses (n= 20)						
	No		*Yes*				*No*		*Yes*				
	Def. not	***Prob. not***	***Prob.***	***Def.***	***Mean (SD)***	***Missing***	***Def. not***	***Prob. not***	***Prob.***	***Def.***	***Mean (SD)***	***Missing***	***p*-value**
Pushing	-	7	11	2	0.20 (0.55)		1	3	9	7	0.45 (0.60)		0.18
Guarding	-	1	10	9	**0.68 (0.37)**		-	2	9	9	**0.63 (0.46)**		0.71
Rubbing	-	2	13	5	**0.53 (0.41)**		-	2	11	6	**0.55 (0.44)**	1	0.84
Limping	-	2	9	9	**0.63 (0.46)**		-	1	8	11	**0.73 (0.38)**		0.46
Restlessness	-	9	10	1	0.08 (0.46)		-	5	10	5	0.38 (0.56)		0.09
Pacing	1	10	8	1	-0.05 (0.58)		-	8	7	5	0.23 (0.64)		0.16
Vocalizations													
Using offensive words	-	8	11	1	0.13 (0.54)		-	5	10	4	0.34 (0.55)	1	0.22
Using pain-related words	-	-	4	15	**0.89 (0.21**)	1	-	1	1	18	**0.90 (0.35)**		0.95
Repeating words	3	12	5	-	-0.33 (0.52)		-	15	3	2	-0.20 (0.55)		0.46
Complaining	-	-	14	6	**0.65 (0.24)**		-	2	9	9	**0.63 (0.46**)		0.83
Shouting	1	10	8	1	-0.05 (0.58)		1	7	11	1	0.10 (0.58)		0.42
Mumbling	2	14	4	-	-0.35 (0.46)		1	9	9	1	0.00 (0.58)		**0.04**
Screaming	1	6	12	1	0.15 (0.56)		-	4	13	3	0.38 (0.48)		0.18
Groaning	-	1	10	8	**0.66 (0.37)**	1	-	-	10	10	**0.75 (0.26)**		0.38
Crying	-	2	13	5	**0.53 (0.41)**		-	1	10	9	**0.68 (0.37)**		0.24
Gasping	1	3	13	3	0.35 (0.54)		1	4	10	5	0.35 (0.61)		1.00
Sighing	-	9	9	2	0.10 (0.58)		-	8	9	3	0.18 (0.59)		0.69

Table 5. Scoring of PAIC-items on question pain-specific: Elderly care physicians versus nurses

	Elderly care Physician (n=20)						Nurses (n=20)					
	Anxiety disorder	**Delirium**	**Dementia**	**Depression**	**Pain**	**Missing**	**Anxiety disorder**	**Delirium**	**Dementia**	**Depression**	**Pain**	**Missing**
Facial expressions												
Pained expression	-	-	-	-	20		-	-	1	1	17	1
Frowning	1	-	-	2	17		2	-	3	5	9	1
Narrowing eyes	3	2	-	-	14		3	-	3	3	10	1
Closing eyes	1	1	3	11	4		2	-	8	4	5	1
Raising upper lip	3	1	2	-	11	3	-	1	3	-	15	1
Opened mouth	5	3	9	-	2	1	2	-	12	-	6	
Tightened lips	2	-	2	3	12	1	1	-	2	1	16	
Clenched teeth	2	1	4	-	11	2	3	-	2	-	14	1
Empty gaze	-	1	12	7	-		-	-	16	4	-	
Seeming disinterested	-	2	6	12	-		-	1	14	5	-	
Pale face	11	2	3	1	1	2	1	1	6	1	10	1
Teary eyed	2	-	2	10	4	2	2	-	3	4	10	1
Looking tense	12	1	-	5	2		6	-	4	1	7	2
Looking sad	1	-	1	18	-		-	-	4	13	1	2
Looking frightened	17	1	1	-	1		12	1	3	-	2	2
Body movements												
Freezing	10	-	1	-	9		2	-	2	1	14	1
Curling up	3	-	1	1	15		6	-	4	-	9	1
Clenching hands	5	-	4	-	10	1	8	-	4	-	7	1
Resisting care	4	2	8	-	5	1	9	-	8	-	5	1

	Elderly care Physician (n=20)						Nurses (n=20)					
	Anxiety disorder	**Delirium**	**Dementia**	**Depression**	**Pain**	**Missing**	**Anxiety disorder**	**Delirium**	**Dementia**	**Depression**	**Pain**	**Missing**
Body movements												
Pushing	7	-	6	1	6		4	-	9	-	6	1
Guarding	1	-	-	-	19		2	-	2	-	16	
Rubbing	1	-	4	-	15		-	-	4	-	16	
Limping	-	-	1	-	19		2	-	1	-	16	1
Restlessness	-	11	8	-	1		-	2	11	-	6	1
Pacing	-	2	17	-	1		1	2	12	1	3	1
Vocalizations												
Using offensive words	1	1	15	1	2		-	-	14	-	5	1
Using pain-related words	-	-	-	-	20		-	-	-	-	20	
Repeating words	-	1	19	-	-		2	-	17	-	1	
Complaining	-	-	1	7	12		1	1	2	7	8	1
Shouting	1	2	15	-	2		3	1	11	1	3	1
Mumbling	2	4	11	3	-		-	-	14	2	3	1
Screaming	2	4	10	-	4		2	2	10	-	6	
Groaning	-	1	-	2	17		1	-	3	-	15	1
Crying	2	2	-	11	5		1	-	3	4	10	2
Gasping	5	2	1	1	7	4	3	-	3	-	14	
Sighing	1	-	2	15	1	1	3	-	1	4	11	1

CHAPTER 6

Pain assessment in impaired cognition: observer agreement in a long-term care setting in patients with dementia

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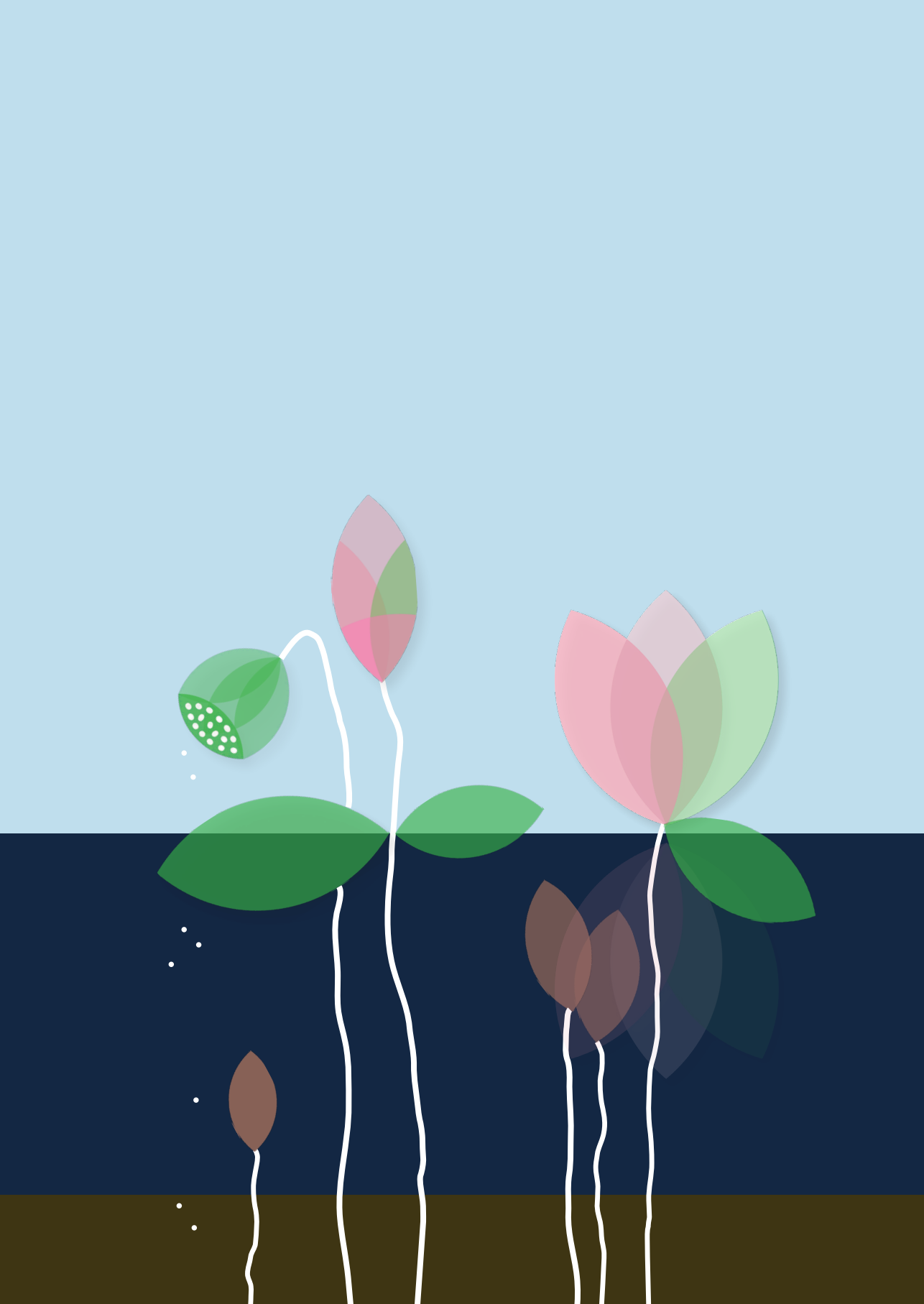

Abstract

Aim

To study the application of the meta-tool Pain Assessment in impaired Cognition (PAIC) in a clini cal setting in patients with moderate to severe dementia.

Materials & methods

Observational study in five Dutch nursing homes, where residents were observed by nurses or nurse-assistants during rest and movement.
Prevalence and observer agreement of individual items were examined.

Results

An observer agreement of ≥70% was found for most items of the body movement domain and vocalization domain, although prevalence of these behaviours was low (especially during rest). Items of the facial expression domain had a percentage agreement <70%, especially during movement, but with high prevalence of behaviours.

Conclusion

The pain assessment in impaired cognition items show promising interobserver and intraobserver agreement in a clinical setting.

Keywords:

dementia, interobserver agreement, intraobserver agreement, nursing home, observational measurement instrument, pain, pain assessment, reliability

Practice points

- Since the identification of pain in dementia is essential to prevent negative consequences on quality of life, the use of reliable and valid measurement instruments is very important.
- Pain Assessment in Impaired Cognition (PAIC) research version is a 'meta-tool', consisting of items from existing observational scales for pain assessment in patients with dementia.
- Prevalence and observer agreement for individual behaviours is unclear for the clinical setting with nursing home residents with moderate to severe dementia.
- Prevalence of the individual items varied. Most items with high prevalence belonged to the facial expression domain during movement, lower prevalence was mainly found for the body movement domain and vocalization domain during rest.
- The Pain Assessment in Impaired Cognition items show promising interobserver and intraobserver agreement in a clinical setting, with observer agreement of ≥70% for most items.

Introduction

Pain in persons with dementia is a serious problem. Not only is it thought to be highly prevalent, but pain also has an important impact on the quality of life. Pain may result in challenging behaviour (e.g., agitation, aggression and depression) and may also cause deterioration of physical functioning[1-3].

Besides the altered perception of pain due to neuropathological changes in dementia[4], diminished cognitive and communicative abilities make it difficult to identify and monitor pain in persons with dementia. The ability to self-report pain is seriously challenged with the progressive nature of dementia and is probably a main reason for the poor pain management reported in hospitals, community and home care[1 5].

Therefore, it is recommended to use reliable and valid observational measurement instruments to identify and measure pain in dementia. Several instruments have been developed that utilize observation of pain-related behaviours, vocalizations and facial expressions. Despite the robust development, these measurement instruments often lack sufficient evidence of psychometric properties (e.g., reliability, face and construct validity, responsiveness and usability) and are not internationally implemented [6]. The European COST initiative 'Pain in impaired cognition, especially dementia', put together items for a new universal meta-tool to measure pain in dementia, in other words, Pain Assessment in Impaired Cognition (PAIC), for use in research and clinical settings [7].

The PAIC was based on the best items in available and acknowledged observational measurement instruments, for example, Pain Assessment in Advanced Dementia (PAINAD)[8], Pain Assessment Checklist for Seniors with Severe Dementia (PACSLAC-D)[9] and Mobilization-Observation-Behaviour-Intensity-Dementia (MOBID-2)[10]. Item selection for the PAIC resulted from scrutiny of the evidence, expert opinion from experimental and clinical researchers and multidisciplinary clinicians and alignment with the American geriatric society criteria[11]. The first version of the PAIC consists of 36 items in three American geriatric society domains: facial expressions, body movements and vocalizations. The facial expression domain comprises 15 items, the body movement domain 10 items and the vocalization domain comprises 11 items (Appendix 1, Chapter 5).

Several items included in the PAIC were assumed by the expert panel to be potentially less reliable or valid than others and more viable for bias. However, to avoid making *a priori* assumptions about the utility of these items in the final PAIC, it was decided to allow further empirical item reduction during the validity and reliability testing.

A reliable and valid measurement instrument is important because, in clinical practice, it often affects decision-making for the individual patient. Therefore, the PAIC was developed to identify and monitor pain, as well as to evaluate the treatment of pain[7]. The PAIC-36 has shown good content validity, especially for the body movement domain[12]. In general, items of all three domains were found to be valid in the measurement of pain in persons with dementia[13 14]. The present study investigated the observer agreement of the Dutch version of the PAIC. Observer agreement is part of the psychometric property 'reliability', which refers to the consistency of a measurement[15].

The aim of this study was to assess two aspects of the observer agreement on all 36 individual items of the Dutch version of the PAIC in a real-life nursing home setting: interobserver agreement (different observers evaluating the same situation) and intra-

observer agreement (same observers evaluating the same situation the next day).
By using real-life observations in a clinical setting, the various behaviours and expressions as presented by persons with dementia within the context of an everyday situation could be taken into account. Therefore, it was expected that the observers could observe almost all items of the PAIC. The observer agreement of the individual items was tested in two different situations: during rest and during movement. By doing so, we could also study whether the prevalence of items was different between these situations. Furthermore, by observing the resident during movement (e.g., making a transfer from bed to chair) it was expected that most items of the PAIC would be more prevalent compared with observations during rest alone, due to pain provocation (often) caused by inducing passive or active movements.

Materials & methods

Pain Assessment in Impaired Cognition

The development of the PAIC-36 (research version) is described elsewhere[7]. The Dutch version of the PAIC-36 (Appendix 2, Chapter 5) was translated following the forward–backward approach of the Guidelines for Establishing Cultural Equivalence of Instruments[12 16]. Each item is rated on a four-point Likert scale indicating the degree of presence of the item, in other words, 0) not at all; 1) slight degree; 2) moderate degree; and 3) great degree.

Setting & study population

Nursing homes within the University nursing home network South Holland (UNC-ZH), The Netherlands[17], were invited to participate in this observational study. In total, five nursing homes were included. Residents from different psychogeriatric wards were selected by the nursing staff and, after receiving an information letter, were asked to participate through their legal representative. Residents with a (clinical) diagnosis of mild to severe dementia (Reisberg global deterioration scale (GDS)-score 5–6–7) were included in the study[18]. The presence of (suspected) pain was not an inclusion or exclusion criterion. Given the high prevalence of pain in persons with dementia, it was expected that residents with and without pain would be included and that all relevant items of the PAIC could be observed. Exclusion criteria were residents with Parkinson's disease, Huntington's disease, Korsakov's syndrome, and chronic psychiatric diagnoses other than dementia-associated diagnoses. In these latter diseases, the observation of pain is more difficult and a significant number of items may not occur in these diseases. Also excluded were residents in a vegetative state or coma, as well as stroke patients with facial paralysis which hampers observation.

Observers

Registered nurses or nurse assistants with a minimum age of 18 years and at least 3 months experience as a care professional for persons with dementia performed the observations.

Procedure

During a session of ±30 min, by means of a training video, the nurses were instructed on how to fill out and practice with the PAIC. The training sessions were short because the PAIC is intended to be a measurement instrument which can reliably be used without extended training. Also, for that reason, no specific information was given about the individual items. Observer agreement of the individual items was tested during rest and movement. For example, an observation during rest could be sitting in a chair; however, it was important that the resident was not asleep or drinking/eating. An observation during movement could include a transfer or repositioning in bed (with or without help) as part of care as usual. Each resident was observed for 5–10 minutes by four different observers (Appendix 1 Scheme of observations):

- Day 1: to establish interobserver agreement the resident was independently observed by two nurses at the same time during a resting situation.
- Day 2: to establish intraobserver agreement the resident that was observed on day 1 was again observed by one of the nurses from day 1.

This same procedure was repeated on days 3 and 4 with the same resident, only this time with different observers and during movement. Different observers were used on days 3 and 4 than used on days 1 and 2 to avoid knowledge about patients' behaviours during rest previously which could influence the ratings during movement.
During the observations on day 1 and 3, one member of the research group was present to supervise the start of the observations and to address any questions. The researcher did not interfere with the rating of the PAIC.
The Medical Ethics Committee of the Leiden University Medical Centre approved this study and gave a waiver of consent. Due to the cognitive impairment of the included residents, written informed consent was obtained from the patients' legal representative. When possible, written informed consent was also obtained from the residents themselves.

Statistical analysis

Descriptive statistics were used to describe the demographic and clinical characteristics of the residents and participating nurses. Data are expressed as percentages or means with standard deviations (SDs).
First, the presence of the individual PAIC items was examined, expressed in percentages, during rest and movement. To analyze the percentage presence, in other words, prevalence of the individual items, the scores of day 1 (first observations during rest) and day 3 (first observation during movement) were dichotomized in 0 ('Not present at all') and 1 ('Present in any degree'). Missing scores were recoded into zero, in other words, not present. The prevalence of the individual items was assessed and compared between rest and

movement. Differences were analyzed using McNemar's test for dichotomous variables. The interobserver and intraobserver agreement of the individual items was assessed by examining the percentage agreement. Agreement parameters indicate how often observers who rated the same item during the same situation chose the same response category, in other words, the probability of two observers choosing the same answer[19 20]. For measurement instruments used in clinical practice, the percentage agreement is more suitable than other measures (e.g., κ) and easier for clinicians to interpret[21]. κ is a relative measure, a measure of reliability, whereas percentage agreement is an absolute measure. In clinical practice, the probability that another rater would give the same answers is of interest to healthcare workers. Therefore, percentage agreement was calculated between the observers for all four response categories and for the dichotomous categories. The four-point Likert scale was dichotomized by recoding the scores as follows: 'Not present at all' and 'Slight degree of presence'= 0, 'Moderate degree of presence' and 'Great degree of presence' = 1. A percentage agreement of ≥70% was considered high. Interobserver agreement was based on scores between observers one and two on day 1, and between observers three and four on day 3. To analyze the intraobserver agreement, scores were used between observer one on day 1 and 2, and between observer three on day 3 and 4. Separate analyses were conducted for the observations during rest and during movement. Analyses were performed with IBM SPSS Statistics version 25.0 for Windows.

Results

Characteristics of residents & observers

Residents were recruited between November 2014 and March 2015 from five different nursing homes. In total, 45 residents met the inclusion criteria and were included in this study. The mean age of the residents was 85.7 (SD 7.0) years, 80% was female, 57% was diagnosed with Alzheimer's disease and 71% was in an advanced stage of dementia (Reisberg GDS score 6–7) (Table 1). The average length of stay in the nursing home was 29.5 (SD 24.5) months.

Of the 28 observers, data on characteristics of four observers were missing (Table 1). All the observers were female; of these, about half were nursing assistants, 33% were registered nurses and 8% were nurses in training. As assessed on a 0–10 Likert scale (higher scores indicating higher level of confidence) nurses felt moderately confident (7.4, SD 2.0) to assess pain in persons with dementia. Furthermore, more than half of the nurses indicated that no pain measurement instrument was used in their organization for daily practice to assess pain in persons with dementia.

Table 1. Characteristics of the study population, residents and observer/raters

Residents (n = 45)	
Age	85.7 (SD: 7.0)
Gender	
Male	9 (20%)
Female	36 (80%)
Length of stay (months; n = 44)	29.5 (SD 24.5)
Dementia severity: GDS (n = 43)	
- GDS 5 (moderate-severe)	11 (26%)
- GDS 6 (severe)	14 (33%)
- GDS 7 (very severe)	18 (42%)
Type of dementia (n = 44)	
- Alzheimer's disease	25 (57%)
- Vascular dementia	3 (7%)
- Mixed dementia	3 (7%)
- Other	1 (2%)
- Not specifies or unknown	12 (27%)
Raters (n = 28)	**N = 4 missing**
Profession	
- Registered nurse	8 (33%)
- Nursing assistant	14 (50%)
- Nurse in training	2 (8%)
Confidence identifying pain in dementia[†]	7.4 (SD: 2.0)
Pain measurement instruments used in organization?	
- Yes	13 (54%)
- No	11 (46%)
How often do you use pain measurement instruments in daily practice?	
- Never	13 (54%)
- < 1 x month	10 (42%)
- 1-2 x month	-
- 1 x week	1 (4%)
- Almost daily	-

[†]Likert scale 0–10, with higher cores indicating a higher level of confidence.
GDS: Global deterioration scale; SD: Standard deviation.

Presence of behaviours described in the individual PAIC-36 items

Table 2 presents the proportion of the behaviour described in the different items that were present (in any degree) during rest and movement.

Facial expression

During rest, four items of the facial expression domain had low item prevalence: 'raising upper lip' (7%), 'clenched teeth' (9%), 'teary eyed' (4%) and 'looking frightened' (11%). During movement, only the items 'raising upper lip' and 'teary eyed' had low prevalence rates: both 9%. During rest, six items had a prevalence rate of ≥ 34%: 'frowning', 'empty gaze', 'seeming disinterested', 'pale face', 'looking tense', and 'looking sad'.
During movement, nine items had a prevalence rate of ≥ 34%, with the highest percentage of 60 and 62% for the items 'empty gaze' and 'looking tense'. Compared with the rest situation, the items 'narrowing eyes' (p = 0.03), 'looking tense' (p = 0.01) and 'looking frightened' (p = 0.001) were significantly more present during movement.

Body movements

During rest, three items had an item prevalence of 2%: 'resisting care', 'limping' and 'pacing'. The item 'pushing' was not present at all. The item 'pacing' was not present during movement. Furthermore, the items 'pushing'' (4%), 'guarding' (7%) and 'rubbing' (7%) also had low item prevalence. Only one item during movement had a prevalence ≥ 34: 'freezing' (44%). Additionally, compared with the rest situation, the items 'freezing' (p = 0.001) and 'resisting care' (p = 0.01) were significantly more prevalent during movement.

Vocalizations

During rest, almost all items had low item prevalence, especially the items 'using pain related words' (2%) and 'screaming' (2%). During movement only three items had a low prevalence: 'using offensive words' (2%), 'screaming' (9%) and 'crying'' (2%). The item 'sighing' had a high item prevalence, that is, 47%. Compared with the rest situation, the items 'using pain-related words' (p = 0.002), 'groaning' (p = 0.02) and 'sighing' (p = 0.004) were significantly more often present during movement.

Table 2. Presence of behaviours described in the PAIC-36 during rest and movement

PAIC item	Rest† (n = 45) Percentage of present (any degree)	Movement† (n = 45) Percentage of present (any degree)	*p*-value
Facial expressions			
Pained expression	20	40	0.06
Frowning	33	42	0.45
Narrowing eyes	18	44	**0.03**
Closing eyes	31	31	1.00
Raising upper lip	7	9	1.00
Opened mouth	22	40	0.10

Table 2. Presence of behaviours described in the PAIC-36 during rest and movement *(continued)*

PAIC item	Rest† (n = 45) Percentage of present (any degree)	Movement† (n = 45) Percentage of present (any degree)	*p*-value
Tightened lips	27	33	0.63
Clenched teeth	9	18	0.29
Empty gaze	49	60	0.36
Seeming disinterested	51	31	0.12
Pale face	42	53	0.38
Teary eyed	4	9	0,69
Looking tense	36	62	**0.01**
Looking sad	38	42	0.83
Looking frightened	11	44	**0.001**
Body movements			
Freezing	13	44	**0.001**
Curling up	13	18	0.79
Clenching hands	18	33	0.14
Resisting care	2	24	**0.01**
Pushing	0	4	0.50
Guarding	16	7	0.34
Rubbing	20	7	0.07
Limping	2	16	0.07
Restlessness	40	20	0.06
Pacing	2	0	1.00
Vocalizations			
Using offensive words	4	2	1.00
Using pain relates words	2	31	**0.002**
Repeating words	4	11	0.45
Complaining	11	18	0.58
Shouting	4	16	0.13
Mumbling	22	31	0.50
Screaming	2	9	0.38
Groaning	9	31	**0.02**
Crying	4	2	1.00
Gasping	7	16	0.29
Sighing	18	47	**0.004**

†Rest: for example, sitting in a chair; Movement: for example, a transfer or repositioning in bed (with/without help) as part of care as usual.Numbers printed bold: ≤0.05 significant.

Observer agreement

Interobserver agreement

Table 3 presents the interobserver agreement of the 36 individual PAIC items during rest and movement. For each item the percentage agreement (for a dichotomous and four-category outcome) is presented.

Facial expressions

During rest, nine items had a high percentage agreement (≥ 70%) for interobserver agreement with regard to the item being present or not: 'pained expression' (84%), 'closing eyes' (78%), 'opened mouth' (73%), 'tightened lips' (73%), 'clenched teeth' (82%), 'teary eyed' (89%), 'looking tense' (73%) and 'looking frightened' (89%). The item with the highest percentage agreement was 'raising upper lip' (91%).
The percentage agreement for the four-category outcome was ≥70% for the items 'pained expression', 'clenched teeth', 'teary eyed', 'looking frightened', and with the highest percentage agreement of 91% also for the item 'raising upper lip'.
During movement, the percentage agreement with regard to the item being present or not was ≥ 70% for the items: 'raising upper lip', ''clenched teeth', 'pale face', 'teary eyed' and 'looking frightened'. The agreement for the four-category outcome was high (both 84%) only for 'raising upper lip' and 'teary eyed'.

Body movements

During rest, all items of the body movement domain had an agreement of ≥ 70% for both four category and dichotomous outcomes except for the item 'restlessness'. This item had a percentage agreement of 64% for the item being present or not and 62% agreement for the four-category outcome. The item 'pushing' had a percentage agreement of 100% for both the dichotomous category and the four-category outcome. The agreement on the items during movement was also high. Eight items of the dichotomous category outcome and seven items of the four-category outcome had an agreement of ≥ 70%, with the highest agreement of 96% for the item 'pacing'.

Vocalizations

During rest, all 11 items of the vocalization domain had a high percentage agreement (≥ 70%) for the dichotomous category outcome. This also applied to the percentage agreement of the four-category outcome, except for the item 'mumbling' (69%).
During movement, ten items had a high percentage agreement for the dichotomous category outcome, with the highest agreement of 93% for the items 'using offensive words' and 'crying'. Only the item 'mumbling' had an agreement of 67%. For the percentage agreement of the items regarding the four-category outcome, only two items had a percentage agreement ≤ 70%: 'mumbling' (58%) and 'sighing' (60%).

Table 3. Interobserver agreement of the PAIC-36 (90 observations in 45 residents)

PAIC item	Interrater reliability			
	Rest†		Movement†	
	Percentage of agreement dichotomous ('yes'/'no')	Perentage of agreement all responses (0-3)	Percentage of agreement dichotomous ('yes'/'no')	Perentage of agreement all responses (0-3)
Facial expressions				
Pained expression	84	82	69	60
Frowning	56	53	38	29
Narrowing eyes	69	69	69	51
Closing eyes	78	69	62	56
Raising upper lip	91	91	87	84
Opened mouth	73	69	60	51
Tightened lips	73	69	69	60
Clenched teeth	82	82	76	69
Empty gaze	67	51	53	40
Seeming disinterested	69	56	64	56
Pale face	67	60	73	69
Teary eyed	89	89	87	84
Looking tense	73	67	69	47
Looking sad	69	53	56	49
Looking frightened	89	87	76	56
Body movements				
Freezing	84	84	60	44
Curling up	89	84	71	69
Clenching hands	82	76	69	60
Resisting care	98	98	78	71
Pushing	100	100	89	89
Guarding	80	78	84	82
Rubbing	82	78	91	89
Limping	96	96	76	71
Restlessness	64	62	78	73
Pacing	98	98	96	96

Table 3. Interobserver agreement of the PAIC-36 (90 observations in 45 residents) *(continued)*

PAIC item	Interrater reliability			
	Rest†		Movement†	
	Percentage of agreement dichotomous ('yes'/'no')	Perentage of agreement all responses (0-3)	Percentage of agreement dichotomous ('yes'/'no')	Perentage of agreement all responses (0-3)
Vocalizations				
Using offensive words	96	96	93	93
Using pain-related words	91	89	80	73
Repeating words	98	86	82	82
Complaining	87	84	73	71
Shouting	100	98	82	78
Mumbling	71	69	67	58
Screaming	96	96	87	84
Groaning	89	89	84	73
Crying	89	89	93	93
Gasping	89	89	84	84
Sighing	78	73	73	60

†Rest: for example, sitting in chair; Movement: for example, a transfer or repositioning in bed (with/without help) as part of care as usual. PAIC: Pain Assessment in Impaired Cognition.

Intraobserver agreement

Table 4 presents the intraobserver agreement of the individual PAIC items for both rest and movement. For each item, the percentage agreement (for a dichotomous and four-category outcome) is presented.

Facial expressions

During rest, only the item 'closing eyes' had a percentage agreement just below 70% for the dichotomous category outcome. The other 14 items had percentages ≥ 70%, with the highest percentage agreement for the item 'teary eyed' (98%). For the scores in the four-category outcome, fewer items had high percentage agreement: eight of 15 items scored ≥ 70%, with the highest score again for the item 'teary eyed' (95%). Compared with rest, only ten items scored ≥ 70% for the dichotomous category outcome during movement, with the highest percentage agreement of 85% for both 'raising upper lip' and 'teary eyed'. The item 'frowning' had the lowest percentage agreement of 55%. This also applied to the four-category outcome. Furthermore, only the items 'closing eyes', 'raising upper lip', 'clenched teeth', 'seeming disinterested' and 'teary eyed' had a percentage agreement of ≥ 70%. Overall, the percentage agreement of the items in the

dichotomous category outcome during both rest and movement were higher compared with the percentage agreement in the four-category outcome.

Body movements

During both rest and movement, almost all items (in both the dichotomous category outcome and the four-category outcome) had a high percentage agreement of ≥ 70%. The lowest percentage agreement was for the item 'restlessness' during rest (63% dichotomous category outcome; 53% four-category outcome) and for the item 'freezing' (65%) during movement (dichotomous category outcome). During rest, the items 'resisting care', 'pushing' and 'limping' had the highest percentage agreement of 98% (for both categories). During movement, the item 'pacing' had the highest percentage agreement (93%) for both categories.

Vocalizations

During rest, all vocalization items had a high percentage agreement for both the dichotomous category outcome and the four-category outcome. The items 'using offensive words' and 'screaming' had the highest agreement of 95%. During movement, only the item 'groaning' had a lower percentage agreement for the dichotomous category outcome (65%) and for the four-category outcome (55%). Also, the items 'using pain-related words' and 'complaining' had a lower percentage agreement: 63%. During movement, the item 'using offensive words' had the highest percentage agreement (95%), followed by the item 'screaming' (88%).

Table 4. Intraobserver agreement of the PAIC-36 (80 observations in 40 residents*)

PAIC item	Interrater reliability			
	Rest†		Movement†	
	Percentage of agreement dichotomous ('yes'/'no')	Percentage of agreement all responses (0-3)	Percentage of agreement dichotomous ('yes'/'no')	Percentage of agreement all responses (0-3)
Facial expressions				
Pained expression	90	78	60	50
Frowning	70	60	55	35
Narrowing eyes	70	70	63	55
Closing eyes	63	55	75	73
Raising upper lip	88	88	85	80
Opened mouth	75	70	60	50
Tightened lips	78	70	65	60
Clenched teeth	85	83	73	70
Empty gaze	70	65	73	68

Table 4. Intraobserver agreement of the PAIC-36 (80 observations in 40 residents*) *(continued)*

	Interrater reliability			
	Rest†		Movement†	
PAIC item	**Percentage of agreement dichotomous ('yes'/'no')**	**Percentage of agreement all responses (0-3)**	**Percentage of agreement dichotomous ('yes'/'no')**	**Percentage of agreement all responses (0-3)**
Facial expressions				
Seeming disinterested	78	65	73	70
Pale face	75	65	83	63
Teary eyed	98	95	85	88
Looking tense	75	68	70	53
Looking sad	83	68	70	58
Looking frightened	76	78	75	68
Body movements				
Freezing	80	80	75	65
Curling up	83	83	85	80
Clenching hands	88	85	75	70
Resisting care	98	98	83	73
Pushing	98	98	85	80
Guarding	80	80	80	75
Rubbing	83	80	90	88
Limping	98	98	73	70
Restlessness	63	53	83	75
Pacing	95	95	93	93
Vocalizations				
Using offensive words	95	95	95	95
Using pain-related words	85	85	73	63
Repeating words	90	85	83	80
Complaining	85	80	70	63
Shouting	88	88	83	78
Mumbling	80	78	85	73
Screaming	95	95	93	88
Groaning	78	78	65	55
Crying	93	93	80	80
Gasping	85	85	85	85
Sighing	80	73	85	74

†Rest: for example, sitting in chair; Movement: for example, a transfer or repositioning in bed (with/without help) as part of care as usual. *Five pairs of observations missing. PAIC: Pain Assessment in Impaired Cognition.

Discussion

This study investigated the observer agreement of the Dutch version of the 36 PAIC items. The results show that both the interobserver and intraobserver agreement of most individual items of the PAIC is good (percentage agreement ≥ 70%). This applied particularly to the items in the body movement and vocalization domains. In comparison to these domains, fewer items in the facial expression domain had good interobserver and intraobserver agreement during both observations in rest and movement.

Regarding the item prevalence of the behaviours described in the different items, seven of 36 items had high item prevalence (> 30%) in both rest and movement: 'frowning', 'closing eyes', 'empty gaze', 'seeming disinterested', 'pale face', 'looking tense', and 'looking sad'. Furthermore, eight of 36 items had a low prevalence rate (< 15%) in both rest and movement: 'raising upper lip', 'teary eyed', 'pushing', 'pacing', 'using offensive words', 'repeating words', 'screaming', and 'crying'.

Most items with a low prevalence rate belonged to the body movement and vocalization domains. The relatively high number of items with low prevalence in the body movement domain was expected; for example, during rest, there is minimal movement of the musculoskeletal system when sitting in a chair[22 23]. However, only four of 15 items of the facial expressions domain had a prevalence rate of <15%. This indicates that pain might also be present during rest, related to other causes besides movement and/or the musculoskeletal system. There may be various causes for this pain. Approximately 5% of nursing home patients with dementia have orofacial pain[24], and pain might also originate from neuropathological changes in the brain, for example, white matter lesions and atrophy, which may cause central pain, also in rest2 [25-27]. This could imply that some persons with dementia are more or less in pain all the time, even in rest. Nevertheless, it is remarkable that the items 'limping' and 'pacing' were present during rest (prevalence of 2%); this might indicate that the observers did not understand the item or that they did not score during actual/real rest.

Regarding observations during movement, the overall prevalence of the individual items was higher compared with observations during rest. This was expected since, during movement, either the resident or the nurse induced physical movement (either active or passive) as part of usual care. For example, mobilizing hips or legs often generates pain originating from the musculoskeletal system. This is a known and frequent cause of pain in elderly persons due to age-related diseases such as osteoporosis and arthritis[22 23]. Although not the topic of this paper, the difference in prevalence of items observed in rest and during movement supports construct validity of the PAIC[28].

Additionally, the latter underlines that it is important that patients with dementia should be observed during different situations/activities, in other words, rest and movement, in order to detect pain accurately. This is supported by the study of Strand et al. which shows strong evidence that specific body movements, such as 'restlessness' and 'guarding', indicate pain[29]. These movements may either be more prevalent or visible during movement or during rest.

It might be assumed that items with low prevalence rates are not informative enough for pain and, therefore, are not suitable for the measurement of pain in persons with dementia. On the other hand, items with low prevalence rates might still be informative,

but only for high pain intensities and may therefore help to encode pain intensities. Additionally, lower inter- and intraobserver agreement might also mean that interpretation of these items is difficult and/or the meaning of the item is not easily understood, making it difficult to score. For example, a study that examined the content validity of the PAIC reported that almost half of the items of the vocalization domain were not interpreted as an expression of pain, but as a symptom of dementia[12].

The present study revealed lower inter- and intraobserver agreement for the facial items compared with the body movement and vocalization domains. This might suggest that facial expressions are more difficult to observe/evaluate in a clinical setting. It has been reported that recognizing and observing facial expressions requires specific training and education[30]. Also, more variation in grading (use of the 4-category outcome) can lead to a lower percentage agreement. This could also apply to the other domains of the PAIC. Furthermore, a possible explanation for the low intraobserver agreement and even lower interobserver agreement is that nurses may not be accustomed to focus on/recognize facial expressions, especially during movement of the resident[31]. At last, facial items can be of (very) short duration and, thus, easily missed.

Regarding the use of different scoring options (dichotomous category outcome versus four-category outcome), more items had a high percentage agreement using the dichotomous category outcome compared with using the four- category outcome. However, using the four-category outcome seems more sensitive to detect (small) changes over time and to monitor treatment effect. On the other hand, filling out only 'yes' or 'no' may be easier for the observer and less time consuming. Moreover, for solely identifying pain, this is sufficient.

Strength & limitations

This was a multicenter observational study performed in five nursing homes. The inter-observer and intraobserver agreement was tested using percentage agreement, as this represents the actual agreement without adjusting for chance agreement (as does, e.g., κ)[20 21]. In clinical practice, since chance agreement cannot be disentangled from actual agreement, adjusting for this is clinically irrelevant. This is why we chose not to report κ statistics. Furthermore, reporting the percentage agreement makes it easier for clinicians to interpret the agreement of the PAIC and decide whether the PAIC is suitable for clinical practice. Additionally, observer agreement was tested in a relatively large population (n = 45) and with a large number of observations[19]. Furthermore, the observations took place in a real-life setting during situations of rest and movement, which represent usual care situations. Moreover, using multiple observers reflects a real-life setting. Additionally, the population is thought to be representative of nursing home residents with high scores on the GDS 7 (42%), indicating very severe dementia[18]. In the more severe stages of dementia, communicative abilities are generally diminished and sometimes even completely absent[32]. In these patients, an observational measurement instrument to identify pain, such as the PAIC, is indispensable.

A possible limitation of the study is that there was variation in the knowledge and/or experience of the observers. Whereas the observers felt relatively confident in identifying pain in persons with dementia (7.4, SD: 2.0), ≤ 50% had never used an observational

measurement instrument to measure pain (Table 1); this might suggest that some observers had difficulty filling out the PAIC. However, all observers received a short training at the beginning of the observations, as PAIC is intended to be used reliably and without specific extensive training. However, variation in the knowledge and experience of the observers might also be considered a strength of this study, as this represents the real-life clinical setting of a nursing home. Nevertheless, more extensive training in using observational pain measurement instruments might lead to higher reliability scores.
Furthermore, there is ongoing discussion regarding which parameter can best be used to examine the reliability of the PAIC. Percentage agreement does not adjust for possible chance agreement. Therefore, percentage agreement represents the realistic amount of observer agreement that actually exists[21]. For the PAIC, examining the percentage agreement is preferred because, besides identifying pain, the PAIC is also applied to measure changes over time, thereby monitoring treatment.

Conclusion

This study shows that the 36 items of the Dutch version of the PAIC-36 have generally good inter- and intraobserver agreement, especially for the body movement and vocalization domains. Although all items were extracted from existing and established scales, it is surprising that some items of the PAIC-36 had low percentage agreement in a clinical setting. A next step in the development and refinement of the PAIC is possible item reduction to increase the probability of successful implementation of the PAIC in daily clinical practice. The decision whether or not to include a specific item needs to be made in combination with other (psychometric) studies from more countries/cultures. Also, the reliability of the facial expression items (and the PAIC items in general) might be further improved by (interdisciplinary) education on pain in persons with dementia and the training of nursing home staff on how to use a pain measurement instrument. Education and training might increase the clinical utility and feasibility of the PAIC.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval and have followed the principles outlined in the Declaration of Helsinki for all human investigations. The Medical Ethics Committee of the Leiden University Medical Centre approved this study and gave a waiver of consent. Due to the cognitive impairment of the included residents, written informed consent was obtained from the patient's legal representative. When possible, written informed consent was also obtained from the residents themselves.

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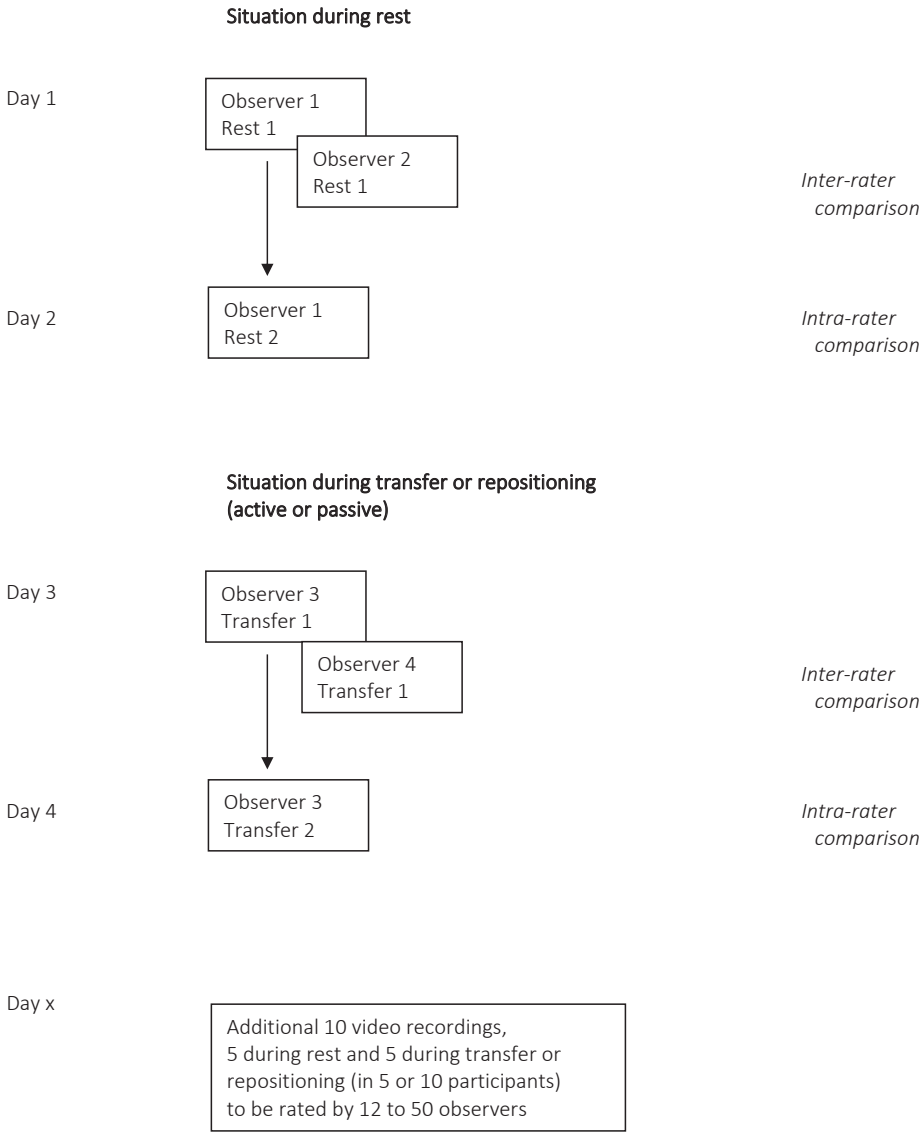
Appendix 1. Scheme of observations for each resident



CHAPTER 7

Observational pain assessment in older persons with dementia in four countries: observer agreement and factor structure of the pain assessment in impaired cognition

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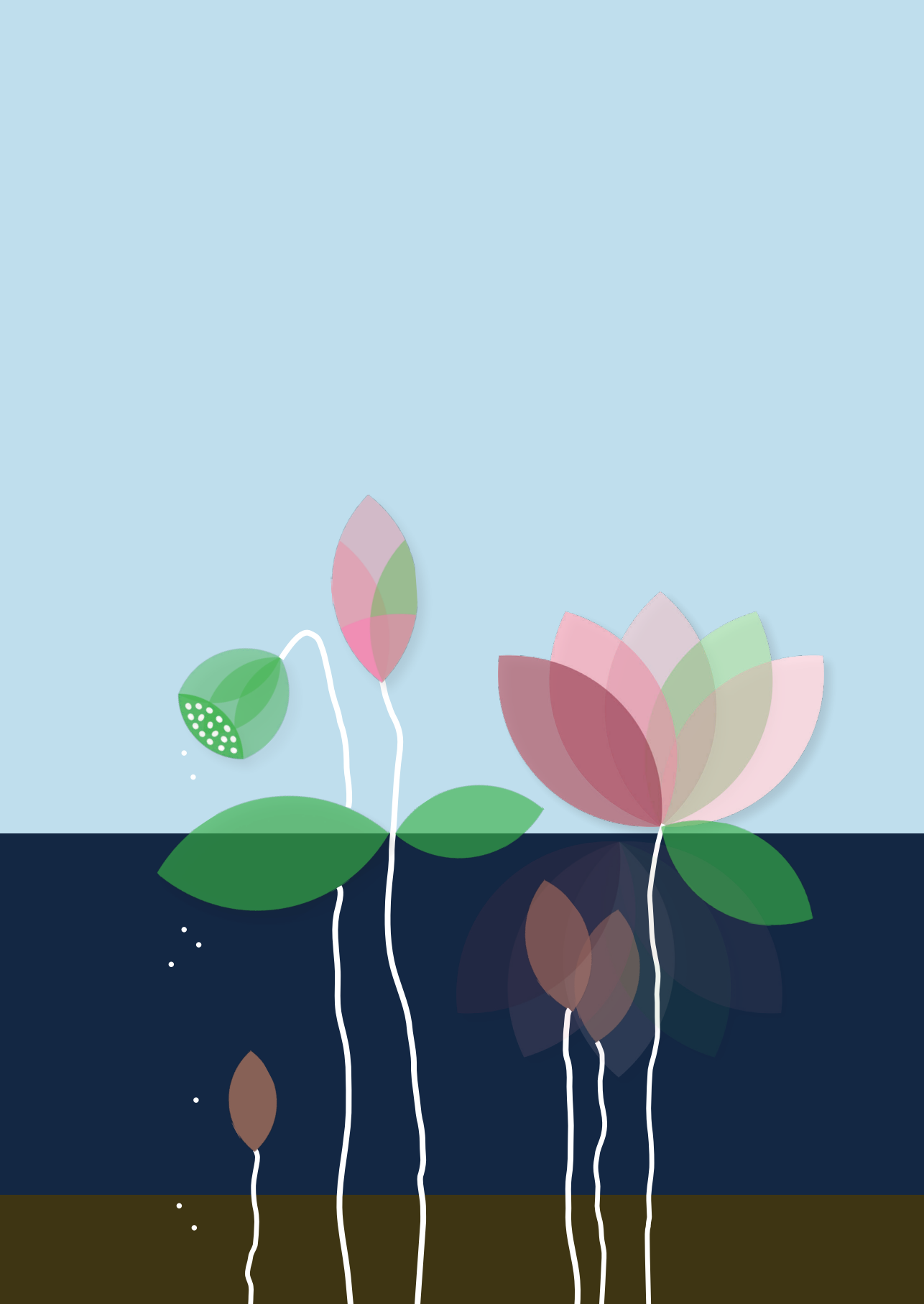
Eur J Pain. 2020 Feb;24(2):279-296. doi: 10.1002/ejp.1484a



Abstract

Background

Recognition of pain in people with dementia is challenging. Observational scales have been developed, but there is a need to harmonise and improve the assessment process. In EU initiative COST-Action TD1005, 36 promising items were selected from existing scales to be tested further. We aimed to study the observer agreement of each item, and to analyse the factor structure of the complete set.

Methods

One hundred and ninety older persons with dementia were recruited in four different countries (Italy, Serbia, Spain and The Netherlands) from different types of healthcare facilities. Patients represented a convenience sample, with no pre-selection on presence of (suspected) pain. The *Pain Assessment in Impaired Cognition* (PAIC, research version) item pool includes facial expressions of pain (15 items), body movements (10 items), and vocalizations (11 items). Participants were observed by health professionals in two situations, at rest and during movement. Intrarater and interrater reliability was analysed by percentage agreement. The factor structure was examined with principal component analysis with orthogonal rotation.

Results

Health professionals performed observations in 40 to 57 patients in each country. Intrarater and interrater agreement was generally high (≥70%). However, for some facial expression items, agreement was sometimes below 70%. Factor analyses showed a 6-component solution, which were named as follows: Vocal pain expression, Face anatomical descriptors, Protective body movements, Vocal defence, Tension, and Lack of affect.

Conclusions

Observation of PAIC items can be done reliably in healthcare settings. Observer agreement is quite promising already without extensive training.

Significance

In this international project, promising items from existing observational pain scales were identified and evaluated regarding their reliability as an alternative to pain self-report in people with dementia. Analysis on factor structure helped to understand the character of the items. Health professionals from 4 countries using 4 different European languages were able to rate items reliably. The results contributed to an informed reduction of items for a clinical observer scale (*Pain Assessment in Impaired Cognition* scale with 15 items: PAIC15).

Introduction

Recognition of pain in people with impaired cognition and communication problems is challenging because of impairment of self-report capacities [1]. International epidemiological research shows that people with dementia typically receive inadequate pain medication and experience inadequate pain management [2]. This may be because people with cognitive impairment do not reliably report when they have pain. In an effort to find an alternative to self-report, in various countries, scales have been developed that rely on observations, but they often lack sufficient psychometric evaluation. For instance, lack of a gold standard in the clinical setting (as opposed to experimental testing) hinders evaluation of validity. Also reliability and clinical utility is tested in small samples of raters in specific clinical settings, and (international) clinical implementation is hampered [3]. At this moment a considerable number of scales is available. There is a need to improve and harmonise the assessment process, as this will help in gathering comparable data and increase applicability across settings.

In the European COST Action TD-1005 "*Pain assessment in patients with impaired cognition, especially dementia*", experimental and clinical researchers together with health professionals aimed to develop a comprehensive and internationally agreed-upon pain assessment scale for older adults with impaired cognition. It was anticipated that the development of this new scale would require an iterative process, in which the loop of evaluation, adaptation and re-testing of items is followed several times [4]. The novel idea was to synthesise existing knowledge about observations of pain in older adults with dementia. For that purpose, all existing observational pain behaviour scales were identified and their items categorised in three groups: facial expressions, vocalizations, and body movements for the *research version of the Pain Assessment in Impaired Cognition* (PAIC, 36 items) [5]. In this way, we built further on the best available expertise. As such, the PAIC can be considered as a 'meta-tool'. For the final PAIC scale, further reduction of number of items was anticipated, using results from various psychometric studies to enhance usability [6].

The setting in which an observational scale will be used will vary between and even within countries [3]. The goal of the EU COST initiative was to develop a scale that can be used by a variety of health professionals in their clinical practice to rate a range of behaviours considered to be indicative of pain in people with dementia. It is important to examine items by using observations of health professionals working in a variety of real-life healthcare settings, in various European countries, as this will result in more robust findings. Specific aims of the present study were: a) to evaluate the interrater agreement and intrarater agreement of individual items and b) to study the factor structure of the PAIC item pool. Factor analysis is used to explore whether individual items can be grouped into meaningful components, for example, pain specific reactions and affective pain consequences.

Methods

Procedure

This was a multicentre, observational study in four countries covering various regions within Europe: Italy, Serbia, Spain, and The Netherlands. Each country was provided with the same study protocol, but implementation varied slightly due to different local conditions.

Health professionals performed observations among persons with dementia in everyday, real-life settings in two conditions: at rest and during movement. Observation was carried out under both conditions as it was expected that movement might induce pain. Also, some items can only be rated during movement of the whole body (e.g., pacing), while others (e.g., facial expressions) are more difficult to assess during gross movement. Examples of situations at rest include sitting in a chair or lying in bed, but excluded moments when drinking, eating, or sleeping. Situations during movement could include repositioning, thus observing a person when he/she moved or was being moved or transferred as part of his/her usual care. On day 1, all participants were seen by two observers who rated all items independently (preferably by observing the same situation together or one after the other within 10 minutes). All patients were rated a third time by one of the health care professionals on day 2. The observations at rest and during movement were on different subsequent days (the exact schedule depended on the situation and feasibility in each country; appendix 1).

Participants – Patients

For each country, participating patients were sought in the health care setting that has a high prevalence of patients with dementia, and in which future use of the PAIC was anticipated, e.g., nursing homes, geriatric hospital wards, or rehabilitation hospitals. It was a convenience sample of patients with a clinical diagnosis of dementia. Pain in any form was no inclusion or exclusion criterion. Given the high prevalence of pain in old individuals, we assumed that there would be a mix of patients with and without pain, in whom a range of items would be observed. We further assumed different levels of cognitive impairment (mild to severe dementia) in patients, and different levels of acquaintance (e.g., no previous, intermittent, or constant contact) of health care professionals with the patient. We excluded patients with Parkinson's disease, Huntington's disease, schizophrenia, Korsakov syndrome, patients in a vegetative state, coma patients and stroke patients with facial impairments that may hamper facial expressions. These groups were excluded either because observation of pain signs is more difficult (because of strong behavioural limitations), or because a substantial number of behaviours covered by the items would not occur in these groups.

Participants – observers

Depending on the care situation in each country, healthcare professionals who would likely use the new scale in the future were chosen as observers. They could be either physicians, nurses, nurse assistants or psychologists (Table 1). A brief training session of 15-30 minutes was held in each facility to inform the observers about the new assessment scale and about the type of items. The PAIC-scoring forms contained a brief written instruction on scoring. The instructions for using the PAIC were intentionally brief as we wanted to determine if the scale could be used reliably with minimal training.

Measures

The research version of the PAIC (*Pain Assessment in Impaired Cognition*) is an observational scale that includes facial expressions of pain (15 items), body movements (10 items), and vocalizations (11 items). The items were chosen following a process that included an extensive literature review of existing tools and several consultation rounds with experts- this process is described in detail elsewhere [5 6].

On the scoring form, for each item a short description of the meaning of the item was provided, for example, frowning 'lowering and drawing brows together', rubbing 'tugging or massaging affected area', shouting 'using a loud voice to express words'. Items were scored on a 4-point scale: 0 'not at all', 1 'slight degree', 2 'moderate degree', and 3 'great degree'. There was an additional column 'not scored', with the options: a 'item is not clear', b 'situation is unsuitable', c 'physical status of person not suitable for scoring', d 'other'. The text was translated and culturally adapted using a forward-backward procedure in seven European languages. For each country, the translation has been checked with a think aloud test [7 8].

Several characteristics of the rating situation, the observer and the patient were measured to describe the study sample: profession of the rater, experience in pain rating, duration of acquaintance with patient, facility (community care, institutional long term care (LTC), hospital care, hospice care), sex and age of the patient, and type of dementia (as stated in the medical chart). Severity of cognitive impairment was measured with the Reisberg Global Deterioration Scale (GDS). This scale describes seven stages of cognitive impairment, where stages 1-3 are pre-dementia stages and stages 4-7 are dementia stages [9].

Ethics and data collection

In each country, a supervising researcher coordinated the study. Ethics approval was obtained in each country, consistent with local procedures (for Italy by the Ethic Committee of Policlinico General Hospital, Bari in February 2015; for Serbia by the ethics committee of the Rehabilitation Clinic of the University of Belgrade School of Medicine 03-2212; for Spain by the Germanes Hospitalàries Hospital Sagrat Cor Martorell Medical Ethics Committee PR-2015-04; for The Netherlands: LUMC Medical Ethical Committee P14.245). Depending on local procedures, appropriate informed (proxy) consent was obtained. Each country collected and archived data on paper, and registered data in a local database. All

datasets were sent to one location in The Netherlands (to MWMdW at LUMC), to form one central research database from which data-cleaning and analyses were conducted. See also publication of Dutch results on reliability [10].

Sample size and statistical analyse

We aimed to recruit 50 patients per country, in total 200 patients from four countries, which is sufficient for factor analysis [4].

First, we examined the ratings of each individual PAIC item: the degree to which certain items were endorsed (or not) on the 4-point scale, missing items, and floor/ceiling effects of the items. In this context, a floor effect emerges when the behaviour described in an item is almost never present. The ceiling effect results from the opposite when a behaviour is almost always present. In both cases, the affected item is of limited value because it cannot indicate variance between persons. Second, reliability was analysed by percentage of agreement in scores on the 4-point scale between raters [11]. Missing scores were recoded to 0, thus assuming that items that were not scored meant that behaviour was not shown. More than 5% missing scores were discussed. For sensitivity analyses, first, percentage agreement was also calculated with dichotomized scores (0=absent; 1,2,3=present), and this was compared with percentage agreement of scores with the 4-point scale. Second, pairs of observations with missing scores were excluded, and this was compared with the percentage agreement of scores (on the 4-point scale) with missing scores recoded to 0. Percentages agreements below 70% were regarded as poor agreement.

An exploratory factor analysis was performed on the sample containing the first observation of each patient in a rest situation, and with no missing scores. We chose not to recode missing scores to 0 as this would influence the correlation between items. The rest situation was chosen as it had the largest sample size, and because situations at rest are not as diverse as situations during movement, meaning that conditions of the measurements can be better standardized. Principal component analysis (PCA) was used with orthogonal (varimax) rotation. The Kaiser-Meyer-Olkin (KMO) statistics were checked to determine the adequacy of the sample size, and also to check KMO values of individual items to be above the limit of 0.5 [12]. The final decision about the number of factors was based on Eigenvalues and scree plot, combined with interpretability of the factors.

Results

Description of setting, observers and patients

In total, 50 healthcare professionals in four countries performed observations in 190 patients, 40 - 57 patients in each country (Table 1). In Italy, observations were done in different hospitals by three physicians, one nurse assistant, and eight psychologists with various degrees of experience of using pain measurement scales in daily practice. Observers in Italy had not known the patients before (56%) or had known them for less than a month (32%). In Serbia, observations were also done in a hospital setting by two nurses and two physicians that were well trained in the use of pain measurement scales. Serbian observers had known the patients for at least 1 week (18%) and up to 6 months (45%). In Spain, observations were done in a community day-care centre and in a day-care hospital facility by two nurses and four nurse assistants who all had experience with using pain measurement scales in daily practice. Spanish observers had known 96% of the patients for several months. In The Netherlands, 14 nursing assistants and 10 registered nurses observed residents in nursing homes. Forty-six percentage of them lacked experience with using pain measurement scales in daily practice, and 42% used these scales less than once a month. The observers had known 78% of the patients for 6 months or more.

Patients were on average 74 – 86 years old. In Italy and Serbia, half were women, and in Spain and The Netherlands, more than three quarters were women. The severity of dementia varied somewhat between countries with an average GDS-score of 4.6 (moderate) to 6.1 (severe). The majority of patients had Alzheimer's disease, except for Italy where the majority had vascular dementia.

Table 1. Characteristics of study population and observers.

	Italy		Serbia		Spain		The Netherlands	
Study population	(n=57)		(n=40)		(n=48)		(n=45)	
Period of data collection	2015		Sep'14-Aug'17		Oct'15-May'17		Nov'14-Oct'15	
Setting								
Community day care	0		0		34	71%	0	
Long-term residential care	0		0		14	29%	45	100%
Hospital care	57	100%	40	100%	0		0	
Length of stay in months, mean (SD)	-		-		-		29.5	(24.5)
Age in years, mean (SD) (range)	74.4	(11.5) (33-89)	81.5	(3.9) (75-89)	77.3	(7.8) (45-92)	85.7	(7.0) (69-103)
Gender, female	28	49%	22	55%	37	77%	36	80%
Dementia severity: Reisberg GDS								
Mean score (SD) (min-max score)	4.8	(2.0) (1-9)	5.7	(0.7) (5-7)	4.6	(0.9) (3-6.5)	6.1	(0.9) (4-7)

Table 1. Characteristics of study population and observers *(continued)*.

	Italy		Serbia		Spain		The Netherlands	
Study population	(n=57)		(n=40)		(n=48)		(n=45)	
Period of data collection	2015		Sep'14-Aug'17		Oct'15-May'17		Nov'14-Oct'15	
Type of dementia								
Alzheimer's disease	5	9%	19	48%	33	67%	25	57%
Vascular dementia	29	52%	13	33%	3	6%	3	7%
Mixed dementia	6	11%	6	15%	5	10%	3	7%
Other	9	13%	0		7	15%	1	2%
Not specified or unknown	7	16%	2	5%	0		12	27%
Acquaintance first observer with client								
Do not know this client	32	56%	0	0%	0	0%	7	16%
Less than 1 week	10	18%	7	18%	0	0%	0	0%
1 week to 1 month	8	14%	18	45%	2	4%	1	2%
Months	4	7%	15	38%	18	38%	2	4%
6 months or more	3	5%	0	0%	28	58%	35	78%
Observers	(n=12)		(n=4)		(n=6)		(n=28)	
Profession								
Physician	3	25%	2	50%	0		0	
Registered nurse	0		2	50%	2	33%	8	33%
Nursing assistant	0		0		4	67%	14	50%
Nurse in training	1	8%	0		0		2	8%
Psychologist	8	67%	0		0		0	
Confidence identifying pain mean (SD)	9.1	(1.4)			8.3	(1.0)	7.4	(2.0)
(min-max score)		(6-10)				(7-10)		
Pain measurement scales used in organization, yes	10	91%	4	100%	6	100%	13	54%
How often do you use pain measurement scales in daily practice?								
Never	2	18%			0		13	54%
Less than once a month	1	9%			0		10	42%
Once or twice a month	0				2	33%	0	
Around once a week	0				1	17%	1	4%
Most days	6	55%			3	50%	0	
Every day	2	18%			0		0	

Note: Missing values for Reisberg GDS n=6 (IT 4, NL 2), type of dementia n=2 (IT 1, NL 1), observer profession n=4 (NL 4), confidence identifying pain n=8 (SB 4, NL 4), pain measurement scales in organization n=5 (IT 1, NL 4), pain measurement scales in daily practice n=9 (IT 1, SB 4, NL 4).

Description of observation

In all countries, patients were rated at rest by one pair of observers. Rest situations could be lying in bed or sitting in a chair. Except for Italy, patients were also observed during movement. Movement situations comprised a short walk, e.g., down a corridor (Serbia, Spain, The Netherlands), transfer from bed to chair or wheelchair, or repositioning in bed (Serbia, The Netherlands).
In Serbia and Spain, patients were rated by one pair of observers. In The Netherlands, the same participants were seen by two pairs of observers, a different pair of observers at rest and during movement situations. In Italy, pairs of observers were not all the same for intrarater and interrater analyses (Appendix 1).

Item scores

Table 2 gives an overview of the distribution of scores on each PAIC item for the first observation of each patient at rest. More categories were used to grade the facial expressions compared to body movements and vocalizations. Facial expressions showed no floor effects: scores 0 'not at all present' for individual items ranged between 44.2% and 89.5% of observations. For body movements and vocalizations, floor effects were acceptable: 3 out of 10 body movements and 3 out of 11 vocalizations had scores of 0 for more than 90% of observations, with the item 'using offensive words' reaching 97.4% with a score of 0. For body movements, score 3 ('great degree') was not used very often: in 6 out of 10 items <1% of observations. There were four items in facial expressions and one item in vocalizations with 0.5% or 1.1% missing scores (that is missing scores in 1 or 2 out of 190 observations). In body movements, two items showed high numbers of missing items: 'guarding' (4.2% missing) and 'limping' (5.8% missing). This was also seen in movement situations, with respectively 5.3% and 8.3% (Appendix 2). The reason mostly given was that the physical status of the patient was not suitable for scoring this item.

Table 2. Scores per item (in percentages) in first observations in rest (n=190)

	Score:	0	1	2	3
	Not rated (missing)	Not at all	Slight degree	Moderate degree	Great degree
Facial expressions					
Pained expression		72.6	14.2	12.6	0.5
Frowning	0.5	70.5	19.5	7.9	1.6
Narrowing eyes		76.8	16.8	5.8	0.5
Closing eyes		76.3	11.6	3.7	8.4
Raising upper lip		89.5	8.4	1.1	1.1
Opened mouth	0.5	77.9	15.3	4.7	1.6
Tightened lips		62.1	23.2	11.1	3.7
Clenched teeth		88.9	7.9	1.6	1.6
Empty gaze	1.1	44.2	35.8	12.1	6.8
Seeming disinterested	1.1	44.7	24.2	20.0	10.0
Pale face		57.9	21.6	18.4	2.1
Teary eyed		87.9	10.0	1.6	0.5
Looking tense		63.7	22.6	12.6	1.1
Looking sad		45.8	37.4	14.2	2.6
Looking frightened		84.2	10.5	4.7	0.5
Body movements					
Freezing		80.0	14.7	4.2	1.1
Curling up		83.7	14.2	1.6	0.5
Clenching hands		78.4	16.8	3.7	1.1
Resisting care		85.8	11.6	2.1	0.5
Pushing		94.7	3.7	1.6	0.0
Guarding	4.2	82.6	10.0	2.6	0.5
Rubbing		89.5	7.9	2.6	0.0
Limping	5.8	90.0	3.2	0.5	0.5
Restlessness		76.8	15.8	4.7	2.6
Pacing		96.8	2.1	1.1	0.0
Vocalizations					
Using offensive words		97.4	1.1	1.6	0.0
Using pain related words		85.8	10.0	3.2	1.1
Repeating words		85.8	11.1	2.6	0.5
Complaining		80.0	15.3	2.1	2.6
Shouting		94.7	3.7	.5	1.1
Mumbling		84.2	12.1	2.6	1.1
Screaming	0.5	95.3	2.1	1.6	0.5
Groaning		81.1	14.7	2.6	1.6
Crying		87.4	8.4	4.2	0.0
Gasping		84.7	13.2	2.1	0.0
Sighing		74.2	20.0	4.7	1.1

Observer agreement of individual items

In both rest and movement situations, there were items of facial expressions with low agreement between observers with percentages below 70 (Table 3), especially in The Netherlands. Five items showed low interrater agreement in three or four countries: 'looking sad' (four countries), 'tightened lips', 'empty gaze', 'seeming disinterested', and 'looking tense'. In The Netherlands, facial items also showed low intrarater agreement for the same observers in two consecutive days (Table 4).

Body movement items generally showed good reliability for both interrater agreement and intrarater agreement, with 7 out of 10 items showing percentages of 70 or higher for all countries. The items 'freezing' and 'clenching hands' showed low interrater agreement in movement in The Netherlands and low intrarater agreement at rest in Spain. 'Restlessness' showed low intrarater and interrater agreement in The Netherlands. Note that for the items 'guarding' and 'limping', missing pairs of observations were above 5%. Sensitivity analyses on observations without pairs of observations that included missing scores showed that percentages agreement were 0-2% lower.

Vocalization items showed good reliability with a few exceptions, for example, for interrater agreement in Serbia at rest for the items 'groaning', 'gasping' and 'sighing'.

In a sensitivity analysis, percentage agreement was analysed after dichotomization of scores, indicating that pain-related behaviours were either present (scores 1 or higher) or absent (scores 0 or missing). As expected, compared to percentages agreement using scores on the 4-point scale, this resulted in higher intrarater and interrater agreement. For Italy and Serbia, all interrater agreement improved over 70% (Appendix 3 and 4).

Table 3. Interrater agreement in percentages.

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement	(n=39)	(n=40)	(n=40)	(n=48)	(n=48)	(n=45)	(n=45)	(n=172)	(n=133)
Facial expressions									
Pained expression	84	90	95	96	79	82	60	88	77
Frowning	85	93	93	81	77	53	29	77	65
Narrowing eyes	87	93	90	81	90	69	51	82	77
Closing eyes	85	95	93	56	90	69	56	75	79
Raising upper lip	90	98	98	98	90	91	84	94	90
Opened mouth	74	93	100	94	85	69	51	83	78
Tightened lips	77	63	73	50	52	69	60	64	61
Clenched teeth	87	83	95	83	83	82	69	84	82
Empty gaze	85	48	68	67	77	51	40	62	62
Seeming disinterested	80	48	68	46	65	56	56	56	62
Pale face	72	93	100	83	90	60	69	77	86
Teary eyed	77	85	88	98	100	89	84	88	91
Looking tense	77	85	93	52	54	67	47	69	63
Looking sad	67	68	78	52	71	53	49	59	65
Looking frightened	87	75	88	83	92	87	56	83	78
Body movements									
Freezing	100	80	68	73	81	84	44	84	65
Curling up	100	78	88	98	100	84	69	90	86
Clenching hands	92	83	90	79	81	76	60	82	77

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement	(n=39)	(n=40)	(n=40)	(n=48)	(n=48)	(n=45)	(n=45)	(n=172)	(n=133)
Body movements									
Resisting care	95	70	73	96	98	98	71	90	81
Pushing	95	95	90	100	100	100	89	98	93
Guarding #	95	98	98	96	98	78	82	91	93
Rubbing	90	100	100	100	98	78	89	92	96
Limping #	100	98	100	98	81	96	71	98	84
Restlessness	100	98	100	81	94	62	73	84	89
Pacing	92	98	95	98	90	98	96	97	93
Vocalizations									
Using offensive words	100	98	98	98	98	96	93	98	96
Using pain related words	92	73	70	100	96	89	73	89	81
Repeating words	95	85	83	94	98	96	82	92	88
Complaining	95	88	93	85	90	84	71	88	84
Shouting	97	98	98	96	94	98	78	97	90
Mumbling	95	83	93	98	92	69	58	86	81
Screaming	95	93	98	98	98	96	84	95	93
Groaning	90	65	85	98	92	89	73	86	84
Crying	95	70	75	98	100	89	93	88	90
Gasping	95	65	83	90	88	89	84	85	85
Sighing	90	68	85	79	81	73	60	77	75

Note: % Agreement with for missing score =0, percentage ≥ 70% in blue.
#Missing pairs of observations for guarding in rest 4.1% and in movement 5.3%; for limping in rest 6.4% and in movement 8.3%.

Table 4. Interrater agreement in percentages.

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement	(n=46)	(n=40)	(n=39)	(n=48)	(n=48)	(n=40)	(n=40)	(n=174)	(n=127)
Facial expressions									
Pained expression	87	98	90	98	90	78	50	90	77
Frowning	91	100	95	75	79	60	35	82	70
Narrowing eyes	85	100	95	88	92	70	55	86	81
Closing eyes	87	98	95	71	96	55	73	78	88
Raising upper lip	94	100	100	98	85	88	80	95	88
Opened mouth	89	90	95	96	79	70	50	87	75
Tightened lips	91	83	87	73	73	70	60	79	73
Clenched teeth	94	93	100	96	88	83	70	91	86
Empty gaze	85	70	77	58	83	65	68	70	76
Seeming disinterested	80	70	74	75	96	65	70	73	81
Pale face	85	93	97	100	100	65	63	86	87
Teary eyed	87	83	87	96	98	95	85	90	91
Looking tense	89	90	97	65	75	68	53	78	75
Looking sad	87	73	77	71	75	68	58	75	70
Looking frightened	78	83	92	85	90	78	68	81	84
Body movements									
Freezing	96	95	74	69	75	80	65	85	72
Curling up	91	85	85	100	100	83	80	90	89
Clenching hands	87	85	97	69	92	85	70	81	87
Resisting care	85	90	77	100	98	98	73	93	84

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement	(n=46)	(n=40)	(n=39)	(n=48)	(n=48)	(n=40)	(n=40)	(n=174)	(n=127)
Body movements									
Pushing	87	93	100	100	100	98	80	94	94
Guarding #	89	98	97	96	98	80	75	91	91
Rubbing	96	98	97	100	100	80	88	94	95
Limping #	96	98	100	100	88	98	70	98	86
Restlessness	89	98	100	79	90	53	75	80	88
Pacing	96	95	97	98	96	95	93	96	95
Vocalizations									
Using offensive words	98	95	97	100	100	95	95	97	98
Using pain related words	94	88	80	100	92	85	63	92	79
Repeating words	96	88	87	98	98	85	80	92	89
Complaining	85	88	97	98	96	80	63	88	86
Shouting	94	100	100	98	100	88	78	95	93
Mumbling	85	88	90	96	90	78	73	87	84
Screaming	98	93	97	100	98	95	88	97	95
Groaning	83	78	82	98	90	78	55	85	76
Crying	96	90	85	100	98	93	80	95	88
Gasping	85	83	82	92	92	85	85	86	87
Sighing	89	83	87	81	75	73	75	82	79

Note: % agreement with for missing score =0, Percentage ≥ 70% in blue.
Missing pairs of observations for guarding in rest 4.0% and in movement 5.5%; for limping in rest 6.3% and in movement 8.7%

Factor analyses

Exploratory factor analyses were performed to explore whether individual items could be grouped into underlying components. This was done in 172 observations, the first observation at rest for each patient. For 18 of the 190 patients, observations were left out due to missing scores.

First, checks were performed to look whether all items could be included in the analysis. A visual check of the correlation matrix showed highest correlation between face (facial expression) item 1 'pained expression' and face item 3 'narrowing eyes' (0.72), and low correlations (majority <0.3 with all other items) for face item 4 'closing eyes', face item 6 'opening mouth', face item 8 'clenched teeth', bm (body movement) item 1 'freezing', bm item 9 'restlessness', bm item 10 'pacing', and voc (vocalization) item 1 'using offensive words'. KMO values of individual items were mostly above 0.7 ('good' for 25 items) or between 0.5-0.7 ('mediocre' for 10 items, with face item 4 'closing eyes' 0.58, bm item 10 'pacing' 0.54, and voc item 1 'using offensive words' 0.58), and below 0.5 for one item (0.48 for face item 8 'clenched teeth'). The four items with KMO values below 0.6 were removed [12] and we also excluded the two items with floor effects of <95% with scores 0 (bm item 10 'pacing' and voc item 1 'using offensive words').

Factor analyses was performed on the remaining 32 items. A KMO statistic of 0.830 confirmed that the sample size was adequate. Correlations between items were sufficiently large, according to Bartlett's test of sphericity (Chi square=3,372 (*df* 496), $p<0.001$). Eigenvalues were >1 for eight components. Visual inspection of the scree plot showed that six components should be retained. Analyses were rerun with this solution enforced on the data. Table 5 shows the factor loadings of the components after rotation. The six components explained 62.6% of the variance.

After inspection of factor loadings, we named the components as follows: 'Vocal pain expression' with seven vocalization items such as sighing, using pain related words, and gasping; 'Face anatomical descriptors' with highest factor loadings on narrowing eyes, teary eyed, and pained expression; 'Protective body movements' with pushing, resisting care, and guarding; 'Vocal defence' with items shouting and screaming; 'Tension' with items tightening lips, looking sad, looking tense, and freezing; and 'Lack of affect' with empty gaze and seeming disinterested. Note that although the item 'curling up' is grouped under component 1, it also has a high loading on component 3 'Protective body movements' (Table 5).

Table 5. Rotated Component Matrix from factor analysis on 32 PAIC items# in 172 observations in rest. Factor loading above 0.5 appear in bold and coloured cell.

PAIC items		Component					
		1	2	3	4	5	6
		Vocal pain expression	Face anatomical descriptors	Protective body movements	Vocal defence	Tension	Lack of affect
F1- pained expression	V11- sighing	**0.71**	0.18	0.08	0.05	0.30	0.00
F2- frowning	V2- using pain related words	**0.69**	0.19	0.14	0.44	0.15	0.04
F3- narrowing eyes	V10- gasping	**0.64**	0.41	0.04	0.11	0.10	0.05
F5 – raising upper lip	V8- groaning	**0.63**	0.23	-0.06	0.33	-0.02	0.24
F6- opening mouth	V6- mumbling'	**0.62**	0.08	0.34	0.47	0.04	0.04
F7- tightening lips	V3- repeating words	**0.61**	0.16	0.33	0.07	-0.01	0.13
F9- empty gaze	V4- complaining	**0.60**	0.30	0.08	0.32	-0.15	0.24
F10- seeming disinterested	BM7- rubbing	**0.58**	-0.14	0.29	0.09	0.20	0.10
F11- pale face	BM8- limping	**0.53**	0.09	0.06	-0.17	0.20	-0.01
F12- teary eyed	F3- narrowing eyes	0.20	**0.76**	0.17	0.12	0.19	0,11
F13- looking tense	F12- teary eyed	0.14	**0.66**	0.04	0.08	0.02	-0.03
F14- looking sad	F1 – pained expression	0.38	**0.64**	0.13	0.10	0.20	0.20
F15- looking frightened	F5 – raising upper lip	0.08	**0.57**	0.29	0.42	0.02	-0.02
BM1- freezing	V9- crying	0.43	**0.55**	0.37	0.18	0.14	0.05
BM2- curling up	F2- frowning	0.25	0.48	0.37	0.18	0.35	0.16
BM3- clenching hands	BM5- pushing	0.01	0.18	**0.75**	0.32	0.11	0.11
BM4- resisting care	BM4- resisting care	0.36	0.14	**0.74**	0.06	0.01	0.12

		Component					
		1	2	3	4	5	6
PAIC items		**Vocal pain expression**	**Face anatomical descriptors**	**Protective body movements**	**Vocal defence**	**Tension**	**Lack of affect**
BM5- pushing	BM6- guarding	0.35	0.08	**0.73**	0.00	0.02	0.08
BM6- guarding	F15- looking frightened	0.01	0.32	**0.56**	0.22	0.35	0.16
BM7- rubbing	BM2- curling up	**0.63**	0.24	**0.54**	-0.12	0.12	0.11
BM8- limping	V5- shouting	0.21	0.18	0.02	**0.81**	0.08	-0.04
BM9- restlessness	V7- screaming	0.08	0.26	0.07	**0.76**	0.00	-0.12
V2- using pain related words	BM9- restlessness	0.14	-0.16	0.24	**0.56**	0.24	0.22
V3- repeating words	F6- opening mouth	-0.01	0.20	0.16	**0.51**	-0.25	0.41
V4- complaining	F7- tightening lips	0.10	-0.02	0.12	0.10	**0.78**	0.04
V5- shouting	F14- looking sad	0.06	0.39	-0.06	-0.01	**0.65**	0.24
V6- mumbling'	F13- looking tense	0.17	0.23	0.23	0.30	**0.65**	0.12
V7- screaming	BM1- freezing	0.15	0.04	-0.01	-0.16	**0.63**	0.04
V8- groaning	BM3- clenching hands	0.42	0.17	0.22	0.21	0.42	0.07
V9- crying	F9- empty gaze	0.06	-0.03	0.14	0.04	0.11	**0.84**
V10- gasping	F10- seeming disinterested	0.12	-0.02	0.11	0.05	0.18	**0.83**
V11- sighing	F11- pale face	0.19	0.33	0.08	-0.08	0.09	**0.65**

Abbreviations: F = Facial expressions, in blue; BM = body movements, in green; V = vocalizations, in pink. # Items F4 closing eyes, F8 clenched teeth, BM10 pacing, VOC1 using offensive words, are excluded from the analysis.

Discussion and conclusions

Recognition of pain in persons with dementia might improve when observational scales are used in daily practice. This is the first study in a European setting to investigate the observer agreement of a large pool of behavioural pain items assembled in the PAIC scale (research version), derived from widely recognized observation scales. For items based on body movements and vocalizations, reliability was generally good. For a number of facial expression items though, agreement between observers was below 70%. This was the case for the items 'looking sad', 'tightened lips', 'empty gaze', 'seeming disinterested' and 'looking tense'. This was seen both in observations at rest and in movement. Poor agreement was especially found in The Netherlands, where the group of observers was large, and experience and education in use of observation scales was low. Facial responses are often quite subtle and fleeting and thus, observers might have had more difficulty noticing them during observation without extensive training. At the same time, it has to be considered that the face items proved to be especially valuable in grading the pain because they were almost free of floor effects, and a high variance of different categories were used to describe the behaviour. This favourable use of more categories for behavioural description by the observer, however, leads to a reduction of observer agreement.

There is strong evidence in the research literature that facial responses are valid for measuring pain and therefore these items are important in observational scales [13]. This suggests that training is probably necessary for the rating of items, especially in grading pain with use of several categories of severity. The need for training was also mentioned by healthcare professionals in a survey across Europe[14] and is planned for the short version of the PAIC scale. [6] For the details of PAIC15 and the associated e-training see: https://paic15.com/nl/start-nl/.

Factor analyses found that individual items could be grouped into six underlying components (Table 5). In the first component, 'vocal pain expression', the majority of vocal items were grouped together. The third group, 'protective body movements', contained many (four out of nine) of the body movement items. Then, we found a factor 'vocal defence', with two vocal items, one body movement, and one face item. The face items were grouped under three components, which we named 'face anatomical descriptors', 'tension', and 'lack of affect'. Lautenbacher et al [15] performed a factor analyses on face items only and found two quite similar components, that is, 'anatomical descriptors' and 'lack of affect', and we adopted the same names. The most important difference between that study and the present study was that the three face items grouping together in the component 'tension' fell in three different components: tightened lips fell in their component 'anatomical descriptors', looking sad into 'lack of affect' and looking tense into 'arousal'. Thus, these factors, which could not be replicated, may be unstable.

Zwakhalen et al. [16] looked at the factor structure of the 24-item PACSLAC-D and found three components. They suggest that some items are more universal pain cues for various target groups, such as facial expressions, while other items are more social-emotional cues, such as mood, aggression and agitation, which may be more specific for patients with dementia. From that perspective, our factors 1 ('vocal pain expression')

and 2 ('face anatomical descriptors') might reflect pain in general, and are the most specific expressions of pain. The body movements that we found in component 1 might also be more universal pain cues compared to body movement items in component 3 ('protective body movements'). These items might be directly or indirectly related to dementia, when the care situation or how people are approached induces protective behaviour. Furthermore, the component 'lack of affect' might also be more specific to dementia itself. This is in line with findings from interviews with health professionals in The Netherlands when studying construct validity [8]. Further validity studies are needed to resolve which items reflect pain in general, pain in dementia or other forms of distress in dementia.

A strength of this study is that it took place in four countries using four different European languages. In this way, it would reflect use of the scale in future daily care situations and patient populations across different cultures. Thus, the development of the PAIC has been a truly international project.

A limitation is that some countries had deviated slightly from the European protocol, with regards to the scheme and number of observations. For example, in The Netherlands two different pairs of observers were involved for each patient, and in Italy observations were only performed at rest and not all patients were observed simultaneously for interrater agreement. This makes comparison somewhat challenging. On the other hand, we planned in advance that the study should be performed in prevalent real-life healthcare conditions in participating countries. This is important, because assessment in daily practice is generally performed whilst providing nursing care [14].

Furthermore, we were most interested in aggregated data, not comparison of data between countries.

To maximize the number of observations to be analysed, we chose to recode missing scores to 0 for the analyses of interrater and intrarater agreement, as if behaviours were not shown. This might not be the case, and percentages present might thus be estimated too low. Another point is that for items that occur rarely, the level of agreement might give a false impression of good reliability. This is especially the case in the sensitivity analysis, where we dichotomized scores. We chose to perform the factor analyses on observations at rest, because we had less observations in movement and the rest condition was more standardized among countries. However, it is possible that different findings would emerge for the test items if we had done the analysis of the items during movement.

This study focussed on scoring and observer agreement of individual items. For intrarater agreement, observations on consecutive days were chosen rather than video recordings. As the observed construct (i.e., observed pain behaviour) is not stable, this might have negatively influenced observer agreement. The high agreement rates, which was achieved under these unfavourable conditions, show that it does not matter whether the patient is observed on one day or the next.

It should be noted that some observational scales score individual items (e.g., PACSLAC-II), some combine items in the response options (e.g., PAINAD), and some score overarching domains (e.g., Abbey Pain Scale and MOBID-2) with or without extensive listing of possible items. (Examples of the tools/forms can be found on internet, for PACLSAC-II, PAINAD, and MOBID-2 on URL: https://geriatricpain.org/assessment/pain-behavior-tool-critique/

list-nonverbal-pain-behavior-tools-2019 and for Abbey pain scale on URL: https://www.apsoc.org.au/PDF/Publications/Abbey_Pain_Scale.pdf (accessed August 6th 2019)). In the latter, pre-existing assumptions (without education) might play a large role in scoring and as such affect the reliability of the scale. Thus, for the PAIC we decided to score individual items. These differences make comparison of former results with the present study difficult. Lichtner et al. [3] reviewed the psychometric properties of observational pain scales, including their reliability. Scale sum-scores and not scores on individual items have been studied: overall, the majority of the assessed tools had moderate to good inter-rater reliability (but limitations in sample sizes) and moderate to good temporal stability.

What are the implications of this study? The EU-COST Action working group set out to study individual items for an observational scale, PAIC. This scale was designed as a meta-tool, systematically looking for and extracting the best items in existing observational scales for pain assessment in dementia [5]. This idea was recently echoed by a US-American research group following a similar line of methodological reasoning [17]. Together with results from other psychometric studies, results of the present study will be used in the item reduction process by means of a Delphi procedure, to form the final PAIC-scale [6]. This is also necessary for feasibility of the measurement scale in daily practice. Training, which has already been planned for the short version of the PAIC scale (PAIC15 [6]) should not only focus on the use of assessment tools but also on the interpretation of the results [14]. For this, further research on total scores will be necessary, for example, how can item scores best be summed and what are the implications of certain (changes in) scores. As individuals and professionals are challenged to understand their role in the dynamic interplay among biological, psychological, and social determinants of pain, training even might embrace this broader context [18]. Ultimately, training should focus on how to incorporate assessments into daily practice when use of observational scale is intended to improve pain management [2 19 20].

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Author contributions

Substantial contributions to conception and design: MdW, AHvD, RdV, TF, AL, BM, WPA. Acquisition of data: MdW, AHvD, LG-L, LK, MdT.
Analysis and interpretation of the data: MdW, AHvD, RdV, LG-L, LK, MdT, MK, SL, FL, BM, JS, WPA. MdW made the first draft, and all authors critially revised the manuscript. All authors approved the final version of the manuscript.

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Conflict of interest disclosures

No conflict of interest was declared.

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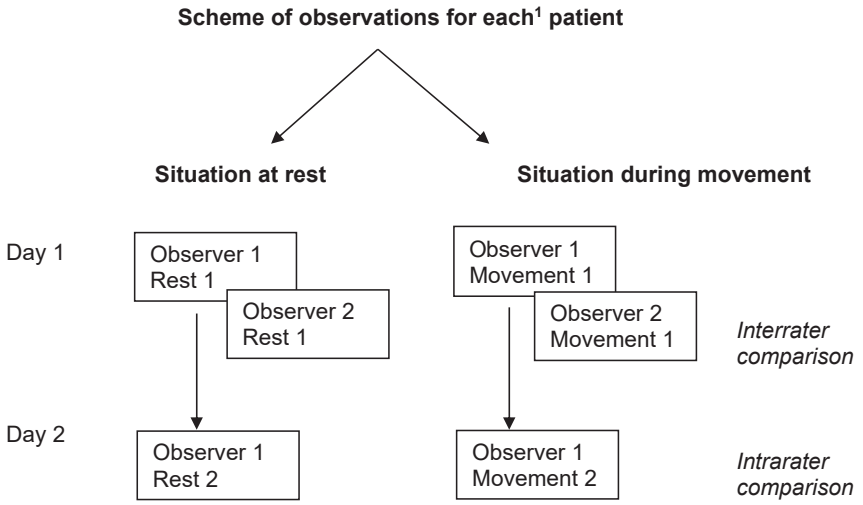
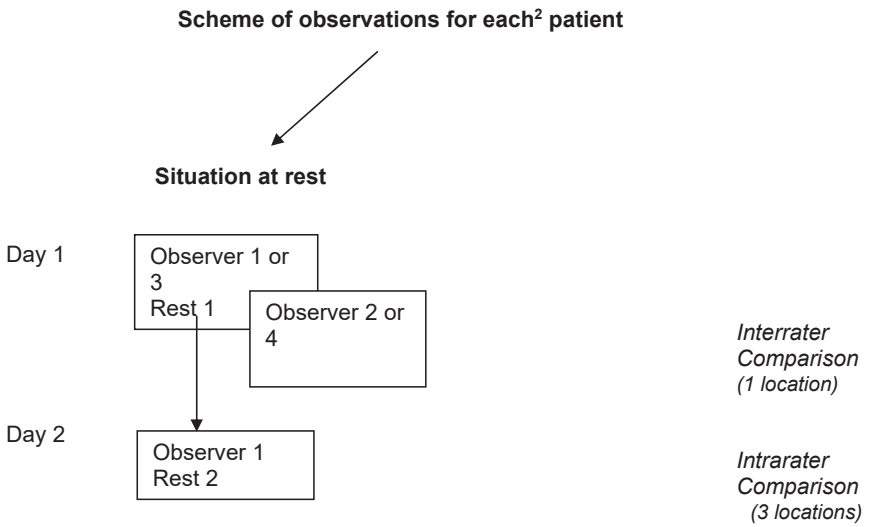
Appendix 1: scheme of observations (version A, B, and C).

Version A (Serbia, Spain)



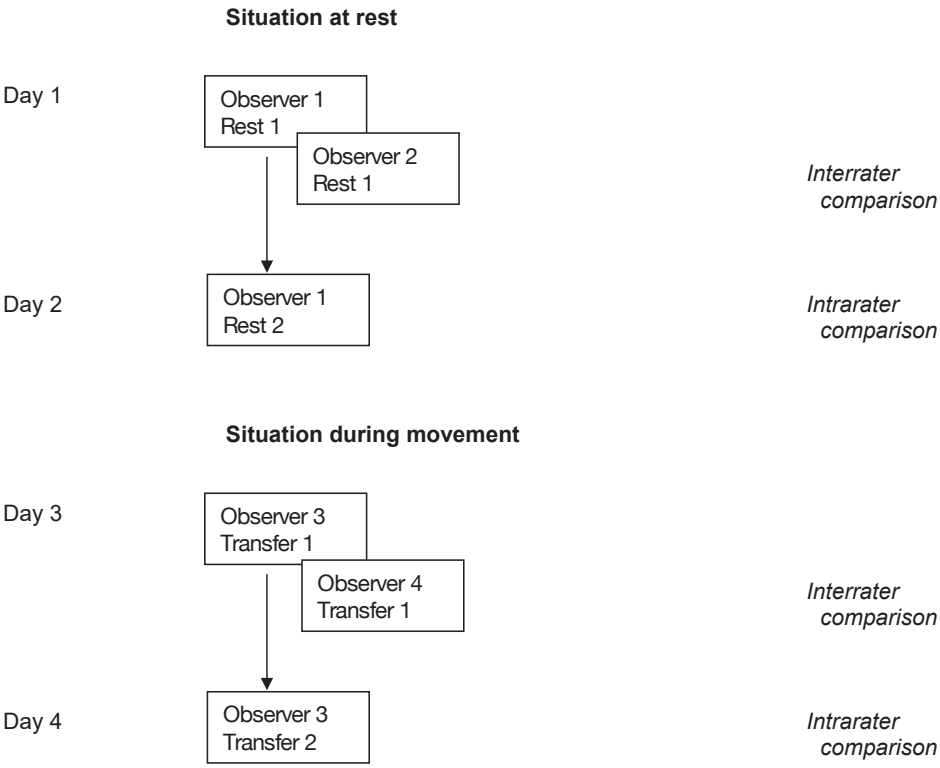
Version B (Italy)



[1] For 1 out of 40 patients in Serbia, observation on day 2 during movement was missing.
[2] Of 57 patients in Italy, 46 were observed twice by the same rater (intrarater comparison), and 39 patients were observed by two observers (interrater comparison).

Version C (The Netherlands)

Scheme of observations for each[3] patient



[3] For 5 out of 45 patients in The Netherlands observations were missing on day 2 and day 4.

Appendix 2. Scores per item (in %) in first observations in movement (n=133).

	Score:	0	1	2	3
	Missing	Not at all	Slight degree	Moderate degree	Great degree
Facial expressions					
Pained expression		68.4	16.5	12.8	2.3
Frowning		66.9	22.6	8.3	2.3
Narrowing eyes		79.7	14.3	4.5	1.5
Closing eyes		86.5	9.8	3.0	0.8
Raising upper lip		90.2	9.0	0.8	0.0
Opened mouth		78.9	13.5	6.0	1.5
Tightened lips		57.1	25.6	14.3	3.0
Clenched teeth		83.5	15.0	1.5	0.0
Empty gaze		54.9	24.1	15.8	5.3
Seeming disinterested		60.2	16.5	18.0	5.3
Pale face		57.1	24.1	15.0	3.8
Teary eyed		88.0	11.3	0.0	0.8
Looking tense		55.6	37.6	6.0	0.8
Looking sad		58.6	23.3	18.0	0.0
Looking frightened		66.2	25.6	6.8	0.5
Body movements					
Freezing		63.9	25.6	7.5	3.0
Curling up		82.7	11.3	5.3	0.8
Clenching hands		75.2	17.3	4.5	3.0
Resisting care		68.4	21.1	7.5	3.0
Pushing		92.5	4.5	1.5	1.5
Guarding	5.3	85.7	8.3	0.8	0.0
Rubbing		95.5	3.8	0.8	0.0
Limping	8.3	72.9	12.8	6.0	0.0
Restlessness		89.5	6.8	3.0	0.8
Pacing		94.7	4.5	0.8	0.0
Vocalizations					
Using offensive words		95.5	3.0	0.8	0.8
Using pain relates words		72.2	18.8	6.8	2.3
Repeating words		85.7	9.8	4.5	0.0
Complaining		79.7	13.5	5.3	1.5
Shouting		90.2	4.5	3.0	2.3
Mumbling		78.9	14.3	4.5	2.3
Screaming	0.8	89.5	6.0	1.5	2.3
Groaning		68.4	20.3	8.3	3.0
Crying		82.7	9.0	7.5	0.8
Gasping		83.5	14.3	2.3	0.0
Sighing		65.4	22.6	11.3	0.8

Appendix 3. Intrarater agreement, percentages for dichotomized scores.

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement after dichotomization	(n=46)	(n=40)	(n=39)	(n=48)	(n=48)	(n=40)	(n=40)	(n=174)	(n=127)
Facial expressions									
Pained expression	94	100	100	98	90	90	60	95	84
Frowning	96	100	100	75	79	70	55	85	78
Narrowing eyes	89	100	100	89	92	70	63	87	85
Closing eyes	91	98	97	81	96	63	75	83	90
Raising upper lip	94	100	100	98	85	88	85	95	90
Opened mouth	91	93	100	96	79	75	60	89	80
Tightened lips	94	90	97	81	85	78	65	86	83
Clenched teeth	94	93	100	93	90	85	73	92	87
Empty gaze	96	95	100	65	85	70	73	81	86
Seeming disinterested	96	100	100	79	100	78	73	88	91
Pale face	91	100	100	100	100	75	83	92	95
Teary eyed	89	85	90	96	98	98	85	92	91
Looking tense	96	93	100	75	83	75	70	85	84
Looking sad	91	90	92	88	79	83	70	88	80
Looking frightened	91	85	95	88	90	78	78	86	87
Body movements									
Freezing	100	95	97	79	75	83	75	89	82
Curling up	100	88	100	100	100	83	85	83	95
Clenching hands	94	95	100	69	92	88	75	86	89
Resisting care	91	90	100	100	98	98	83	95	94

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement after dichotomization	(n=46)	(n=40)	(n=39)	(n=48)	(n=48)	(n=40)	(n=40)	(n=174)	(n=127)
Pushing	91	98	100	100	200	98	85	97	95
Body movements									
Guarding #	89	98	100	96	98	80	80	91	93
Rubbing	96	100	100	100	100	83	90	95	97
Limping #	96	100	100	100	92	98	73	98	88
Restlessness	91	98	100	81	90	63	83	83	86
Pacing	96	95	97	98	96	95	93	96	95
Vocalizations									
Using offensive words	100	95	97	100	100	95	95	98	98
Using pain relates words	96	93	100	100	94	85	73	94	89
Repeating words	100	95	100	98	98	90	83	96	94
Complaining	89	90	100	98	96	85	70	91	89
Shouting	96	100	100	98	100	88	83	95	95
Mumbling	94	90	100	96	90	80	85	90	91
Screaming	100	93	97	100	98	95	93	97	96
Groaning	87	80	95	98	90	78	65	86	84
Crying	96	90	100	100	98	93	80	95	93
Gasping	89	83	97	92	92	85	85	87	91
Sighing	91	88	100	81	75	80	85	85	86

Note: % agreement for scores after dichotomization to not present (0) or present (1-3), for missings score=0, percentage ≥ 70% in blue.
missing pairs of observations for guarding in rest 4.0% and in transfer 5.5%; for limping in rest 6.3% and in transfer 8.7%

Appendix 4. Interrater agreement, percentages for dichotomized scores.

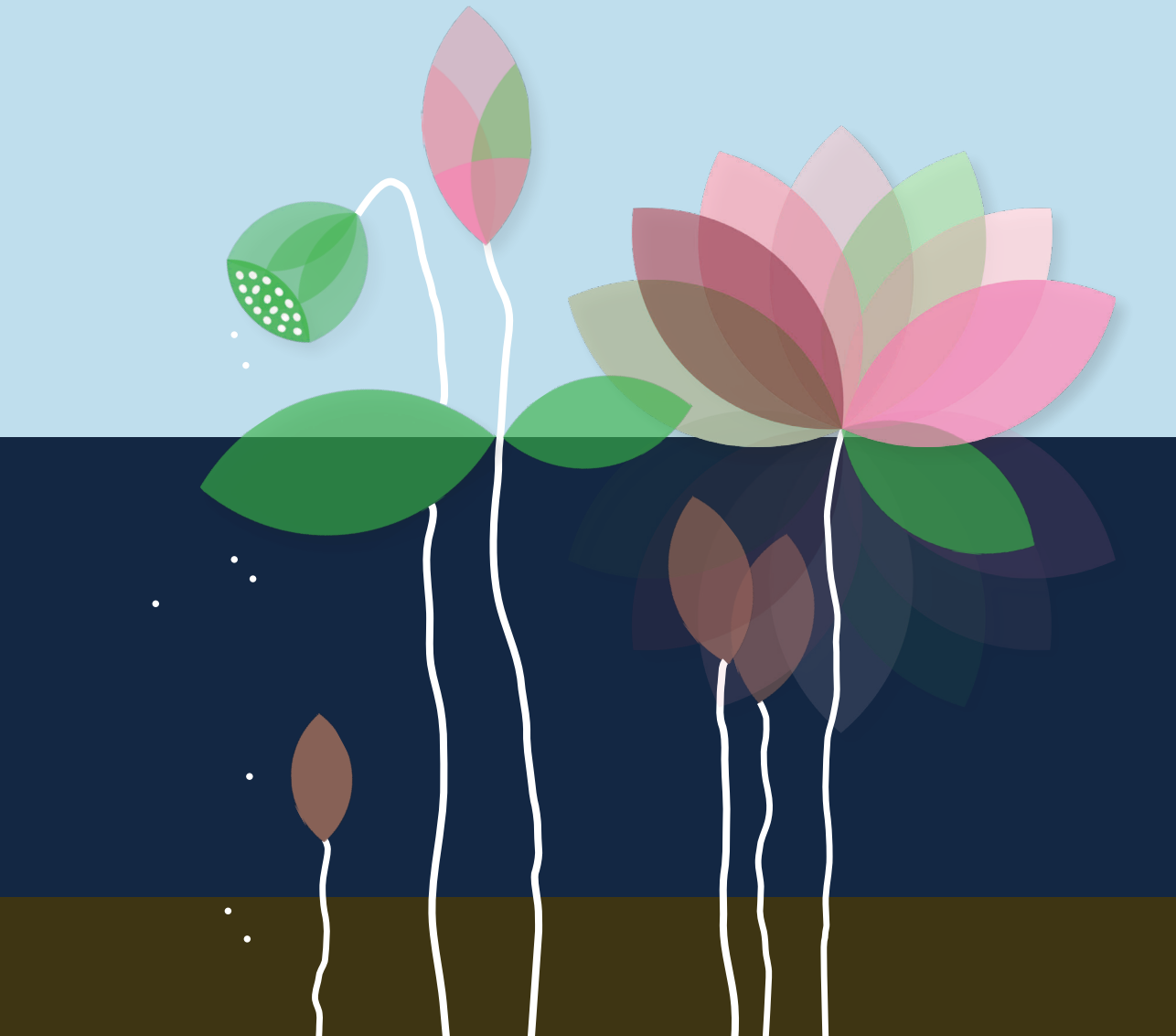
	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement after dichotomization	(n=39)	(n=40)	(n=40)	(n=48)	(n=48)	(n=45)	(n=45)	(n=172)	(n=133)
Facial expressions									
Pained expression	90	98	100	96	83	84	69	92	84
Frowning	90	100	100	81	79	56	38	81	71
Narrowing eyes	97	98	100	81	90	69	69	86	86
Closing eyes	87	95	93	60	90	78	62	79	81
Raising upper lip	92	98	98	98	90	91	87	95	91
Opened mouth	74	93	100	94	88	73	60	84	82
Tightened lips	80	85	95	54	56	73	69	72	72
Clenched teeth	90	85	98	83	83	82	76	85	85
Empty gaze	87	95	100	71	81	67	53	79	77
Seeming disinterested	90	100	100	50	67	69	64	76	76
Pale face	80	100	100	83	100	67	73	82	87
Teary eyed	80	85	88	98	100	89	87	88	92
Looking tense	77	90	100	54	56	73	69	73	74
Looking sad	80	90	93	63	75	69	56	74	74
Looking frightened	92	80	95	83	92	89	76	86	87
Body movements									
Freezing	100	93	98	73	83	84	60	87	80
Curling up	100	80	98	98	100	89	71	92	90
Clenching hands	92	88	100	83	81	82	69	86	83
Resisting care	95	88	100	96	98	98	78	94	92

	Italy	Serbia		Spain		The Netherlands		Total	
	Rest	Rest	Movement	Rest	Movement	Rest	Movement	Rest	Movement
Interrater agreement after dichotomization	(n=39)	(n=40)	(n=40)	(n=48)	(n=48)	(n=45)	(n=45)	(n=172)	(n=133)
Pushing	95	95	95	100	100	100	89	98	95
Guarding #	95	98	100	96	98	80	84	92	94
Rubbing	90	100	100	100	98	82	91	93	96
Limping #	100	100	100	98	83	96	76	98	86
Restlessness	100	98	100	83	94	64	78	86	90
Pacing	92	98	98	98	92	98	96	97	95
Vocalizations									
Using offensive words	100	98	98	98	100	96	93	98	96
Using pain relates words	95	80	100	100	96	91	80	92	92
Repeating words	95	90	95	94	98	98	82	94	92
Complaining	95	90	98	85	90	87	73	89	87
Shouting	97	100	98	96	94	100	82	98	91
Mumbling	95	90	98	98	92	71	67	88	85
Screaming	97	93	100	98	98	96	87	96	95
Groaning	95	78	100	98	92	89	84	90	92
Crying	97	88	100	98	100	89	93	93	98
Gasping	100	70	95	90	88	89	84	87	89
Sighing	92	85	100	79	83	78	73	83	85

Note: % agreement for scores after dichotomization to not present (0) or present (1-3), percentage ≥ 70% in blue.
missing pairs of observations for guarding in rest 4.1% and in transfer 5.3%; for limping in rest 6.4% and in transfer 8.3%

CHAPTER 8

Summary and General discussion



The primary aim of this thesis was to investigate the complex relationship between pain, neuropsychiatric symptoms, and ADL functioning in dementia. In part II, we aimed to study the psychometric properties of the PAIC observational pain assessment instrument. In this final chapter, the main findings are summarized and critically discussed. In addition, methodological considerations are discussed. Finally, implications for clinical practice are presented and recommendations are made for further research.

Summary of main findings

Part I. Relationship between pain, neuropsychiatric symptoms, and ADL functioning

Chapter 2 | The current state of evidence regarding the challenges of pain management in persons with dementia

This narrative review explores evidence from relevant and recent literature regarding four key perspectives of pain management. First, from a biological perspective the impact of neuropathological changes of the brain in dementia leads to a change in the nociception of pain: the intensity of pain and affective response is different. Furthermore, loss of communicative skills hampers the self-report of pain, and therefore the detection of pain. Consequently, pain assessment (second perspective) should focus on behavioural expressions of pain such as agitation and aggression, for example by using observational measurement instruments with good psychometric properties. Additionally, there is ample evidence of undertreatment and inadequate treatment of pain in persons with dementia (third perspective). The fourth key perspective debates the lack of interdisciplinary education and training of healthcare professionals (fourth perspective). There is an urgent need for evidence-based guidelines.

Chapter 3 | The strength of associations between pain, neuropsychiatric symptoms, and physical functioning in persons with dementia

Despite the increased attention for pain in dementia, this systematic review shows that only few studies have explored the association between pain, neuropsychiatric symptoms (NPS) and physical functioning. Most evidence was found for a positive association between pain and depression, followed by a positive association between pain and agitation/aggression. Physical functioning was often not the main topic of the included studies. There was little evidence for the association between pain, transfers, and bathing. All associations found in this review were relatively weak. This may be the result of inadequate assessment; use of valid measurement instruments was often lacking.

Chapter 4 | The relationship between the course of pain and change in ADL functioning, both in general and regarding specific ADL functions

This longitudinal study showed that pain is associated with ADL functioning cross-sectionally. Residents with pain (PACSLAC-D score ≥4) were more ADL dependent than residents without pain.

Moreover, a change in pain within the first 3 months of follow-up predicted a decline in ADL functioning over the 6-month follow-up period, independent of dementia severity. Specifically, a decline was found in the ADL-activities 'transferring' and 'feeding'.

Part II. Pain assessment in impaired cognition: PAIC

Chapter 5 | Content validity of the Dutch version of the Pain Assessment in Impaired Cognition scale

First, the PAIC (36 items) was translated into Dutch and content validity was examined. Overall, the study showed good content validity and it suggests that especially the items of the body movement domain correspond well with the clinical experience of the Elderly Care Physicians (ECP) and nurses in Dutch nursing homes. Compared to the body movement domain, lower content validity was found for a number of items of the facial expression domain and, to a lesser extent, for items of the vocalizations domain. Interestingly, the think-aloud test performed in this study revealed differences between physicians and nurses in the notions of pain characteristics. For example, unlike ECPs, nurses found the item 'freezing' specific for pain.

Chapter 6 | Observer agreement on the individual 36 items of the Dutch version of the PAIC in a real-life nursing home setting

This observational study in five Dutch nursing homes showed that the 36 items of the Dutch version of the PAIC have promising intra- and interobserver agreement. The items of the domains of body movements and vocalizations in particular showed good observer agreement. In the facial expression domain, there were fewer items with good observer agreement.

Chapter 7 | Observer agreement and factor structure of each of the 36 items of the Pain Assessment in Impaired Cognition scale

Finally, in a multicentre observational study, which took place in four European countries, the inter- and intraobserver agreement, and factor structure of the PAIC (36 items) was analyzed. Results showed that reliability of especially the items of the body movement and vocalizations domains was generally good. For five items of the facial expression domain ('looking sad', 'tightened lips', 'empty gaze', 'seeming disinterested', and 'looking tense'), the agreement between observers was below 70%. This was true for observations during rest and during movement. Poor agreement was found especially in the Netherlands, where education and training in the use of observational measurement instruments was low. Furthermore, factor analysis showed individual items could be clustered into six underlying components: 1) vocal pain expression; 2) face anatomical descriptors; 3) protective body movements; 4) vocal defence; 5) tension; and 6) lack of effect.

Interpretation and critical discussion of findings and methodology

The evidence presented in this thesis builds on the existing evidence that the management of pain in persons with dementia is challenging. However, it narrows it down by dividing the challenges into four areas of interest: neuropathology, pain assessment, analgesic treatment, training and education. This thesis focusses especially on the relationship between pain and ADL functioning, and on pain assessment by examining the psychometric properties of the PAIC observational pain instrument.
The following section addresses the methodological strengths and limitations that should be considered when interpretating the results presented in this thesis. First, the design of the study investigating the relationship between pain and ADL functioning, including follow-up and statistical analyses, will be discussed. In the second part, we will elaborate on issues related to the development of the PAIC, including psychometric testing and item overlap.

Part I. Pain and ADL functioning

The systematic review on the complex relationship between pain, NPS and ADL functioning does not provide satisfactory results in terms of causality (Ch. 3). Especially the relationship between pain and ADL functioning was underexposed and we found no longitudinal study investigating this relationship. In order to examine if, and how, a change in pain influences ADL functioning in dementia we performed a longitudinal study with linear regression analyses. We investigated the effect of pain on ADL functioning in general, but also on specific ADL activities. This provides more in-depth information on which ADL activity is affected most by pain.
A key finding in Chapter 4 of this thesis is that pain has an impact on ADL functioning in dementia, irrespective of dementia severity.[1] This is an important finding, because a decline in ADL functioning is often interpreted as a sign of increasing dementia severity, whereas it can also be caused by pain.[2-4] However, due to the fluctuation of pain and ADL functioning over time, there is a need to reflect on choices regarding statistical analyses.
As there is a partially reciprocal relationship between dementia, pain, NPS and ADL functioning (see introduction Figure 1) unravelling single pathways is difficult. Besides linear regression analyses, other statistical approaches were explored, such as multilevel modelling for longitudinal data. This would account for dependency in data, e.g., residents within organizations, but also for dependency in repeated measures on the individual level. However, correlations at the unit of organization level (different wards) were negligible. Furthermore, multilevel modelling would enable the use of all available data, including those lost to follow-up at three months. Even so, the inclusion of pain as a time varying covariate did not provide a clearer view on the relationship, as we aimed to stay close to daily clinical practice.
Therefore, we chose a more simplified statistical approach of linear regression analyses with the change in pain score during the first three months of follow-up as a predictor for ADL functioning at six months follow-up.

Furthermore, to examine the relationship between pain and ADL functioning, data from the STA-OP! trial was used (Ch. 4). ADL functioning was not a primary subject of interest and data collection was at 3 and 6 months follow-up. A longer follow-up period might have captured more changes. In a Norwegian study, for example, the course of ADL functioning in persons with dementia was examined over a follow-up period of 36 months with biannual measurements.[2] The study showed that ADL impairment increased with the progression of dementia, and the association between dementia severity and ADL impairment was stable over time. This stability of the relationship of ADL and dementia severity over time might suggest that a longer follow-up period, compared to the follow-up period used in the STA-OP! trial (6 months), or frequent measurements of ADL functioning is not necessary. However, this could be different for the relationship between pain and ADL, because pain can be acute or chronic and may fluctuate over time. Also, in the Norwegian study the assessment started immediately after admission to the nursing home. The onset of a decline in ADL functioning can be pinpointed more precisely when multiple measurements in follow-up studies start at admission. The downside of a longer follow-up period is a larger number of dropouts due to, for example, death, transfer to other facilities, but also an increasing number of refusals to be tested due to worsening of cognitive status.[5 6] To accommodate the loss to follow-up, one could shorten the time period needed by including an intervention that potentially forces a change in pain and ADL functioning, e.g., an analgesic trial. This shorter follow-up period, for example a period of 8-10 weeks[7] may be more feasible in clinical practice. A shorter follow-up period could also eliminate possible barriers which hamper successful implementation of research in long-term care, such as understaffing/high workload, high staff turnover, lack of time, and lack of financial resources.[8 9]

Part II. Pain Assessment in Impaired Cognition: PAIC

The PAIC was developed in a European group of experimental and clinical researchers. The goal was to develop an internationally agreed upon observational measurement instrument, with thoroughly investigated psychometric properties, an ultimately valid and reliable tool, which is sensitive to change. The tool should be suitable for use in a research and clinical setting, and facilitate international research on pain management in dementia. The results presented in this thesis regarding the initial development of the PAIC (hereinafter referred to as PAIC36) were used in refining the final version of the PAIC (hereinafter referred to as PAIC15).

In the process of examining the research version of the PAIC36, a total of 36 promising items were studied. These items were selected from 12 existing pain observation instruments, which makes this instrument a meta-tool. Across Europe, several studies have been conducted in the road map for an optimal instrument for research and practice.[10] Three of these studies are described in this thesis.

For the validity of the PAIC36, the think-aloud test among nurses and elderly care physicians (ECPs) was an important step.[11] This think-aloud test is not often used in the development of instruments, but it is very appropriate for research in our setting. Performing this test with potential users provided insight into the thought processes that determine the user's response to an item and whether the items are understood as they were intended.

However, we did not take full advantage of all available expert input. Other potential users, such as physiotherapists, psychologists, and occupational therapists, were not part of the study. Their clinical opinion, but also their cultural beliefs and experience in pain management, is missing. As these healthcare professionals play a significant role in guiding and treating residents with pain, this might have an adverse effect on the instrument's reliability and validity.[12] This is especially important considering the results of the content validity study (Ch. 5), in which we found that nurses and ECPs do not speak the same language when it comes to pain. A valid and reliable measurement instrument could close this 'linguistic' gap.

By contrast, one of the strengths of the multicentre observational study (Ch. 7) is that it took place in four countries (Italy, Serbia, Spain and the Netherlands). This means that the PAIC36 was studied in culturally different clinical settings which facilitates cross-cultural research on pain in persons with dementia. Due to globalization and migration, many countries have very diverse populations. In order to provide patient-centred care, understanding the cultural and ethnic background of residents as well as healthcare professionals is important.[13] Especially considering that many cultural aspects influence different domains of pain: physical, psychological, spiritual, and social. In other words, people with different cultural backgrounds respond differently to pain.[14]

In the Dutch study described in Chapters 5 and 6, these cultural patterns were not addressed during, for example, the think-aloud test. Healthcare professionals' attitudes and beliefs about pain are associated with the content of the health advice given to the resident or their relative.[15] For example, when a nurse believes that it is important to avoid certain tasks and rest when having low back pain, this will be the advice given to the resident. In order to provide adequate pain management, healthcare professionals need to be aware not only of their own attitudes and beliefs about pain, but also of the cultural background of the resident and how this may influence their experience of pain, and their personal needs regarding pain management.

During the psychometric testing of the PAIC36, a short training was given to the nurses, about different aspects of observing a resident. This included, for example, not performing other tasks while observing and not giving a personal interpretation of the different items, but also practicing filling out the PAIC36 using a videoclip. Despite these efforts, observer agreement of the facial items of the Dutch version of the PAIC36 (Ch. 6) was low compared to the domains of body movement and vocalizations.[16] This is remarkable, as we know that facial expressions are the most valid expressions, certainly in laboratory settings.[17 18] A possible explanation could be that observing 36 items during a relatively short period of time is challenging. Also, nurses may not have followed the instructions provided during the training. Perhaps a more plausible explanation is that nurses are unaware of the fleeting and variable nature of facial expressions. We know that nurses and other healthcare professionals find facial expressions most difficult to interpret.[19 20] Healthcare professionals seem to recognize changes in behaviour or a decline in ADL functioning more quickly than they recognize changes in facial expressions.[21 22]

It could be worthwhile to investigate the correct use of the PAIC15 and how *well* the observation is executed, both in studies and in everyday practice. This could provide valuable information for future educational training and implementation programmes.

Item overlap and development of the PAIC15

As previously mentioned, the interplay between pain, NPS, ADL functioning in dementia is complex. This is also reflected by the overlap of items between measurement instruments, such as the Katz-ADL scale and the Reisberg Global Deterioration Scale (GDS), but also items of the PACSLAC-D and CMAI that measure pain and agitation respectively. This does not aid the unravelling of the relationship. For example, the items concerning assisted bathing, eating and toileting are incorporated in both the Katz-ADL scale and the Reisberg GDS. Physical aggression items, such as hitting and kicking, are both incorporated in the PACSLAC-D and CMAI. Overlapping items weaken the discriminant validity of a measurement instrument and this may have led to an overestimation of the relationship between pain and ADL functioning in dementia presented in this thesis (Ch. 3, 4). [23] During the development of the PAIC36, steps were taken to minimize overlap of items between the different constructs of pain, NPS and ADL functioning in dementia. The PAIC36 'research version' consisted of 36 items and item reduction was completed through 7 steps: 1) gathering empirical evidence on individual items (Ch. 5, 6, 7); 2) item difficulty (Ch. 5); 3) inter-rater reliability (Ch. 6, 7); 4) construct validity; 5) content validity (Ch. 5); 6) feedback external reviewers; and 7) consensus meeting with expert panel.[24] For example, the items 'crying', 'looking sad', and 'seeming disinterested', which might also indicate a depression, were excluded. The item reduction process resulted in the exclusion of 21 items, leading to the final version of the PAIC: PAIC15.

A very important and unique part in developing the PAIC15, was the use of experimental pain.[24] In this way it became clearer which item/behaviour truly was a result of pain, reducing possible overlap with items of behavioural observation tools even further. In clinical studies mimicking experimental pain by including guided movement is advised, since pain is more likely to occur during movement.[24]

Not having a 'gold standard' for pain in persons who cannot communicate remains a problem in the validation of observational pain instruments. Recently a study in the field of biomedics showed interesting results on the positive correlation between pain biomarkers in saliva and the score of the PAINAD scale, one of the oldest pain observation scales.[25] Pain biomarkers, tumour necrosis factor receptor type II (sTNF-RII) and secretory IgA (sIgA), were determined in the saliva of persons with moderate to severe cognitive impairment. This technique is rather simple, safe, non-invasive, and therefore a promising strategy to reinforce the validity of pain measurement instruments, such as PAIC15.

Although the final version of the PAIC15 warrants further refinement in terms of sensitivity to change/responsiveness, first results on cut-off scores are underway[26] and COSMIN recommendations have been followed, resulting in the most promising observational measurement instrument available so far.

In summary, the psychometric evaluation of the PAIC presented in this thesis not only results in a promising measurement instrument, but also provides useful information for the development and improvement of educational programmes that contribute to the utilization of the PAIC15.

Implications for clinical practice and organizational aspects

Several implications for future clinical practice and organizational aspects result from this thesis.

Despite the growing body of evidence, including this thesis, concerning the relationship between pain in dementia and its consequences and the quest for the optimal observational measurement instrument, regular assessment and guidelines are poorly implemented in clinical practice (Ch. 2 and 3). Moreover, research has shown that implementing an observational measurement instrument is not enough to reduce pain in persons with dementia.[27] In order to facilitate successful pain management, we need to think beyond measurement instruments and focus on a systematic approach of pain.[28]
In the Netherlands, the Dutch association for elderly care physicians, Verenso, developed a national guideline for the multidisciplinary recognition and treatment of pain in vulnerable elderly.[29]
There are several points of concern, some resulting directly from this thesis, and some suggestions.

Organizational aspects

1. Implementation of a multidisciplinary pain team

A pain team can formulate a pain protocol adjusted to the healthcare organization, for example the nursing home.[30] Preferred participants in pain teams are a nurse, occupational therapist, psychologist, physiotherapist and an elderly care physician. This team can facilitate training and feedback, consultation, the availability of assessment instruments (and their implementation in electronic patient file systems) and availability of information materials and different types of interventions.

2. Individualized patient care and treatment plan

Next to organizational tasks, the pain team can support an interdisciplinary approach in the team that treats the patient, which allows for developing such an individualized care and treatment plan. This plan should incorporate non-pharmacological as well as pharmacological interventions.

3. Collaboration between physicians and nurses (Ch. 5.)

For a proposed care and treatment plan to be successful, it is important that physicians collaborate closely with the nursing staff. Nurses are the eyes and ears of the team, making them the patients' advocates. By involving the nursing staff, treating pain becomes a team responsibility.

4. Use a stepwise approach (Ch. 2.)

Using a stepwise or systematic approach incorporating an observational pain measurement instrument is important. The STA-OP! programme is an example of such a stepwise approach. STA-OP! has proven to be successful in reducing pain as well as challenging behaviour.[31-33]

5. Improve implementation

However, implementing (new) evidence-based guidelines or measurement instruments is a challenging endeavour. It requires commitment from healthcare organizations and policymakers. Over the years, some important findings emerged which may help to improve implementation strategies.[34] For example, barriers to effective pain management can be grouped into three themes: patient related (sensory and cognitive impairment, fear of addiction), caregiver related (lack of knowledge, difficulty communicating with family or physician), and system related (lack of funding, lack of standardized approaches, lack of education, high workload and staff turnover).[35 36]

Whilst the patient- and caregiver-related barriers can be incorporated in educational programmes, the system-related barriers are the most challenging. This should be the focus during implementation of evidence-based pain guidelines. In this light, Verenso developed an implementation protocol for the multidisciplinary guideline on pain; recognition and treatment of pain in frail elderly.[37] Special attention was paid to the organizational aspects of the implementation process, combined with evident and reproducible policy reports. Also, the University Network of Eldery Care of the University Medical Center in Groningen (UNO-UMCG) is currently investigating the implementation of the PAIC15 in two Dutch nursing homes (https://huisartsgeneeskunde-umcg.nl/effectiviteit-van-pijninterventies).

6. Use pain champions

A cornerstone of successful adherence to a newly implemented guideline and practice change, is the use of motivational leaders, or so-called pain champions.[8 34] They can be the go-to person for all nursing staff, the connector between nursing staff and physician, and the driving force behind integrating the observation of pain in routine care.[22 34]

Education and interdisciplinary learning and training

1. Interdisciplinary training (Ch. 2, 4 and 5)

A prerequisite for adequate pain management is integrating and facilitating continuous education and training of healthcare professionals in elderly care.[32 38 39]
As previously mentioned, this thesis showed a mismatch concerning the notion of pain between nurses and physicians working in nursing homes (Ch. 5). This reflects the gap in the knowledge of both nurses and physicians. Pain is subjective and difficult to recognize in persons with dementia. However, the consequences of pain, as presented in this thesis, are more easily recognized by nursing staff.[31 39 40] For instance, nurses observe changes in behaviour, but are often unable to distinguish whether changes in behaviour are caused as part of NPS in dementia, or by pain. Misinterpretation is also likely to occur in case of a change in ADL functioning: decline in ADL functioning is ascribed to an increase in dementia severity (Ch. 4). Therefore, it is important to develop an educational training programme with a special focus on interdisciplinary training and a multidimensional approach to pain.
Key components of an educational training programme should cover important patient- and care-related topics such as the perception, expression, recognition, and assessment of

pain, with special attention for a change in ADL functioning. Also, the pharmacological and non-pharmacological treatment of pain should be addressed as well as cultural aspects of pain.[22] Furthermore, it is important to raise awareness about 'red flag-conditions' which are known to cause pain, such as co-morbidities (e.g., osteoporosis, cardiovascular disease, cancer), performing certain activities (e.g., getting dressed, transferring), but also pain as an occupational disease resulting from previous profession such a being a hairdresser or a construction worker. The individual's biography is an important element in the assessment of pain.[41 42] Admission to the nursing home should be the starting point for documenting a resident's pain history, including coping strategies.[43-45]

2. What type of education?

Besides the topics of a pain education training programme, it is equally important to look into how such programmes are operationalized. In the course of the development of PAIC, an e-learning course was created (https://www.free-learning.nl/modules/paic15/start.html). This e-learning course includes background information on the different domains and items of the PAIC15, but predominately includes training videos on how to use the PAIC15 correctly. However, training videos alone may not change nurses' behaviour.[46 47] It is therefore necessary to combine several educational interventions. Few studies have been conducted on educational interventions in pain management in nursing homes. As a result, a combination of interactive training workshops, interdisciplinary discussions of case reports, training videos and e-learning seems most promising to enhance knowledge and improve skills in pain management.[7 34 48 49]

Recommendations for future research

Based on the results of this thesis, several recommendations can be made for future research.

As discussed earlier, more longitudinal research is needed on all aspects of pain management, for example, a more in-depth examination of the relationship between pain and ADL functioning using different statistical approaches. However, intervention studies on educational training programmes and large-scale pain management testing programmes are also important subjects of interest.

Investigating the relationship between pain and ADL functioning

Although not widely accepted in medical research, case studies, or n-of-1 trials, could be an alternative way to investigate the relationship between pain, NPS and ADL functioning.[50] A lot of research involves interventions tailored to a group of individuals. N-of-1 trials are considered to be the most ideal study design to investigate causality on an individual level.[51] As stated throughout this thesis, the relationship between pain, ADL, NPS and dementia is reciprocal and therefore difficult to investigate in large clinical trials where the heterogeneity of the study sample is substantial. N-of-1 trials use key elements of clinical trials (i.e., randomization, blinding) but have a more flexible approach in which participants serve as their own control. Furthermore, series of n-of-1 trials can highlight individual differences and reveal characteristics related to responders and non-responders. A meta-

analysis of multiple n-of-1 trials can reveal evidence which can be applied to a whole group of individuals[52]. More importantly, participants benefit directly from the intervention.
Pursuing n-of-1 trials, especially in dementia care, could be a key factor in closing the gap between evidence-based medicine, derived from large clinical trials (often with high heterogeneity), and real clinical practice where individualized patient care is the core business.
Furthermore, applying different statistical approaches, such as multilevel modelling, allows for studying the dynamic interplay between pain, NPS and ADL functioning in dementia. Multilevel modelling can be used to examine different trajectories of pain, NPS, and ADL functioning, as well as how these trajectories are interrelated over time.
Also, another statistical approach, such as mediation analysis, could be used to explain the mechanisms that underlie the relationship between pain (independent variable), NPS, ADL functioning, and dementia severity (dependent variables). In this way, the main mechanisms by which pain affects NPS and ADL functioning in persons with dementia could be revealed, providing, among other things, important information for the development of more effective interventions.[53]

Pain assessment with PAIC15

To contribute to the usage and implementation of PAIC15 in clinical practice, several additional studies are needed (Ch. 5, 6, 7). It is important to collect evidence on cut-off scores for different pain intensities. As mentioned, first results on cut-off scores for possible and probable pain are underway.[26] Future research on cut-off scores should also include severe pain. Perhaps it is possible to examine whether a specific score would be suggestive of a specific treatment or drug. Furthermore, investigating the sensitivity to change, for example by initiating analgesic trials, is an important part of future research. Especially since a recent double-blinded randomized placebo-controlled trial investigating the validity of the German PAINAD showed insufficient sensitivity to change/responsiveness.[54]
Additionally, the feasibility of PAIC15 must be examined in persons with other neurodegenerative diseases, such as Parkinson's disease, Huntington's disease, and persons with cerebrovascular accidents that have aphasia and facial paralyses.[55 56] Studies on the use of PAIC15 in patients with aphasia are underway (Carolien de Vries, LUMC), and studies in Huntington's disease are in the design phase (Gregory Sprenger, LUMC). All of these groups, including Parkinson's, face many challenges regarding the usability of pain observation scales such as PAIC15. These include evaluation of motor symptoms and facial expressions, because these may be affected heavily by the primary disease, and thus the expression of pain may be hampered.[57]
Further, it might also be worthwhile to investigate the feasibility of the PAIC15 in persons with young onset dementia. It is conceivable that, for example, ageism does not play a significant role in pain behaviour in young onset dementia and that pain behaviour in this group might therefore be different.
Lastly, testing PAIC15 in different clinical settings, such as hospitals, rehabilitation centres, but also in primary care. In the Netherlands, an increasing number of persons with dementia live at home. It might be interesting to test whether PAIC15 can also be used

by informal caregivers or family. A recent study by Bentur et al., showed promising results about the use of pain assessment tools by family members.[58]

Non-pharmacological and pharmacological treatment of pain

The evidence for efficient treatment with analgesics, such as paracetamol and opioids, is scarce (Ch. 2), resulting in both over- and undertreatment of pain.[59] Little is known about medication dosage, titrating analgesics, and optimal duration of analgesic use. This is one of the reasons physicians are reluctant to prescribe opioids, also known as opiophobia.[60] A much safer way to treat pain are non-pharmacological interventions, such as massage and music therapy, exercise and movement therapies (e.g., rocking chair), but also using the robotic seal PARO.[61-65]

However, strong study designs on non-pharmacological treatment options in dementia patients are lacking. To achieve adequate pain management, large-scale analgesic trials combined with non-pharmacological interventions are necessary.

Novel technologies

Despite the development of PAIC15, pain assessment in persons with dementia still faces many challenges. These often originate from the barriers mentioned before, such as lack of time and difficulty differentiating pain from other forms of discomfort.

An interesting focus of research could therefore be the application of modern technology, such as automatic pain assessment systems.[66 67] In the past 5 years interest in this complementary diagnostic is increasing, and the results are very promising.[66 67] However, most systems have been developed for young or middle-aged individuals and are not yet suitable for older individuals.

For example, wrinkles which could lead to false positives. Therefore, research is needed in the field of geriatric medicine, and in the future automatic pain assessment systems may lead to better pain management and a reduction in the workload of nursing staff.

Overall conclusion

Recommendations from this thesis may lead to further improvement of pain management in persons with dementia. The most important recommendation is that besides challenging behaviour, a decline in ADL functioning should also serve as a red flag for the presence of pain. Therefore, the clinical message is: if there is a decline in ADL functioning, do not automatically attribute it to the progression of dementia but check for other causes. Pain is definitely a cause to be considered.

The development of PAIC was the starting point for creating a robust valid, reliable, and international meta-tool which can be used in clinical as well as research practice. At present, research on psychometrics, clinical utility and feasibility of PAIC15 is ongoing. Throughout this thesis, important suggestions are made for much-needed educational training programmes and implementation strategies.

Follow-up on Hans

Hans, who suffers from Lewy body dementia and Parkinson's disease, suddenly expressed challenging behaviour such as agitation, and verbally and even physically aggressive behaviour towards other residents and nursing staff. There was also a change in his ADL functioning: his wife noticed that there were more OFF moments and that he was limping with his right foot. The nursing staff elaborated on possible causes for his sudden change in behaviour and mobility. They consulted with the elderly care physician (ECP), psychologist, and physiotherapist. Together with the nursing staff, the psychologist evaluated the agitated and aggressive behaviour, among other things by measuring the agitated behaviour with the Cohen Mansfield Agitation Inventory (CMAI). His score of 86 (range 29-203) indicated significant agitated behaviour. Furthermore, a physical examination by the ECP and physiotherapist resulted in the identification of increased muscle stiffness, postural instability, and difficulty walking. During walking, Hans frequently moaned and sometimes had a pained expression on his face. In addition, the nursing staff filled out the PAIC15 for three consecutive days, during rest and during movement. The PAIC15-scores were especially high during movement: 31 (range 0-45). This led to a follow-up physical examination by the ECP, with special focus on locomotion. An ingrown toenail of the great toe of the left foot was found. After a partial avulsion of the lateral edge of the nail plate and matrixectomy, the pain was alleviated. Within the next week, Hans' walking pattern improved and the frequent OFF moments decreased. Moreover, the agitated and aggressive behaviour disappeared.

A multidisciplinary approach of a change in behaviour and ADL functioning, use of observational measurement instruments, with special attention for the presence of pain, can significantly contribute to the quality of life.

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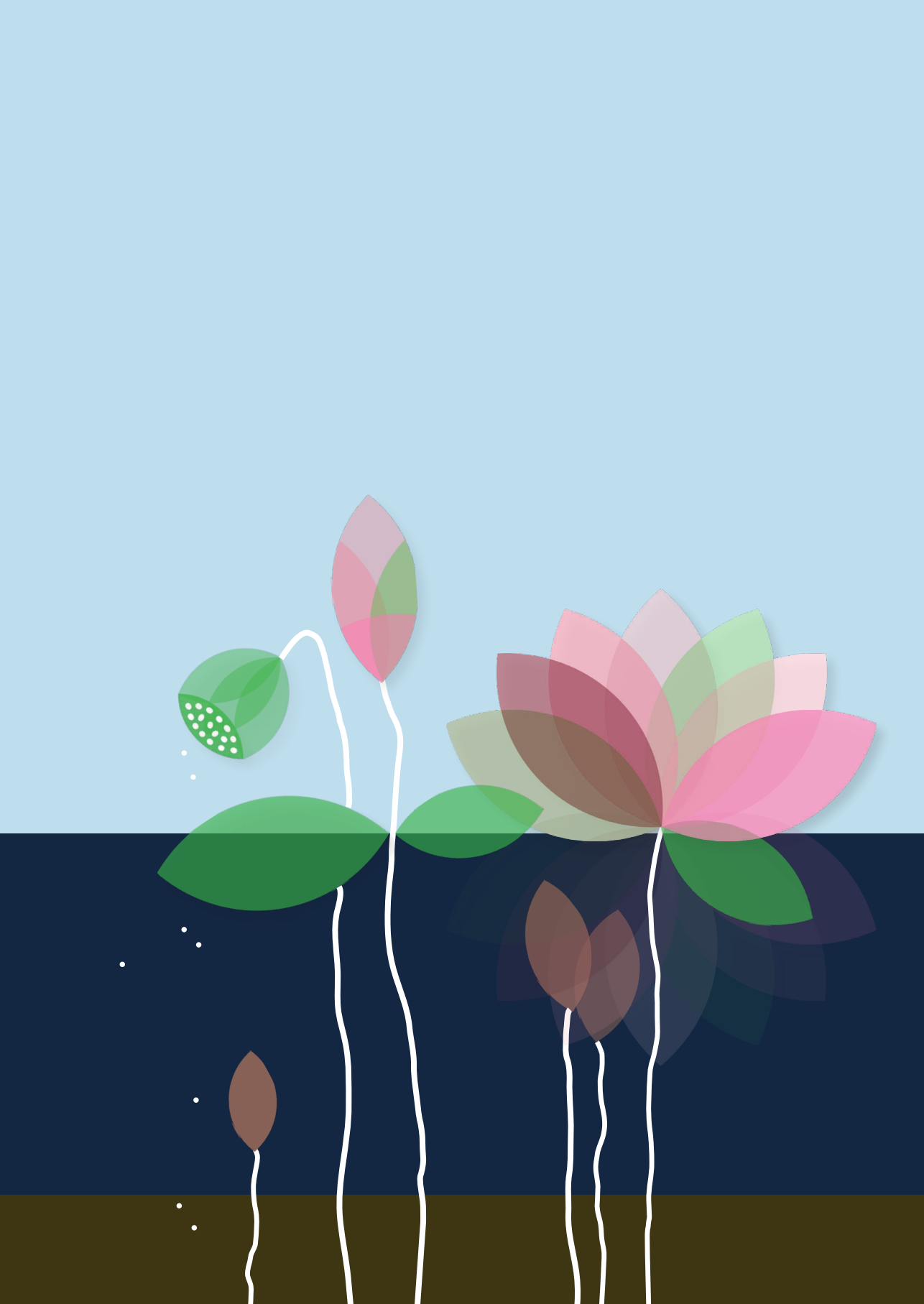
Samenvatting (Summary in Dutch)
Dankwoord
Curriculum vitae
List of publications



Samenvatting

Dementie is wereldwijd een van de meest voorkomende ziekten waarbij iemand achteruitgaat in functioneren. Het is een syndroom dat zich kenmerkt door geheugenverlies, problemen met het denken en begrijpen, veranderingen in gedrag en problemen met het uitvoeren van dagelijkse activiteiten. Dementie is niet alleen overweldigend en ingrijpend voor de mensen die de diagnose krijgen, maar ook voor hun naasten.
De meest voorkomende oorzaken van dementie zijn de Ziekte van Alzheimer, vasculaire dementie, Lewy body dementie en fronto-temporale dementie (FTD).
Het is een progressieve ziekte welke niet te genezen is. Uiteindelijk sterft iemand aan de gevolgen van dementie, bijvoorbeeld door een longontsteking.
De neuropathologische veranderingen in het brein zorgen naast geheugenverlies en verlies van communicatieve vaardigheden, ook voor probleemgedrag zoals agitatie en agressie. Daarnaast hebben de veranderingen ook invloed op het waarnemen en het verwerken van pijn.

Pijn bij mensen met dementie

Ouder worden is een risicofactor voor het ontwikkelen van dementie, maar ook voor ziekten die gepaard gaan met pijn, bijvoorbeeld osteoporose en cardiovasculaire ziekten zoals een hartinfarct of een herseninfarct. Men kan dus verwachten dat mensen met dementie ook pijn hebben: uit eerder onderzoek blijkt dat de prevalentie rond de 60 tot 80% ligt.
Om te begrijpen hoe de relatie tussen pijn en dementie in elkaar zit, is het belangrijk de definitie van pijn te kennen. De definitie volgens de International Association for the Study of Pain (IASP) luidt als volgt:
'Pijn is een onplezierige, sensorische en emotionele gewaarwording. Deze wordt geassocieerd met actuele of potentiele weefselbeschadiging of beschreven in termen van beschadiging.'
Wellicht kunt u zich voorstellen dat deze definitie minder toepasbaar is op mensen met dementie gezien het gebruik van de term 'emotionele gewaarwording'. Onderzoek naar de emotionele reactie op pijn bij mensen met dementie laat tegenstrijdige resultaten zien: zowel een verhoogde als verlaagde emotionele reactie werd gevonden. Bovendien tasten de neuropathologische veranderingen, zoals witte stof schade en atrofie, verschillende onderdelen van het brein aan die betrokken zijn bij de verwerking van een pijnprikkel. Bijvoorbeeld de somatosensore cortex, welke o.a. verantwoordelijk is voor het lokaliseren van de pijn, de hippocampus, waar het pijngeheugen gelegen is en de amygdala, welke verantwoordelijk is voor de emotionele ervaringen van de pijn. Daarnaast heeft pijn drie verschillende dimensies: biologisch, psychologisch en sociaal. Deze dimensies zijn onderling met elkaar verbonden en resulteren uiteindelijk in een persoonlijke ervaring en expressie van pijn. Daar komt bij dat de communicatieve vaardigheden bij mensen met dementie, ook aangetast zijn en dat het verbaliseren van pijn moeilijk, en soms geheel niet mogelijk is.
Al deze veranderingen tezamen zorgen voor een complexe relatie tussen pijn en dementie en veroorzaken verschillende problemen. Het herkennen van pijn bij iemand met dementie en het uiteindelijk instellen van een adequate behandeling, is een uitdaging.

Probleemgedrag

Agitatie, agressie, maar ook depressie en apathie zijn voorbeelden van neuropsychiatrische symptomen, ofwel probleemgedrag. Tijdens het ziektebeloop van dementie komt probleemgedrag veel voor. Dit is een van de belangrijkste redenen voor opname in een zorginstelling. Zorgverleners interpreteren probleemgedrag vaak niet als het gevolg van een onvervulde behoefte, bijvoorbeeld de aanwezigheid van onbehandelde pijn. Probleemgedrag wordt vaak behandeld met psychofarmaca, zoals haldol en lorazepam. Echter, de oorzaak van het probleemgedrag wordt daarmee niet aangepakt. Het gebruik van dergelijke medicatie is geassocieerd met ernstige bijwerkingen zoals een toename van cognitieve achteruitgang, valpartijen, cardiovasculaire incidenten en zelfs overlijden. Om te voorkomen dat onvervulde behoeften, zoals onbehandelde pijn, inadequaat worden behandeld, is het belangrijk dat probleemgedrag zoals agitatie en agressie opgemerkt wordt als een signaal, een rode vlag. Deze rode vlag dient aanleiding te geven tot verder onderzoek naar pijn als mogelijke oorzaak voor het probleemgedrag.

Fysiek functioneren

Fysiek functioneren of Activiteiten van het Dagelijks Leven (ADL) zijn fundamentele vaardigheden welke nodig zijn om activiteiten zoals wassen, kleden, eten en lopen, zelfstandig te kunnen uitvoeren. Wanneer het niet mogelijk is deze activiteiten zelfstandig uit te voeren, is men afhankelijk van anderen en wordt er vaak een beroep gedaan op bijvoorbeeld thuiszorg of zorginstellingen.
Met de achteruitgang van de dementie, gaat ook het ADL functioneren achteruit. Dit is een natuurlijk gevolg van de neuropathologische veranderingen in het brein welke ook de dementie veroorzaken. Met andere woorden, een achteruitgang in ADL functioneren is te verwachten, vooral in de laatste fase van de dementie. Desalniettemin is achteruitgang in ADL functioneren een complex fenomeen; naast de dementie zijn er ook andere factoren die een achteruitgang in ADL functioneren kunnen veroorzaken. Apathie en depressie, medicatiegebruik zoals antipsychotica (bijvoorbeeld haldol en lorazepam), maar ook pijn zijn voorbeelden van dergelijke factoren. Het is echter onduidelijk wat het (toegevoegde) effect van pijn op het ADL functioneren van mensen met dementie is.

Verpleeghuiszorg in Nederland

De zorg voor mensen met een gevorderde tot vergevorderde dementie vindt vaak plaats in verpleeghuizen op zogenoemde psychogeriatrische afdelingen. Het aantal personen met dementie in 2021 in Nederland wordt geschat op 290.000 mensen. Een geschatte 70.245 daarvan waren opgenomen in een zorginstelling, bijvoorbeeld een verpleeghuis. In het verpleeghuis wordt geïntegreerde, multidisciplinaire medische en paramedische zorg verleend door een multidisciplinair team bestaande uit een psycholoog, ergotherapeut, fysiotherapeut en een specialist ouderengeneeskunde. Daarnaast is er een zorgteam wat 24 uur per dag, 7 dagen per week de zorg verleent en zij zijn ook onderdeel van het multidisciplinaire team. Nederland is het enige land ter wereld wat een medisch specialisme ouderenzorg heeft.

Beoordeling van pijn

Door de complexe interactie tussen dementie, pijn, probleemgedrag en ADL is het herkennen van pijn moeilijk, vooral wanneer het verbaliseren van pijn nauwelijks of zelfs niet mogelijk is. Verschillende verbale en non-verbale gedragingen en veranderingen kunnen duiden op de aanwezigheid van pijn. Bijvoorbeeld zuchten, kreunen, ijsberen, agressie en een veranderd slaappatroon. Wanneer zelfrapportage van pijn niet meer lukt, is directe observatie van de bewoner en daarbij gebruik maken van een pijnobservatieschaal, de meest belangrijke methode om pijn bij mensen met dementie te herkennen. De afgelopen jaren zijn er verschillende pijnobservatieschalen ontwikkeld, bijvoorbeeld de PACSLAC-D en de PAINAD. De psychometrische eigenschappen van deze instrumenten zijn echter niet goed onderzocht en door ontwikkeld. Ook zijn er verschillen in hoe de observatieschalen in de praktijk worden gebruikt en ontbreekt er een internationale standaard.

Het werk in dit proefschrift beschrijft de relatie tussen pijn, probleemgedrag en ADL functioneren bij mensen met een gevorderde tot vergevorderde dementie.
Dit proefschrift bestaat uit twee delen. Het eerste deel beschrijft deze complexe relatie, met speciale aandacht voor het effect van pijn op ADL functioneren. Het tweede deel richt zich op de ontwikkeling en onderzoek van de psychometrische eigenschappen van een nieuwe observatieschaal om pijn bij mensen met dementie te kunnen meten: PAIC (Pain Assessment in Impaired Cognition).

Deel I. Relatie tussen pijn, probleemgedrag en ADL functioneren

In hoofdstuk 2 worden vier belangrijke perspectieven van pijn management besproken.
Allereerst het biologisch perspectief waaruit blijkt dat er tegenstrijdige onderzoeksbevindingen zijn over de impact van de neuropathologische veranderingen in het brein op de pijnbeleving. Er lijkt ook een verschil in pijnbeleving te zijn tussen de verschillende vormen van dementie. Mensen met vasculaire dementie lijken bijvoorbeeld meer pijn te ervaren in vergelijking met mensen met FTD.
Het tweede perspectief beschrijft de beoordeling van pijn. Door onder andere het verlies van communicatieve vaardigheden, is het verbaal uiten van pijn moeilijk en moet de beoordeling van pijn verschoven worden naar het observeren van gedragingen die kunnen wijzen op de aanwezigheid van pijn, zoals agitatie en agressie. Hiervoor kunnen pijnobservatieschalen gebruikt worden. Wat betreft de behandeling van pijn (derde perspectief), blijkt dat er maar weinig bewijs is voor adequate inzet van pijnmedicatie, zoals paracetamol. Een systematische en stapsgewijze aanpak van pijn kan hierin ondersteunen. Daarin is zowel aandacht voor een medicamenteuze aanpak als ook voor een niet-medicamenteuze aanpak, bijvoorbeeld het inzetten van snoezelen of fysiotherapie. Als vierde en laatste perspectief worden organisatorische en onderwijskundige aspecten besproken. Het gebrek aan interdisciplinair onderwijs en training van zorgmedewerkers tezamen met een grote behoefte aan evidence based richtlijnen, maakt dat pijnmanagement in de dagelijkse praktijk een grote uitdaging is.

Pijn bij dementie heeft de afgelopen decennia veel aandacht gekregen. Uit hoofdstuk 3 blijkt echter dat er maar weinig studies zijn die de relatie tussen pijn, probleemgedrag en ADL functioneren hebben onderzocht en dat er vaak geen gebruik werd gemaakt van valide meetinstrumenten.
Hoofdstuk vier beschrijft een longitudinale studie naar het effect van pijn op het ADL functioneren. Daarbij is het effect van pijn op het ADL functioneren in het algemeen, maar ook op specifieke ADL-verrichtingen, onderzocht. De resultaten uit deze studie laten zien dat pijn effect heeft op het ADL functioneren, onafhankelijk van het stadium van de dementie. Dit is een belangrijk gegeven, omdat met de progressie van de dementie het ADL functioneren ook achteruitgaat. Met andere woorden: een achteruitgang in ADL functioneren bij een bewoner met dementie kan ook komen door de aanwezigheid van pijn. Er mag niet louter vanuit worden gegaan dat de achteruitgang veroorzaakt wordt door de progressie van de dementie.

In hoofdstuk 3 wordt nog een ander opvallend detail beschreven, namelijk het niet tot nauwelijks gebruik maken van gevalideerde meetinstrumenten om pijn bij mensen met dementie te kunnen meten. Dit maakt het ontrafelen van de complexe relatie tussen pijn, probleemgedrag en ADL functioneren nog moeilijker. In deel 2 van dit proefschrift worden de ontwikkeling en de psychometrische eigenschappen van de PAIC beschreven: een nieuw instrument om pijn bij mensen met dementie te kunnen meten.

Deel II. Het meten van pijn met de PAIC

Uit hoofdstuk 2 en 3 blijkt dat het voor de beoordeling van pijn bij dementie essentieel is gebruik te maken van betrouwbare en gevalideerde pijnobservatieschalen, maar dat in de dagelijkse praktijk deze niet of nauwelijks worden toegepast. Hierdoor besloot een groep internationale wetenschappers een nieuwe pijnobservatieschaal te ontwikkelen, welke gebaseerd is op de beste meetinstrumenten die er tot nu toe ontwikkeld zijn, om uiteindelijk te komen tot een internationale standaard. Deze pijnobservatieschaal heet Pain Assessment in Impaired Cognition; PAIC. De PAIC bevat de allerbeste items (in totaal 36) afkomstig uit 12 bestaande pijnobservatieschalen, waaronder de PACSLAC en de PAINAD. De items zijn verdeeld over 3 domeinen:
1) gezichtsuitdrukkingen, 2) lichaamsbewegingen en 3) stemgeluiden.
Hoofdstuk 5 beschrijft de content validiteit van de Nederlandse versie van de PAIC36. De content validiteit beschrijft in hoeverre de items van de PAIC36 meten wat we daadwerkelijk willen meten, namelijk pijn. Alle 36 items van de PAIC36 werden voorgelegd aan 20 specialisten ouderengeneeskunde (SO) en 20 verzorgenden/verpleegkundigen. Per item moesten zij aangeven of het item indicatief en/of specifiek was voor pijn of juist specifiek voor een andere aandoening, bijvoorbeeld voor een depressie of dementie. De resultaten laten zien dat de items van de PAIC36 over het algemeen een goede content validiteit hebben. Opvallend was dat SO's en verzorgenden/verpleegkundigen vaak anders over de items dachten. Er was vooral weinig overeenstemming betreffende de items van het domein 'gezichtsuitdrukkingen'. De meeste overeenstemming werd gevonden over de items van het domein 'lichaamsbewegingen'. Het verschil in overeenstemming suggereert dat SO's en verzorgende/verpleegkundigen niet dezelfde taal spreken wanneer het over pijn gaat en dat er daarom behoefte is aan interdisciplinair onderwijs en training.

Een volgende stap in de ontwikkeling van de PAIC36 was het onderzoeken van de betrouwbaarheid van het meetinstrument: of de observaties tussen verschillende beoordelaars vergelijkbaar zijn (observer agreement).
Hoofdstuk 6 beschrijft een observationele studie welke verricht is in vijf Nederlandse verpleeghuizen (Stichting Zorggroep Florence, Topaz, Woonzorgcentrum Haaglanden, Saffier de Residentie). In deze verpleeghuizen werden in totaal 45 bewoners met een gevorderde tot vergevorderde dementie geobserveerd door zorgmedewerkers (observatoren). De observaties vonden plaats tijdens rust en tijdens beweging. Van elk item van de PAIC36 werd vervolgens de prevalentie en de observer agreement onderzocht. Deze studie laat zien dat vooral de items uit de domeinen 'lichaamsbewegingen' en 'stemgeluiden' een hoge observer agreement hebben (>70%). De prevalentie van deze items was echter laag, vooral tijdens rust. De items van het domein 'gezichtsuitdrukkingen' hadden een lager percentage observer agreement (<70%), vooral tijdens beweging. De prevalentie van deze items was echter wel hoog. Uit deze studie kan geconcludeerd worden dat de observer agreement van de items van de PAIC36 veelbelovend zijn in een klinische setting.

Naast de validiteit en betrouwbaarheid van de Nederlandse versie van de PAIC36, wordt in hoofdstuk 7 de PAIC36 op internationaal niveau onderzocht. De observer agreement werd onderzocht en er werd een factoranalyse uitgevoerd. In deze multi-center observationele studie, welke plaats heeft gevonden in vier verschillende landen (Italië, Servië, Spanje en Nederland), werden in totaal 190 personen met dementie geïncludeerd. Zij waren afkomstig uit verschillende klinische settingen. Alle deelnemers werden, net als in de Nederlandse studie (hoofdstuk 6), geobserveerd door zorgmedewerkers tijdens rust en beweging. Resultaten uit deze internationale studie laten zien dat de observer agreement van de verschillende items over het algemeen hoog was (>70%). Ook hier zagen we dat observer agreement van enkele items van het domein 'gezichtsuitdrukkingen' lager was. Een opvallende bevinding was dat er vooral in Nederland een lagere overeenstemming gevonden werd. Mogelijk omdat juist in Nederland minder onderwijs en training in het gebruik van dergelijke meetinstrumenten gegeven wordt.
Er werd ook een factoranalyse uitgevoerd. De factoranalyse werd gebruikt om te kijken of er onderliggende factoren/patronen zijn in de verschillende items. Items die vergelijkbare patronen hebben worden bij elkaar geplaatst. De factoranalyse liet zes onderliggende patronen/factoren zien: verbale expressie van pijn, (anatomisch gestandaardiseerde) gezichtsuitdrukkingen, beschermende lichaamsbewegingen, verbaal verzet, gespannenheid en verminderde emotionele reactie.
Op basis van de resultaten uit zowel hoofdstuk 5, 6 en 7 kan geconcludeerd worden dat observaties middels de PAIC36 goed uitgevoerd kunnen worden. Echter, een pijnobservatieschaal bestaand uit 36 items is te omvangrijk om te implementeren in de praktijk. Itemreductie was daarom een belangrijke stap in de ontwikkeling van de PAIC en de resultaten zoals beschreven in hoofdstuk 5, 6 en 7 hebben daaraan bijgedragen.
Uiteindelijk heeft dit geleid tot de definitieve klinische pijnobservatieschaal: PAIC15. Op dit moment lopen er verschillende onderzoeken naar de implementatie en effectiviteit van de PAIC15, waaronder bij het Universitair Netwerk voor de Care sector Zuid-Holland (UNC-ZH) in Leiden en bij het Universitair Netwerk Ouderenzorg (UNO-UMCG) in Groningen.

De klinische praktijk

Uit het eerste deel van dit proefschrift komt naar voren dat pijnmanagement bij mensen met dementie, waaronder het regulier gebruik van pijnobservatieschalen, slecht geïmplementeerd is. Daarentegen is ook uit onderzoek gebleken dat de implementatie van een pijnobservatieschaal alleen niet voldoende is om de pijn bij mensen met dementie te verlagen. Het is dus belangrijk dat we verder denken dan alleen meetinstrumenten en ons richten op een systematische aanpak van pijn. Verenso heeft daarom de multidisciplinaire richtlijn 'Pijn; Herkenning en behandeling van pijn bij kwetsbare ouderen' opgesteld.
Echter, er zijn verschillende aandachtspunten, zowel op organisatieniveau als aandachtspunten betreffende interdisciplinair onderwijs/training. Op organisatieniveau is het vooral belangrijk om een multidisciplinair pijnteam te implementeren, een individueel zorg- en behandelplan op te stellen, goede samenwerking tussen artsen en verpleging, gebruik maken van een evidence based programma zoals STA-OP! en aandacht voor implementatiestrategieën waarin het o.a. belangrijk is om aandacht te hebben voor implementatie barrières. Als laatste is het van belang om gebruik te maken van zogeheten 'pain champions'. Zij vormen de brug tussen de verpleging en artsen en fungeren als de drijvende kracht achter het integreren van de pijnobservatie in de dagelijkse praktijk.
Uit hoofdstuk 5 blijkt dat verpleging en artsen niet dezelfde taal spreken en daarom is het van belang dat er aandacht is voor interdisciplinaire onderwijsvormen en dat er verschillende vormen van onderwijs en training gecombineerd worden.

Conclusie

De resultaten en aanbevelingen die in dit proefschrift beschreven worden kunnen bijdragen aan het verbeteren van het pijnmanagement bij mensen met dementie. Denk aan de suggesties met betrekking tot onmisbare onderwijs- en trainingsprogramma's en implementatie strategieën. Een van de belangrijkste bevindingen is dat, naast probleemgedrag, ook achteruitgang in het ADL functioneren een rode vlag is voor de aanwezigheid van pijn. De klinische boodschap is dan ook: wanneer er een achteruitgang in ADL functioneren wordt opgemerkt, moet dit niet automatisch toegeschreven worden aan de progressie van de dementie. Er moeten ook andere oorzaken overwogen worden waarvan pijn absoluut tot de differentiaaldiagnose behoort. Voor nog diepgaander onderzoek betreffende deze relatie zijn er meer longitudinale studies nodig met diverse analysetechnieken. Daarnaast zijn N=1 studies ook een mooie manier om deze relatie nader te onderzoeken.

De ontwikkeling van de PAIC markeerde het startpunt van het creëren van een robuust, valide, betrouwbaar en internationaal meta-tool om pijn te kunnen meten bij mensen met dementie. Een instrument wat zowel in de kliniek als in wetenschappelijk onderzoek gebruikt kan worden. Momenteel wordt er nog steeds onderzoek gedaan naar de PAIC15, onder andere naar de uitvoerbaarheid en klinische bruikbaarheid bij andere doelgroepen.

Dankwoord

Het zit erop! Ein-de-lijk is mijn proefschrift af. Het was een geweldig avontuur met pieken en dalen, maar bovenal een ontzettend mooie uitdaging zowel op professioneel als op persoonlijk vlak. Promoveren doe je niet alleen, er zijn een aantal belangrijke mensen die elk op hun eigen manier aan dit proefschrift hebben bijgedragen.

Wilco, jouw enthousiasme en passie voor het vak ouderengeneeskunde en in het bijzonder het wetenschappelijk onderzoek hebben mij overgehaald om als eerste in Leiden het aioto-traject te starten. Als jij niet in Leiden was gekomen, was ik wellicht geen specialist ouderengeneeskunde geworden en misschien niet eens gepromoveerd. Ik ben blij dat het anders gelopen is. Bedankt voor je persoonlijke en flexibele begeleiding. Het was een voorrecht om met jou samen te mogen te werken en hopelijk kunnen we dit blijven voortzetten.

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Het combineren van onderzoek en opleiding was niet mogelijk geweest zonder de ondersteuning en flexibiliteit van de opleiding tot specialist ouderengeneeskunde.
Paul Went (voormalig hoofd opleiding tot specialist ouderengeneeskunde): bedankt dat je deze kritische aios in 2011 de ruimte hebt gegeven om als aioto-so te starten. Ook dank aan jou, Victor Chel, voor het vrijmaken van uren om te besteden aan mijn promotieonderzoek.
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Mijn speciale dank gaat uit naar Hans en zijn vrouw. Dank dat ik een klein stukje van Hans zijn reis door de dementie mocht gebruiken om dit proefschrift kracht bij te zetten.

Lieve familie, schoonfamilie en vrienden, bedankt voor de belangstelling en interesse tijdens mijn promotieonderzoek. Lieve schoonpap en -mam, bedankt voor de steun en het inspringen daar waar nodig, maar bovenal dank voor al het oppassen op de groeiende kinderschare.

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Curriculum Vitae

Annelore Hermine van Dalen-Kok was born on October 2nd, 1984 in Leidschendam. She attended secondary school in Leidschendam at the Veurs College where she started at MAVO and eventually obtained her VWO diploma in 2003. That same year she started the study Medicine at the Leiden University, where she obtained her Medical Doctor's degree in 2009. After this she went to work at nursing home Westhoff, Stichting Zorggroep Florence in Rijswijk. In September 2010, she started the post academic training to become an elderly care physician in Leiden. In 2011 she was the first elderly care physician trainee in the Netherlands who combined her training with PhD research at the Department of Public Health and Primary Care (PHEG) of the Leiden University Medical Center (LUMC). She completed the training to become an elderly care physician in July 2017. Since then, she has been working in the nursing home 'Mariahoeve' in The Hague, where she focusses on the care for persons with young-onset dementia. In January 2022 she became the program leader of the young-onset dementia care program at Stichting Zorggroep Florence. Besides her clinical work, Annelore also was a lecturer in the scientific educational program for the elderly care physicians in training at the PHEG-LUMC. At present she is a guest lecturer 'pain and dementia', for the master students of geriatric physiotherapy at the Hogeschool Utrecht. She will continue her research at the University Network for the Care Sector South Holland (UNC-ZH) within the research theme 'Quality of life in people with dementia'. Annelore is married to Alex and together they have three sons, Liam (9), Luuk (5) and Levi (2).

List of publications

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