How, why and where it hurts - breaking down pain syndrome among nursing home patients with dementia. A cross-sectional analysis of the COSMOS trial

Shunta Wagatsuma, MD student[1 α], Taizo Yamaguchi, MD student[1], Line I. Berge, MD, PhD[2,3], Bettina Husebo, MD, PhD[2,4], Torstein F. Habiger, MD, PhD student[2], Rui Nouchi, PhD[5,7], Renira C. Angeles, PhD[2,6]

[α] *Shunta Wagatsuma and Taizo Yamaguchi are both first authors*

[1]Tohoku University, The School of Medicine, Sendai, Japan

[2]Department of Global Public Health and Primary Care, University of Bergen, Norway

[3] NKS Olaviken Gerontopsychiatric Hospital, Bergen, Norway

[4] Municipality of Bergen, Norway

[5]Institute of Development, Aging and Cancer (IDAC), Tohoku University, Sendai, Japan

[6]NORCE Norwegian Research Centre

[7]Smart Aging Research Center, Tohoku University, Sendai, Japan

Corresponding author:

Renira C. Angeles, Postdoctoral Research Fellow rean@norceresearch.no

Abstract

Background: Between 40-60% of nursing home patients with dementia suffer from chronic and acute pain despite increasing their analgesic drug prescription.

Objective: Determine the locations and intensity of pain and the association between quality of life (QoL) and four stratified pain - analgesic groups: 1) pain – analgesics treatment, 2) pain - no analgesics, 3) no pain - analgesics, and 4) no pain - no analgesics.

Design: Multicenter, multicomponent cluster randomised controlled COSMOS trial.

Data and Methods: 723 nursing home patients were enrolled at baseline; 463 were completely evaluated for the presence of pain and included in the cross-sectional analyses.

ANCOVA were used to compare pain and QoL across pain - analgesics groups.

Measurements: Cognitive function (Mini-Mental-State Evaluation, MMSE), Quality of Life in Late stage of Dementia (QUALID) and Dementia-Specific QoL (QUALIDEM), Mobilization–Observation–Behavior–Intensity–Dementia Pain Scale (MOBID-2), and number of analgesic drug prescription.

Results: 78% had moderate to severe dementia; 74% were female, and the mean age was 86.7. Almost 44% reported clinically significant pain. 69% had ≥ 2 pain locations, especially in the musculoskeletal system. 33.5% had pain receiving analgesics, 10% had pain with no analgesics, and 27% had no pain receiving analgesics. Patients evaluated with clinically significant pain intensity scores had lower QoL (<.001) compared to assessments relying on different pain locations.

Conclusion: Untreated musculoskeletal and multi-located pain is still common in nursing home patients with dementia. A significant share without pain receives analgesics. Proper pain assessment and regular re-assessment are prerequisites for the prescribing and deprescribing of analgesics. Pain intensity scores are more significantly connected to QoL. This must be stressed when evaluating pain and QoL.

Keywords: pain, pain assessment, dementia, analgesics, nursing home, quality of life

Introduction

Approximately 40-60% of nursing home patients with dementia regularly experience pain (Achterberg et al., 2010; van Kooten et al., 2016). Both the prevalence of pain and dementia increases with age, in particular chronic pain, and around 5% of people over 65 years old have a diagnosis of dementia, rising to over 50% in those aged over 90 years (WHO, 2012). In late stage dementia, when language, daily function and cognition are impaired, disclosing needs (Corbett et al., 2012; Herr et al., 2006; Husebo et al., 2010), such as the experience of acute and chronic pain, location of pain, pain intensity, treatment of pain and the side-effects of the treatment, becomes difficult (Husebo et al., 2016).

Measuring pain among people with dementia is demanding due to different practices and

interpretations in nursing homes. How to determine suitable pain management is one of the main challenges in the treatment and care of pain within this group (Achterberg et al., 2013). Nonetheless, it is of great importance, as a range of studies have shown that pain is negatively associated with QoL (Cordner et al., 2010; Beerens et al. 2013; Flo et al., 2014).

There is little evidence of efficient treatment with analgesics for nursing home patients with dementia (Achterberg et al., 2013), and despite extensive use of pain assessment tools, the share of untreated pain among patients with cognitive decline in nursing homes is still high (Corbett et al., 2012). Compared to patients with no dementia in a nursing home setting (52%), patients with dementia have lower probability of receiving analgesics, and the prevalence is 46.8% (de Souto Barreto et al., 2013). Moreover, the rate has increased the last two decades (Sandvik et al., 2016). Despite increasing opioid prescriptions in people with dementia (Erdal et al., 2018; Hunnicutt et al., 2018), nursing home residents remain in pain (Griffoen et al., 2019). Notably, the rise in opioid prescriptions is particularly high among patients with dementia living at home (Jensen-Dahm et al., 2015).

This is important due to the possibility of polypharmacy in relation to numerous pain medications in people with limited ability to report medication side-effects (Buffum et al., 2001). For example, nursing home residents with dementia and pain using paracetamol, opioids, or both, reported lower QoL than patients not using analgesics (van Dam et al., 2019).

In studies showing the inefficacy of analgesics, there were no regular assessments with

validated pain instruments (Husebø et al., 2014). Assessments are most efficient if they are based on the observation of the patient's pain behavior during daily movements (Husebo et al., 2014). One recommended tool is the MOBID-2 because, in addition to assessing pain intensity, it differentiates the location of the bodily pain, which is relevant for proper management (Husebo et al., 2010). MOBID-2 also differentiates between pain location, which is relevant for the clinician since different locations of pain may require different treatment approaches.

This paper has two objectives. One is to provide the patient characteristics and clinical variables related to MOBID-2 pain intensity, pain location and pain location frequencies among nursing home patients with dementia. Our second goal is to explore the association between QoL and the various domains of MOBID-2, stratified according to the presence of pain and use of analgesic. The analyses use baseline data measurements from the Norwegian COSMOS trial, conducted in 2014-2015 (Husebo et al., 2019).

Methods

Study Design

COSMOS is a multi-center single-blinded controlled trial. COSMOS is an acronym of the intervention's four elements: to enhance nursing home staff's awareness of information concerning the Communication of advanced care planning, Systematic pain management, Medication review and Organization of activities. COSMOS includes long-term nursing home patients aged 65 or more (Husebo et al., 2015; Husebo et al., 2019), and excludes people with schizophrenia and a life expectancy of less than 6 months. The clusters (1 cluster = 1 nursing home unit) are randomised into intervention (N=297) or

control groups (N=248) (Husebo et al., 2019).

Outcome Measures

The location, frequency, and intensity of pain were measured by the MOBID-2 Pain Scale, a validated two-part proxy-rater pain assessment instrument, which is applicable to patients with moderate to severe dementia who are no longer able to report own pain (Husebo, 2017; Husebo et al., 2010). In MOBID-2 Part I, the instrument focused on nociceptive, musculoskeletal pain during active, guided movements of the trunk and extremities. Five active movement items were explored: (1) open both hands, (2) stretch both arms towards head, (3) stretch and bend both ankles, knees and hips, (4) turn over in bed to both sides and (5) sit at bedside. Trained nursing home staff carefully instructed the patient on each location's movement and scored the intensity of pain from 0 (no pain) to 10 (severe pain) based on the patient`s typical behaviour of pain such as pain noises, facial expression and defence. In MOBID-2 Part II, pain that might be related to internal organs, head and skin were evaluated in accordance with observed pain behaviour during the last week and documented on a body chart with respect to potential pain locations. The total pain intensity score (range 0-10) was defined as clinically significant if the pain score was greater than 2/10.

The QoL was assessed by two measurements. The Quality of Life in Late-Stage Dementia Scale (QUALID) was based on the caregivers` evaluation of the patients` typical behaviour during their daily life activities (Weiner et al., 2000). This was composed of 11 items using a 5-point scale for each category (range 11 – 55, best and worst QoL, respectively) (Benhabib et al., 2013; Sanches-Valdeon et al., 2019). The Quality of Life

Dementia Scale (QUALIDEM) is an 18-item instrument, divided into 6 subscales: Care relationship, Positive affect, Negative affect, Restless tense behaviour, Social relations and Social isolation (Ettema et al., 2007). The maximum score is 54 points; lower score means poor QoL (Dichter et al., 2019).

We stratified our sample into four groups based on the pain intensity and regular analgesics history (ATC code: N02A -opioids), N02B - other analgesics (except for opioids) and antipyretics, and N02C - antimigraine medicine: 1) pain – no analgesics (MOBID-2 total score ≥ 3 with 1 or more regular analgesics), 2) pain – no analgesics, 3) no pain - analgesics (MOBID-2 total score < 3 and one or more regular analgesics), and 4) no pain – no analgesics.

Other measures

The severity of dementia was measured by the Mini Mental Status Examination (MMSE). This assessment instrument was a simple way to quantify the cognitive impairment with an 11-item test, whose maximum score was 30-points (Folstein et al., 1975). A lower score indicated poorer cognitive function and severe dementia. The following cut-off points for MMSE score were used: severe dementia (0-11), moderate dementia (12-17), and mild dementia (18-23) (Engedal et al., 1988; Teri et al., 2000).

Activities of Daily Living (ADL) was assessed by the Physical Self-Maintenance Scale (Lawton and Brody, 1969; Fish, 2011). ADL was proxy-rated and based on 6 categories: feeding, bathing, toileting, dressing, moving, and grooming. Each category had 5 items, and the range of total score was 0 - 30. A lower score indicated more independent daily activities. Data on use of analgesics (classified in ATC code: N02a, N02b and N02c) were

extracted from their medical record. Among them, the regular analgesics data (0 or ≥ 1) were used to stratify participants into pain - analgesics groups.

Statistics

The analysis of covariance (ANCOVA) and Bonferroni tests were used to compare the variables of the four stratified pain - analgesics groups. In addition, the ANCOVA was used to assess QoL stratified by different pain - analgesics groups. The QoL (QUALID and QUALIDEM) was the dependent variable. Each of the pain variables and analgesic variables were independently coded in the analysis. The effect of gender was adjusted since there was a gender ratio difference in the sample. The permutation test was conducted with ANCOVA due to non-normal distribution, as it further controlled the rate of type I errors (Camargo et al., 2008). Missing data was handled with listwise deletion, and the p-value threshold was less than .05 as statistically significant. All analyses were conducted using “Psych” and “ImPerm” packages in R version 3.6.3.

Results

723 patients were enrolled from 33 nursing homes. In Table 1, the baseline data included 545 patients from 67 units in 31 nursing homes, and 463 residents were completely evaluated regarding pain intensity by MOBID-2. The mean age was 86.7 years; 74% were women and 78% of the sample had moderate to severe dementia with mean MMSE score of 10.9 (Table 1). On average, the total pain intensity score was 2.6 (range: 0-10), with multiple pain locations; most had more than one (mean 2.3) pain location (range: 0-10). The sample average for QUALIDEM was 39.8 (range: 0 - 54) and 21 for QUALID. ADL was 17.4 (range: 0-30), and it was significantly higher for the group with pain and regular

analgesics treatment, compared with the no pain – analgesic treatment group. As shown in Table 1, most of the pain stemmed from old fractures (11.4%) and the musculoskeletal system (8.4%). For the pain with analgesics group, old fractures, arthritis (6.5%) and musculoskeletal were the most frequent sources of pain. Less frequent sources of pain for either group were cancer (4.5%) and osteoarthritis (3.9%).

A total of 98.5% of the patients were prescribed regular medications, 93.7% on demand. On average, every patient received 7.5% of regular medications, 3.3% on demand (Table 2). The mean number of regular medications was 9.4% for the pain and analgesics group. In the two groups encompassing patients with analgesic treatment, patients were prescribed regular analgesics 1.5 times per day. In the category "other analgesics and antipyretics", analgesics (0.5 times) were prescribed more than opioids (0.4 times).

Table 3 shows intensity scores across 10 pain locations, including pain frequency for all groups. The pain – analgesics group (33.5%) had highest pain intensity in the legs (3.4) and hips (2.7). The back and pelvis were the second most intensive pain locations reported. Both pain groups had up to 4 and 3.2 pain locations (Table 3). For the pain – analgesics group, 2.6 was on average reported for the musculoskeletal system (range: 0-5). The differences between the pain - analgesic groups are significant at the 1 % level. Patients with no pain and no analgesic treatment had high QoL score (<.001), while patients with pain and analgesic had the lowest average QoL score (37.3) when using QUALIDEM. Similarly, patients with no pain and no analgesic had on average the highest QoL score when assessed by QUALID (18.9) (Table 1). The poorest QoL score was reported in the pain - analgesic group (24.5).

Table 1 about here

Table 2 about here

Table 3 about here

Table 4 demonstrates the results from the ANCOVA analysis of QoL across the pain - analgesics groups using the MOBID-2 pain intensity score. The Bonferroni's post hoc test for total intensity shows that there is a significant association between analgesics and QoL across the reference group (pain – analgesics group) and patients in the pain - no analgesic group. The coefficient for the association is ≥0.5 meaning that the two groups differed by a 0.5 standard deviation or more. There is also a significant difference between patients with pain on analgesics and patients with no pain nor analgesic treatment. Both effects are significant at the 10 % level. The results in Table 4 suggest that patients on regular analgesics reported poor QoL regardless of their pain intensity.

There is a significant association between analgesics treatment and QoL, and patients with pain in multiple location treated with regular analgesics had poorer QUALID ($P<0.001$). In the same way, the interaction term between pain location frequency and analgesics was significantly associated with QUALIDEM. Among patients on analgesics treatment with pain in multiple locations, QUALIDEM was lower compared to patients not on regular analgesics ($P< 0.009$). The Bonferroni test showed a high mean difference (0.666) between patients with a high frequency on regular analgesic versus patients with a lower frequency on analgesic ($P< 0.001$).

We tested how pain in the musculoskeletal system and analgesics treatment are associated with QoL. Table 4 shows that patients with musculoskeletal pain and analgesics had a poorer QoL ($P<0.001$) compared to all other groups; however, the interaction term (musculoskeletal pain*analgesic) showed almost no association, and this is also insignificant (for both QoL measurements). There are significant mean differences across groups. It is particularly high (0.560) between patients with musculoskeletal pain on analgesics and patients with no pain but still on regular analgesics. This finding remains significant when using the total intensity score and frequency of pain.

Patients who had high leg pain intensity treated with regular analgesics also had lower QoL compared to patients with the same pain syndrome but no analgesics. For QUALID and QUALIDEM, the mean differences are low ($P<0.050$). Patients with no leg pain and no regular analgesics experience higher QoL compared to patients who receive these drugs.

Table 4 about here

Discussion

This study aims to investigate the locations and intensity of pain in nursing home patients with dementia and explore the association between the QoL and four pain - analgesic groups. We found that almost 44% reported clinically significant pain, while 69% had ≥2 different pain locations, most frequently related to the musculoskeletal system. Further, 34% of the patients were in pain when receiving analgesics, 10% were in pain with no analgesics, and 27% had no pain but still received analgesics. Only 29.6% had no pain without any pain management. Patients evaluated with clinically significant pain intensity

scores had lower QoL (<.001) compared to evaluations on different pain locations.

Pain intensity

The study shows that overall pain intensity was highest in the group with regular analgesics prescription. The pain - analgesics group had the highest score in total intensity, as well as the highest intensity in specific location and frequency. This suggests that patients who had relatively more pain also received the most analgesics treatment. The most frequent pain diagnoses concerned old fracture and musculoskeletal system related pain, but also arthritis, cancer and osteoporosis. This is fairly in line with previous findings by Hoffmann et al. (2014), who investigated pain diagnoses in 1 848 people with dementia and found that the most common cause of pain was a musculoskeletal pain diagnosis such as back pain followed by pain due to arthritis osteoarthritis. This coincides with findings from Husebo et al. (2008), who assessed pain diagnoses, location and intensity by MOBID-2 across different levels of dementia.

Pain location

Across all stratified pain – analgesics group, the most common pain is related to the musculoskeletal system, located in the legs. The second most intensive pain in a specific location concerned the back and pelvis. Pain in the head and skin were less prevalent, but not completely absent, while pain related to the heart and other internal organs was rather low. This is in line with previous research (Husebo et al., 2010; Husebo et al., 2008). As demonstrated by MOBID-2 (Husebo et al., 2010), the differentiation between pain related to the musculoskeletal system, internal organs, head, and skin is relevant for the clinician, since different locations of pain may require different treatment approaches.

Pain location, frequency and pain assessment

The study also shows that most patients had more than one pain location (up to 4). Our findings highlight the importance of using a pain assessment tool that not only assesses the prevalence of pain, but also the location of pain. Other pain assessment tools such as the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) and Pain Assessment in Advanced Dementia scale (PAINAD) rely mainly on observing typical behaviour that might be related to pain (e.g. vocalisation, agitation, defence) but not the location of pain (van t'Hof et al., 2011; Warden et al., 2003). It is important for the clinician to identify different pain locations, as different causes can warrant different treatment options. For example, back pain caused by compression fractures in the spine has different treatment options than muscular pain originating from the shoulder (Greenberg, 2014; McCarthy et al., 2016). The use of a pain assessment tool such as MOBID-2 helps the physician and nurse to discover different pain locations and thereby aide in the selection of treatment options.

QoL

The main finding in the second part of our analysis is that QoL is lowered in pain groups using one or more regular analgesics compared to pain groups with no prescription. The groups using analgesics are also the groups using most regular opioids (Table 1). The lowered QoL in the pain - analgesics group may be due to low duration, low dose, high intensity of pain, side-effects or less regular pain assessment. The power of the association with QoL is lower across the four pain - analgesics groups for specific pain location, i.e. musculoskeletal related pain, and leg pain – compared to variables describing total

intensity and frequency of pain location.

In other words, there are larger significant differences between the groups with self-reported QoL when using total score and frequency. The stronger association (<.001) between reduced QoL, pain intensity score and musculoskeletal pain, compared to location such as the leg, suggests that it is the total intensity score rather than the locality of pain that determines the QoL in nursing home patients with dementia. Musculoskeletal pain and leg pain are more weakly connected to QoL compared to the use of total intensity score (Table 4). This is in line with van Dam et al. (2019) who found no effect on QoL when patients received paracetamol treatment.

Pain treatment

The study shows that nearly 34% of nursing home patients with severe dementia experience pain despite analgesic drug prescription. 10% of those in pain are not regularly scheduled for analgesics treatment, and 27% of the patients with no pain are regularly scheduled to receive pain management.

The reason why pain still persists among patients in the pain - analgesic group may be due to small doses, the wrong type of analgesics or factors such as frequent campaigns by The Norwegian Medical Associations that influence the use of medications, for instance, by encouraging their members to reflect on their own practice of prescribing opioid treatment. The 27% on analgesics treatment in this group may in fact still suggest overtreatment. However, it may also mean optimal treatment, as they would probably be in pain if analgesics treatment were absent. The 10% who are not treated with analgesics may be treated in a way not informed by the data, or their pain may be undetected by staff. Table 1 also shows that when analgesics are needed for people with dementia with

significant pain on regular analgesics, opioids tend to be prescribed on demand. Analgesics are necessary, but patients suffer from multiple types of pain and there is a risk that analgesics alone come short when discriminating between multiple locations.

By regulation, examination of medication for patients in Norwegian nursing homes is required a minimum of once per year. Pain assessments and additional reviews beyond this requirement vary, including for patients with dementia. Pain management in vulnerable groups is preferably conducted in an interdisciplinary setting (Achterberg et al., 2020). Proper assessments are not the only crucial part of pain management; however, the effect of the initiated treatment should be regularly controlled to avoid pain despite treatment and patients with dementia with no pain being listed as on the medication.

As both analgesic treatment and valid and effective pain assessment tools are required for the most efficient treatment of pain, educational training for nursing and care staff in improving pain assessment and the analgesic-prescribing practice for patients with dementia can be valuable. The use of analgesics has increased from 34.9% in 2000 to 57.6 % in 2011, and similarly the use of opioids rose from 1.9% to 17.9% in the same period (Sandvik et al., 2016). Nevertheless, despite the prescription, patients using opioids are still in pain (Griffioen et al., 2019), and the prevalence of opioid use is 32.4 %, although opioid use is lower among people with the most severe cognitive impairment (Erdal et al., 2018; Hunnicutt et al., 2018). Patients with dementia need to be assessed using an observational pain assessment tool (Corbet et al., 2016) to determine whether they suffer from pain (Sandvik et al., 2016).

Our analysis is the first to confirm these results with a relatively large sample size in a

dementia context, yielding the high generalisability of our findings. Our study is the first assessment of pain intensity and different pain locations that examines the differences between groups in QoL that are not strictly based on intensity score, as the intensity of specific body parts such as legs, and frequency of specific parts such as muscle and skeleton, are also taken into account.

Limitations and further research

Our cross-sectional study does not address the duration of pain nor the duration of treatment with analgesics, and assumptions regarding the association between QoL and the duration of treatment and/or pain cannot be made. A high frequency of analgesics prescriptions does not necessarily mean that appropriate treatment is being given to the right individual at the right time. Further, our data only shows treatment with pain analgesics, but different types of pain are not necessarily best treated with analgesics. For example, antiepileptic and antidepressant agents are often prescribed for neuropathic pain. Another limitation to our study is the measurement of QoL. Although, we have validated used measurements specifically for people with dementia in a care setting there are known challenges to measuring QoL among patient with cognitive impairment. Proxy-rated-generated QoL such as QUALIDEM and QUALID provides second hand information compared to, for instance, subjectively rated well-being – which is a challenge among nursing home patients with dementia. Further, we utilized total score of the instruments, and did not test sensitivity of each items.

Our dichotomisation of pain, i.e. clinically significant pain versus non-clinically significant pain, may oversimplify the picture. There is a large range in scores in the group experiencing pain, and the likelihood of being prescribed one or more analgesics may

increase the more severe pain, which may partly explain our finding of lower QoL in pain groups using one or more analgesics compared to pain groups with no regular analgesics. We did not consider analgesic treatment prescribed on demand.

Our study implies several important directions for future research. Future studies should investigate pain in different body parts among nursing home residents with dementia compared to residents with no dementia. As there are difficulties in drawing conclusions on the duration of pain and pain analgesics based on cross-sectional studies, a longitudinal design involving nursing home residents with pain and dementia should be prioritised. When evaluating the connection between pain and QoL it must be stressed that there is a high within-variance of one type of pain assessment instrument. Our findings first and foremost motivate more comparisons *within* pain assessment tools. Finally, our sample consisted mostly of women (74%), and thus the question of whether there are true gender differences in pain expression remains unexplored.

Conclusions

Untreated musculoskeletal and multi-located pain is still common in nursing home patients with dementia. However, a significant share of patients receives analgesics with no pain, possibly suggesting that they are successfully treated. Proper pain assessment and regular re-assessment are prerequisites for prescribing and deprescribing analgesics in people with advanced dementia. Pain intensity scores are a more satisfactory measurement when evaluating pain and QoL.

Proper assessments are not the only crucial part of pain management, but the effect of the initiated treatment should also be regularly controlled to avoid pain despite treatment and patients with dementia but no pain being listed as on the medication.

In a research context, an expansion of observational pain assessment that analyses locations and total intensity in a dementia context for cross-country analysis should be translated. An important health policy implication for dementia care is the increasing problem with the use of opioids, other analgesics, and regular medications in Norwegian nursing homes. There is a pressing need to restructure pain assessment and pain management, as well as implement systematic checks concerning when to start, stop, or continue opioid therapy in people with dementia.

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Conflict of interests

None reported

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Tables

Table 1 Baseline demographics, pain intensity, pain location and pain frequency across pain – analgesics groups

	Total population (n=463)	Pain - analgesics (n=155)	Pain - no analgesics (n=47)	No pain - analgesics (n=124)	No pain - no analgesics (n=137)	*P*-value
% of sample		33.5	10.2	26.8	29.6	
Female (%)	74.1	76.8	85.1	75	66.4	0.056
Age (SD)	86.7 (7.4)	87.1(7.0)	86.7(8.2)	86.2(7.2)	86.7 (7.7)	0.834
MMSE score (SD)	10.9 (7.7)	11.1 (7.9)	11.2 (7.6)	11.0 (7.8)	10.4 (7.5)	0.973
Mild dementia (%)	22.1	23.2	26.8	25.0	16.9	
Moderate dementia (%)	26.8	24.6	24.4	26.7	30.0	
Severe dementia (%)	51.0	52.1	48.7	48.3	53.1	
Pain intensity (SD)	2.6 (2.6)	5.2 (1.9)	4.5 (1.6)	0.8 (0.9)	0.5(0.8)	<0.001
Pain location (SD)	2.3 (2.3)	4.0 (2.1)	3.2 (2.3)	1.3 (1.7)	0.9 (1.7)	<0.001
QUALID (SD)	21.2 (7.3)	24.5(7.9)	20.1 (7.5)	20.2 (6.9)	18.9 (5.5)	<0.001
QUALIDEM (SD)	39.8 (8.7)	37.3 (9.0)	17.1 (5.4)	17.1 (4.9)	16.6 (4.9)	<0.001
ADL (SD)	17.4 (5.3)	18.3 (5.4)	17.1 (5.4)	17.1 (5.4)	16.6(5.5)	0.046
Pain diagnosis (%)						
Old fractures	11.4	11.6	12.8	8.9	13.1	
Muscleskeletal	8.4	9.7	8.5	8.9	6.6	
Arthritis	7.8	11.0	4.3	6.2	6.6	
Cancer	4.5	3.9	2.1	4.0	6.6	
Osteoporosis	3.9	2.6	4.3	4.8	4.4	
Abdominal	2.2	1.9	2.1	3.2	1.5	
Neuropathy	1.5	0.6	2.1	2.4	1.5	
Skin, gangrene	0.4	0.6		0.8		
Urological	0.9	0.6		2.4		
Migraine, headache	0.2	0.6				
Contractures	0.2	0.6				

SD - Standard Deviation
p < .05 p < .01** p< .001****

Table 2 Regular and required medications across pain – analgesics group

	Total population (n=463)	Pain - analgesics (n=155)	Pain - no analgesics (n=47)	No pain -on analgesics (n=124)	No pain - no analgesics (n=137)	*P*-value
All kinds of regular medications (SD)	7.6(3.8)	9.4 (3.8)	7.0 (4.3)	7.9 (3.2)	5.4 (3.1)	<0.001
Regular analgesics, all - N02a, N02b and N02c (SD)	0.9(0.8)	1.5(0.6)		1.4(0.5)		<0.001
Regular opioids (SD)	0.4(0.6)	0.6(0.6)		0.5(0.6)		<0.001
Regular other analgesics and antipyretics (SD)	0.5(0.5)	0.9(0.3)		0.8(0.4)		<0.001
Regular antiepileptics	0.1(0.4)	0.1(0.4)	0.1(0.4)	0.1(0.4)	0.1(0.3)	0.935
All kinds of required medications	3.3(2.1)	3.7(2.0)	2.9(2.0)	3.4(2.3)	2.9(2.0)	<0.001
Total number of analgesics	1.0(0.7)	1.0(0.7)	0.7(0.7)	0.9(0.7)	0.9(0.6)	0.528
Total number of opioids	0.4(0.6)	0.6(0.7)	0.2(0.4)	0.4(0.5)	0.2(0.4)	<0.001
Other analgesics and antipyretics	0.5(0.5)	0.4(0.5)	0.6(0.5)	0.5(0.5)	0.7(0.5)	<0.001

SD - Standard Deviation
p < .05 p < .01** p< .001****

Table 3 Pain intensity, -location, and -frequency analysis across pain – analgesics group

	Total population (n=463)	Pain - analgesics (n=155)	Pain - no analgesics (n=47)	No pain - on analgesics (n=124)	No pain - no analgesics (n=137)	*P*-values for difference between groups	Total population (n=463)
MOBID-2 pain intensity score (0-10) mean, SD							
① Hands	0.5(1.4)	1.0 (2.0)	0.7 (1.6)	0.3 (1.0)	1.4(0.4)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) 0.045	0.5(1.4)
② Arms	1.1(2.2)	2.3(2.9)	1.6(2.4)	0.4(1.2)	0.3(0.9)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) <0.001 (2) - (3) 0.005	1.1(2.2)
③ Legs	1.6(2.4)	3.4(2.8)	2.2(2.7)	0.6(1.2)	0.2(0.7)	(1) - (4) <0.001 (1) - (3) <0.001 (1) - (2) <0.003 (2) - (4) <0.001 (2) - (3) <0.001	1.6(2.4)
③ Hips	1.3(2.3)	2.7(2.9)	2.0(2.8)	0.3(0.8)	0.3(0.9)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) <0.001 (2) - (3) <0.001	1.3(2.3)
④⑤ Back, pelvis	1.0(2.0)	2.2(2.7)	1.5(2.5)	0.2(0.6)	0.2(0.5)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) <0.001 (2) - (3) <0.001	1.0(2.0)
⑥ Head	0.7(1.7)	1.4(2.3)	1.1(2.3)	0.1(0.5)	0.1(0.5)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) 0.002 (2) - (3) 0.002	0.7(1.7)

⑦ Heart	0.3(1.1)	0.6(1.4)	0.7(1.7)	0.1(0.4)	0.1(0.3)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) 0.001 (2) - (3) 0.002	0.3(1.1)
⑧ Abdomen	0.4(1.2)	0.8(1.7)	0.6(1.8)	0.1(0.4)	0.1(0.4)	(1) - (4) <0.001 (1) - (3) <0.001	0.4(1.2)
⑨ Pelvis	0.7(1.7)	1.7(2.3)	0.9(2.0)	0.2(0.5)	0.2(0.7)	(1) - (4) <0.001 (1) - (3) <0.001 (1) - (2) 0.016 (2) - (4) 0.016 (2) - (3) 0.033	0.7(1.7)
⑩ Skin	0.7(1.6)	1.3(2.4)	1.2(1.8)	0.2(0.5)	0.2(0.7)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) 0.001 (2) - (3) <0.001 (1) - (2) 0.014	0.7(1.6)
Total intensity	2.6(2.6)	5.2 (1.9)	4.5(1.6)	0.8(0.9)	0.5(0.8)		2.6(2.6)
MOBID-2 number of pain locations (0-10) mean, SD							
MOBID-2, Part I ①-⑤ (0-5)	1.5(1.6)	2.6(1.5)	1.9(1.6)	1.0(1.3)	0.5(1.0)	(1) - (4) <0.001 (1) - (3) <0.001 (1) - (2) 0.024 (2) - (4) <0.001 (2) - (3) <0.001 (3) - (4) 0.043	1.5(1.6)
MOBID-2 Part II, ⑦-⑨ (0-3)	0.4(0.8)	0.9(0.9)	0.6(0.9)	0.2(0.5)	0.2(0.5)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) 0.001 (2) - (3) 0.005	0.4(0.8)
Head (0-1)	0.2(0.4)	0.4(0.5)	0.2(0.4)	0.1(0.2)	0.1(0.3)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (3) 0.026	0.2(0.4)
Skin (0-1)	0.2(0.4)	0.2(0.4)	0.4(0.5)	0.1(0.3)	0.9(1.7)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) <0.001 (2) - (3) <0.001	0.2(0.4)

Total number of pain locations	2.3(2.3)	4.0(2.1)	3.2(2.3)	1.3(1.7)	0.9(1.7)	(1) - (4) <0.001 (1) - (3) <0.001 (2) - (4) <0.001 (2) - (3) <0.001	2.3(2.3)

SD - Standard Deviation
n for Pain and Medications variables indicate the number of those who suffer from each pain, or consumes more than 1 medication.
p < .05 p < .01** p< .001****

Table 4 ANCOVA analysis of pain intensity, pain location and pain frequency and QoL across pain - analgesic treatment groups

Associations	**QUALID (η^2)**	**QUALIDEM (η^2)**	**Bonferroni's post hoc test**		
	(n=462)	(n=446)			Cohen's d
			*Intensity*analgesics*		
Total pain intensity score	0.051***	0.014**	pain/analgesic - pain/no analgesics.	0.572*** [0.329-0.814]	0.342***[0.099-0.584]
Analgesics	0.023***	0.015***	pain/analgesics - no pain/analgesics	0.563*** [0.229-0.896]	0.488**[0.150-0.826]
Intensity*analgesics	0.007*	0.003			
Pain ≥3. No interaction effect found using QUALIDEM.					
	(n=437)	(n=421)	*Frequency*analgesics*		
Pain frequency	0.057***	0.023***	High freq./analg. - low freq./analgesics	0.660***[0.400-0.920]	0.469***[0.208-0.730]
Analgesics	0.025***	0.014*	High freq./analg. - High freq./no analgesics	0.493***[0.201-0.784]	0.402**[0.098-0.705]
Frequency*analgesics	0.011*	0.010*			
Pain frequency: low freq. (no. of pain locations ≦1), high freq. (≧ 2 ≦10). Analgesics: Analgesics (no. of analgesics ≧1), no analgesics (no. of analgesics =0)					
	(n=452)	(n=435)	*Musculoskeletal (MS)-analgesics*		
Musculoskeletal pain dummy	0.046***	0.014**	MS/analgesics – no pain/analgesics	0.560*** [0.292-0.828]	0.360**[0.091-0.629]
Analgesics	0.024***	0.014**	MS/analgesics – MS/no analgesics	0.522*** [0.253-0.791]	0.388**[0.111-0.665]
Musculoskeletal*analgesics	0.005	0.004			
No. of musculoskeletal pain: high (≥1), no pain (=0). Analgesics: high (≥1), no analgesics (=0)					
	(n=471)	(n=453)	*Leg pain*analgesics*		

Leg pain intensity	0.028***	0.003	Leg pain/analgesic - leg pain/no analgesic	0.449**[0.116-0.782]	0.373*[0.025-0.720]
Analgesics	0.026***	0.019***	No pain/analgesic - no pain/no analgesic	0.346**[0.107-0.585]	0.261*[0.017-0.504]
Leg pain*analgesics	0.001	0.000			
Leg pain intensity: high ≥1, low =0. Analgesics: high ≥1, no med.=0					

p < .05 p < .01** p < .001****