JAMDA 22 (2021) 1692–1698

JAMDA

journal homepage: www.jamda.com

Original Study

Managing Pain and Psychosis Symptoms in Nursing Home Patients: Results from a Cluster-Randomized Controlled Trial (COSMOS)

Torstein F. Habiger MD [a,*], Wilco P. Achterberg PhD [a,b], Elisabeth Flo-Groeneboom PhD [a,c], Janne Mannseth PhD [a], Bettina S. Husebo PhD [a,d]

[a] Department of Global Public Health and Primary Care, Centre for Elderly and Nursing Home Medicine, University of Bergen, Bergen, Norway
[b] Department of Public Health and Primary Care, Centre for Elderly and Nursing Home Medicine, Leiden University Medical Centre, Netherlands
[c] Department of Clinical Psychology, Faculty of Psychology, University of Bergen, Bergen, Norway
[d] Municipality of Bergen, Bergen, Norway

Keywords:
Pain
psychosis symptoms
nursing home
dementia
opioid analgesics

A B S T R A C T

Objectives: In nursing homes (NHs), 30% to 60% of patients experience daily pain and >80% have dementia. This can lead to neuropsychiatric symptoms, including psychosis symptoms such as delusion. We investigated if there was a relationship between pain and psychosis symptoms over time. We also aimed to investigate the effect of a multicomponent intervention (COSMOS) on pain, psychosis symptoms, and analgesic prescription.

Design: COSMOS is a cluster-randomized, single blinded, controlled trial. Each NH unit was defined as a cluster and randomized to either the COSMOS intervention or care as usual. The COSMOS intervention is a multicomponent intervention, consisting of staff training in communication, pain treatment, medication review, organization of activities, and safety. The intervention lasted for 4 months with a follow-up at month 9.

Setting and Participants: Sixty-seven units from 33 Norwegian NHs in 8 municipalities. The study included 723 patients aged ≥65 years, residing at the NH ≥2 weeks before inclusion. Patients with a life expectancy <6 months were excluded.

Measures: Pain was measured using the Mobilization-Observation-Behavior-Intensity-Dementia Pain Scale. Psychosis symptoms were measured using the Neuropsychiatric Inventory—NH version. Measurements were performed at baseline, and months 4 and 9.

Results: Multilevel Mixed-Effect statistical analysis found that psychosis symptoms as a group (odds ratio [OR] 2.03, $P = .009$), and delusion (OR 2.12, $P = .007$) were associated with pain over time. No significant intervention effect on psychosis symptoms was observed. Compared with the control group, people with dementia in the intervention group experienced less musculoskeletal pain (β: −0.47, $P = .047$). Analgesic prescription was not affected by the intervention.

Conclusion and Implications: Pain is associated with psychosis symptoms, and pain assessment should be done when making treatment decisions on psychosis symptoms in NH patients. The COSMOS intervention improved musculoskeletal pain in people with dementia, but not psychosis symptoms, and there is need for further studies on treatment of psychosis symptoms in NH patients.

The nursing home (NH) population is heterogenic, with people experiencing many different acute and chronic conditions; over 80% have dementia.[1] Pain is common, and 30% to 60% of NH patients suffer from daily pain.[2,3] People with dementia are at risk of having untreated pain due to difficulties in reporting their own pain location and pain intensity, and this can in turn lead to reduced quality of life (QoL) and increased neuropsychiatric symptoms (NPS).[4–6] Due to these difficulties, physicians and nurses often have to rely on proxy rating or observation of behavioral signs to assess and treat the pain.[7]

The University of Bergen, the Norwegian Research Council (Protocol code: 222113) and Rebecca Ege Hegermanns Foundation financed the study. The funders had no role in study-design, data collection, data analyses, data interpretation, or writing of the article itself.

The authors declare no conflicts of interest.

* Address correspondence to Torstein F. Habiger, MD, Department of Global Public Health and Primary Care, Centre for Elderly and Nursing Home Medicine, University of Bergen, Alrek helseklynge, Årstadveien 17, Block D, 5018 Bergen, Norway.

E-mail address: Torstein.Habiger@uib.no (T.F. Habiger).

https://doi.org/10.1016/j.jamda.2021.05.008

More than 90% of people with dementia experience at least 1 NPS during the course of their disease.[8] Such symptoms can be detrimental for patients, family, and caregivers alike and seriously affect patients' QoL.[9,10] NPS can be grouped together in clusters according to coexistent symptoms, such as agitation, mood, and psychosis, the latter consisting of delusion and hallucination.[11,12] Psychosis symptoms are common in an NH, with prevalence varying between 14% and 30%,[1,13,14] and are often the result of dementia or delirium.[15] Studies have previously found that psychosis symptoms in people with dementia are associated with reduced QoL and admission to an NH.[16–18] An association between pain and delusion, but not hallucinations has also been found.[19,20]

Psychosis symptoms can be triggered by different medications that can cause unwanted side effects, such as delirium.[15,21] Further, polypharmacy is common in an NH population, and studies have shown that regular medication reviews are necessary to decrease the risk of unnecessary drug prescriptions, as well as unwanted side effects.[22,23] Guidelines on the treatment of psychosis symptoms recommend nonpharmacological measures as the first-line approach and highlight the importance of treating possible underlying causes.[24,25] Previous studies have found that other NPSs, such as agitation, can benefit from nonpharmacological measures; however, the effect on psychosis symptoms is uncertain.[26] If nonpharmacological measures are insufficient, treatment with antipsychotics is recommended in the acute phase for a limited time.[24,25] Several studies, including a randomized placebo-controlled discontinuation trial of antipsychotic medication by Ballard et al.,[27] have found that mortality increases and QoL is reduced in patients receiving antipsychotic medication.[28]

Systematic assessment and treatment of pain have the possibility to benefit more than pain.[29–31] Husebo et al.[29] investigated the effect of systematic pain treatment on agitation in people with dementia, where agitation was reduced in response to pain treatment. Secondary analyses from the same study also show positive effects on mood symptoms as well as psychosis symptoms.[30,31]

The COSMOS trial was designed to improve the QoL of NH patients through better COmmunication, Systematic assessment and treatment of pain, Medication review, Organization of activities and Safety, thus the acronym COSMOS.[32,33] As the intervention included elements that previous studies have found to improve both pain and psychosis symptoms, we aimed to analyze whether the multicomponent intervention could improve pain and psychosis symptoms in people with and without dementia. We hypothesized that the intervention would have a positive effect on both pain and psychosis symptoms. We also wanted to determine if the use of analgesics changed in response to the intervention, as well as the characteristics, such as QoL, of patients with pain using analgesics.

Further, baseline data from the COSMOS study found an association between pain and psychosis symptoms[19]; we aimed to investigate if this association persisted over time by analyzing the control group patients who received their usual care.

Methods

This study was based on secondary analyses from the COSMOS trial. The study was a multicenter cluster-randomized, single blinded controlled trial performed from 2014 to 2015, aimed at improving patients' QoL through the implementation of a multicomponent intervention. The study enrolled 723 patients from 33 NHs and 67 different NH units in Norway. The entire study protocol and a description of the COSMOS intervention have previously been published in full elsewhere,[32,33] hence a summary is presented.

Inclusion and Exclusion Criteria

Patients ≥65 years who had stayed at the NH for at least 2 weeks were included. Patients with a <6 months' life expectancy were excluded from the study.

Randomization and Intervention

Each NH unit was defined as a cluster and randomized to receive either the COSMOS intervention or care as usual. The COSMOS intervention components were based on current state-of-the-art evidence,[7,26,34–36] and was implemented through a 2-day education seminar for NH staff, as well as a medication review for all units during the intervention period. All NHs participated with at least 2 staff members who were put in charge of implementing the COSMOS intervention at their respective NH units. The intervention period lasted for 4 months, with a follow-up at month 9. Data collection was performed at baseline, month 4, and month 9. All assessments were performed by NH staff who knew the patient well.

Outcome Measures

Pain was assessed using the Mobilization-Observation-Behavior-Intensity-Dementia-2 (MOBID-2) Pain Scale. The scale has been thoroughly tested for validity, reliability, and responsiveness.[37,38] MOBID-2 consists of 2 parts, where part 1 assesses musculoskeletal pain through 5 actively guided movements during which the raters are encouraged to look for pain behavior. Part 2 consist of 5 items and assesses pain coming from head, skin, and internal organs. For each item, raters assess the patients' pain on a Numerical Rating Scale (NRS) from 0 to 10, where 0 represents no pain and 10 represents the worst pain possible. Finally, raters take all assessments into account and rate the patient's total pain score on an NRS from 0 to 10. A total pain score ≥3 is viewed as clinically significant pain.

Psychosis symptoms were measured using the Neuropsychiatric Inventory–Nursing Home Version (NPI-NH).[39] The NPI-NH measures the frequency and severity of 12 different NPSs (eg, agitation, delusion, and depression in the last week before assessment). Frequency (F) is measured on a scale from 0 to 4, where 0 represents not present, and 4 represents present daily. Severity (S) is measured on a scale from 1 to 3, where 1 represents mild symptom severity and 3 represents a severe symptom with high stress on the patient. The scores for frequency and severity are multiplied to generate a score for each symptom ranging from 0 to 12. A score ≥4 is considered a clinically significant symptom.[40] Previous factor analyses of NPS have found different symptom clusters, among others the psychosis symptom cluster, which consists of delusion and hallucinations.[11,12]

Other secondary outcome measures include the Cornell Scale for Depression in Dementia (CSDD),[41] and the Quality of Life in late-stage Dementia (QUALID).[42] Information concerning medication and diagnoses were obtained from the patients' medical records. Analgesics were defined as the group N02 in the Anatomical Therapeutic Chemical (ATC) classification system, which was further subdivided into opioid analgesics (N02A) and nonopioid analgesics (N02B and N02C). In addition, cognitive function was assessed using the Mini Mental State Examination (MMSE).[43]

Statistics

Analyses were performed by TFH in collaboration with a statistician (JM). The intervention effect on pain and psychosis were analyzed using Multilevel Mixed-Effect Linear Regression, with random

intercept for clusters and time as a categorical variable. The association between pain and psychosis over time in the control group was investigated using Multilevel Mixed-Effect Logistic regression with maximum likelihood estimation and random intercept for clusters. A clinically significant symptom of psychosis, representing the presence of 1 or more symptoms of psychosis, was defined as the dependent variable, and a clinically significant MOBID-2 score (≥3) was established as an independent variable. The same analysis was conducted for the individual symptoms of psychosis. Associations were adjusted for the effect of time, defined as a categorical variable, age, dementia severity, and use of opioids. Model fit was evaluated using Akaikes Information criterion.[44]

Ethics

Information about the COSMOS study and its implications was provided for all patients. Consent was obtained in written and verbal form from patients with the cognitive ability to provide it. For patients lacking this ability, presumed consent was obtained from the patients' next of kin or legal guardian after explaining the study procedure. The trial was approved by the Regional Committee for Medical and Health Research Ethics, West Norway (REK 2013/1765) and registered at clinicaltrials.gov (NCT02238652).

Results

A total of 723 patients were enrolled; 178 were excluded, leaving 545 patients to be included in the study. A total of 297 patients were randomized to the intervention group, with 248 allocated to the control group. A total of 73.8% of patients were women, with an average age of 86.7 years (Table 1).

There was no significant intervention effect on the total score of the MOBID-2 Pain Scale from baseline to month 9 (β −0.23; 95% confidence interval [CI] −0.88 to 0.42; $P = .49$) (Table 2). A significant positive intervention effect was found for MOBID-2 part 1 for people with dementia from baseline to month 9 (β −0.45; 95% CI −0.90 to −0.01; $P = .047$), but not for MOBID-2 part 2 (Figure 1). The number of patients using opioids increased nonsignificantly from baseline to month 9 in both groups, from 31.5% to 38.0% in the control group (odds ratio [OR] 1.31; $P = .20$) and from 30% to 35% in the intervention group (OR 1.26; $P = .27$). There was no significant intervention effect on the use of opioid analgesics (OR 0.95; 95% CI 0.53–1.70; $P = .86$).

The number of people with pain in the intervention group who did not use analgesics decreased from 24.3% to 19.4% from baseline to month 4, and remained stable at month 9 (Table 3). The number of people in the control group with a MOBID-2 score ≥3 who did not use analgesics steadily increased from baseline (19.1%) to month 9 (26.3%) (Table 3). The difference between the control and intervention groups, and changes within groups were not significant at either time point (Table 3). Patients in the intervention group with a MOBID-2 score ≥3 who used analgesics experienced more NPS (F 5.7; $P = .001$) compared with patients with a MOBID-2 score <3 at baseline and month 4 (Table 4). In the control group, the same was found at month 9 (F: 4.5; $P = .005$), but no such difference was observed at baseline and month 4 (Table 4). Patients with a MOBID-2 score ≥3 using analgesics had lower QoL than other patients at all time-points in both the control and intervention groups (Table 4).

Pain and psychosis symptoms as a group (OR 2.03; 95% CI 1.19–3.45; $P = .009$), and delusion individually (OR 2.12; 95% CI 1.23–3.63; $P = .007$) were significantly associated over time. There was no significant association between pain and hallucinations (OR 1.47; 95% CI 0.66–3.29; $P = .35$). Patients who used antipsychotic medication were more likely to experience pain than patients not using antipsychotic medication (OR 1.78; 95% CI 1.02–3.10; $P = .043$). There was no significant intervention effect on psychosis symptoms – either as a cluster (β 0.23; 95% CI −0.92 to 1.37; $P = .70$) or for the individual symptoms delusion and hallucinations (Table 2).

Table 1
Baseline Characteristics

Item	Control (n = 248)	Intervention (n = 297)	*P* Value	Total (n = 545)
Women (%)	186 (75.0)	216 (72.7)	.548	402 (73.8)
Age (SD)	87.0 (7.2)	86.5 (7.7)	.405	86.7 (7.5)
Weight in kg (SD)	63.4 (14.3)	64.5 (14.1)	.388	64.0 (14.2)
Height in m (SD)	1.64 (0.09)	1.63 (0.09)	.288	1.64 (0.09)
Dementia diagnosis (%)	155 (62.5)	196 (66.0)	.396	351 (64.4)
MMSE (SD)	11.4 (7.9)	10.4 (7.6)	.172	10.8 (7.8)
FAST (SD)	5.5 (1.4)	5.6 (1.4)	.187	5.6 (1.4)
ADL total (SD)	16.9 (5.5)	17.7 (5.2)	.099	17.4 (5.3)
Regular drugs (SD)	7.8 (3.8)	8.0 (3.8)	.466	7.9 (3.8)
CMAI total (SD)	42.6 (15.5)	42.0 (15.1)	.729	42.3 (15.3)
NPI-total score (SD)	17.9 (21.1)	17.5 (19.5)	.737	17.7 (20.2)
Psychosis cluster (SD)	2.9 (5.5)	2.3 (4.4)	.213	2.6 (4.9)
Delusion (%)	48 (21.0)	46 (16.0)	.149	94 (18.2)
Hallucinations (%)	24 (10.2)	23 (8.1)	.396	47 (9.0)
Agitation/Aggression (%)	54 (22.5)	71 (24.6)	.577	125 (23.6)
Depression (%)	46 (19.7)	79 (27.7)	.033	125 (24.1)
Anxiety (%)	58 (24.5)	66 (23.2)	.725	124 (23.8)
Euphoria (%)	10 (4.2)	10 (3.4)	.639	20 (3.8)
Apathy (%)	28 (11.8)	50 (17.4)	.075	78 (14.9)
Disinhibition (%)	37 (15.5)	50 (17.2)	.599	87 (16.4)
Irritability (%)	77 (32.1)	91 (31.4)	.862	168 (31.7)
Aberrant motor behavior (%)	32 (13.3)	29 (10.0)	.233	61 (11.5)
Nighttime disturbance (%)	44 (18.3)	63 (21.6)	.331	107 (20.1)
Appetite disturbance (%)	20 (8.5)	26 (9.1)	.818	46 (8.9)
Cornell total score (SD)	7.5 (6.6)	6.8 (5.7)	.484	7.1 (6.1)
MOBID-2 total score (SD)	2.8 (2.8)	2.3 (2.4)	.106	2.5 (2.6)
Analgesic drugs (%)	156 (62.9)	165 (55.6)	.083	321 (58.9)
Opioids (%)	78 (31.5)	89 (30.0)	.708	167 (30.6)
Psychotropic drugs (%)*	177 (71.4)	209 (70.4)	.903	386 (70.8)
Antipsychotics (%)	30 (12.1)	48 (16.2)	.177	78 (14.3)
Anxiolytics (%)	58 (23.4)	56 (18.9)	.195	114 (20.9)
Hypnotics And Sedatives (%)	79 (31.9)	82 (27.6)	.279	161 (29.5)
Antidementia drugs (%)	38 (15.6)	44 (15.2)	.898	82 (15.4)
Antidepressants (%)	99 (40.6)	119 (41.0)	.914	218 (40.8)

ADL, Activities of Daily Living; CMAI, Cohen Mansfield Agitation Inventory; FAST, Functional Assessment Staging.
*N05A, N05B, N05C, N06A, N06D in the ATC-register.

Discussion

Pain was significantly associated with psychosis symptoms, and delusion over time, but not with hallucinations. This is important for clinicians, as it suggests that a thorough pain assessment is essential before making treatment decisions concerning psychosis symptoms. This is to our knowledge the first study to investigate the relationship between pain and psychosis symptoms over time. The COSMOS intervention had a positive effect on musculoskeletal pain in people with dementia, highlighting the importance of a thorough pain assessment and treatment strategy in NHs.

The total MOBID-2 pain score was not reduced in response to the COSMOS intervention. Musculoskeletal pain was, however, reduced in people with dementia. The reason that musculoskeletal pain was reduced in people with dementia in the intervention group compared with the control group, and not for the total population, can be explained by the ability of the MOBID-2 pain scale to detect pain in people with dementia. Patients without cognitive impairment are able to report their own pain and the effect of pain treatment, or lack thereof, which assists the physician's decision making.[7] The assessment of musculoskeletal pain can also be more straightforward compared with the assessment of pain from the internal organs, head, and skin, as musculoskeletal pain can be provoked by active

Table 2
Effect of Intervention Compared With Control on Pain and Psychosis Symptoms*

Item	Total Population					
	Baseline to Month 4			Baseline to Month 9		
	β-coefficient	95% CI	*P* Value	β-coefficient	95% CI	*P* Value
MOBID-2 total score	−0.11	−0.74 to 0.53	.740	−0.23	−0.88 to 0.42	.490
MOBID-2 part 1	−0.07	−0.50 to 0.35	.734	−0.40	−0.84 to 0.05	.079
MOBID-2 part 2	−0.12	−0.40 to 0.15	.369	−0.02	−0.30 to 0.26	.885
Psychosis cluster-total	−0.19	−1.29 to 0.91	.736	0.23	−0.92 to 1.37	.696
Delusion	−0.06	−0.80 to 0.68	.872	0.19	−0.57 to 0.96	.619
Hallucinations	−0.06	−0.63 to 0.50	.823	0.01	−0.58 to 0.59	.979
	Patients With dementia					
MOBID-2 total score	−0.14	−0.80 to 0.51	.668	−0.23	−0.89 to 0.43	.495
MOBID-2 part 1	−0.13	−0.57 to 0.30	.545	−0.45	−0.90 – −0.01	**.047**
MOBID-2 part 2	−0.11	−0.39 to 0.16	.421	−0.09	−0.37 to 0.19	.531
Psychosis cluster-total	−0.23	−1.39 to 0.92	.694	0.28	−0.91 to 1.48	.646
Delusion	0.07	−0.71 to 0.85	.852	0.41	−0.40 to 1.22	.326
Hallucinations	−0.24	−0.83 to 0.35	.419	−0.18	−0.79 to 0.43	.567

Note: Bold values are statistically significant ($P < .05$).
*Analyzed using Multilevel Mixed-Effect Linear Regression.

movements, as in part 1 of the MOBID-2 Pain Scale. Our findings are partly in line with a previous study by Sandvik and colleagues,[45] who found that a Stepwise Protocol for Treating pain reduced pain in NH patients with dementia and behavioral disturbances. However, in contrast to our study, this study focused primarily on the treatment of pain and found an intervention effect on the total pain score, not only on musculoskeletal pain.[45] In the COSMOS study, no significant intervention effect on pain was found, although the number of patients with pain increased over time in the control group and decreased in the intervention group. This may suggest that the intervention group could have benefited from the COSMOS intervention to a certain degree.

The use of analgesics was high in both groups, especially the number of patients using opioids on a regular basis, which increased from 30% to >35% from baseline to month 9 in both the control group and intervention group. A previous study found a rise in the use of opioids in Norwegian NHs from 2000 to 2011, from 1.9% to 17.9%.[46] Our findings suggest that this trend has continued, which is particularly worrisome considering the possible side effects from long-term opioid use and risk of polypharmacy in people with dementia.[47,48] A recent study by Erdal et al.[49] investigating the effect of analgesic treatment on depression in NH patients with dementia found that patients being prescribed a buprenorphine transdermal patch had a significantly higher chance of dropping out of the study due to adverse events. This highlights the importance of being thorough in evaluating the risk of possible side effects in patients, before and during the prescription of an opioid analgesic.

When investigating the characteristics of patients with and without pain using and not using analgesics, we observed that patients with pain who used analgesics had lower QoL and more NPS than other patients. This supports previous studies, which have found pain to be associated with NPS and poor QoL.[5,50] However, it was unexpected that no significant differences were found between patients' QoL scores concerning those with pain using analgesics and those with pain not using analgesics, as the aim with analgesic prescription is to reduce the patient's pain and improve their QoL. In future studies, this could be an important focus point when investigating the effect of long-term analgesic use in NH patients. If

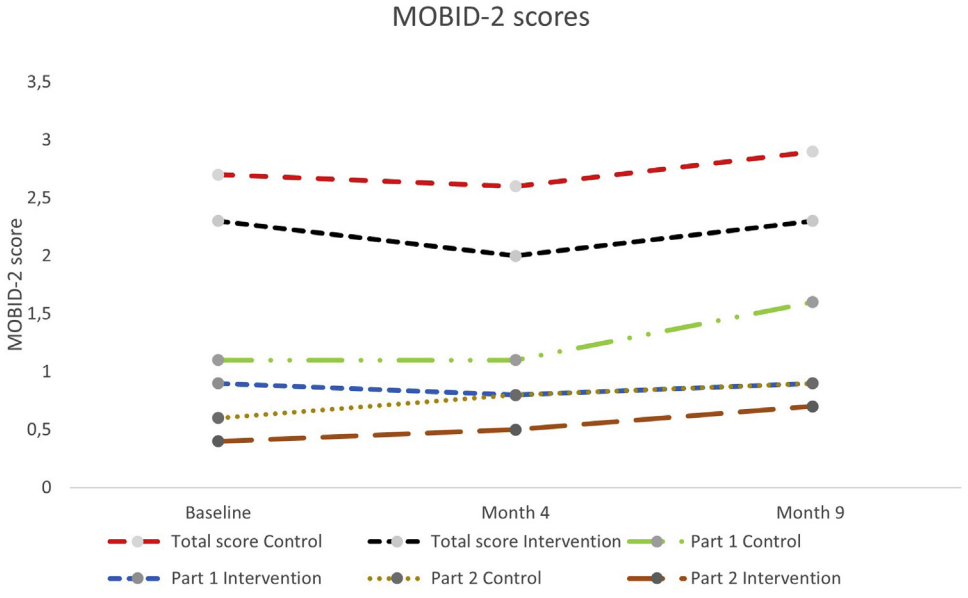

Fig. 1. Progression of pain scores (MOBID-2) in people with dementia. MOBID-2 part 1: Musculoskeletal pain (Significant invention effect), MOBID-2 part 2: Pain from internal organs, head, and skin.

Table 3
Use of Analgesics in People With and Without Clinically Significant Pain (MOBID-2 ≥3)

	Control (n = 202)		Intervention (n = 251)	
Baseline (χ^2 Control vs. Intervention: $\chi^2 = 4.08$, $P = .253$)	MOBID-2 ≥3	MOBID2 <3	MOBID-2 ≥3	MOBID2 <3
Uses analgesics (% of pain group)	76 (80.9)	57 (52.8)	78 (75.7)	65 (43.9)
No analgesics (% of pain group)	18 (19.1)	51 (47.2)	25 (24.3)	83 (56.1)
Month 4 (χ^2 Control vs. Intervention: $\chi^2 = 5.19$, $P = .158$)	Control (n = 185)		Intervention (n = 208)	
	MOBID-2 ≥3	MOBID2 <3	MOBID-2 ≥3	MOBID2 <3
Uses analgesics (% of pain group)	64 (77.1)	51 (50.0)	58 (80.6)	61 (44.9)
No analgesics (% of pain group)	19 (22.9)	51 (50.0)	14 (19.4)	75 (55.1)
Month 9 (χ^2 Control vs. Intervention: $\chi^2 = 4.20$, $P = .241$)	Control (n = 174)		Intervention (n = 184)	
	MOBID-2 ≥3	MOBID2 <3	MOBID-2 ≥3	MOBID2 <3
Uses analgesics (% of pain group)	56 (73.7)	49 (50.0)	51 (79.7)	54 (45.0)
No analgesics (% of pain group)	20 (26.3)	49 (50.0)	13 (20.3)	66 (55.0)

long-term use of opioid analgesics causes more harm through unwanted side effects than benefit, more focus on frequent reevaluation of long-term use of opioid analgesics is needed.

As hypothesized, psychosis symptoms and pain were associated over time, as was the individual symptom delusion, but not hallucinations. This is in line with previous cross-sectional findings from the baseline data of the COSMOS study.[19] Previous studies have found a cross-sectional association between pain and delusion, such as Tosato et al.,[20] who found a relationship between pain and delusion in 2822 NH patients with dementia from 8 countries. As this is the first study that investigates the longitudinal relationship between pain and psychosis symptoms, our finding adds important knowledge regarding psychosis symptoms in NH patients. If psychosis symptoms, and especially delusion, are associated with pain, then a thorough assessment of pain should be a prerequisite when deciding on treatment options for psychosis symptoms, and aid in reducing the use of psychotropic medication to those who benefit the most from them. This is further highlighted by our finding that use of antipsychotic medication was associated with pain. If psychosis symptoms are triggered by underlying pain, then treatment of the underlying factor would be preferred rather than treating only the overt symptoms.

In contrast to our hypothesis, no significant intervention effect on psychosis symptoms was found. This diverges from a previous study from 2016, where systematic pain assessment and treatment in 352 patients with dementia and behavioral disturbances reduced psychosis symptoms.[31] It is important to keep in mind that only 94 (18%) patients in the COSMOS study experienced at least 1 psychosis symptom at baseline,[19] limiting the potential to discover an intervention effect. The 2 studies also differ regarding the type of intervention. Where the 2016 study only focused on systematic pain assessment and treatment, this was only 1 part of the COSMOS trial, which includes components with the ability to reduce psychosis symptoms, such as organization of activities and medication review. Despite this, psychosis symptoms were not reduced, which underlines the complexity in treating psychosis symptoms in NH patients and that there is no one-size-fits-all treatment. Guidelines state that nonpharmacological options should be the first-line treatment, but knowledge concerning the effect of such treatments is sparse and our study is one of few that investigates the effect of nonpharmacological options.

Table 4
Characteristics of Different Pain-Analgesics Groups

Item – Mean (SD)	No Pain No Analgesics	No Pain Using Analgesics	Pain No Analgesics	Pain Using Analgesics	*P* Value*
	Baseline				
	Control				
NPI-Total score	14.8 (16.8)	12.0 (16.5)	10.5 (13.1)	20.0 (24.4)	.121
NPI-Psychosis score	2.6 (4.6)	1.4 (3.5)	1.4 (3.1)	3.4 (6.0)	.107
Cornell score	5.4 (5.6)	4.8 (4.4)	8.4 (5.6)	9.6 (7.5)†,‡	<.001
MMSE total	11.0 (8.4)	11.5 (7.9)	13.0 (8.7)	12.4 (7.7)	.720
QUALID total	18.1 (5.5)	20.0 (6.6)	19.7 (7.1)	24.4 (8.2)†,‡	<.001
	Intervention				
NPI-Total score	11.9 (14.5)	16.3 (19.3)	17.2 (17.3)	25.2 (23.9)†	.001
NPI-Psychosis score	1.1 (2.7)	1.4 (3.6)	2.3 (5.4)	4.2 (5.7)†,‡	<.001
Cornell score	4.5 (4.1)	7.4 (6.4)	6.5 (5.5)	8.7 (6.2)†	.001
MMSE total	10.1 (7.0)	10.6 (7.8)	10.6 (6.6)	9.7 (7.9)	.902
QUALID total	19.3 (5.5)	20.2 (7.2)	20.4 (7.9)	24.6 (7.8)†,‡	<.001
	Month 4				
	Control				
NPI-Total score	12.5 (16.6)	9.7 (15.0)	18.4 (20.3)	16.9 (17.7)	.126
NPI-Psychosis score	2.0 (3.6)	1.8 (3.9)	2.4 (5.3)	3.3 (5.1)	.313
Cornell score	5.9 (5.8)	5.9 (5.9)	7.2 (4.5)	8.1 (6.3)	.237
MMSE total	12.7 (8.1)	12.3 (7.2)	11.4 (7.8)	9.8 (8.2)	.270
QUALID total	18.6 (5.5)	19.9 (6.2)	20.6 (6.9)	23.4 (7.6)†,‡	.001
	Intervention				
NPI-Total score	6.2 (6.9)	10.7 (13.2)	13.2 (9.5)	16.5 (18.9)†	.001
NPI-Psychosis score	0.7 (1.7)	0.9 (1.8)	3.5 (6.7)†,‡	2.3 (4.2)†	.002
Cornell score	4.9 (5.3)	6.9 (5.0)	8.0 (6.1)†	8.8 (6.5)†	.014
MMSE total	10.5 (6.3)	11.3 (9.0)	10.9 (6.7)	10.8 (7.8)	.958
QUALID total	18.9 (6.0)	20.6 (7.1)	25.4 (7.5)	24.3 (8.6)†,‡	<.001
	Month 9				
	Control				
NPI-Total score	14.6 (20.4)	8.9 (12.3)	23.3 (24.4)	22.3 (22.3)‡	.005
NPI-Psychosis score	2.6 (4.9)	1.2 (2.6)	2.8 (6.1)	3.9 (5.2)	.032
Cornell score	5.4 (5.7)	5.1 (4.3)	7.9 (6.1)	10.1 (7.6)†,‡	<.001
MMSE total	12.0 (7.0)	11.5 (7.8)	11.2 (10.4)	10.3 (8.3)	.764
QUALID total	17.9 (5.3)	20.2 (6.2)	22.2 (7.4)	24.7 (8.5)†,‡	<.001
	Intervention				
NPI-Total score	12.8 (19.2)	15.1 (16.6)	10.3 (7.3)	19.0 (21.6)	.321
NPI-Psychosis score	1.9 (4.7)	1.9 (3.2)	0.5 (1.7)	2.5 (4.6)	.529
Cornell score	5.0 (3.7)	6.7 (4.9)	5.7 (5.6)	9.0 (6.7)†	.009
MMSE total	10.5 (6.6)	9.4 (7.5)	11.7 (8.5)	8.7 (7.8)	.499
QUALID total	20.4 (7.3)	21.1 (6.4)	19.1 (4.7)	24.6 (8.9)†	.011

*One-way analysis of variance (with Bonferroni correction for multiple tests).
†Significantly different from the No Pain – No Analgesics group.
‡Significantly different from the No Pain – Using Analgesics group.

Strengths and Limitations

This is one of the largest multicomponent intervention studies performed in a NH setting, and it includes a broad NH population both with and without dementia. This increases the generalizability of our findings. There is also a strength in using the MOBID-2 Pain Scale, which has been thoroughly tested for reliability and responsiveness for change. A limitation is that the study was powered with respect to QoL and not for pain and psychosis symptoms. It is a limitation that we only had data on type of pharmacological pain treatment, not dosage, or if nonpharmacological measures had been taken. There was also no assessment concerning the type of psychosis, or if the psychosis symptoms were chronic or acute in nature. A limitation also lies in the lack of knowledge regarding the duration of current pain and pain

treatment at baseline, which is important to consider when interpreting the results.

Conclusions and Implications

Pain, psychosis symptoms as a group, and delusion were significantly associated over time, highlighting the importance for clinicians to assess pain when making treatment decisions on psychosis symptoms. The COSMOS intervention had no significant effect on psychosis symptoms. The COSMOS intervention had a significant effect on musculoskeletal pain in patients with dementia, but not on the total pain score, which shows the need for systematic pain assessment and treatment in patients with dementia. The use of opioid analgesics increased in both groups and was not affected by the COSMOS intervention, which shows the importance of frequent reassessment of opioid prescriptions.

Acknowledgments

Tony Elvegaard, Christian Gulla, and Irene Aasmul took part in the data collection. TFH thanks the Medical Students Research Program and the University of Bergen for all their support. We also thank the Norwegian Ministry of Health and Care services, as well as the GC Rieber foundation for their financial support to the Center for Elderly and Nursing Home Medicine.

References

1. Selbaek G, Kirkevold O, Engedal K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes. Int J Geriatr Psychiatry 2007;22:843–849.
2. Achterberg WP, Gambassi G, Finne-Soveri H, et al. Pain in European long-term care facilities: Cross-national study in Finland, Italy and The Netherlands. Pain 2010;148:70–74.
3. van Kooten J, Smalbrugge M, van der Wouden JC, et al. Prevalence of pain in nursing home residents: The role of dementia stage and dementia subtypes. J Am Med Dir Assoc 2017;18:522–527.
4. Flo E, Gulla C, Husebo BS. Effective pain management in patients with dementia: Benefits beyond pain? Drugs Aging 2014;31:863–871.
5. van Dalen-Kok AH, Pieper MJ, de Waal MW, et al. Association between pain, neuropsychiatric symptoms, and physical function in dementia: A systematic review and meta-analysis. BMC Geriatr 2015;15:49.
6. Wagatsuma S, Yamaguchi T, Berge LI, et al. How, why and where it hurts-breaking down pain syndrome among nursing home patients with dementia: A cross-sectional analysis of the COSMOS trial. Pain Manag Nurs 2021;22:319–326.
7. Corbett A, Husebo B, Malcangio M, et al. Assessment and treatment of pain in people with dementia. Nat Rev Neurol 2012;8:264–274.
8. Selbaek G, Engedal K, Benth JS, et al. The course of neuropsychiatric symptoms in nursing-home patients with dementia over a 53-month follow-up period. Int Psychogeriatr 2014;26:81–91.
9. Helvik AS, Engedal K, Wu B, et al. Severity of neuropsychiatric symptoms in nursing home residents. Dement Geriatr Cogn Dis Extra 2016;6:28–42.
10. van Kooten J, van der Wouden JC, Sikkes SAM, et al. Pain, neuropsychiatric symptoms, and quality of life of nursing home residents with advanced dementia in The Netherlands: A cross-sectional study. Alzheimer Dis Assoc Disord 2017;31:315–321.
11. Cheng ST, Kwok T, Lam LC. Neuropsychiatric symptom clusters of Alzheimer's disease in Hong Kong Chinese: Prevalence and confirmatory factor analysis of the Neuropsychiatric Inventory. Int Psychogeriatr 2012;24:1465–1473.
12. Selbaek G, Engedal K. Stability of the factor structure of the Neuropsychiatric Inventory in a 31-month follow-up study of a large sample of nursing-home patients with dementia. Int Psychogeriatr 2012;24:62–73.
13. Bergh S, Holmen J, Saltvedt I, et al. Dementia and neuropsychiatric symptoms in nursing-home patients in Nord-Trondelag County. Tidsskr Nor Laegeforen 2012;132:1956–1959.
14. Roen I, Selbaek G, Kirkevold O, et al. Resourse use and disease course in dementia - nursing Home (REDIC-NH), a longitudinal cohort study; design and patient characteristics at admission to Norwegian nursing homes. BMC Health Serv Res 2017;17:365.
15. Reinhardt MM, Cohen CI. Late-life psychosis: Diagnosis and treatment. Curr Psychiatry Rep 2015;17:1.
16. Wetzels RB, Zuidema SU, de Jonghe JF, et al. Determinants of quality of life in nursing home residents with dementia. Dement Geriatr Cogn Disord 2010;29:189–197.
17. Wergeland JN, Selbaek G, Bergh S, et al. Predictors for nursing home admission and death among community-dwelling people 70 years and older who receive domiciliary care. Dement Geriatr Cogn Dis Extra 2015;5:320–329.
18. Connors MH, Ames D, Woodward M, et al. Psychosis and clinical outcomes in Alzheimer Disease: A Longitudinal Study. Am J Geriatr Psychiatry 2018;26(3):304–313.
19. Habiger TF, Achterberg WP, Flo E, et al. Psychosis symptoms in nursing home residents with and without dementia-Cross-sectional analyses from the COSMOS study. Int J Geriatr Psychiatry 2019;34:683–691.
20. Tosato M, Lukas A, van der Roest HG, et al. Association of pain with behavioral and psychiatric symptoms among nursing home residents with cognitive impairment: results from the SHELTER study. Pain 2012;153:305–310.
21. Duran CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. Eur J Clin Pharmacol 2013;69:1485–1496.
22. Potter K, Flicker L, Page A, et al. Deprescribing in frail older people: A randomised controlled trial. PLoS One 2016;11:e0149984.
23. Frankenthal D, Lerman Y, Kalendaryev E, et al. Intervention with the screening tool of older persons potentially inappropriate prescriptions/screening tool to alert doctors to right treatment criteria in elderly residents of a chronic geriatric facility: A randomized clinical trial. J Am Geriatr Soc 2014;62:1658–1665.
24. Kales HC, Gitlin LN, Lyketsos CG. Management of neuropsychiatric symptoms of dementia in clinical settings: Recommendations from a multidisciplinary expert panel. J Am Geriatr Soc 2014;62:762–769.
25. Helsedirektoratet. Nasjonal faglig retningslinje om demens. 3 ed. Oslo, Norway: Helsedirektoratet; 2017.
26. Testad I, Corbett A, Aarsland D, et al. The value of personalized psychosocial interventions to address behavioral and psychological symptoms in people with dementia living in care home settings: A systematic review. Int Psychogeriatr 2014;26:1083–1098.
27. Ballard C, Hanney ML, Theodoulou M, et al. The dementia antipsychotic withdrawal trial (DART-AD): Long-term follow-up of a randomised placebo-controlled trial. Lancet Neurol 2009;8:151–157.
28. Ito E, Berge LI, Husebo BS, et al. The negative impact of psychotropic drug use on quality of life in nursing home patients at different stages of dementia: Cross-sectional analyses from the COSMOS Trial. J Am Med Dir Assoc 2020;21:1623–1628.
29. Husebo BS, Ballard C, Sandvik R, et al. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: Cluster randomised clinical trial. BMJ 2011;343:d4065.
30. Husebo BS, Ballard C, Fritze F, et al. Efficacy of pain treatment on mood syndrome in patients with dementia: A randomized clinical trial. Int J Geriatr Psychiatry 2014;29:828–836.
31. Habiger TF, Flo E, Achterberg WP, et al. The interactive relationship between pain, psychosis, and agitation in people with dementia: Results from a cluster-randomised clinical trial. Behav Neurol 2016;2016:8.
32. Husebo BS, Ballard C, Aarsland D, et al. The effect of a multicomponent intervention on quality of life in residents of nursing homes: A randomized controlled trial (COSMOS). J Am Med Dir Assoc 2019;20:330–339.
33. Husebo BS, Flo E, Aarsland D, et al. COSMOS-improving the quality of life in nursing home patients: Protocol for an effectiveness-implementation cluster randomized clinical hybrid trial. Implement Sci 2015;10:131.
34. Flo E, Husebo BS, Bruusgaard P, et al. A review of the implementation and research strategies of advance care planning in nursing homes. BMC Geriatr 2016;16:24.
35. Husebo BS, Achterberg W, Flo E. Identifying and managing pain in people with Alzheimer's disease and other types of dementia: A systematic review. CNS Drugs 2016;30:481–497.
36. Ballard C, Howard R. Neuroleptic drugs in dementia: Benefits and harm. Nat Rev Neurosci 2006;7:492–500.
37. Husebo BS, Strand LI, Moe-Nilssen R, et al. Mobilization-Observation-Behavior-Intensity-Dementia Pain Scale (MOBID): Development and validation of a nurse-administered pain assessment tool for use in dementia. J Pain Symptom Manage 2007;34:67–80.
38. Husebo BS, Ostelo R, Strand LI. The MOBID-2 pain scale: Reliability and responsiveness to pain in patients with dementia. Eur J Pain 2014;18:1419–1430.
39. Selbaek G, Kirkevold O, Sommer OH, et al. The reliability and validity of the Norwegian version of the Neuropsychiatric Inventory, nursing home version (NPI-NH). Int Psychogeriatr 2008;20:375–382.
40. Margallo-Lana M, Swann A, O'Brien J, et al. Prevalence and pharmacological management of behavioural and psychological symptoms amongst dementia sufferers living in care environments. Int J Geriatr Psychiatry 2001;16:39–44.
41. Alexopoulos GS, Abrams RC, Young RC, et al. Cornell scale for depression in dementia. Biol Psychiatry 1988;23:271–284.
42. Weiner MF, Martin-Cook K, Svetlik DA, et al. The quality of life in late-stage dementia (QUALID) scale. J Am Med Dir Assoc 2000;1:114–116.
43. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
44. Bozdogan H. Akaike's information criterion and recent developments in information complexity. J Math Psychol 2000;44:62–91.
45. Sandvik RK, Selbaek G, Seifert R, et al. Impact of a stepwise protocol for treating pain on pain intensity in nursing home patients with dementia: A cluster randomized trial. Eur J Pain 2014;18:1490–1500.

46. Sandvik R, Selbaek G, Kirkevold O, et al. Analgesic prescribing patterns in Norwegian nursing homes from 2000 to 2011: Trend analyses of four data samples. Age Ageing 2016;45:54–60.
47. Erdal A, Ballard C, Vahia IV, et al. Analgesic treatments in people with dementia - how safe are they? A systematic review. Expert Opin Drug Saf 2019; 18(6):511–522.
48. Husebo BS, Kerns RD, Han L, et al. Pain, complex chronic conditions and potential inappropriate medication in people with dementia. Lessons learnt for pain treatment plans utilizing data from the Veteran Health Administration. Brain Sci 2021;11:86.
49. Erdal A, Flo E, Aarsland D, et al. Tolerability of buprenorphine transdermal system in nursing home patients with advanced dementia: A randomized, placebo-controlled trial (DEP.PAIN.DEM). Clin Interv Aging 2018;13:935–946.
50. van Dam PH, Caljouw MAA, Slettebo DD, et al. Quality of life and pain medication use in persons with advanced dementia living in long-term care facilities. J Am Med Dir Assoc 2019;20:1432–1437.