

## **Epidemiology of pain in people with dementia living in care homes: Longitudinal course, prevalence and treatment implications**

**Running title:** Epidemiology of pain in people with dementia living in care homes

### **Abstract**

**Introduction** Knowledge regarding the longitudinal course, impact, or treatment implications of pain in people with dementia living in care homes is very limited.

**Methods** We investigated the people with dementia living in 67 care homes in London and Buckinghamshire, UK. Pain, dementia severity, neuropsychiatric symptoms, depression, agitation, and quality-of-life were measured using appropriate instruments at baseline (N=967) and after nine months (n=629).

**Results** Baseline prevalence of pain was 35.3% (95%CI 32.3-38.3). Pain severity was significantly correlated with dementia severity, neuropsychiatric symptoms, depression, agitation, and quality-of-life at both time-points. Regular treatment with analgesics significantly reduced pain severity. Pain was significantly associated with more antipsychotic prescriptions. Pain was significantly associated (OR=1.48; 95%CI 1.18-1.85) with all-cause mortality during follow-up.

**Conclusions** Pain is an important determinant of neuropsychiatric symptoms, mortality, quality-of-life, and antipsychotic prescriptions. Improved identification, monitoring, and treatment of pain are urgent priorities to improve the health and quality-of-life for people with dementia.

**Key words:** Pain; Dementia; Analgesics; Quality of Life; Mortality; Depression

## Introduction

There are 850,000 people with dementia in the UK, representing a major public health issue that costs the UK economy over £26 billion each year <sup>1</sup>. One third of people with dementia reside in long-term care facilities <sup>2</sup>. These individuals have highly complex treatment and care needs resulting from moderate to severe dementia, associated mental health symptoms, medical comorbidity, and communication difficulties <sup>3</sup>. Pain is common in people with dementia living in care homes, and is a major contributor to the challenge of care. Pain is often associated with medical co-morbidities, particularly musculoskeletal conditions and long-term neuropathic conditions such as diabetes <sup>4,5</sup>. Despite widely available treatment options, pain is often unrecognised or untreated because of difficulties in identifying and assessing pain in this patient group. Impairment in verbal communication, and insight into their condition is inherent in the later stages of dementia, thus hindering timely diagnosis and effective pain management <sup>6</sup>.

Despite the importance of pain as a key driver of health and wellbeing in people with dementia in care homes, there is a concerning lack of consensus regarding its prevalence and epidemiology in these settings. Within the evidence base, studies principally evaluating the prevalence, nature, and mental health correlates of pain in people with dementia living in care homes are few in number, and usually based on modest samples <sup>5,7</sup>, often including people without dementia, with disparate prevalence estimates for pain ranging from 19.8% to 73.0% <sup>8,9</sup>. Three large longitudinal studies have been published, involving 3926, 5761, and 372 care home residents across European care homes, and reporting a prevalence of pain of 48.4%, 50%, and up to 67.6% respectively <sup>7-9</sup>. However, none of these studies employed validated observational pain assessment instruments designed specifically for measuring pain in people

with dementia and communication difficulties, and thus detailed interpretation of the outcomes cannot be made <sup>8,9</sup>.

Initial evidence suggests that pain may be associated behavioural symptoms <sup>10</sup> including agitation, aggression, and depression <sup>11,12</sup>, and the risk of polypharmacy in people with dementia. These issues are major drivers of Quality of Life (QoL), which suggests a potential association, but no study has examined the specific impact of pain and its intensity on QoL. More robust studies are needed to establish the true correlations between pain and these important health-related outcomes. To date, no study has utilised standardised measures of neuropsychiatric symptoms to examine association with pain.

There is a clear need for robust evaluation of the epidemiology, associations and impacts of pain in people with dementia to build on the current evidence base and inform the development of optimal pathways for assessment, monitoring and treatment. Despite the importance of pain as a clinical issue in dementia, the guidance available for physicians is limited. A recent review of available guidelines has identified only three clinical guidelines for managing pain in dementia, of which none are tailored for the unique environment presented by a care home <sup>6</sup>. Such lack of robust clinical guidelines adds to the difficulties in optimally managing pain and related mental health symptoms in this population, and highlights the need to fully understand the issues around pain management in this setting. Hence, this research aimed to conduct the first comprehensive large longitudinal study examining the nature, prevalence, and impact of pain exclusively in people with dementia living in care homes using a validated pain measure, and to assess the longitudinal course of pain and its associations with mental health symptoms and quality of life in people with dementia.

## **Methods & Materials**

### *Study design*

This longitudinal study used data from the Well-being and Health for People with Dementia (WHELD) NIHR programme, and has been ethically approved (National Research Ethics Service Committee South Central - Oxford C Reference: 13/SC/0281).

### *Setting*

67 care homes were recruited across sites in South London, North London, and Buckinghamshire, UK. Suitable care homes were initially searched using local care home directories. Care homes were included, if at least 60% of their residents had dementia and they demonstrated minimum acceptable standard of care according to the Care Quality Commission (CQC). Care homes that received local authority special support, had insufficient staffing resource, were undergoing systematic service improvement programmes or another research, or anticipated major internal changes within the next 12 months were excluded. Consent for care home involvement was obtained from the management of the homes.

### *Participants*

All residents in the participating care homes meeting diagnostic criteria for dementia, and having a score of one or greater on the Clinical Dementia Rating Scale (CDRS)<sup>13</sup> were invited to participate. If residents lacked capacity, informed consent was obtained with the involvement of a nominated or personal consultee, who represented the residents' interests,

and wishes in accordance with the Mental Capacity Act, 2005. Cluster sizes (the number of recruited participants per care home) varied from 12 to 25 participants.

### *Outcome measures*

Pain was assessed using the Abbey pain scale (APS)<sup>14</sup>. APS is a brief observational pain assessment instrument, designed specifically for measuring pain in people with dementia, who cannot verbalise. APS includes six non-verbal indicators of pain, vocalisation, facial expression, change in body language, behavioural change, physiological change, and physical changes, which are rated absent (0), mild (1), moderate (2), or severe (3). Total APS score ranges from zero to 18, and pain is considered to be present when the total APS score is three and above. Total scores between three and seven indicate mild pain, moderate pain is defined as scores between eight and 13, and severe pain is defined as a score of 14 and above. APS also categorises the type of pain as acute, acute on chronic, or chronic<sup>14</sup>. The Functional Assessment Staging Tool (FAST)<sup>15</sup>, a validated functional assessment scale in people with dementia, was employed to assess the severity of dementia. Agitation, depression, and mental health symptoms in dementia of the participants were evaluated using the Cohen-Mansfield Agitation Inventory (CMAI)<sup>16</sup>, Cornell Scale for Depression in Dementia (CSDD)<sup>17</sup>, and Neuropsychiatric Inventory-Nursing Home version (NPI-NH)<sup>18</sup>, respectively. QoL of the participants were systematically assessed by the caregiver version of assessment of quality of life for people with dementia (DEMqoL-Proxy)<sup>19</sup>, and by the Quality of Life in Late-Stage Dementia (QUALID) scale<sup>20</sup>. Higher DEMqoL-Proxy scores indicate better QoL, while lower QUALID scores reflect better QoL. Trained research assistants completed the assessments at baseline, and after nine months.

### *Statistical analyses*

Participants' characteristics, their clinical profile, and APS scores were initially analysed by descriptive statistics. Differences between subgroups were analysed by appropriate tests of statistical significance. Correlations between APS scores and FAST, CSDD, CMAI, DEMQoL-Proxy, and QUALID scores were assessed using Spearman's rank-order correlation with Bonferroni corrections at baseline and at the follow-up. Associations between the changes in pain severity and the changes in mental health symptoms and QoL were evaluated using three-level mixed effects linear regression models with maximum likelihood estimation method. These models included age, gender, baseline FAST stage, and regular treatment with analgesics at baseline as covariates. Individual participants were nested within a level, the nursing homes, that in turn nested within a higher level, the three recruiting sites. Although FAST stages were naturally ordered, they were modelled as linear effects to increase the power of the statistical analyses. Clustered robust standard errors for the estimated regression coefficients were calculated with the recruiting sites as the clustering variable. Association between the presence of pain at baseline and all-cause mortality during follow-up was analysed by a three-level mixed effects logistic regression model. All analyses were performed using the statistical software STATA 13.1 (StataCorp, Texas, USA).

## **Results**

### *Participant characteristics*

967 people with dementia living in 67 nursing homes were included in this study, of whom 629 (65.0%) completed follow-up at nine months. Among the 338 (35.0%) participants that did not complete the study, 125 (13.0%) withdrew, and 213 (22.0%) died during follow-up.

The participants, who withdrew, did not differ significantly ( $\chi^2=0.15$ ;  $df=1$ ;  $p=0.70$ ) from others on the presence of pain at baseline. Table-1 presents the socio-demographic and clinical characteristics of the participants with and without pain at baseline.

### *Prevalence and nature of pain*

341 participants (35.3%) had pain, defined by total APS score of three and above, at baseline. The majority of participants had mild pain, which was predominantly chronic (Table-2). 197 participants experienced pain at nine months, with a similar predominance of mild chronic pain. Table-2 shows the full data regarding the prevalence and nature of pain among participants with mild, moderate, moderately severe, or severe dementia at baseline and follow-up.

### *Treatment with analgesics*

377 (39.0%; 95%CI 35.9 to 42.1%) participants had received regular analgesics at least for one month at baseline. 245 (65.0%) of them completed follow-up. Among the completers, 171 (69.8%; 95%CI 64.1 to 75.6%) participants were receiving regular analgesics at follow-up, and 74 (30.2%; 95%CI 24.5 to 36.0%) stopped receiving regular analgesics. 109 (28.4%) of the 384 completers, who had not received analgesics at baseline, had started regular analgesics at follow-up. Regular treatment with analgesics at baseline significantly reduced the severity of pain ( $\beta=-0.88$ ; 95%CI -1.57 to -0.20;  $p=0.01$ ) at the follow-up, after adjusting for the effects of age, gender, and baseline severity of dementia.

### *Longitudinal course and correlates of pain*

Participants with and without pain at baseline did not differ significantly in their gender, age, ethnicity, or the number of years lived in the care homes. People experiencing pain showed significantly higher agitation, depressive symptoms, overall mental health symptoms, and worse QoL at baseline and follow-up after Bonferroni corrections, and significant associations were also demonstrated between changes in pain and changes in these symptoms (Table 3, Table 4). Change in pain severity was significantly associated with the changes in the NPI-NH domain C (Agitation/Aggression) scores of participants that completed follow-up, after adjusting for the effects of age, gender, baseline dementia severity, and baseline treatment with analgesics. The associations between the changes in pain severity and the changes in other NPI-NH domain scores of participants that completed follow-up were not statistically significant (Table 5).

Participants experiencing pain at follow-up were significantly more likely to receive antipsychotics ( $\chi^2=3.92$ ;  $df=1$ ;  $p=0.048$ ). Pain at baseline was significantly associated (OR=1.48; 95%CI 1.18 to 1.85;  $p=0.001$ ) with all-cause mortality during follow-up. This association remained statistically significant (AOR=1.34; 95%CI 1.07 to 1.68;  $p=0.01$ ) after adjusting for the effects of age, gender, and baseline dementia severity. Analgesic treatment was common within the cohort, with the largest proportion of participants receiving regular paracetamol, a considerable number receiving non-steroidal anti-inflammatories and opioids and a small number receiving gabapentin, topical analgesia and neurticeutical preparations for joint pain.

209 participants who experienced clinically significant pain completed the study, of whom 82 (39.2%) showed significant pain at follow-up. Pain resolved in 127 (60.8%) participants. 115



(27.4%) of the 420 participants, who completed the study and did not have pain at baseline, developed incident pain. Table 6 presents socio-demographic and clinical profiles of the participants with persistent or resolved pain. Participants with more severe pain and associated mental health symptoms at baseline were significantly more likely to suffer from persistent pain at follow-up. Moreover, persistent pain was associated with greater agitation, depressive symptoms, overall mental health symptoms and worse QoL than participants, whose pain resolved, at the follow-up. Among the 98 completers with chronic pain at baseline 48 (49.0%) experienced pain at follow-up. Among the 111 completers with acute or acute on chronic pain at baseline, 39 (35.1%) experienced pain at follow-up.

## **Discussion**

This study is the largest longitudinal study conducted to date that has utilised validated scales to establish the prevalence, impact, and associations of clinically-significant pain, and key health-related outcomes in people with dementia living in care homes. The study confirms the widespread prevalence of pain in this group, and provides robust data regarding the longitudinal course of pain, and its association with severity of dementia, neuropsychiatric symptoms, and all-cause mortality of people with dementia, after adjusting for the effects of potential confounders. Importantly, it is also the first study to report the longitudinal association between severity of pain and QoL.

Several novel findings have implications for practice. Firstly, it is interesting to note the considerable fluctuation of pain within the cohort, with a significant proportion of individuals experiencing resolution of pain or developing incident pain. These findings highlight the

complexity and subjectivity of pain as a clinical condition, particularly when it is linked to multiple co-morbidities, and thus part of a complex set of interrelated symptoms. This work clearly indicates the importance of regularly assessing pain on an ongoing basis in order to optimise the identification and treatment of pain, and maximise the knock-on effect on QoL, neuropsychiatric symptoms, and mortality in these individuals<sup>21-24</sup>. The study also reports a clear association between pain and increased antipsychotic use, which may be related to misdiagnosis or mistreatment of pain in these individuals, and further highlights the importance of prompt assessment.

Secondly, the study also reports improved outcome of pain in people receiving analgesics at baseline, which highlights the value of prompt analgesic treatment in this patient group. There are few studies of analgesia in people with dementia, and the majority are focussed on the impact of treatment on neuropsychiatric symptoms rather than ongoing pain. This work indicates the potential for sustained benefit of analgesics on persistent pain, which warrants further investigation. Finally, there is a distinct group of individuals within the cohort with both neuropsychiatric symptoms and pain at baseline who continued to experience persistent pain at follow-up. This is an important patient group with multi-morbidity, who should be prioritised for intensive treatment and monitoring, and for whom specific treatment pathways are needed.

These findings offer the rationale for clear, accessible, tailored guidance for use in care home settings, indicating the importance of pain assessment and treatment in addressing or reducing the risk of other clinically relevant health outcomes such as behaviour and mortality. Despite the availability of caregiver rating and observational assessment instruments, they are not regularly used in practice. This study has demonstrated the concurrent validity of pain, assessed

using the APS, which is a brief and simple tool that is commonly available in care homes<sup>25</sup>. These findings indicate that promotion of the APS for general use by staff as part of pain management guidance would be a positive step towards regular, accurate pain assessment in usual care. There is a clear need to ensure care staff at all seniorities and positions receive clear, evidence-based training on assessing, managing, and treating pain in people with dementia, including understanding the fluctuating nature of pain, and recognising high priority, and at-risk individuals for rapid treatment. No such training or management interventions currently exist, and there is a concerning lack of accessible guidance in the UK or worldwide, particularly for care home settings<sup>6</sup>. Any new guidance should be informed by the outcomes of this study in addition to the growing body of evidence relating to timely assessment and effective non-drug and pharmacological treatment options for use in care home settings.

The study both confirms and provides novel data regarding the association of pain with key health-related outcomes. Prevailing evidence clearly describes the associations between pain and agitation, physical aggression, depression, and overall mental health symptoms in dementia<sup>11,12,21-24</sup>. This pattern is confirmed in this study, which further provides a longer follow-up period, and more robust multivariate analysis in comparison to previously published studies. The findings also correlate with a recent small study in eight nursing facilities in Pennsylvania (N=103) which reported that people with dementia experiencing higher levels of pain had significantly higher rates (OR = 6.31; 95%CI 1.91 to 20.77) of all-cause mortality over three months. Our findings confirm this association with a larger sample size, longer duration of follow-up, and robust multivariate analysis. Association between severity of pain and mortality is difficult to interpret due to the low number of participants with severe pain at baseline (n=4). However, mortality in people with mild and moderate pain at baseline were within a similar range. Importantly, to date no studies have systematically evaluated the

longitudinal association between severity of pain and QoL in people with dementia living in care homes. This study is the first to investigate and establish this link. Overall, the evidence of association between pain and key outcomes including major neuropsychiatric symptoms and QoL highlights the importance of pain in the overall health and wellbeing of people with dementia in care home settings.

This study reports a prevalence of pain of between 35.3% and 31.3% across the time course. Interestingly, this is lower than the prevalence reported in previous studies in European nursing home residents including people with and without dementia (up to 50%)<sup>8,9</sup>, community-dwelling individuals (63.5%)<sup>26</sup>, and acute care settings (up to 57.0%)<sup>27</sup>. It is also lower than figures of 47% to 68% published in smaller care home studies from the Netherlands and Northern Ireland<sup>5,7</sup>. This discrepancy is likely due to the clinically-relevant criteria that were followed in this study, ensuring that the diagnostic threshold of pain was determined by APS score. It may also be related to the inclusion criteria for the study which required homes to demonstrate a minimum acceptable standard of care according to the CQC. The lower pain prevalence may also be related to the 39% use of analgesics at baseline.

This is a large, robust study that provides novel and important data within the field. The study has clear strengths, including the robust design, large sample size, high retention of surviving participants and long follow-up period compared with previous studies, in addition to the precision of the design which ensured the exclusive recruitment of people with dementia living in care homes and assessment of pain through a validated, sensitive and appropriate observational pain assessment instrument. Selection bias was minimised by including all eligible consenting residents in the participating care homes. There are limitations to

acknowledge. Further data on the type and dosage of analgesics were not available, including reasons for halting their use during the period of the study, and the pragmatic nature of this trial allowed including people with multiple concurrent medications. Furthermore, our analyses considered all subtypes of dementia as one category and it may be of interest to investigate the patterns reported here in various subtypes of dementia in the future.

## **Conclusions**

The study confirms the widespread prevalence of pain amongst people with dementia living in care homes, and provides novel data regarding the longitudinal course of pain and its association with severity of dementia, neuropsychiatric symptoms, all-cause mortality and QoL. The clear association between pain and these key health outcomes highlights the importance of pain in the overall health and wellbeing of people with dementia in care home settings and the need to improve guidance on pain management in these settings.

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### **Competing interests**

All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

**Table 1:** Socio-demographic and clinical characteristics of the people with dementia, who suffered from pain<sup>a</sup>, and those, who did not experience pain at baseline (N=967)

Characteristic		With pain <sup>a</sup> (n=341) n (%) / Mean (SD)	Without pain (n=626) n (%) / Mean (SD)	$\chi^2$ (df)/ z <sup>b</sup>	p value
Female gender		251 (73.6)	432 (69.0)	2.25 (1)	0.13
Age in years		85.28 (8.71)	84.17 (9.13)	-1.56 <sup>b</sup>	0.91
Ethnicity: White		322 (94.4)	590 (94.3)	0.01 (1)	0.91
Number of years lived in nursing homes		2.31 (2.19)	2.41 (2.35)	0.37 <sup>b</sup>	0.71
FAST	Mild	25 (7.3)	63 (10.1)	16.26 (3)	0.001
	Moderate	19 (5.6)	67 (10.1)		
	Moderately severe	196 (57.5)	368 (58.8)		
	Severe	101 (29.6)	128 (20.5)		
Abbey pain scale total score		5.40 (2.50)	0.60 (0.81)	-26.57 <sup>b</sup>	<0.001
NPI-NH total score		18.12 (16.89)	12.07 (13.00)	-5.95 <sup>b</sup>	<0.001
CMAI total score		53.54 (22.42)	45.46 (16.86)	-5.68 <sup>b</sup>	<0.001
CSDD total score		8.52 (5.39)	4.98 (4.43)	-10.49 <sup>b</sup>	<0.001
DEMQoL total score		98.41 (13.50)	103.16 (12.33)	5.63 <sup>b</sup>	<0.001
QUALID total score		24.86 (7.66)	19.80 (6.68)	-10.41 <sup>b</sup>	<0.001
Co-morbid mental health diagnoses		73 (21.4)	109 (17.4)	2.31 (1)	0.13
Treatment with analgesics <sup>c</sup>		198 (58.1)	179 (28.6)	80.60 (1)	<0.001

Currently on antipsychotic medication	61 (17.9)	97 (15.5)	0.93 (1)	0.34
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<sup>a</sup> Abbey pain scale total score three and above; <sup>b</sup> Two-sample Wilcoxon rank-sum test z value; <sup>c</sup> Participant has been receiving regular treatment with analgesics at least for a month at baseline. Analgesic treatments included: Paracetamol, Non-Steroidal Anti-inflammatories, Opioids, Topical administrations, Gabapentin and neuraceutical preparations; FAST: Functional assessment staging test; NPI-NH: Neuropsychiatric inventory-nursing home version; CMAI: Cohen-Mansfield agitation inventory; CSDD: Cornell scale for depression in dementia; DEMQoL: Assessment (Proxy) of quality of life for people with dementia; QUALID: Quality of life in late-stage dementia scale.



**Table 2:** Prevalence and nature of pain<sup>a</sup> among the participants with differing levels of severity of dementia<sup>b</sup> at baseline (N=967) and at the follow-up (n=629)

Nature of pain	Mild n (%)		Moderate n (%)		Moderately severe n (%)		Severe n (%)	
	Baseline (n=88)	Follow-up (n=52)	Baseline (n=86)	Follow-up (n=32)	Baseline (n=564)	Follow-up (n=345)	Baseline (n=229)	Follow-up (n=200)
Mild <sup>c</sup>	23 (26.1)	4 (7.7)	15 (17.4)	3 (9.4)	153 (27.1)	98 (28.4)	85 (37.1)	59 (29.5)
Moderate <sup>d</sup>	2 (2.3)	0 (0.0)	4 (4.7)	0 (0.0)	40 (7.1)	17 (4.9)	15 (6.6)	12 (6.0)
Severe <sup>e</sup>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.5)	1 (0.3)	1 (0.4)	3 (1.5)
Acute	9 (10.2)	2 (3.9)	5 (5.8)	1 (3.1)	51 (9.0)	23 (6.7)	32 (14.0)	22 (11.0)
Acute on chronic	3 (3.4)	0 (0.0)	3 (3.5)	1 (3.1)	57 (10.1)	15 (4.4)	18 (7.9)	11 (5.5)
Chronic	13 (14.8)	2 (3.9)	11 (12.8)	1 (3.1)	88 (15.6)	78 (22.6)	51 (22.3)	41 (20.5)
Total score <sup>f</sup> (Mean (SD))	1.60 (0.26)	0.71 (0.17)	1.53 (0.26)	0.56 (0.21)	2.40 (0.12)	2.24 (0.15)	2.59 (0.18)	2.59 (0.22)

<sup>a</sup> Pain was assessed by the Abbey pain scale (APS); <sup>b</sup> Severity of dementia was assessed by the Functional assessment staging test (FAST); <sup>c</sup> Total APS scores between three and seven; <sup>d</sup> Total APS scores between eight and 13; <sup>e</sup> Total APS scores 14 and above; <sup>f</sup> Total APS score.

**Table 3:** Clinical correlates of pain<sup>a</sup> among people with dementia living in nursing homes at baseline (N=967) and at the follow-up (n=629)

Clinical variable	Baseline		Follow-up	
	$\rho^b$	$p^c$	$\rho^b$	$p^c$
Age in years	0.04	1.00	0.03	1.00
FAST stage	0.14	< 0.001	0.19	< 0.001
NPI-NH total score	0.19	< 0.001	0.27	< 0.001
CMAI total score	0.19	< 0.001	0.31	< 0.001
CSDD total score	0.37	< 0.001	0.40	< 0.001
DEMQoL total score	-0.22	< 0.001	-0.30	< 0.001
QUALID total score	0.36	< 0.001	0.40	< 0.001

<sup>a</sup> Abbey pain scale total score; <sup>b</sup> Spearman correlation coefficients; <sup>c</sup> p values after Bonferroni correction for multiple testing; FAST: Functional assessment staging Test; NPI-NH: Neuropsychiatric inventory-nursing home version; CMAI: Cohen-Mansfield agitation inventory; CSDD: Cornell scale for depression in dementia; DEMQoL: Assessment (Proxy) of quality of life for people with dementia; QUALID: Quality of life in late stage dementia scale.

**Table 4:** Associations between changes in pain severity<sup>a</sup> and changes<sup>b</sup> in neuropsychiatric symptoms as well as quality of life of participants that completed follow-up (n=629)

<b>Dependent variable<sup>c</sup></b>	<b><math>\beta^d</math></b>	<b>95% CI of <math>\beta^e</math></b>	<b>z</b>	<b>p</b>
CMAI total score	0.69	0.19 – 1.19	2.73	0.006
Physically aggressive behaviours <sup>f</sup>	0.26	0.10 – 0.41	3.25	0.001
Physically non-aggressive behaviours <sup>f</sup>	0.16	-0.08 – 0.40	1.29	0.196
Verbally aggressive behaviours <sup>f</sup>	0.09	-0.02 – 0.20	1.66	0.097
Verbally non-aggressive behaviours <sup>f</sup>	0.13	-0.07 – 0.33	1.25	0.211
NPI-NH total score	0.29	0.06 – 0.52	2.51	0.012
CSDD total score	0.44	0.34 – 0.54	8.28	< 0.001
DEMqoL total score	-0.59	-0.68 – -0.51	-13.81	< 0.001
QUALID total score	0.60	0.43 – 0.76	6.97	< 0.001

<sup>a</sup> Abbey pain scale (APS) total score at baseline was subtracted from APS total score at the follow-up; <sup>b</sup> Scores at baseline were subtracted from corresponding scores at the follow-up; <sup>c</sup> Each row represents a three-level mixed effects linear regression model with maximum likelihood estimation method. Change in pain severity between the two time-points was included as the independent variable. Age and gender of participants, baseline dementia severity, measured by Functional Assessment Staging Test, and baseline treatment with analgesics were included as co-variables. Individual participants were nested within a level, the nursing homes, that in turn nested within a higher level, the sites; <sup>d</sup> Regression coefficients; <sup>e</sup> Clustered robust standard errors were calculated with the sites as the clustering variable; <sup>f</sup> Subscale of Cohen-Mansfield Agitation Inventory (CMAI); NPI-NH: Neuropsychiatric inventory- nursing home version; CSDD: Cornell scale for depression in dementia; DEMqoL: Assessment (Proxy) of quality of life for people with dementia; QUALID: Quality of life in late stage dementia scale.

**Table 5:** associations between the changes in pain severity<sup>a</sup> and the changes in each of these NPI-NH domains<sup>b</sup> of participants that completed follow-up.

Dependent variable <sup>c</sup>	$\beta^d$	95% CI of $\beta^e$	z	p
A. Delusions	0.03	-0.03 – 0.08	1.04	0.30
B. Hallucinations	0.01	-0.02 – 0.05	0.71	0.48
C. Agitation/Aggression	0.12	0.06 – 0.17	3.99	< 0.001
D. Depression/Dysphoria	0.06	-0.01 – 0.13	1.80	0.07
E. Anxiety	-0.01	-0.05 – 0.04	-0.27	0.79
F. Elation/Euphoria	0.02	-0.01 – 0.05	1.18	0.24
G. Apathy/Indifference	0.05	-0.10 – 0.19	0.66	0.51
H. Disinhibition	0.00	-0.04 – 0.04	0.13	0.90
I. Irritability/Lability	0.03	-0.09 – 0.16	0.52	0.60
J. Aberrant motor behaviour	0.01	-0.09 – 0.12	0.28	0.78
NPI-NH total score	0.29	0.06 – 0.52	2.51	0.01

<sup>a</sup> Abbey pain scale (APS) total score at baseline was subtracted from APS total score at the follow-up; <sup>b</sup> Scores at baseline were subtracted from corresponding scores at the follow-up; <sup>c</sup> Each row represents a three-level mixed effects linear regression model with maximum likelihood estimation method (*mixed changeNPIA changepain analgesicBLR age gender FASTBL if completedFU==1 || site: || CareHome\_ID: , vce(cluster site) nolog*). <sup>d</sup> Regression coefficients; <sup>e</sup> Clustered robust standard errors were calculated with the sites as the clustering variable.

**Table 6:** Socio-demographic and clinical profile of the people, who experienced persistent pain<sup>a</sup> (n=82), and the people, whose pain resolved<sup>b</sup> (n=127) at the follow-up

Characteristic		Persistent pain <sup>a</sup>	Resolving pain <sup>b</sup>	$\chi^2$ (df)/ z <sup>c</sup>	p value
		n (%) / Mean (SD)	n (%) / Mean (SD)		
Female gender		65 (79.3)	92 (72.4)	1.24 (1)	0.27
Age in years at baseline		83.57 (9.48)	84.95 (8.67)	0.60 <sup>c</sup>	0.55
Ethnicity: White		76 (92.7)	119 (93.7)	0.08 (1)	0.77
FAST at baseline	Mild	6 (7.3)	13 (10.2)	5.74 (3)	0.13 <sup>d</sup>
	Moderate	9 (11.0)	4 (3.2)		
	Moderately severe	44 (53.7)	76 (59.8)		
	Severe	23 (28.1)	34 (26.8)		
APS score at baseline		5.90 (2.80)	4.96 (2.18)	-2.38 <sup>c</sup>	0.02
Type of pain at baseline	Acute	18 (22.0)	45 (35.4)	4.30 (2)	0.12
	Acute on chronic	21 (25.6)	27 (21.3)		
	Chronic	43 (52.4)	55 (43.3)		
NPI-NH total score	Baseline	22.27 (19.76)	15.12 (14.48)	-2.94 <sup>c</sup>	0.003
	Follow-up	20.37 (16.25)	12.34 (13.67)	-4.14 <sup>c</sup>	<0.001
CMAI total score	Baseline	58.83 (23.82)	51.20 (20.46)	-2.51 <sup>c</sup>	0.01
	Follow-up	55.74 (21.05)	46.21 (20.15)	-4.13 <sup>c</sup>	<0.001
CSDD total score	Baseline	9.56 (5.46)	7.37 (4.93)	-2.91 <sup>c</sup>	0.004
	Follow-up	7.02 (5.18)	4.17 (4.09)	-4.45 <sup>c</sup>	<0.001
DEMQoL total score	Baseline	96.22 (13.99)	100.70 (13.03)	2.47 <sup>c</sup>	0.01
	Follow-up	99.20 (13.09)	106.63 (9.91)	5.02 <sup>c</sup>	<0.001
QUALID total score	Baseline	26.49 (7.70)	22.76 (6.82)	-3.59	<0.001
	Follow-up	26.44 (8.39)	19.92 (6.09)	-5.93	<0.001
Comorbid mental health diagnoses at baseline		21 (25.6)	25 (19.7)	1.02 (1)	0.31
Receiving analgesics <sup>e</sup>	Baseline	52 (63.4)	72 (56.7)	0.93 (1)	0.33
	Follow-up	53 (64.6)	69 (54.3)	2.18 (1)	0.14
Receiving APD	Baseline	16 (19.5)	23 (18.1)	0.06 (1)	0.80
	Follow-up	15 (18.3)	19 (15.0)	0.41 (1)	0.52

<sup>a</sup> Abbey pain scale (APS) total score three and above at both time-points; <sup>b</sup> APS total score was three and above at baseline, but it was less than three at the follow-up; <sup>c</sup> Two-sample Wilcoxon rank-sum test z value; <sup>d</sup> Fisher's exact test p value was 0.138; <sup>e</sup> Participant has been receiving regular treatment with analgesics at least for a month; FAST: Functional assessment staging test; NPI-NH: Neuropsychiatric inventory-nursing home version; CMAI: Cohen-Mansfield agitation inventory; CSDD: Cornell scale for depression in dementia; DEMQoL: Assessment (Proxy) of quality of life for people with dementia, APD: Antipsychotic Drugs

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