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Original Study

# From Admission to Death: Prevalence and Course of Pain, Agitation, and Shortness of Breath, and Treatment of These Symptoms in Nursing Home Residents With Dementia

Simone A. Hendriks MD [a], Martin Smalbrugge MD, PhD [a], Francisca Galindo-Garre PhD [b], Cees M.P.M. Hertogh MD, PhD [a], Jenny T. van der Steen PhD [a,*]

[a] Department of General Practice and Elderly Care Medicine and EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands
[b] Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

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A B S T R A C T

*Objectives:* Burdensome symptoms frequently develop as part of the dementia trajectory and influence quality of life. We explore the course of symptoms and their treatment during nursing home stay to help target adequate symptom management.
*Design:* Data were collected as part of the Dutch End of Life in Dementia study, a longitudinal observational study with up to 3.5 years of follow-up. Physicians performed assessments at baseline, semiannually, and shortly after death of pain, agitation, shortness of breath, and treatment provided for these symptoms.
*Setting:* Long-term care facilities (28) in the Netherlands.
*Participants:* Newly admitted nursing home residents (372) in variable stages of dementia.
*Measurements:* We described prevalence and course of symptoms, and treatment provided for these symptoms. We used generalized estimating equations to evaluate the longitudinal change in symptoms and their treatment, and the associations between the symptoms of pain and agitation, as well as between stage of dementia and symptoms.
*Results:* Pain was common (varying from 47% to 68% across the semiannual assessments) and frequently persistent (36%–41% of all residents); it increased to 78% in the last week of life. Agitation was the most common symptom (57%–71%), and also frequently persistent (39%–53%), yet it decreased to 35% in the last week of life. Shortness of breath was less common (16%–26%), but it increased to 52% at the end of life. Pain was not significantly associated with agitation. Advanced dementia was associated with more pain only. Treatment changed in particular at the end of life. Pain was treated mostly with acetaminophen (34%–52%), and at the end of life with parenteral opioids (44%). Agitation was mostly treated nonpharmacologically (78%–92%), and at the end of life anxiolytics were the most frequently prescribed treatment (62%). Overall, aerosolized bronchodilators were the most frequently prescribed treatment for shortness of breath (29%–67%), but at the end of life, this was morphine (69%).
*Conclusion:* Pain and agitation were common and frequently persisted in residents with dementia during nursing home stay, but symptom management intensified only at the end of life. Symptom control may be suboptimal from admission, and a stronger focus on symptom control is needed at an earlier stage than the end of life.



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* Address correspondence to Jenny T. van der Steen, PhD, Department of General Practice and Elderly Care Medicine, EMGO Institute for Health and Care Research, VU University Medical Center, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands.
*E-mail address:* j.vandersteen@vumc.nl (J.T. van der Steen).

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Burdensome symptoms frequently occur in patients with dementia, while adequate symptom control is important to maintain or improve quality of life.[1] In the United States and Western Europe, most people with dementia are eventually admitted to, and die in long-term care facilities.[2,3] Pain, agitation, and shortness of breath are the most prevalent and important symptoms at the end of life.[4] At any given time, 12% to 76% of nursing home residents are in pain and prevalence may increase when death approaches,[4,5] and up to 80% present with challenging behavior.[6,7] More severe dementia may be associated with more pain[8,9] and with more agitation.[10,11] The rates of shortness of breath vary widely, from 8% to 80%.[4] Optimal symptom control needs a holistic approach because symptoms may be interrelated; for example, pain may be associated with agitation.[12–15]

These findings are from work that has several specific limitations. First, study populations are often limited to advanced dementia,[5] whereas in the Netherlands, half of all patients with dementia may die before having reached this stage.[16] Second, most studies are limited to the period shortly before dying,[4] whereas symptoms present earlier.[1] Last, data collection is frequently limited to retrospective collection or fixed periods per individual.[12,17] In addition, there are few studies on how specific symptoms are managed with pharmacological and nonpharmacological treatment.[9]

To achieve adequate symptom control in dementia, a better understanding is needed of the longitudinal course of symptoms and the treatment provided.[18] Therefore, the objectives of this study were to explore changes in symptoms and provided treatment in Dutch nursing home residents in variable stages of dementia during their nursing home stay. We report on the prevalence and course of pain, agitation, and shortness of breath. We explore the longitudinal association between pain and agitation, and between stage of dementia and symptoms. Furthermore, we report on specific pharmacological and nonpharmacological treatment provided for pain, agitation, and shortness of breath during nursing home stay.

## Methods

### *Data Collection*

Data were collected as part of a longitudinal observational study, the Dutch End of Life in Dementia study. Between 2007 and 2011, data were prospectively and retrospectively collected on 491 residents in 34 long-term care facilities, nursing homes, and affiliated residential homes. In this article, we used only prospectively collected data from 28 facilities (23 nursing homes and 5 residential care facilities that the physicians visit from their nursing home practice) on 372 newly admitted residents. Elderly care physicians, who are certified after 3 years of training, employed by the nursing homes were responsible for data collection. The residents had a physician's diagnosis of dementia in all possible stages. A total of 372 residents were enrolled on admission between January 2007 and July 2009; during the study period, 218 residents died before summer 2010.[16]

Individual assessments were performed for a maximum period of 3.5 years (January 2007–July 2010; and survival was monitored for an additional year, until summer 2011). The baseline measurement was carried out 8 weeks after admission, and it was followed by a maximum of 5 semiannual assessments. We refer to the baseline measurement and the semiannual assessments as regular assessments. In case of death during the study period, a questionnaire about the last week of life was completed within 2 weeks after death, and we refer to this questionnaire as the after-death assessment. The study protocol was approved by the Medical Ethics Review Committee of the (VU University Medical Center in Amsterdam), and written consent was obtained from all participants or their families.

### *Measurements*

The diagnosis of dementia was based on international guidelines.[19–22] Type of dementia was assessed with a prestructured item comprising the categories Alzheimer disease, vascular dementia, Alzheimer disease and vascular dementia, Lewy body/Parkinson disease, and other. Advanced dementia (versus less advanced dementia) was defined as a maximum score of 7 on the Global Deterioration Scale (GDS)[23] and a score of 5 or 6 on the Cognitive Performance Scale (CPS, range 0–6).[24]

The physicians assessed frequency of pain and shortness of breath as "never," "rarely" (<5 days a month), "sometimes" (5–10 days per month), "often" (11–20 days/month), and "almost daily" (>20 days per month). The frame of reference was the previous month for the baseline assessments, and the 3 months before the semiannual assessments (frequency on average per month over last 3 months). During the last week of life, the physicians assessed frequency of pain and shortness of breath as "never," "rarely" (≤1 day), "sometimes" (2–3 days), "often" (4–5 days), and "almost daily" (6–7 days). We dichotomized into "never" versus "other" for all assessments. Prevalence of agitation, such as restlessness, calling out, resistance to care, verbal aggression, or physical aggression was assessed as present or not, during the month before baseline, the 3 months before the semiannual assessments, and during the last week of life.

Treatment provided for pain, agitation, and shortness of breath was assessed using prestructured items. The categories for pain treatment were nonpharmacological (eg, physiotherapy, occupational therapy, transcutaneous electrical neurostimulation, massage); acetaminophen (paracetamol); nonsteroidal anti-inflammatory drugs (NSAIDs); oral narcotic; parenteral narcotic (including transdermal patch), each separately assessed as PRN ("as needed") only or scheduled dose; other; and no therapy. Treatment provided for agitation comprised nonpharmacological treatments (eg, 1:1 sitter, separate, involve family to participate in care), trunk or limb restraints, antipsychotic medication, anxiolytic or hypnotic medication, other, and no therapy. Finally, treatment of shortness of breath was prestructured as oxygen, morphine, aerosolized bronchodilators, diuretics, other, and no therapy.

### *Analyses*

We analyzed the results by taking 2 perspectives, one prospective, reporting on consecutive regular follow-up assessments, and the other retrospective, anchoring the after-death assessment and following back to the last regular assessment. For the follow-back analyses, we selected the last regular assessment before death from the assessments 1 through 6. For each assessment, we described symptom prevalence. To investigate the individual course of symptoms in more detail, we calculated the following frequency parameters for each consecutive assessment: persistence of a symptom and persistence of no symptom, incidence, and resolution of a symptom relative to the total number of residents at the assessments concerned. A symptom persisted if it occurred on 2 consecutive assessments, or a symptom was persistently absent if it did not. Incidence was defined as a symptom present at one assessment but not present at the previous assessment. We defined resolution as presence of a symptom at one assessment but not at the next assessment. For each assessment, we described the targeted treatment and for the most frequently provided treatments we calculated the proportion of continued treatment in case of a persistent symptom.

To evaluate the longitudinal associations (change in symptoms, and change in treatment), we used the generalized estimating equation (GEE) model, with an exchangeable correlation structure. We evaluated 5 models of longitudinal associations. Three models used assessment as the independent predictor with repeated contrast

levels: (1) change in symptoms; (2) course of symptoms, with persistency and persistency of no symptoms; (3) change in provided treatment. Further, we evaluated the longitudinal association between (4) pain and agitation, with agitation as the dependent variable and pain as the independent variable. The final model (5) represented the association between the stage of dementia (less advanced dementia versus advanced dementia was the independent variable) and the presence of symptoms. For models 1, 3, 4, and 5, we separately analyzed the follow-up perspective (the regular assessments 1 through 6), and the follow-back perspective (last regular assessment and the after-death assessment). For model 2, we analyzed the follow-up perspective only, because at least 3 assessments are needed for the analysis of the course of symptoms (change in persistency). For the follow-up perspective analyses, we adjusted for the last regular assessment before death. For all follow-back perspective analyses, we adjusted for the exact number of days between the 2 assessments. We defined a significant difference as a *P* value less than .05. A significant change between 2 consecutive assessments indicates a change at the population level (ie, change in the total proportion of residents with a symptom) or at an individual level (ie, the individual change in symptoms). Detail on the statistical analyses is available on request. Analyses were performed with PASW 20.0 (SPSS, Inc., Chicago, IL 2013).

## Results

### *Residents*

Most residents were women, 9% had advanced dementia at admission and 38% at death. The most common type of dementia was Alzheimer disease (46%; Table 1). Through follow-up, the number of residents decreased across consecutive assessments because residents died or reached the conclusion of data collection (possible from assessment [A] 3 onward). In total, 218 residents died during follow-up, with a median survival time of 8 months from admission. In case of death, the median length of time between the last regular assessment and the after-death assessment was 13 weeks (25th percentile = 8, 75th percentile = 21). The median length of time between the day of death and the day the physician completed the after-death questionnaires was 16 days (first quartile = 1 day, second quartile = 8 days, third quartile = 32 days, fourth quartile = 214 days). Ten residents were lost to follow-up because they moved to another long-term care facility, or the physician withdrew from data collection. Detail on number of residents through data collection is available from online resource Figure 1.

**Table 1**
Resident Characteristics

| Characteristics | n = 372 | |
|---|---|---|
| Female, % | 70 | |
| Age at admission, mean (SD) | 84 | (7) |
| Age at death, mean (SD)* | 85 | (7) |
| Median length of stay until death, mo (25th percentile, 75th percentile)* | 8 | (4, 17) |
| Type of dementia, % | | |
| Alzheimer disease | 46 | |
| Vascular | 23 | |
| Alzheimer and vascular | 18 | |
| Lewy body/Parkinson disease | 5 | |
| Other types | 8 | |
| Advanced dementia at admission, %† | 9 | |
| Advanced dementia at death, %* | 38 | |
| Residence before admission, % | | |
| Private home | 32 | |
| Residential home/other nursing home | 42 | |
| General/psychiatric hospital | 19 | |
| Other | 7 | |

*Percentage refers to 213 residents who died during the follow-up period with completed after-death assessments.

†Percentage refers to 329 residents. This is because for the residents who died before or shortly after the baseline assessment, we used a shortened baseline assessment, to complete only the data of resident characteristics that we deemed not particularly vulnerable to recall bias.

### *General Patterns of Change in Symptoms Over Time*

Overall, the prevalence of pain, agitation, and shortness of breath changed marginally across the regular assessments (Table 2, online resource Figures 2–4). Moreover, we found only 2 significant changes: the prevalence of pain at A2 was significantly higher than at A1, and the prevalence of shortness of breath was significantly higher at A3 compared with at A2. In the last week of life, however, the (overall) prevalence of pain and shortness of breath increased, while the prevalence of agitation decreased significantly (Table 2, online resource Figures 2–4), as detailed in the following sections.

### *Pain*

Table 2 (and online resource Figure 2) provides details on the prevalence of and change in pain, and shows the course over the consecutive assessments. Across the regular assessments, the prevalence of pain varied from 47% to 68%, and the prevalence at A2 was significantly higher than at A1 ($P = .004$; Table 2). Pain persisted

**Table 2**
The Prevalence and Change in Symptoms Over 2 Consecutive Assessments

| Symptom | Assessment | | Prevalence | | Change |
|---|---|---|---|---|---|
| | | (n; m)* | % | n | *P*† |
| Pain | A1 | (327; 7) | 52 | 171 | |
| | A2 | (221; 30) | **61** | 134 | **.004** |
| | A3 | (170; 36) | 68 | 115 | .093 |
| | A4 | (120; 18) | 58 | 70 | .135 |
| | A5 | (77; 9) | 56 | 43 | .693 |
| | A6 | (34; 3) | 47 | 16 | .350 |
| | A<†‡ | (162; 33) | 67 | 108 | |
| | A†§ | (211; 6) | **78** | 165 | **.011** |
| Agitation | A1 | (328; 6) | 57 | 188 | |
| | A2 | (221; 30) | 58 | 128 | .941 |
| | A3 | (170; 36) | 62 | 105 | .263 |
| | A4 | (120; 18) | 57 | 68 | .208 |
| | A5 | (77; 9) | 66 | 51 | .258 |
| | A6 | (34; 3) | 71 | 24 | .894 |
| | A<†‡ | (163; 30) | 58 | 94 | |
| | A†§ | (213; 4) | **35** | 75 | **<.001** |
| Shortness of breath | A1 | (327; 7) | 19 | 62 | |
| | A2 | (219; 32) | 18 | 39 | .891 |
| | A3 | (170; 36) | **24** | 41 | **.018** |
| | A4 | (120; 18) | 16 | 19 | .059 |
| | A5 | (77; 9) | 25 | 19 | .144 |
| | A6 | (34; 3) | 26 | 9 | .813 |
| | A<†‡ | (163; 30) | 28 | 46 | |
| | A†§ | (213; 4) | **52** | 111 | **<.001** |

As also described in the Methods section, for the follow-up perspective analyses (A1 through A6) we adjusted for the last regular assessment before death. For the follow-back perspective analyses (A<† through A†), we adjusted for the length of time between these 2 consecutive assessments.
The complete output of the GEE analyses is available on request.
online resource Figures 2–4 present detail about the course of symptoms.

*(n; m) = Number of residents per assessment; number of missing values.

†GEE with repeated contrast between 2 consecutive assessments. The *P* value is an indication for change over time over 2 consecutive assessments at a population level and at an individuals level. Therefore, even when the total proportion of a symptom is unchanged, significance change is possible due to change of individual patterns. We defined a $P < .05$ as significant, and prevalence and *P* values of significant changes are bolded.

‡A<† = The last regular assessment before death is one of A1 through A6.

§A† = The after-death assessment.

**Table 3**
Longitudinal Associations

| Association | Assessment | Unadjusted OR | 95% Wald CI | | Adjusted* OR | 95% Wald CI | |
|---|---|---|---|---|---|---|---|
| | | | Lower | Upper | | Lower | Upper |
| Pain and agitation | A1-A6 | 1.2 | 0.95 | 1.6 | 1.2 | 0.95 | 1.6 |
| | A<†‡ – A†§ | 1.3 | 0.81 | 1.2 | 1.4 | 0.86 | 2.3 |
| Advanced dementia and pain | A1-A6 | **1.9** | **1.3** | **2.7** | **1.8** | **1.2** | **2.6** |
| | A<†‡ – A†§ | 1.7 | 1.0 | 3.1 | 1.7 | 0.94 | 3.2 |
| Advanced dementia and agitation | A1-A6 | 1.3 | 0.87 | 2.0 | 1.3 | 0.88 | 2.0 |
| | A<†‡ – A†§ | 0.84 | 0.53 | 1.3 | 0.87 | 0.54 | 1.4 |
| Advanced dementia and Shortness of breath | A1-A6 | 1.3 | 0.90 | 2.0 | 1.3 | 0.85 | 2.0 |
| | A<†‡ – A†§ | 0.89 | 0.56 | 1.4 | 1.0 | 0.63 | 1.7 |

GEE for longitudinal associations. In case of A<†-A†: we adjusted for the length of time between these 2 consecutive assessments. We defined a $P < .05$ as significant and ORs of significant associations are bolded.

*In case of A1 through A6, we adjusted for the last regular assessment before death.

‡A<† = The last regular assessment before death is one of A1 through A6.

§A† = The after-death assessment.

in many residents (ie, in 36%–41%) across the consecutive regular assessments. Further, the proportion of persistent pain at A3 was significantly ($P = .006$) higher than at A2. At 20% to 35%, the proportion of residents without pain on 2 consecutive regular assessments was much lower. Only at A3 versus A2 did we find a significantly ($P = .017$) lower proportion of residents with persistent absence of pain. An intermittent course of pain in some residents is illustrated by incidence proportions of 6% to 24%, and resolution of pain proportions of 10% to 13% across the consecutive regular assessments.

Further, over the last weeks of life the (overall) prevalence of pain increased significantly (from 67%) to 78% ($P = .011$; Table 2). We also found a significantly ($P = .009$) smaller proportion of residents with persistent absence of pain at the after-death assessment (versus the last regular assessment before death).

### *Agitation*

Table 2 (and online resource Figure 3) shows the prevalence of and change in agitation, and shows the course over the consecutive assessments. Across the regular assessments, agitation was the most prevalent symptom, varying from 57% to 71%, and it did not differ significantly between the assessments. Agitation persisted in 39% to 53% of all residents. There were no significant changes in the proportion of persistency between the consecutive regular assessments. At 9% to 25%, the proportion of residents with absence of agitation on 2 consecutive regular assessments was much smaller and it did not change significantly. An intermittent pattern of agitation occurred in some residents, with 6% to 17% incident agitation, and 11% to 18% resolution of agitation.

Yet, in the last week of life, the prevalence of agitation decreased significantly (from 58%) to 35%.We also found a significantly ($P < .001$) larger proportion of residents with persistent agitation at the after-death assessment (versus the last regular assessment before death).

### *Shortness of Breath*

Table 2 (and online resource Figure 4) shows the prevalence of and change in shortness of breath, and shows the course over the consecutive assessments. The prevalence of residents with shortness of breath varied from 16% to 26%, and was significantly higher at A3 than at A2 (in line with Table 2).

The proportion of residents with persistent shortness of breath was small with 8% to 18% over the consecutive regular assessments. There were no significant changes in the proportion of persistency. The proportion of residents with persistently absent shortness of breath was 62% to 75%. Only at A3 versus A2 did we find a significantly ($P = .003$) lower proportion of residents with persistently absent shortness of breath. The proportions residents with incident shortness of breath ranged 6% to 13%, and 3% to 13% for resolution of shortness of breath.

In the last week of life, the prevalence of shortness of breath increased substantially and significantly (from 28%) to 52%, and we also found a significantly ($P < .001$) smaller proportion of residents with persistently absent shortness of breath at the after-death assessment (versus the last regular assessment before death).

### *Association Between Pain and Agitation*

Across the regular assessments, the prevalence of simultaneously reported pain and agitation in residents varied from 29% to 42%, and in the last week of life it was 27%. We found a positive but insignificant longitudinal association between presence of pain and agitation across the regular assessments (adjusted odds ratio [OR] 1.2; confidence interval [CI] 0.95–1.6) and across the last regular assessment and the after-death assessment (adjusted OR 1.4; CI 0.86–2.3; Table 3).

### *Association Between the Stage of Dementia and the Presence of Symptoms*

We found a significant longitudinal association between advanced dementia (versus less advanced dementia) and pain across the regular assessments (adjusted OR 1.8; CI 1.2–2.6), but insignificant across the last regular assessment and the after-death assessment (adjusted OR 1.7; CI 0.94–3.2; Table 3). We did not find a significant association between advanced dementia and agitation (A1 through A6: adjusted OR 1.3; CI 0.88–2.0; A<†–A†: adjusted OR 0.87; CI 0.54–1.4; Table 3). We also did not find an association between advanced dementia and shortness of breath (A1 through A6: adjusted OR 1.3; CI 0.85–2.0; A<†–A†: adjusted OR 1.03; CI 0.63–1.7; Table 3).

### *Treatment of Pain*

Table 4 shows the treatment provided for the symptoms. Over the regular assessments, pain was most frequently treated with non-pharmacological treatments (24%–34%) and acetaminophen (paracetamol, 34%–52%). We found a significantly higher percentage of acetaminophen only at assessment 3 versus 2, and a significantly higher percentage of oral narcotics at A3 versus A2. Continued non-pharmacological treatment across the regular assessments ranged from 35% to 67%, and for acetaminophen from 48% to 80%.

**Table 4**
Treatment Provided for Symptoms per Assessment and Change Over 2 Consecutive Assessments

| Symptom | Treatment*% | Assessment | | | | | | | | Change *P* Value‖ |
|---|---|---|---|---|---|---|---|---|---|---|
| | | A1 | A2 | A3 | A4 | A5 | A6 | A<†‡ | A†§ | |
| Pain (n) | | (171) | (133) | (114) | (70) | (42) | (16) | (108) | (157) | |
| | Nonpharmacological | 27 | 26 | 24 | 34 | 31 | 25 | 26 | 11 | ↓.005 |
| | Acetaminophen PRN | 26 | 34 | 29 | 21 | 29 | 44 | 26 | 11 | ↓.002 |
| | Acetaminophen | 40 | 34 | **49**[1↑] | 52 | 52 | 38 | 49 | 43 | .252 |
| | NSAID PRN | 1 | 4 | 3 | 3 | 2 | 6 | 2 | 1 | .423 |
| | NSAID | 13 | 15 | 11 | 15 | 12 | 13 | 14 | 9 | .269 |
| | Oral narcotic PRN¶ | 1 | 1 | 2 | 0 | 0 | 0 | 1 | 4 | .307 |
| | Oral narcotic¶ | 5 | 2 | **8**[2↑] | 6 | 2 | 0 | 6 | 10 | .203 |
| | Parenteral narcotic PRN¶ | 0 | 1 | 0 | 3 | 0 | 6 | 2 | **17** | ↑.002 |
| | Parenteral narcotic¶ | 4 | 2 | 2 | 0 | 7 | 0 | 5 | **44** | ↑<.001 |
| | Other | 4 | 4 | 7 | 4 | 2 | 6 | 6 | 1 | .091 |
| | No therapy | 16 | 11 | 11 | 4 | 10 | 6 | 11 | **4** | ↓.018 |
| Agitation (n) | | (188) | (128) | (103) | (69) | (51) | (24) | (94) | (68) | |
| | Nonpharmacological | 86 | 86 | 88 | **78**[3↓] | **92**[4↑] | 88 | 85 | **50** | ↓<.001 |
| | Trunk and limb restraints** | 11 | **5**[5↓] | 2 | 4 | 4 | 4 | 13 | 3 | .104 |
| | Antipsychotics | 46 | 45 | 37 | 33 | 27 | 38 | 59 | **44** | ↓.007 |
| | Anxiolytics | 29 | 30 | 31 | 29 | 33 | 29 | 41 | **62** | ↑.032 |
| | Antidepressant drug‡‡ | 3 | 2 | **11**[6↑] | 6 | 8 | 8 | 5 | 3 | .305 |
| | Other | 7 | 9 | 12 | 17 | 12 | 8 | 4 | 9 | .171 |
| | No therapy¶ | 0 | 0 | 1 | 0 | 0 | 4 | 0 | 4 | ¶ |
| Shortness of breath (n) | | (62) | (39) | (41) | (19) | (17) | (9) | (46) | (106) | |
| | Limiting physical exertion‡‡ | 8 | 10 | 15 | 5 | 18 | 11 | 11 | **1** | ↓.019 |
| | Aerosolized bronchodilators | 38 | 36 | 32 | 53 | 29 | 67 | 30 | **16** | ↓.041 |
| | Diuretics | 27 | 26 | 12 | 32 | 29 | 11 | 37 | **12** | ↓.008 |
| | Antibiotic¶,‡‡ | 21 | 18 | 12 | 11 | 18 | 0 | 11 | **2** | ↓.040 |
| | Oxygen¶ | 5 | 8 | 0 | 11 | 0 | 0 | 4 | **32** | ↑.002 |
| | Morphine¶ | 2 | 0 | 0 | 0 | 0 | 0 | 2 | **69** | ↑<.001 |
| | Other therapy | 15 | 10 | 12 | 16 | 12 | 0 | 15 | 14 | .965 |
| | No therapy | 19 | 23 | 29 | 21 | 18 | 11 | 13 | 10 | .386 |

↓ = Lower percentage/↑ = higher percentage: Significant change in GEE analyses with repeated contrasts between 2 consecutive regular assessments and change between the last regular assessment before death and the after-death assessment. We defined a $P < .05$ as significant. Only significant changes are reported, in case of the semiannual assessments, and prevalence of significant changes are bolded.
In case of 2 consecutive regular assessments we adjusted for the last regular assessment before death. In case of the last regular assessment before death and the after-death assessment, we adjusted for the length of time between these 2 consecutive assessments.
[1↑] $P = .003$, [2↑] $P = .041$, [3↓] $P = .023$, [4↑] $P = .006$, [5↓] $P = .036$, [6↑] $P = .013$. Coefficients of the GEE analyses are available on request.
*Receiving more than 1 treatment is possible.
‡A<† = The last regular assessment before death is one of A1 to A6.
§A† = The after-death assessment.
‖GEE analyses with repeated contrast between A<† and A†.
¶GEE analysis with repeated contrast is not possible between assessments with a proportion of 0%, thus only assessments with a proportion >0% were included in the GEE analyses.
**Strictly regulated within legal framework.
‡‡Not separately assessed but derived from the category "other."

Compared with the last regular assessment, at the after-death assessment, a significantly larger proportion of residents received parenteral narcotics PRN (increase from 2% to 17%) or parenteral narcotics (from 5% to 44%). A significantly smaller proportion of residents received nonpharmacological treatment (decrease from 26% to 11%), acetaminophen PRN (from 26% to 11%), and a significantly smaller proportion received no therapy (from 11% to 4%).

### *Treatment of Agitation*

Over the regular assessments, treatment provided for agitation was mostly nonpharmacological (78%–92%), or with antipsychotics (27%–46%) or anxiolytics (29%–33%; Table 4). We found only a few significant changes between the regular assessments. Across the regular assessments, continued nonpharmacological treatment ranged from 88% to 100%, continued use of antipsychotics from 58% to 74%, and continued use of anxiolytics from 50% to 75%.

Compared with the last regular assessment, at the after-death assessment, a significantly smaller proportion received nonpharmacological treatment (from 85%–50%), and antipsychotics (from 59% to 44%), and a significantly larger proportion of residents received anxiolytics (from 41% to 62%; Table 4).

### *Treatment of Shortness of Breath*

The most frequently provided treatments for shortness of breath across the regular assessments were aerosolized bronchodilators (29%–67%) and diuretics (11%–32%; Table 4). We did not find significant changes between the regular assessments. Across the regular assessments, continued aerosolized bronchodilators ranged from 33% to 100%, and continued diuretics from 0% to 50% (only 1–7 residents).

Compared with the last regular assessment, the after-death assessment showed a significantly larger proportion of residents receiving morphine (increase from 2% to 69%) and oxygen (from 4% to 32%). Limiting physical exertion (from 11% to 1%), aerosolized bronchodilators (decrease from 30% to 16%), diuretics (from 37% to 12%), and antibiotics (from 11% to 2%) were prescribed significantly less often (Table 4).

## Discussion

Dementia is a disease without a cure, and many people diagnosed with dementia will die with or of this disease. Burdensome symptoms frequently develop during the disease trajectory. Therefore, adequate symptom control to maintain or improve quality of life should be one

of the most important care goals.[1] To our knowledge, (Dutch End of Life in Dementia) is the first study that describes the longitudinal course, from admission to a nursing home until death, of burdensome symptoms and provided treatment for patients in variable stages of dementia. Agitation was persistent and the most common symptom, yet it decreased at the end of life. Pain was also common and persistent and increased in the last week of life. Shortness of breath was less common, but it often persisted and increased at the end of life. We found no significant longitudinal association between pain and agitation. We found a positive significant longitudinal association between advanced dementia and pain, but not at the end of life and there was no association with other symptoms. Pharmacological management of symptoms was more intensive at the end of life. Parenteral opioids, morphine, and anxiolytics were prescribed substantially more frequently at the end of life.

Many residents were in pain, consistent with the pain prevalence observed in previous studies.[25,26] Of note, in our earlier analyses of symptoms at the end of life[17], we also reported pain prevalence over the last week of life, but we reported lower percentages because we dichotomized differently, combining "never" with "rarely." It should be noted that residents already suffered from pain shortly after admission. Acetaminophen was frequently provided, which is in line with guideline recommendations,[27] but in view of frequently persisting pain, it is remarkable that the treatment was intensified only at the end of life. Perhaps this is because physicians are more inclined to accept side effects, such as sedation, in case of a nearing death, or due to increasing pain or a new origin of pain at the end of life, requiring a different treatment strategy. Reports in the literature support the value of stepped approaches of analgesia administration, both for the treatment of pain and as an important component of the management of agitation,[8,27] because pain may be the underlying cause of behavioral symptoms.[8,9] However, we found no significant association between pain and agitation. Absence of an association has been reported in more studies.[12–15] Ahn and Horgas[14] reported that the relationship between pain and disruptive behaviors depends on the type of behaviors examined, and found that pain is positively correlated with disruptive behaviors that do not involve locomotion (eg, aggression and agitation).

Agitation was highly prevalent shortly after admission and often persisted. Agitation did not tend to increase over time. This is in line with a study of Selbaek et al,[10] which also had a long follow-up period, but reported on aggression only. Nonpharmacological approaches based on person-centered care combined with medication review should be the first-line approach for treatment of agitation in people with dementia.[1,28,29] Nonpharmacological treatments were frequently provided in our study, as well as antipsychotics and anxiolytics. These psychotropic drugs were continued in more than half of the residents with persistent agitation, despite the recommendation that these psychotropic drugs be reduced or discontinued within 3 months, because of possible limited benefits in longer-term therapy.[29–31] An explanation for less agitation reported at the end of life may be the worsening condition at the end of life, or the sedative effect of opioids at the end of life. Shortness of breath was less common and persisted in only a small proportion of residents; however, at the end of life, shortness of breath is increasingly present and may be attributed to different causes, such as pneumonia and heart failure.

Diagnosing symptoms and symptom management is challenging in residents with dementia. It is remarkable that overall, despite almost all residents dying with a palliative goal of care,[32] nonpharmacological types of treatment decreased at the end of life, although we do not know if some were also replaced by other types of nonpharmacological treatment. This suggests that the available nonpharmacological treatment is not suitable at the end of life, and that tailored treatment is not available or not offered. Further intervention research is needed to improve symptom management and to develop more evidence-based guidelines for pharmacological and nonpharmacological treatment. A strong focus on palliative care needs is recommended from admission. Research should focus on the *how* of providing comfort, with optimal treatment of symptoms to improve the quality of life of patients with dementia.[1]

### *Strengths and Limitations*

The strength of our study is the inclusion of residents in all stages of dementia, making the results representative of a wide population of nursing home residents with dementia. Our findings apply to institutional long-term care rather than to community settings. International differences in health care systems potentially reduce generalizability. Elderly care medicine is a separate specialty in the Netherlands, and elderly care physicians are employed by the nursing homes, and have patient contact frequently.[33,34] They work with low-educated nursing staff. However, this system does not necessarily result in a better recognition of symptoms and treatment. Further, through the long follow-up period and the adoption of 2 temporal perspectives, we investigated the full period from admission until death, and for most residents, from both perspectives. In addition, our study was unique in that it we provided detailed information on symptom management, such as type of medication.

Some limitations should be acknowledged. First, to allow for longitudinal analyses, we collapsed the response options for frequencies of pain and shortness of breath. However, the full response options showed similar patterns and stable distributions across assessments. Of all residents, 18% to 25% "rarely" had pain, 12% to 25% "sometimes," 3% to 10% "often," and 7% to 17% had pain "almost daily." Across the assessments, 6% to 18% had shortness of breath "rarely," 8% to 20% "sometimes," 1% to 9% "often," and 3% to 9% had shortness of breath "almost daily." Second, we used the physician's evaluation of symptoms. In approximately half of the cases (52%) the same physician completed all assessments, in 35% the resident was assessed by 2 physicians, in 11% by 3 physicians, and in 2% by 4 physicians. The median length of time between the day of death and the day the physician completed the after-death questionnaire was 16 days. However, recall bias may be limited, because physicians could rely on both the chart and their own memory. Accordingly, we found no significant correlation between length of time and symptom levels (pain: $r = -0.058$, $P = .405$; agitation: $r = 0.048$, $P = .482$; shortness of breath: $r = 0.030$, $P = .666$). Third, the statistical power was adequate for analyzing, but the analyses of change in treatment were less powerful, because of the reduced sample sizes of those receiving specific treatments. Further, unfortunately, we cannot draw conclusions about the most effective treatment for symptom relief, because of the observational study design, and we did not assess treatment that effectively resolved symptoms. We did not assess the intensity of symptoms or change in dosage of medication, and we did not specify nonpharmacological treatment. Finally, we did not consider changes in (co)morbidity and underlying change in causation and nature of symptoms.

## Conclusion

Pain and agitation are common and frequently persist. Symptom control may be suboptimal in patients in variable stages of dementia during nursing home stay in the Netherlands. We recommend a strong focus on palliative care and palliative care needs with meticulous assessment and subsequent treatment of burdensome symptoms, from admission until the end of life. Our observations call for further research into interventions targeted at pain and agitation and

the relation between both symptoms. This will contribute to the development of evidence-based guidelines for treatment of burdensome symptoms in patients with dementia.

## Supplementary Data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.jamda.2014.12.016.

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