

**Original Article**

# Dying With Dementia: Symptoms, Treatment, and Quality of Life in the Last Week of Life

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**Abstract**

**Context.** Burdensome symptoms present frequently in dementia at the end of life, but we know little about the symptom control provided, such as type and dosage of medication.

**Objectives.** To investigate symptom prevalence and prescribed treatment, explore associations with quality of life (QOL) in the last week of life, and examine symptom prevalence by cause of death of nursing home residents with dementia.

**Methods.** Within two weeks after death, physicians completed questionnaires about symptoms and treatment in the last week for 330 nursing home residents with dementia in the Dutch End of Life in Dementia study (2007–2011). We used linear regression to assess associations with QOL, measured by the Quality of Life in Late-Stage Dementia scale. Causes of death were abstracted from death certificates.

**Results.** Pain was the most common symptom (52%), followed by agitation (35%) and shortness of breath (35%). Pain and shortness of breath were mostly treated with opioids and agitation mainly with anxiolytics. At the day of death, 77% received opioids, with a median of 90 mg/24 hours (oral equivalents), and 21% received palliative sedation. Pain and agitation were associated with a lower QOL. Death from respiratory infection was associated with the largest symptom burden.

**Conclusion.** Symptoms are common in dementia at the end of life, despite the large majority of residents receiving opioids. Dosages may be suboptimal with regard to weighing of effects and side effects. Future research may employ observation on a day-to-day basis to better assess effectiveness of symptom control and possible side effects. *J Pain Symptom Manage* 2014;47:710–720. © 2014 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

**Key Words**

*Dementia, end-of-life care, palliative care, symptoms, symptom control, treatment, opioids, palliative sedation*

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## Introduction

Worldwide mortality rates of death with dementia have increased and so has awareness that patients with dementia need palliative care in the last phase of life. This has generated a considerable research interest in end-of-life care for patients with dementia.<sup>1</sup> A high symptom burden and inappropriate treatment at the end of life have been reported.<sup>1,2</sup> However, these reports lack detail on how specific symptoms are being treated, for example, which pharmacological treatment is being provided to relieve pain and shortness of breath at the end of life. Moreover, many reports are limited to nursing home residents with advanced dementia, whereas about half of patients may die before having reached this stage.<sup>3</sup>

Burdensome symptoms present frequently in the last phase of life, as Mitchell et al.<sup>2</sup> reported. Pain and shortness of breath are the most prevalent symptoms at some point in the process of dementia, with a peak when death approaches. The rates of these symptoms vary widely, from 12% to 76% for pain, and from 8% to 80% for shortness of breath.<sup>1</sup> Agitation is less frequently studied but was reported in 20%–54% of nursing home residents with advanced dementia at the end of life.<sup>2,4,5</sup>

We know little about types of medication administered to treat burdensome symptoms, and more specifically, the use and dosages of opioids and palliative sedation in residents with dementia at the end of life. Symptom control is an important factor in maintaining or improving quality of life (QOL) in end-of-life care.<sup>6–8</sup> So far, treatment has been mostly empirical or based on general palliative care guidelines, which are not tailored to dementia.<sup>1,2,9,10</sup>

In this study, we report on burdensome symptoms and on specific pharmacological and nonpharmacological treatments provided for the most important symptoms in the last week of life of nursing home residents in variable stages of dementia. We report on the use of opioids as important drugs to treat pain and shortness of breath and explore associations with QOL in the last week of life and symptom prevalence related to direct causes of death.

## Methods

### Data Collection

Data were collected as part of the Dutch End of Life in Dementia (DEOLD) study.<sup>3</sup> The primary aims of the study were to describe quality of dying and end-of-life care and assess associated factors. This observational study employed both prospective (on admission) and retrospective (after death) recruitment of residents. Data were collected between 2007 and 2011 in 34 long-term care facilities. The mean number of beds per facility was 82, ranging from 11 to 210 beds. Dutch nursing homes employ elderly care physicians, certified after three years of training,<sup>11</sup> who were responsible for data collection in nursing homes and affiliated residential homes. The residents had a physician's diagnosis of dementia of any stage and a family representative able to understand and write Dutch or English.

Prospectively, 372 residents were enrolled on admission; 218 (59%) died within the data collection period, resulting in 213 cases with complete physician after-death assessments. Retrospectively, 119 of 121 eligible residents were enrolled, resulting in 117 physician assessments. For analyses, we selected the 330 residents with complete physician after-death reports, involving 103 physicians. No longer than two weeks after death, written questionnaires were completed by physicians or, in part, by nurses under supervision of the physician. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Center in Amsterdam.

### Measurements

The diagnosis of dementia was based on international guidelines.<sup>12–15</sup> Type of dementia was assessed with a prestructured item comprising the categories Alzheimer's disease, vascular dementia, Lewy body/Parkinson's disease, and other. Advanced dementia (vs. less advanced dementia) was defined as a Global Deterioration Scale score of 7<sup>16</sup> and a Cognitive Performance Scale score of 5 or 6.<sup>17</sup>

The level of consciousness that most frequently occurred during the last week was scored as: awake and alert, awake, awake but drowsy looking, falling asleep, light sleep, or deep looking sleep. The physicians scored this

item in 53% of cases and nurses in 47%. They assessed frequency of pain and shortness of breath during the last week of life as: never, rarely ( $\leq 1$  day), sometimes (2–3 days), often (4–5 days), and almost daily (6–7 days). We dichotomized these assessments as never or rarely vs. sometimes, often, and almost daily.<sup>2</sup> Prevalence of agitation was described with the examples restlessness, resistance to care, calling out, or verbal and physical aggression and was assessed as present or not in the last week of life.

Treatment provided for pain, shortness of breath and agitation was assessed using pre-structured items. The categories for pain treatment were nonpharmacological (e.g., physiotherapy, occupational therapy, transcutaneous electrical neurostimulation, massage), paracetamol (acetaminophen), nonsteroidal anti-inflammatory drugs, oral opioid or parenteral opioid (each separately assessed as “as needed” only or scheduled dose), other, and no therapy. Treatment provided for shortness of breath was prestructured as: oxygen, opioids, aerosolized bronchodilators, diuretics, scopolamine, suctioning, intubation, other, and no therapy. Similarly, treatment of agitation comprised nonpharmacological treatments (e.g., 1:1 sitter, separate, involve family to participate in care), trunk or limb restraints, antipsychotic medication, anxiolytic or hypnotic medication, other, and no therapy.

Physicians reported the type and dosage of opioids that were given during the last 24 hours of life. They further reported the dosage pattern in the last three days, visualized graphically as no increase, gradual increase, or large increase on the last day. We converted all opioid dosages into oral morphine equivalents (OMEs) to allow for comparison of dosages between opioid types.<sup>18</sup> Physicians reported how many hours before death opioid administration started. Palliative sedation was defined as continuous deep sedation or sleep until death.<sup>19</sup> Physicians reported the type and dosage of drugs they provided for palliative sedation and how many hours before death palliative sedation was started.

QOL of residents in the last week of life was measured with the 11-item Quality of Life in Late-Stage Dementia (QUALID)<sup>20</sup> scale, which was translated and tested in an independent Dutch population.<sup>21</sup> The minimum and best summed score is 11 points; the maximum and

worst score is 55 points. The physicians completed QUALID in 51% of cases and nurses in 49%. Analogous to the Dutch death certificate, physicians registered the causes of death. For analyses, we used the three most common immediate causes of death (Part 1a of the Dutch death certificate). Cardiovascular disorders were defined as diseases of the circulatory system, and respiratory infection was defined as pneumonia, other lower respiratory tract infections, or upper respiratory infections.

### *Statistical Analyses*

We used t-tests for independent samples, Chi-square tests, and Gamma correlations to compare subgroups where appropriate, as well as Spearman’s correlation coefficients. We report the results for the total sample, and when different, separately for the prospectively and retrospectively recruited samples. To assess variability in prescribing at the physicians’ level, we estimated the intraclass correlation coefficient (ICC), using the formula:  $ICC = \text{variance in intercept} / (\text{variance in intercepts} + 3.29)$ .<sup>22</sup> Random intercepts were used at the physicians’ level for use of opioids and palliative sedation. Linear regression models were developed to evaluate associations with QOL, with the QUALID score as the dependent variable and symptoms of pain, shortness of breath, and agitation as the independent variables. We adjusted for simultaneously occurring symptoms, use of morphine during the last 24 hours, level of consciousness, and advanced vs. less advanced dementia.

In all analyses, fewer than 5% of values were missing, except for 6.0% missing values in treatment for agitation and 5.5% of QUALID scores, after having imputed with item means if a maximum four of 11 items were missing (3%). An additional 3.5% of cases was missing in the regression analyses because of missing independent variables. Analyses were performed with PASW 20.0 (SPSS, Inc., Chicago, IL).

## **Results**

### *Characteristics*

Most residents were female, and almost half (43%) had Alzheimer’s disease (Table 1). Almost all residents (99%) died in the facility, except for four residents (1%), who died in

Table 1  
Resident Characteristics

| Characteristics                                | (N = 330)  |
|--|------------|
| Female, %                                      | 67         |
| Age at death, mean (SD)                        | 85.2 (7.4) |
| Advanced dementia, %                           | 43         |
| Type of dementia, %                            |            |
| Alzheimer's disease                            | 43         |
| Vascular                                       | 24         |
| Alzheimer's and vascular                       | 19         |
| Lewy body/Parkinson's disease                  | 6          |
| Other types                                    | 9          |
| Residence before admission, %                  |            |
| Private home                                   | 36         |
| Residential home/other nursing home            | 40         |
| General/psychiatric hospital                   | 18         |
| Other  | 6          |
| Physicians' expectation of residents' death, % |            |
| Expected                                       | 64         |
| Expected, yet sooner than anticipated          | 22         |
| Neither expected nor unexpected                | 3          |
| Unexpected                                     | 11         |

a hospital. The populations recruited prospectively and retrospectively differed in two ways: advanced dementia, which was present in 38% and 53% of cases, respectively, and mean length of stay, 10.5 months (range 0.2–37.7) and 30.2 months (range 0.2–178.4), respectively.

### Symptoms

Fig. 1 shows the proportions of residents with symptoms of pain, shortness of breath and agitation in the last week of life. Pain was reported in 52% of the residents. Agitation and shortness of breath were both reported in 35% of the residents. Symptom prevalence did not differ between residents with advanced and less advanced dementia (pain: 55% vs. 50%,  $P = 0.34$ ; shortness of breath: 31% vs. 38%,  $P = 0.16$ ; agitation: 33% vs. 38%,  $P = 0.37$ , respectively). Presence of one of the symptoms was reported in 39% of residents, two symptoms in 32%, all three symptoms in 6%, and 23% were free from these symptoms. Pain and agitation without shortness of breath was present in 15% of residents.

### Treatment of Symptoms

Table 2 shows the treatments prescribed to address the specific symptoms in the last week of life. At least one type of opioid (oral or parenteral) was provided to 73% of residents in pain (not shown in table). Opioids were administered as monotherapy in 43% of cases, and 57% of residents received

combination therapy, mostly with paracetamol (acetaminophen) (87%). Nonpharmacological treatment was combined with analgesics in all but one resident who received nonpharmacological treatment exclusively.

Shortness of breath was treated with opioids in 71% of cases and in 58% with combination therapy, mostly (74%) with oxygen. Aerosolized bronchodilators and/or diuretics were prescribed to 31% (not shown in table).

For agitation, nonpharmacological therapy was provided to 62% of residents. A combination with pharmacological treatment was prescribed in 71% of these cases (48/68). Overall, at least one type of medication was provided to 79% of residents. Anxiolytic or hypnotic medications were the most frequently prescribed types (57%). The combination of anxiolytic or hypnotic medications with antipsychotic medication was prescribed to 30% of residents (not shown in table).

### Opioids

Overall (for any symptom), in the last 24 hours before death, 77% of residents received opioids; this differed between the prospectively (74%) and retrospectively (84%;  $P = 0.03$ ) recruited samples. The variance at the physicians' level of the proportion of prescribed opioids was 0.05 (SE 0.3), with an ICC of 0.02. Fig. 2 shows that the proportion of residents receiving opioids increased every day in the week before death, with a larger increase in the last two days before death.

The median duration of receiving opioids until death was 48 hours (25th percentile, 96 hours; 75th percentile, 19 hours before death). The median total opioid dosage was 90 mg (OME) in the last 24 hours (25th percentile, 52; 75th percentile, 150 OME). The most frequently used method of administration was by injection (88%) (Table 3).

The dosage pattern of opioids of the last three days was described as no increase in 51% of the residents, a gradual increase in 24%, and a large increase in the last day in 25% of cases. A pattern of larger increase (none, gradual, large) of opioid dosages correlated significantly with the dosage in the last 24 hours ( $r = +0.30$ ,  $P < 0.001$ ) and with the duration of using opioids until death ( $r = +0.20$ ,  $P = 0.002$ ).

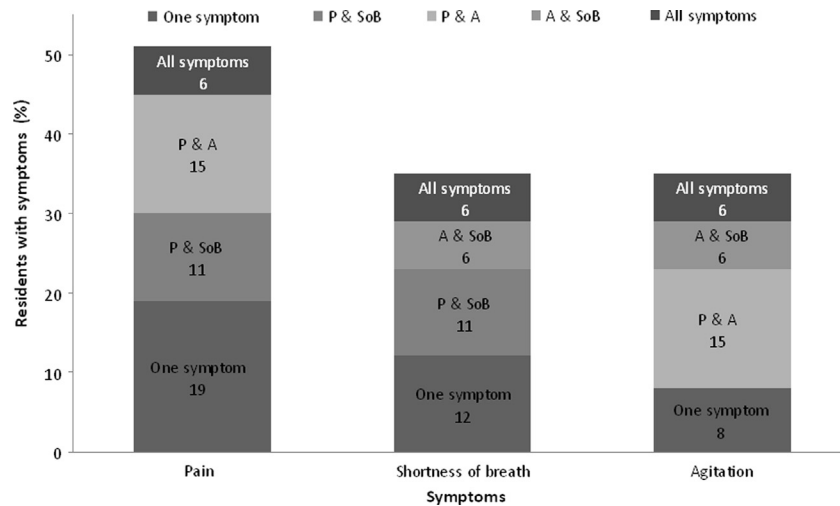


Fig. 1. Nursing home residents with symptoms of P, SoB, and A in the last week of life. P = pain; SoB = shortness of breath; A = agitation.

### Palliative Sedation

Of all residents, 21% received palliative sedation: 17% of the prospectively and 28% of the retrospectively recruited sample ( $P = 0.015$ ). The variance at the physicians' level of use of palliative sedation was 0.39 (SE 0.38), with an ICC of 0.11. The proportion of all residents who received palliative sedation increased strongly two days before death (Fig. 2). The median duration of receiving sedative medication until death was 24 hours (25th percentile, 48; 75th percentile, 12 hours before death). Midazolam was the most commonly prescribed drug (86%), with a median dosage of 30 mg/24 hours (Table 4). In 61% of residents, midazolam was prescribed as monotherapy, and in 33%, it was combined with morphine. Oxazepam, haloperidol, and levomepromazine were only provided as additional to midazolam (5%).

### Relationship of Symptoms With QOL

The mean QUALID score was 28.8 (SD 9.0). The mean QUALID score of residents did not differ significantly whether scored by a physician or a nurse (28.6 vs. 29.2;  $P = 0.61$ ). The median level of consciousness was "falling asleep" and did not differ whether assessed by a physician or a nurse ( $P = 0.86$ ).

QUALID correlated significantly with pain and with agitation but not with shortness of breath (Table 5). Residents with agitation had a 6.1 points higher (worse) mean

QUALID score than residents without agitation. Furthermore, the mean QUALID score for residents with pain was 4.0 points higher than residents with otherwise similar symptom levels but without pain.

### Causes of Death Related to Symptoms

The three most common direct causes of death were dehydration/cachexia (38%), cardiovascular disorders (19%), and respiratory infection (18%). Most respiratory infections (82%) concerned pneumonia, and 18% were other lower and upper respiratory infections. Fig. 3 shows the association of causes of death with symptoms. In residents who died from dehydration/cachexia, pain was the most frequently reported symptom. Residents who died with cardiovascular disorders frequently presented with pain and shortness of breath, and in residents who died with respiratory infection, shortness of breath was the most frequently occurring symptom. Respiratory infection related to the largest symptom burden.

### Discussion

To our knowledge, DEOLD is the first study that describes the last week of life of nursing home residents with variable stages of the dementia, focusing in detail on treatment provided for the most important burdensome symptoms, and on use of opioids and palliative

Table 2  
Treatment Provided for Symptoms in the Last Week of Life

| Symptom (n)               | Treatment <sup>a</sup>            | n   | % <sup>b</sup> | PRN Only, % |
|---------------------------|-----------------------------------|-----|----------------|-------------|
| Pain (169)                | Parenteral opioids                | 109 | 67             | 15          |
|                           | Paracetamol (acetaminophen)       | 97  | 60             | 7           |
|                           | NSAID                             | 28  | 17             | 1           |
|                           | Oral opioids                      | 22  | 13             | 2           |
|                           | Nonpharmacological                | 17  | 10             |             |
|                           | Other                             | 2   | 1              |             |
| Shortness of breath (115) | No therapy                        | 2   | 1              |             |
|                           | Opioids                           | 79  | 71             |             |
|                           | Oxygen                            | 48  | 43             |             |
|                           | Aerosolized bronchodilators       | 22  | 20             |             |
|                           | Diuretic                          | 17  | 15             |             |
|                           | Scopolamine                       | 14  | 13             |             |
|                           | Other                             | 6   | 5              |             |
|                           | Nonpharmacological <sup>c</sup>   | 5   | 4              |             |
| Agitation (116)           | No therapy                        | 5   | 4              |             |
|                           | Suctioning                        | 4   | 4              |             |
|                           | Nonpharmacological                | 68  | 62             |             |
|                           | Anxiolytic or hypnotic medication | 62  | 57             |             |
|                           | Antipsychotic medication          | 54  | 50             |             |
|                           | Other                             | 6   | 6              |             |
|                           | Trunk or limb restraints          | 5   | 5              |             |
|                           | Antidepressant drug <sup>c</sup>  | 5   | 5              |             |
|                           | No therapy                        | 3   | 3              |             |

PRN = as needed; NSAID = nonsteroidal anti-inflammatory drug.

<sup>a</sup>Receiving more than one treatment for a specific symptom is possible.

<sup>b</sup>Total percentages do not refer to total numbers with symptoms because of missing treatment (six cases for treatment of pain, two for type of opioid, three for shortness of breath, and seven for agitation, so refer to 163 cases in pain, 112 with shortness of breath, and 109 with agitation).  
<sup>c</sup>Not separately assessed but derived from the category "other."

sedation. The distressing symptoms pain (52%), shortness of breath (35%), and agitation (35%) were common. Pain and shortness of breath may even be underestimated in our study because we combined the frequencies "never" and "rarely" into "no presence of

symptoms" for reasons of clinical relevance. The prevalence of pain rises to 80% if pain "rarely" is included, and similarly, the prevalence of shortness of breath rises to 57%. Death from respiratory infections was associated with more burdensome symptoms than

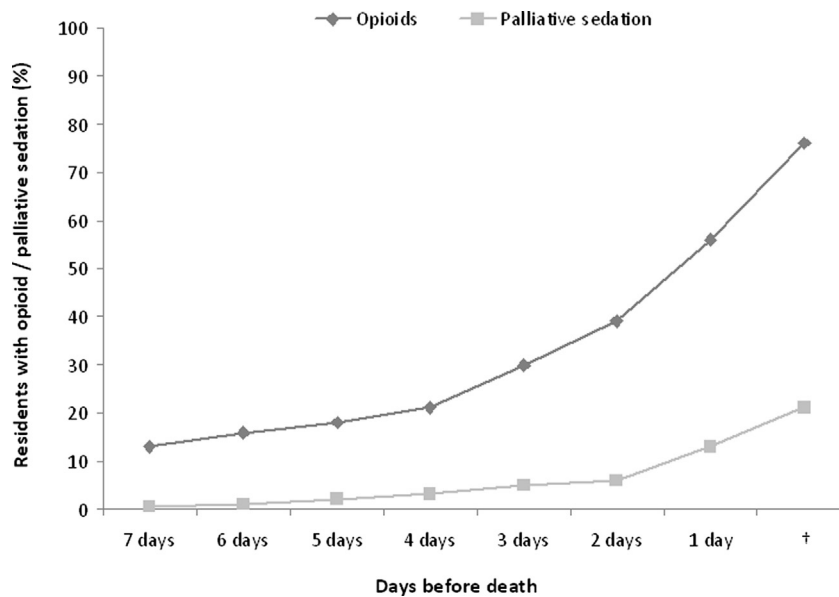


Fig. 2. Proportions of residents receiving opioids and palliative sedation over the days before death.



Table 3  
Opioid Dosage in the Last 24 Hours Before Death (N = 251)

| Opioid Type or Administration            | % <sup>a</sup> | OME, mg Over Last 24 Hours |                 |                 |
|--|----------------|----------------------------|-----------------|-----------------|
|  |                | Median                     | 25th Percentile | 75th Percentile |
| Fentanyl patch                           | 12             | 60                         | 30              | 60              |
| Pump                                     | 10             | 90                         | 60              | 180             |
| Subcutaneous bolus injection             | 88             | 90                         | 30              | 120             |
| Tramadol drops                           | 2              | 20                         | 7               | 28              |
| Controlled-release tablets               | 1              | 10                         | 10              | 10              |
| Oxycodone tablets                        | 0.4            | 40                         | 40              | 40              |
| Drink                                    | 0.4            | 5                          | 5               | 5               |
| Summed dosage ( $\geq 1$ type of opioid) |                | 90                         | 52              | 150             |

OME = oral morphine equivalents.

<sup>a</sup>Total percentages do not refer to total numbers with opioids because receiving more than one type of opioid was possible and there were seven missing cases of type of opioid.

death from cardiovascular disorders or dehydration/cachexia. Distressing symptoms were mostly treated pharmacologically. Furthermore, QOL in the last week was worse in residents with pain or agitation, despite the large majority of all residents (77%) receiving opioids and one-fifth (21%) receiving palliative sedation until death.

We found substantially more pain (52% vs. 25%) but only slightly more shortness of breath (35% vs. 32%) and agitation (35% vs. 33%) in comparison with the Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life (CASCADE) study.<sup>2</sup> These differences cannot be explained by dichotomizing the presence of symptoms but may be affected by a difference in time frame (symptoms on, at most, 1 day in the last week vs. maximum 4 days per month over the last 3 months, respectively).<sup>2,23</sup> Furthermore, symptom prevalence did not differ between those with advanced dementia (in which CASCADE was limited) and less advanced dementia.<sup>2</sup> The observed differences may be interpreted in three ways. First, the physicians in DEOLD may have reported more symptoms,

as they were asked directly and could rely on both the chart and their own memory, whereas in the CASCADE study, the data were mostly obtained from chart reviews by research assistants (for agitation, the nurse was interviewed as well).<sup>2</sup> In contrast to the U.S., the Dutch physicians are employed by the nursing homes, resulting in physicians having a first-hand understanding and intimate knowledge of the patient.<sup>24</sup> Second, generalizability for the nation differed: DEOLD facilities performed “average” on general quality indicators,<sup>3</sup> whereas CASCADE facilities performed better than average.<sup>2,23</sup> Third, symptom control may be suboptimal in Dutch long-term care facilities and of lower standards than in the U.S. This is supported by research findings that indicated more favorable U.S. family reports compared with Dutch family reports on comfort in the last week of life.<sup>25</sup>

The finding that death from respiratory infections was associated with more burdensome symptoms is in line with earlier research observations, where death with pneumonia compared with death after intake problems was associated with higher levels of

Table 4  
Palliative Sedation: Type of Medication and Dosages (N = 67)

| Sedation Medication   | % <sup>a</sup> | mg/24 Hours |                 |                 |
|-----------------------|----------------|-------------|-----------------|-----------------|
|                       |                | Median      | 25th Percentile | 75th Percentile |
| Midazolam             | 86             | 30          | 15              | 30              |
| Morphine <sup>b</sup> | 39             | 90          | 90              | 180             |
| Diazepam              | 3              | 15          | 10              | 10              |
| Haloperidol           | 3              | 3           | 1               | 1               |
| Oxazepam              | 2              | 10          | 10              | 10              |
| Levomepromazine       | 2              | 50          | 50              | 50              |

<sup>a</sup>Total percentages do not refer to total numbers with palliative sedation because of two missing cases of type of medication.

<sup>b</sup>mg/24 hours in oral morphine equivalents.

Table 5  
Association of Symptoms With Quality of Life  
(QUALID<sup>a</sup> Score)

| Symptom               | Coefficient <sup>b</sup> | 95% CI      |
|-----------------------|--------------------------|-------------|
| Pain                  |                          |             |
| Unadjusted            | 5.5                      | 3.5 to 7.5  |
| Adjusted <sup>c</sup> | 4.0                      | 2.1 to 6.0  |
| Shortness of breath   |                          |             |
| Unadjusted            | 0.1                      | -2.1 to 2.3 |
| Adjusted <sup>c</sup> | 0.7                      | -1.2 to 2.6 |
| Agitation             |                          |             |
| Unadjusted            | 6.6                      | 4.6 to 8.6  |
| Adjusted <sup>c</sup> | 6.1                      | 4.2 to 8.1  |

QUALID = Quality of Life in Late-Stage Dementia.

<sup>a</sup>The minimum and best score is 11 points; the maximum and worst score is 55 points.

<sup>b</sup>Unstandardized regression coefficients from linear regression models.

<sup>c</sup>Adjusted for advanced dementia, use of morphine during the last 24 hours, level of consciousness and pain, shortness of breath, or agitation. The adjustment for specific symptoms differs according to which symptom is analyzed (e.g., analysis of pain was adjusted for shortness of breath and agitation).

discomfort.<sup>26,27</sup> In another Dutch study, dehydration/cachexia was a common cause of death as well.<sup>28</sup> Dutch elderly care physicians rarely provide tube feeding in case of intake problems,<sup>29</sup> and this implies that death from dehydration/cachexia is an acceptable scenario.

We found a significant association between pain and agitation, and lower QOL measured by the QUALID scale. Santangelo,<sup>30</sup> in dementia patients more generally, also found lower QOL in patients with pain. These findings are in contrast with the findings from Cordner et al.<sup>6</sup> who used the Alzheimer

Disease-Related Quality of Life scale and found that residents with pain identified at the end of life had a better QOL. This might be explained by more adequate treatment, although the percentage of residents treated with medication was similar.

Opioids were the most frequently provided medication for pain and were prescribed as monotherapy in almost half of the cases. This is inconsistent with pain guideline recommendations<sup>18</sup> of prescribing opioids supplementary to nonsteroidal anti-inflammatory drugs and paracetamol (acetaminophen). Yet in the terminal phase, reducing and avoiding burdening interventions (i.e., oral and rectal medication) is important, and monotherapy with parenteral opioids may be preferred.

Almost one-sixth (15%) of residents experienced both pain and agitation. There may be underuse of effective pain medication in cases of agitation because unrecognized pain may cause agitation<sup>31-33</sup> and, therefore, possibly also overuse of anxiolytics, which were used mostly for agitation in line with Dutch guidelines for behavior problems.<sup>34</sup> However, physicians also should be aware of the risk of delirium (with agitation as an important symptom) because of the accumulation of opioids in the last phase of life (caused by renal dysfunction). In these cases, the dosage of opioids should be decreased in the dying phase, as side effects may involve an increased symptom burden.

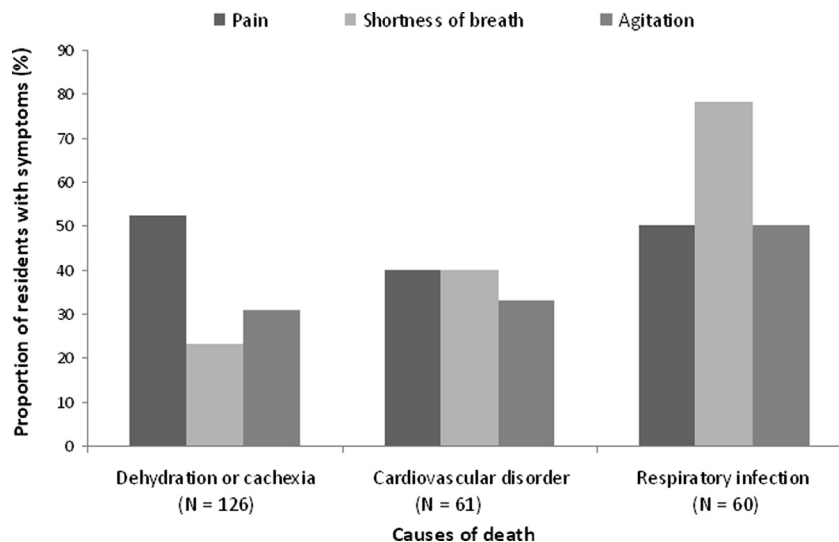


Fig. 3. Proportion of symptoms in the last week of life related to the three main immediate causes of death.



We found no association between shortness of breath and QOL measured by the QUALID scale. Caprio et al.<sup>7</sup> found a positive association between dyspnea and quality of dying as evaluated by families with a scale that also included psychosocial aspects. They explained this by shortness of breath attracting more caregiver attention in these patients than other symptoms.<sup>7</sup> It may be viewed as a more alarming symptom and, therefore, followed by more prompt treatment, such as parenteral opioids, which is in line with general palliative care guidelines.<sup>18</sup> This might result in faster relief of shortness of breath and limited negative effects on QOL measured over the full last week, as was done in this study.

We observed a gradual increase in use of opioids, with a median duration of 48 hours until death and a median dosage of 90 OME in the last 24 hours. The course of dementia and the nearing of death are less predictable than, for example, in patients with cancer.<sup>35</sup> This may result in this specific pattern of increase in use of opioids in the last few days of life. Alternatively, an increased symptom burden may present later, that is, closer to death, than in cancer.

Our results showed a substantially higher frequency of palliative sedation (21%) in comparison with European studies concerning all deaths nationwide (2.5%–8.5%)<sup>36</sup> but lower compared with palliative care settings (15% to >60%).<sup>37–42</sup> In 2005, a national guideline on palliative sedation was released in The Netherlands, which recommended that to warrant sedation at the end of life, the patient's condition should be irreversible, with death expected within at most one to two weeks.<sup>10,19,43</sup> ICC we found in this study (0.11) reflects substantial clustering of using palliative sedation within physician practices. This may raise questions as to whether the physicians applied the definitions and guidance consistently.

Different percentages for using opioids and palliative sedation between prospectively and retrospectively recruited samples were found, which were not explained by differences in proportions of advanced dementia. The retrospective data were collected in only six nursing homes with two physician teams, and prescribing practices may have differed between physician teams.

### *Limitations*

The present study has some limitations that warrant comment. First, this study is based on cross-sectional analyses; consequently, we cannot interpret relationships between symptoms, their treatment, QOL, and direct causes of death as causal. Accordingly, we cannot draw conclusions about the most effective treatment for symptom relief. Second, our findings are limited to long-term care settings. In The Netherlands, up to 92% of patients with dementia may die in these settings,<sup>44</sup> so our findings are, to a large degree, representative of dying with dementia in The Netherlands.

### *Conclusion and Recommendations*

Current symptom control may be improved in Dutch long-term care facilities. Our observations call for further research into interventions targeted at pain and agitation in this population. Concerning pain and shortness of breath, which are common despite frequent treatment with opioids, the dosages of opioids may be suboptimal with regard to weighing of effects and side effects. Future research may employ observation on a day-to-day basis to better address effectiveness of symptom control and possible side effects at the end of life, employing observational or ethically acceptable experimental designs. This will contribute to the development of practice guidelines for this specific patient population in palliative care.

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