The Practice of Continuous Palliative Sedation in Elderly Patients: A Nationwide Explorative Study Among Dutch Nursing Home Physicians

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OBJECTIVES: To study the practice of continuous palliative sedation (CPS) by Dutch nursing home physicians in 2007.

DESIGN: A structured retrospective questionnaire.

SETTING: Nationwide nursing home physician study in the Netherlands.

PARTICIPANTS: One thousand two hundred fifty-four nursing home physicians received a questionnaire concerning their last case of CPS in 2007; 54% (n = 675) responded.

MEASUREMENTS: Characteristics of CPS and requests for euthanasia were measured.

RESULTS: Three hundred sixteen patients were described. The majority had cancer or dementia. The most-reported refractory symptoms were pain (52%), anxiety (44%), exhaustion (44%), dyspnea (40%), delirium (24%), loss of dignity (18%), and existential distress (16%). In 98% of cases, CPS was aimed at symptom relief. Of patients with cancer, 17% had previously requested euthanasia. The mean starting dose of midazolam was 31 mg every 24 hours (range 0–240 mg/24 h), and the mean end dose was 48 mg every 24 hours (range 0–480 mg/24 h).

CONCLUSION: In addition to physical symptoms, anxiety, exhaustion, loss of dignity, and existential distress are often mentioned as refractory symptoms in the decision to start CPS by nursing home physicians. Furthermore, close to one in five patients with cancer had made a previous request for euthanasia. The dosage range of midazolam in this study fits the recommendations of the Dutch national guideline on palliative sedation, although international studies show smaller dosage ranges. Finally, prospective research about the acceptability and assessment of non-physical symptoms as indications for CPS is recommended.


Key words: palliative sedation; elderly; nursing home; cancer; dementia

Since the 1990s, there has been a growing interest in palliative care in the Netherlands. Although historically administered in people with cancer, palliative care is increasingly administered to patients without cancer too. Despite improvements in palliative care, some symptoms remain hard to treat or relieve. If one or more symptoms in a patient who is dying cause unbearable suffering, and conventional modes of treatment are not effective or fast acting enough (so-called refractory symptoms), an indication arises to administer palliative sedation.

The third national Dutch study on end-of-life decisions was the first to report on the practice of what was then referred to as terminal sedation in the Netherlands.1 In response to this study, the Dutch government stressed the need for a national guideline on palliative sedation.2 In 2005, the Royal Dutch Medical Association (RDMA) issued a national guideline on palliative sedation.3,4 Despite this guideline, the practice of palliative sedation remained a controversial subject. Furthermore, a Dutch study found that continuous deep sedation was being used increasingly more often, whereas the use of euthanasia was decreasing.5 This suggested that palliative sedation was possibly being administered as an alternative to euthanasia.

Although the RDMA guideline gives a comprehensive framework for clinical decision-making, the recommendations are mainly expert-based. The methodological, practical, and ethical challenges involved limit research on palliative sedation. In particular, research on palliative sedation in a population of frail and elderly patients has
proved to be problematic for nursing home physicians. The available studies indicate that the refractory symptoms are mostly anxiety, pain, and dyspnea. The drugs most often administered are benzodiazepines, and in most cases the duration of continuous deep sedation is 7 days or less, no life-shortening effect is reported, and artificial hydration is withheld.\(^5\)\(^-\)\(^\text{13}\) In 2005, it was estimated that nursing home physicians used continuous deep sedation in conjunction with end-of-life decisions in 5.9% of all deaths.\(^7\) However, all but one of these studies originated from before the introduction of the RDMA guideline, and data were obtained mostly from limited samples. Furthermore, these studies often neglected to consider the practices of nursing home physicians (characterized by a large percentage of elderly patients without cancer) separately from other care settings such as hospitals and home care (with mainly patients with cancer).\(^14\) Nursing home physicians find it difficult to define patients as terminally ill or to predict their life expectancy, and the pattern of symptom prevalence is different from that of patients with cancer.\(^14\) It was therefore hypothesized that in patients with cancer, the refractory symptoms for continuous palliative sedation (CPS) would differ from those of patients without cancer. Moreover, the difficulty of predicting life expectancy of people without cancer could complicate the administration of CPS, because a precondition for its use within the RDMA guideline is that death will ensue within 1 to 2 weeks. More insights into this specific group of patients shall contribute to the further development of guidelines on palliative sedation and could provide more-targeted palliative care. There is an international demand for more research on monitoring national trends and patterns in end-of-life care, such as (continuous) palliative sedation, including the administration of artificial nutrition and hydration, the drugs and dosages administered, and the interval between the administration of sedating drugs and death.\(^15\),\(^16\)

The practice of CPS by Dutch nursing home physicians was therefore investigated in a nationwide study. Special attention was paid to differences in the administration of CPS to the subgroups of patients with cancer and dementia.

**METHODS**

**Respondents**

All registered members of the Dutch Association of Nursing Home Physicians were eligible for the study (n = 1,441). Because of a parallel ongoing study on palliative sedation in the Amsterdam and Rotterdam regions, 187 of the 292 members in this region were excluded. A structured retrospective questionnaire was sent to the remaining 1,254 nursing home physicians in February 2008. A return envelope was sent with the questionnaire, and full confidentiality was assured. After 3 weeks, all physicians received a reminder to return the questionnaire so as to maximize the response rate. Data collection ended in May 2008.

**Questionnaire**

The questionnaire was a revised version of a previously reported questionnaire.\(^9\) The original questionnaire was adapted to nursing home patients and piloted by 20 nursing home physicians, which resulted in some minor modifications. In the questionnaire, palliative sedation and refractory symptoms were defined according to the RDMA national guideline.\(^3\) Palliative sedation was defined as “deliberately lowering a patient’s level of consciousness in the final stage of life,” and a symptom was considered refractory if “none of the conventional modes of treatment were effective or fast-acting enough, and/or if these modes of treatment were accompanied by unacceptable side-effects.” It was clearly stated in the questionnaire that the study explicitly focused on CPS, defined as “sedation continued until death.”

The questionnaire consisted of 38 closed-ended questions and six open questions and was divided into two parts. The first part included questions about the respondent’s age, sex, years of clinical experience with end-of-life care (<5, 5–15, ≥16), whether they had at some time administered CPS (yes/no), and whether they were aware of the RDMA guideline on palliative sedation (yes/no). In addition, their knowledge of the contents of the guideline was assessed on a 5-point scale (poor to excellent). Each respondent was also asked about the number of patients who died in 2007 (0, 1–5, 6–10, 11–20, 21–50, ≥50) and the exact number of occasions on which CPS was administered in 2007. The second part addressed the practice of CPS in the most-recent case in 2007, with an explicit request to retrieve the information from the patient’s medical file. This part included questions about the patient’s age, sex, and primary disease (dementia, cancer, cardiovascular disease, pulmonary disease, nervous system disease, other diagnosis). When respondents filled in more than one primary diagnosis, it was registered as “multiple.” In the questionnaire, no distinction was made between informed consent (yes/no) from the patient or the patient’s legal representative. The indicating symptoms for CPS were pain, dyspnea, delirium, anxiety, vomiting, nausea, exhaustion, existential distress, loss of dignity, and other (more than one answer possible). The aim of CPS was defined as symptom relief, life shortening, or other (more than one answer possible). The respondents were asked whether a previous request for euthanasia had been reported. The physician judged the life expectancy before the start of CPS (1–4, 5–7, 8–14, ≥15 days), and the duration of the CPS was defined in the exact number of days. In addition, whether the respondent expected a life-shortening effect of CPS (yes/no), whether CPS provided symptom relief according to the respondents (4-point scale: no, hardly, partially, completely), and what the level of consciousness of the patient was at the time adequate symptom relief was attained from CPS (6-point scale: alert and oriented, drowsy, eyes closed follow directives, eyes closed partially responding to physical stimuli, eyes closed not responding to physical stimuli, disturbed brainstem function) was asked about. Respondents were also asked what the patient’s intake was before the start of CPS (0, 1–500, 501–1,500, ≥1,501 mL) and whether they withheld, withdrew, started, or continued artificial hydration and feeding. To determine which medication was used to facilitate the start and continuation of CPS, the respondents were asked to fill in a maximum of three drugs, in order of rank, stating the starting and end dose (mg/24 h) and the route of administration.

**Analysis**

Descriptive analysis was performed using proportions for categorical variables and means ± standard deviations for any continuous variables.
continuous variables, using SPSS version 14.0.2 (SPSS, Inc., Chicago, IL). The goodness-of-fit test was used to determine the representativeness of the registered nursing home physicians in the study of the total population of registered nursing home physicians. The duration of CPS was categorized, in categories similar to those used in the question to assess life expectancy before the start of CPS, for the analyses. To study the differences in the administration of CPS to patients with cancer and dementia, Pearson chi-square and Fisher exact tests were used. All P-values were two sided, and an alpha of .05 was considered to indicate statistical significance.

RESULTS

Respondents
Six hundred seventy-five of the 1,254 physicians returned the questionnaire (54% response rate) (Figure 1). In 2007, 28 respondents were not actively practicing and were excluded from the analysis, resulting in a study population of 647 respondents. For sex (P = .10; goodness-of-fit test) and age (P = .87; goodness of fit test), the respondents were representative of the total population of registered nursing home physicians.

The majority of the respondents were women (65%). Mean age was 45 (range 25–65). Eighty percent of the nursing home physicians had more than 5 years of experience with palliative care, and 72% had at some time administered CPS. Almost all of them knew about the RDMA guideline on palliative sedation (98%). Fifty-two percent rated their level of knowledge about the contents of the guideline as good to excellent, and 12% rated their knowledge as moderate to poor (Table 1).

Forty-nine percent (n = 316) of the respondents indicated that they had used CPS in 2007; 307 of these provided information about the exact number of occasions on which CPS was administered in 2007 (9 missing); 60% (n = 185) administered CPS once or twice, and 22% (n = 69) administered CPS three to five times. One nursing home physician indicated that she had administered CPS to 30 patients in 2007. According to the data, a maximum of 15% of all patients who died in 2007 in the Netherlands and were treated by nursing home physicians received CPS.

Patients
Three hundred sixteen cases were described, mostly women (57%) of high age. The majority of the patients had cancer or dementia (Table 2). In all but one case, patient informed consent was obtained from the patient or the relative who was the patient’s legal representative.

Characteristics of CPS
Eighty-two percent of patients were treated with CPS for two or more refractory symptoms, mostly pain, anxiety, exhaustion, or dyspnea (Table 3). If there was only one refractory symptom (n = 55), it was usually dyspnea (n = 16), pain (n = 12), or exhaustion (n = 10). In one case, existential distress was reported as the only refractory symptom.

In 98% of cases, symptom relief was the aim of CPS. In 2% of cases, the co-intention was life shortening, whereas 1% (n = 2) had shortening of life as the sole intention. In 12% of cases, a previous request for euthanasia had been reported.

In 94% of the patients, life expectancy was 7 days or less, and the duration of CPS was 7 days or less in 97% of

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>25–39</td>
<td>189 (29)</td>
</tr>
<tr>
<td>40–54</td>
<td>339 (52)</td>
</tr>
<tr>
<td>55–65</td>
<td>118 (18)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>419 (65)</td>
</tr>
<tr>
<td>Male</td>
<td>228 (35)</td>
</tr>
<tr>
<td><strong>Experience, years</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>129 (20)</td>
</tr>
<tr>
<td>5–15</td>
<td>269 (42)</td>
</tr>
<tr>
<td>&gt;15</td>
<td>247 (38)</td>
</tr>
<tr>
<td><strong>Ever administered CPS</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>184 (29)</td>
</tr>
<tr>
<td>Yes</td>
<td>461 (72)</td>
</tr>
<tr>
<td><strong>Aware of guideline on palliative sedation</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 (2)</td>
</tr>
<tr>
<td>Yes</td>
<td>634 (98)</td>
</tr>
<tr>
<td><strong>Knowledge of contents of guideline</strong></td>
<td></td>
</tr>
<tr>
<td>Good to excellent</td>
<td>334 (52)</td>
</tr>
<tr>
<td>Reasonable</td>
<td>236 (37)</td>
</tr>
<tr>
<td>Moderate to poor</td>
<td>74 (12)</td>
</tr>
</tbody>
</table>

Data were missing for one physician on age and awareness of guideline on palliative sedation, for two physicians on experience and ever administered continuous palliative sedation (CPS), and for three physicians on knowledge of contents of guideline.
the cases. The mean duration of the CPS was 2.8 days (median 2.0, range 0–21 days). Twenty-six percent of all physicians estimated that CPS had shortened life.

According to the respondents, CPS provided complete symptom relief in 89% of the cases. At the time adequate symptom relief by CPS was attained, 47% of the patients had a level of consciousness varying from alert to responding to physical stimuli. Fifty-one percent of the patients were not responsive to physical stimuli, and 2% had a very deep level of unconsciousness, with disturbed brainstem function.

Hydration and Nutrition

Eighty-two percent of the patients had an intake of no more than 500 mL the day before CPS started, and 17% had no intake (Table 4). Three patients who received artificial hydration and nutrition had an intake of more than 1,500 mL a day.

In 98% of cases, no artificial hydration was administered during CPS. In the group of patients who received artificial hydration before the start of CPS (n = 20), administration was discontinued in 15 and continued in five. Artificial hydration was started in one patient.

Drugs

To facilitate the start and continuation of CPS, 91% of the patients were administered midazolam, 64% received morphine, and 18% were prescribed haloperidol (Table 5).

In 65% of cases, a combination of a benzodiazepine (midazolam, diazepam, clorazepate dipotassium, clonazepam) and an opioid (morphine, fentanyl) was prescribed, 30% were administered a benzodiazepine without an opioid, and 3% were prescribed an opioid without a benzodiazepine.

With the exception of two patients, midazolam was administered subcutaneously. The mean starting dose of midazolam was 31 mg every 24 hours (median 30 mg/24 h), the mean end dose was 48 mg every 24 hours (median
Table 4. Nutrition and Hydration (N = 316 Patients)

<table>
<thead>
<tr>
<th>Intake before the start of CPS, mL</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>53 (17)</td>
</tr>
<tr>
<td>1–500</td>
<td>201 (65)</td>
</tr>
<tr>
<td>501–1,500</td>
<td>52 (17)</td>
</tr>
<tr>
<td>&gt;1,500</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Artificial hydration</td>
<td></td>
</tr>
<tr>
<td>Discontinued</td>
<td>15 (5)</td>
</tr>
<tr>
<td>Continued</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Started</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Not started</td>
<td>293 (93)</td>
</tr>
<tr>
<td>Artificial feeding</td>
<td></td>
</tr>
<tr>
<td>Discontinued</td>
<td>12 (4)</td>
</tr>
<tr>
<td>Continued</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Started</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Not started</td>
<td>293 (94)</td>
</tr>
</tbody>
</table>

Data were missing for two patients on artificial hydration, four patients on artificial feeding, and six patients on intake before the start of continuous palliative sedation (CPS).

30 mg/24h). The dose range of midazolam at the start of sedation was 0 to 240 mg every 24 hours, and the dose range at the time of death was 0 to 480 mg every 24 hours. Two patients received a benzodiazepine other than midazolam at the start of sedation, which was changed to midazolam later on. In four patients, the administration of midazolam was ceased 24 hours or more before death. For morphine, which was given subcutaneously in all cases, the mean starting dose was 47 mg every 24 hours (median 30 mg/24 h), and the mean end dose was 65 mg every 24 hours (median 60 mg/24 h).

Primary Disease

Comparing the administration of CPS to patients with cancer and dementia, there were only statistically significant differences between a previous request for euthanasia (cancer 17%, dementia 0%; \( P < .001 \), Fisher exact test), a life expectancy of 4 days or less before the start of the CPS (cancer 64%, dementia 78%; \( P = .03 \), Pearson chi-square test), and an absence of intake before the start of the CPS (cancer 11%, dementia 33%; \( P = .001 \), Pearson chi-square test). No statistically significant differences were found between patients with cancer or dementia in distribution of refractory symptoms, level of consciousness at the time adequate symptom relief was attained, or duration and effect of CPS (data not shown).

DISCUSSION

To the authors’ knowledge, this is the first nationwide Dutch study to provide insight into the practice of CPS by nursing home physicians in a population of frail older adults with a high percentage of patients suffering from terminal cancer and dementia. The vast majority of Dutch nursing home physicians have experience with administering CPS at some time. In 2007, most patients were elderly women and had two or more refractory symptoms. The most frequent of these were pain, anxiety, exhaustion, and dyspnea. In almost all cases, symptom relief was the aim, and in 12% of cases, a previous request for euthanasia had been reported. Life expectancy and duration of the CPS were 7 days or less in almost all patients. In general, nursing home physicians judged CPS to be effective in relieving refractory symptoms. More than half of the patients were unresponsive to physical stimuli at the time adequate symptom relief was attained and must be qualified as being in deep and continuous sedation. For 82% of patients, intake was less than 300 mL before the start of CPS, and in most cases artificial hydration was withheld during CPS. Midazolam was the most frequently used drug. The administration of CPS to patients with cancer and dementia differed significantly with respect to the following factors: previously made request for euthanasia, life expectancy of 4 days or less, and absence of intake before the start of CPS.

Care should be taken when comparing the figures of this study with the results of previous international studies. First, this study did not include temporary or intermittent palliative sedation, and the questionnaire used the term “continuous palliative sedation.” Most studies performed over the past decade have focused on continuous deep sedation, which covers just 53% of the cases in the current study. Second, the Netherlands is the only country where nursing home medicine exists as an independent medical specialism with its own specific training program. In other countries, general practitioners or other physicians take care of these patients. Within these constraints, some of the results of the current study will be compared here with those of previous studies.

The distribution of symptoms considered refractory in this study is in line with previous studies although the current study found a higher frequency of loss of dignity.

Table 5. Six Most-Frequently Used Drugs to Facilitate the Start and Continuation of Continuous Palliative Sedation

<table>
<thead>
<tr>
<th>Drug</th>
<th>n (%)</th>
<th>mg/24/h, Mean ± Standard Deviation (Range)</th>
<th>Administration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>289 (91)</td>
<td>30.6 ± 26.1 (0–240)</td>
<td>47.7 ± 56.8 (0–480)</td>
</tr>
<tr>
<td>Morphine</td>
<td>201 (64)</td>
<td>47.5 ± 49.7 (0–600)</td>
<td>65.5 ± 64.7 (5–600)</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>57 (18)</td>
<td>6.3 ± 5.6 (1–30)</td>
<td>6.0 ± 6.6 (0–30)</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>22 (7)</td>
<td>35.3 ± 36.8 (0–150)</td>
<td>50.8 ± 32.3 (8–150)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>17 (5)</td>
<td>1.48 ± 0.98 (0.29–3.60)</td>
<td>1.58 ± 0.95 (0.29–3.60)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>13 (4)</td>
<td>25.4 ± 13.9 (10–60)</td>
<td>24.0 ± 20.1 (0–60)</td>
</tr>
</tbody>
</table>

Data were missing for nine patients.
(18% vs 6.5%) and exhaustion (44% vs 13%) and a lower frequency of anxiety (44% vs 65.2%). The RDMA guideline explicitly mentions exhaustion as a contributor to refractory suffering because its presence may exacerbate suffering, and it is a determining factor of the patient’s endurance. This may lead to the conclusion that palliative sedation is the only reasonable option left. Furthermore, little is known about the pathogenesis of exhaustion, so conventional modes of treatment may be less successful than treatments for other symptoms at the end of life.

The presence of loss of dignity and existential distress is consistent with previous research, although some authors have questioned whether viewing existential suffering as a symptom or a medical state is justified, but given the involvement of physicians with dying patients, existential distress cannot be separated from the domain of medicine and can therefore be a part of the indication for palliative sedation. The RDMA guideline does not define this state but instead describes or characterizes it in the text: “In such cases, this existential suffering cannot be alleviated by communication or spiritual support. These patients have often been through a great deal of distress, are often extremely ill and weak, close to death, and have a range of physical complaints, some of them often severe. The patient’s body has reached its end, literally and figuratively, and everything that needed saying has been said and there is the feeling that one’s existence is empty or meaningless (existential suffering).”

In a retrospective study, it is not possible to determine the precise reason for the patient’s existential suffering. Despite the vagueness of the term, existential suffering often proves to be an important reason for discussing end-of-life decisions. A prospective study to determine exactly what happens in these cases would be worthwhile.

In 2004, it was reported that 59% of all nursing home physicians performed continuous deep palliative sedation with the (co)intention of hastening death. The current study found a considerably lower percentage (2%). In 12% of all cases, and 17% of patients with cancer, a previous request for euthanasia had been reported. These percentages are higher than found in previous research in nursing home populations, with percentages of 6.5% and 9% found. This might indicate that CPS is used as an alternative to euthanasia in some cases. Why a euthanasia request was not granted in such cases needs to be investigated.

Whether artificial nutrition and hydration should be forgone in CPS is a subject of ongoing debate. In other European countries, continuous deep sedation in nursing homes and residential homes is frequently administered with artificial nutrition and hydration. The current study shows that nursing home physicians in the Netherlands mostly do not administer artificial fluids. The minimal intake before sedation in the vast majority of the study population could be a contributing factor in this decision by nursing home physicians. It could be argued that artificial hydration is medically futile, hampers the natural dying process, and may result in additional suffering, whereas withholding artificial hydration will not influence survival.

The general consensus is that midazolam is the drug of choice for inducing CPS because of its fast onset of action, the ease of titration, and the option of rapid reversibility. Morphine is not considered to be a suitable drug for inducing CPS. The current study revealed a higher frequency of a benzodiazepines being used to induce and maintain CPS than previous nursing home physician studies (95% vs 75–89%) and found a lower frequency of an opioid without a benzodiazepine being used for this purpose (3% vs 10–26%). This shift is probably because of the publication of the RDMA guideline, as well as media attention to the issue and the ongoing debate among physicians. Despite these changes in practice, it was found that nursing home physicians increased the mean dose of morphine during CPS. Morphine is usually continued as a symptom-directed treatment, but benzodiazepines are administered to induce sedation.

Almost all other studies show smaller dose ranges, with a lower maximum dose of midazolam than in the current study, although the mean dose of midazolam used in the current study was lower than or similar to that in most other studies. Furthermore, only nine patients received an end dose of midazolam greater than 120 mg every 24 hours, and the dose range was consistent with the recommendations of the RDMA guideline. Moreover, continuous deep palliative sedation was administered in only 53% of cases, suggesting that the doses used were proportional to patients’ needs, although little is known about the pharmacokinetics of midazolam in a frail, elderly population. Further research is needed to support the medication recommendations of the RDMA guideline.

Despite the specific pathophysiology and symptomatology of each primary underlying disease, no statistically significant differences were found between the distribution of refractory symptoms in patients with cancer and dementia. In addition, no statistically significant differences were found in outcomes of CPS, such as symptom relief and duration.

There was a statistically shorter life expectancy in terminally ill patients with dementia than in patients with cancer before the start of CPS. The fact that more patients with dementia had no intake before the start of CPS might have helped the physician to determine that death would ensue within 1 or 2 weeks. In addition, it suggests that whether nutrition or hydration will be withheld during CPS is discussed more frequently for patients with cancer than for those with dementia.

This is the first nationwide study of the practice of CPS by Dutch nursing home physicians. Nevertheless, these findings should be interpreted within the constraints of a questionnaire study. First, there were limitations with respect to the study population. Although the respondents were representative regarding sex and age of the total population of registered nursing home physicians, a portion of nursing home physicians in the Amsterdam and Rotterdam regions were excluded, and the response rate was only 54%. Possible differences between respondents and nonrespondents, as well as the excluded physicians in the Amsterdam and Rotterdam regions, with respect to the practice of CPS cannot be excluded. Second, although clear definitions of palliative sedation and refractory symptoms in the questionnaire were used, items such as loss of dignity and existential distress were not defined. Also primary disease was not defined using, for example, the International Classification of Diseases. Third, refractoriness of suffering was not determined by investigating the etiology of each type of
suffering, what types of treatment had been attempted before sedation, and how symptoms were recognized, especially in patients with dementia. Fourth, respondents may have had difficulty recalling patient characteristics, although recall bias was probably limited because of the instruction to use data extracted from the medical file.

This study shows that, in addition to physical symptoms, nursing home physicians often mention anxiety, exhaustion, loss of dignity, and existential distress as refractory symptoms in the decision to start CPS. Furthermore, close to one in five patients with cancer had made a previous request for euthanasia. The dosage range of midazolam in this study fits the recommendations of the Dutch national guideline on palliative sedation, although international studies show smaller dosage ranges. Further prospective research about the acceptability and assessment of nonphysical symptoms as indications for CPS and the optimal medication scheme for CPS in frail elderly patients is recommended. Finally, adequate palliative care with careful assessment of potential reversible factors and nonseating alternatives should be the keystone of treatment before starting palliative sedation.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions: van Deijck had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: van Deijck, Krijnsen, Hasselaar, Verhagen, Vissers, and Koopmans. Acquisition of data: van Deijck and Krijnsen. Analysis and interpretation of data: van Deijck, Krijnsen, Hasselaar, Verhagen, Vissers, and Koopmans. Preparation of manuscript: van Deijck, Krijnsen and Koopmans. Critical revision of manuscript for important intellectual content and final approval: van Deijck, Krijnsen, Hasselaar, Verhagen, Vissers, and Koopmans. Statistical analysis: van Deijck, Krijnsen, Hasselaar, and Koopmans.

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