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Original Article

The Practice of Continuous Deep Sedation Until Death in Flanders (Belgium), The Netherlands, and the U.K.: A Comparative Study

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Abstract

Context. Existing empirical evidence shows that continuous deep sedation until death is given in about 15% of all deaths in Flanders, Belgium (BE), 8% in The Netherlands (NL), and 17% in the U.K.

Objectives. This study compares characteristics of continuous deep sedation to explain these varying frequencies.

Methods. In Flanders, BE (2007) and NL (2005), death certificate studies were conducted. Questionnaires about continuous deep sedation and other decisions were sent to the certifying physicians of each death from a stratified sample (Flanders, BE: $n = 6927$; NL: $n = 6860$). In the U.K. in 2007–2008, questionnaires were sent to 8857 randomly sampled physicians asking them about the last death attended.

Results. The total number of deaths studied was 11,704 of which 1517 involved continuous deep sedation. In Dutch hospitals, continuous deep sedation was significantly less often provided (11%) compared with hospitals in Flanders, BE (20%) and the U.K. (17%). In U.K. home settings, continuous deep sedation was more common (19%) than in Flanders, BE (10%) or NL (8%). In NL in both settings, continuous deep sedation more often involved benzodiazepines and lasted less than 24 hours. Physicians in Flanders combined continuous deep sedation with a decision to provide physician-assisted death more often. Overall, men, younger patients, and patients with malignancies were more likely to receive

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continuous deep sedation, although this was not always significant within each country.

Conclusion. Differences in the prevalence of continuous deep sedation appear to reflect complex legal, cultural, and organizational factors more than differences in patients' characteristics or clinical profiles. Further in-depth studies should explore whether these differences also reflect differences between countries in the quality of end-of-life care. J Pain Symptom Manage 2012;44:33–43.

Key Words

Continuous deep sedation until death, continuous deep sedation, palliative sedation, end-of-life care

Introduction

Dying with dignity and without pain are characteristics of what people consider to be a "good death."[1–5] Although palliative medicine has made improvements in controlling symptoms at the end of life, some terminally ill patients still experience "refractory symptoms," uncontrollable and unresponsive to conventional therapies and optimal palliative care.[6–8] As an option of last resort, palliative sedation, that is, reducing the patient's consciousness and thus the awareness of suffering, may be used.[9,10] Palliative sedation can vary from mild to deep sedation and can be used intermittently or continuously. Continuous deep sedation until death can be considered an extreme form of palliative sedation; it has been described by some (especially if accompanied by withdrawal of clinically assisted hydration and nutrition) as a form of "slow euthanasia."[11]

There appears to be significant and substantial variation in the prevalence of continuous deep sedation between countries and over the years. A study across six European countries in 2001–2002 reported a prevalence ranging from 3% (Denmark) to 9% (Italy) of all deaths. In Flanders, Belgium (BE), its incidence was estimated to be 8% and in The Netherlands (NL) 6%.[10] More recent studies with comparable designs showed an increase in the incidence of sedation. In Flanders, BE in 2007, its incidence was estimated to be 15% of all deaths.[12] In NL in 2005, this was 8%.[13] In the U.K. in 2008, its prevalence was 17% of all deaths.[14] Further details of the methods used in these studies are given in the section below.

Continuous deep sedation until death is a heavily debated practice with regard to its indications and performance and also its relationship with life-shortening end-of-life practices, such as euthanasia.[6,15,16] Some national and international guidelines for the use of sedation have been published to educate clinicians and also to show patients and families that continuous deep sedation until death is an acceptable medical end-of-life procedure.[6,17–21] Official national guidelines are available in NL and BE, respectively, presented by the Royal Dutch Medical Association and the Federation for Palliative Care Flanders.[17,22]

The causes of variation between countries in the use of continuous deep sedation in end-of-life care have not yet been investigated. Therefore, we focused on three countries for which we had the most recent and comparable data. This study assessed Flanders, BE, NL, and the U.K., in hospital and home settings, for the frequency of continuous deep sedation until death, the characteristics of patients who received sedation, and other characteristics of the practice to gain insights into what causes variable rates of sedation.

Methods

We conducted post hoc comparative analyses using data on end-of-life decision-making practices that were collected separately in Flanders, BE,[12] NL,[13,23] and the U.K.[14,24] Because we had only access to data from Flanders and not from the Walloon provinces of BE, we will use Flanders instead of BE in the following sections.

Study Design

Flanders and NL. In Flanders (in 2007) and NL (in 2005), large-scale death certificate studies were conducted.[12,13,23] All deaths in these countries are reported to either the Flemish Ministry of Public Health in BE or the central death registry of Statistics Netherlands by means of a death certificate that is signed by the reporting physician. Stratified samples of Flemish and Dutch residents aged one year or older at the time of death who died between June and November 2007 (Flanders) or between August and November 2005 (NL) were drawn. All deaths that occurred in these periods were proportionally stratified for month of death and province of death (in BE, Flanders consists of five provinces). Some deaths, however, have a higher likelihood of being preceded by one or more end-of-life decisions (ELDs).[25,26] Therefore, we assigned deaths to one of four strata according to cause of death and corresponding estimated likelihood of an ELD, ranging from stratum 0: "Cause of death implies that an ELD is certain" to stratum 3: "Cause of death implies that an ELD is improbable." We adopted disproportionate sampling, and sampling fractions were larger for groups in which it was more likely that an ELD would be made. For each sampled death certificate of nonsudden deaths, the attending physician was sent a questionnaire. The response rate was 58% (3623 of 6202 questionnaires) for Flanders and 78% (5342 of 6860 questionnaires) for NL.[12,13,23,27]

United Kingdom. In the U.K., a random sample of working U.K. medical practitioners with different specialties was drawn from Binley's database (www.binleys.com), a regularly updated national database describing the medical workforce. An initial mailing of questionnaires and two follow-up reminders were sent between November 2007 and April 2008. Anonymity was guaranteed.[14] The response rate was 42% (3733 of 8857 questionnaires).[14,24] The death certificate method could not be used in the U.K. because this survey method is highly restricted because of privacy legislation.[28]

Questionnaire

In all countries, the questionnaire contained structured questions about the end-of-life decision-making process. The questionnaire was virtually identical to the ones used in previous studies.[24,25,29]

In Flanders and NL, the key question about continuous deep sedation was as follows: "Was the patient continuously and deeply sedated until death by the use of one or more drugs?" Subsequently, it was asked which medication was given for sedation and at what time before death continuous sedation of the patient was started. In the U.K., the sedation question was as follows: "Was the patient continuously and deeply sedated until death or kept in a coma before death?" Subsequently it was asked which medication was given for sedation and at what time before death continuous sedation of the patient was started.

The question about physician-assisted death (PAD) in all countries was as follows: "Was death caused by the use of a drug prescribed, supplied, or administered by you or a colleague with the explicit intention of hastening the end of life (or of enabling the patient to end his or her own life)? If yes, who administered this drug (i.e., introduced it into the body)?" For Flanders, NL, and the U.K., PAD includes euthanasia, physician-assisted suicide, and life shortening not on request. Patients' sociodemographic characteristics (sex, age, cause and place of death) were collected from the death certificates for Flanders and NL and from the questionnaires for the U.K.

Statistical Analysis

The percentages reported for Flanders and NL were weighted to adjust for the disproportionate case sampling and differences in response rates in relation to the patient's sex, age, province (Flanders), marital status (NL), region of residence (NL), and place and cause of death. After adjustment, the percentages were extrapolated to cover a 12-month period to reflect all deaths in Flanders in 2007 and NL in 2005. For U.K. analyses, all data were weighted by both physician specialty and cause of death to make these mirror national proportions, except where indicated otherwise. Also, data were weighted to adjust for the fact that different physicians attend different numbers of deaths per annum. Data were analyzed using SPSS (SPSS, Inc., Chicago, IL). For the comparison between and within countries, we calculated 95% confidence intervals (CIs).

Ethical Considerations

Approval for the Belgian study was received from the Ethical Review Boards of the University Hospitals of the Vrije Universiteit Brussel and Ghent University. Positive recommendations were received from the Belgian Medical Disciplinary Board and the Belgian Federal Privacy Commission. Ethical approval or informed consent was not needed for the Dutch study because the data collection was anonymous. Ethical approval for the U.K. study was granted by the South East Research Ethics Committee REC 07/H1102/94.

Results

Characteristics of Deaths

The total number of studied deaths was 11,704 (Table 1). The U.K. sample contained more people of younger age (<80 years) (60%) compared with Flanders (50%) and NL (52%). In all countries, cardiovascular and malignant diseases were the most frequent causes of death. In the U.K., there were significantly more people dying from nervous system diseases (8%) than in Flanders (4%) and NL (3%). Patients more often died in a hospital in the U.K. (83%) than in Flanders (50%) and NL (32%).

Frequency of Continuous Deep Sedation

The total number of deaths involving continuous deep sedation until death was 1517 (Table 2). Continuous deep sedation was used less frequently in NL (8%) than in Flanders (15%) and the U.K. (17%). Sedation was significantly less often performed in Dutch hospitals (11%) compared with Flanders (20%) and the U.K. (17%) and significantly more often at home in the U.K. (19%) compared with

Table 1
Characteristics of Deaths

Variables	Flanders	NL	U.K.
Number of deaths per year[a]	54,880	13,0870	579,697
Response percentage	58	78	42
Number of studied cases	3623	5239	2842
Sex			
Male	50 (48–52)	49 (47–50)	50 (46–53)
Female	50 (48–52)	51 (50–53)	50 (47–54)
Age[b]			
1–64	17 (16–19)	19 (18–20)	33 (30–37)
65–79	33 (31–35)	33 (31–34)	27 (24–30)
≥80	50 (48–52)	49 (47–50)	40 (37–43)
Cause of death[c]			
Malignancies	29 (29–30)	29 (28–30)	27 (24–30)
Cardiovascular	34 (32–35)	32 (31–34)	34 (30–37)
Respiratory	12 (11–13)	11 (9–12)	13 (11–16)
Nervous system	4 (3–4)	3 (2–3)	8 (6–10)
Other	22 (20–23)	26 (24–27)	18 (15–20)
Place of death[d]			
Hospital	50 (48–52)	32 (31–34)	83 (81–85)
Home	24 (22–25)	28 (26–29)	10 (9–12)
Other	27 (25–28)	40 (39–42)	7 (6–8)

NL = The Netherlands; BE = Belgium.
Data are weighted % (95% CI). In Flanders and NL, percentages are weighted for stratification and nonresponse. In the U.K., percentages are weighted for physician's specialty and cause of death. Also, data were weighted to adjust for the fact that different physicians attend different numbers of deaths per annum. Note: Flanders is a region of BE.
Missing cases, Flanders (*n*): place of death (1). Missing cases, NL (*n*): sex (868), age (818), cause of death (987), and place of death (837). Missing cases, U.K. (*n*): sex (60), cause of death (178), and place of death (16).
[a]Flanders data are for 2007; NL data are for 2005; and the U.K. data are for 2008.
[b]Deaths of infants younger than one year were not included in the samples for all countries (NL [1% ($n=122$)] and the U.K. [1% ($n=27$)]). In the U.K., age group 1–64 was 1–69 years and age group 65–79 was 70–79 years.
[c]Cerebrovascular disease is included in cardiovascular diseases for Flanders, NL, and the U.K.
[d]In Flanders, hospital includes hospital deaths; home includes deaths in own home of deceased; and other place of death includes deaths in care homes and other places not specified. In NL, hospital includes hospital deaths; home includes deaths in own home of deceased; and other place of death includes deaths in care homes, nursing homes, and other places not specified. In the U.K., hospital includes hospital and hospice deaths; home includes deaths in own home of deceased; and other place of death includes deaths in care homes and deaths not categorized as occurring in hospital or home.

Table 2
Frequency of Continuous Deep Sedation

Variables	Flanders	NL	U.K.
Number of studied cases	561	501	455
All settings	15 (13–16)	8 (7–9)	17 (14–19)
Hospital	20 (17–22)	11 (9–13)	17 (14–20)
Home	10 (8–12)	8 (7–9)	19 (13–25)
Other	9 (8–12)	6 (5–7)	7 (3–11)

Data are weighted % (95% CI).

Flanders (10%) and NL (8%). In Flanders and NL, sedation was significantly less often performed for patients dying at home than in the hospital, respectively, 10% vs. 20% (Flanders) and, respectively, 8% vs. 11% (NL). In the U.K., these percentages were not significantly different (19% vs. 17%).

Characteristics of Patients Who Received Continuous Deep Sedation

Continuous deep sedation was most often administered to patients younger than 80 years in all countries and both settings (hospital: 67%–74%; home: 73%–77%) (Table 3). In hospitals in all countries, sedation was most often performed for malignancies (28%–32%) and cardiovascular diseases (22%–29%), in rather comparable frequencies. At home, malignancy was the cause of death in most deaths that involved sedation (74%–86%). This did not differ significantly between the countries studied.

Characteristics of Continuous Deep Sedation

Medication. In all countries, benzodiazepines (sometimes combined with opioids and/or other drugs) were more often used than opioids alone to induce continuous deep sedation, especially in the home setting (Table 4). This was statistically significant for Flanders and the U.K. In NL, the proportion induced with benzodiazepines (sometimes combined with opioids and/or other drugs) was higher than in Flanders and the U.K. but only reached statistical significance for NL compared with Flanders. For the home setting, these proportions were 89% (NL) vs. 72% (Flanders) and 81% (U.K.) and for the hospital setting, 76%, 55%, and 58%, respectively.

Duration. Continuous deep sedation lasted, in most cases, for one week or less in all countries and both settings (hospital: 90%–93%; home: 91%–96%). In both settings, sedation was more likely to last for less than 24 hours in NL (hospital: 54%; home: 43%) compared with Flanders (hospital: 35%; home: 27%) and the U.K. (hospital: 38%; home: 20%). This reached statistical significance for NL compared with Flanders.

Table 3
Characteristics of Patients Who Received Continuous Deep Sedation

	Hospital			Home		
Variables	Flanders	NL	U.K.	Flanders	NL	U.K.
Number of studied cases	270	176	296	190	180	119
Sex						
Male	52 (45–59)	58 (48–67)	59 (50-68)	50 (42–58)	58 (50–66)	52 (37–68)
Female	48 (45–55)	42 (33–52)	41 (33–50)	50 (42–58)	42 (34–50)	48 (33–64)
Age[a]						
1–64	26 (21–32)	27 (20–35)	49 (40–58)	29 (23–35)	38 (31–46)	45 (28–61)
65–79	41 (34–48)	45 (36–55)	25 (18–32)	44 (36–53)	39 (32–47)	31 (18–45)
≥80	33 (26–40)	28 (20–38)	26 (19–34)	27 (20–36)	23 (16–31)	24 (14–34)
Cause of death[b]						
Malignancies	30 (29–32)	32 (25–40)	28 (20–37)	78 (76–81)	86 (76–92)	74 (64–84)
Cardiovascular	29 (25–33)	22 (15–31)	24 (17–32)	13 (9–18)	4 (1–12)	13 (6–20)
Respiratory	15 (11–19)	9 (4–19)	16 (9–22)	0	3 (1–10)	5 (0–9)
Nervous system	4 (2–7)	2 (1–6)	9 (2–16)	4 (2–8)	2 (0–7)	4 (0–9)
Other	23 (17–29)	35 (27–46)	22 (15–29)	5 (2–14)	6 (2–15)	4 (1–7)

Data are weighted % (95% CI).
Number of studied cases (*n*) in all settings: Flanders (561), NL (501), and the U.K. (455).
[a]In the U.K., age group 1–64 was 1–69 years and age group 65–79 was 70–79 years.
[b]U.K. cause of death: weighted by specialty only.

Table 4
Characteristics of Continuous Deep Sedation

Variables	Hospital			Home		
	Flanders	NL	U.K.	Flanders	NL	U.K.
Number of studied cases	270	176	296	190	180	116
Medication						
Benzodiazepines, opioids, and/or other	55 (48–62)	76 (66–83)	58 (49–67)	72 (63–79)	89 (82–93)	81 (71–90)
Only opioids	28 (22–35)	16 (10–25)	22 (15–29)	25 (18–33)	9 (5–16)	17 (7–26)
Opioids and other (excluding benzodiazepines)	10 (6–15)	3 (1–10)	12 (6–18)	3 (1–9)	2 (1–6)	3 (0–7)
Only other	7 (4–12)	5 (2–12)	8 (4–12)	1 (0–4)	0	0
Duration						
0–24 hours	35 (28–42)	54 (44–63)	38 (29–47)	27 (21–33)	43 (36–51)	20 (2–38)
1–7 days	55 (48–62)	36 (27–45)	55 (46–64)	64 (56–72)	53 (45–61)	73 (56–90)
>1 week	10 (7–16)	11 (6–18)	8 (3–12)	9 (5–18)	4 (2–8)	8 (0–15)
In conjunction with PAD[a]	10 (7–15)	3 (1–6)	1 (0–3)	19 (13–27)	8 (5–14)	3 (0–8)

PAD = physician-assisted death.
Data are weighted % (95% CI).
Number of studied cases (*n*) in all settings: Flanders (561), NL (501), and U.K. (455).
Missing cases: U.K. hospital (*n*): Medication (29), Duration (29).
[a]For Flanders, NL, and the U.K., PAD includes euthanasia, physician-assisted suicide, and life shortening not on request.

Continuous Deep Sedation in Conjunction With a Decision for Physician-Assisted Dying. In Flanders, in both settings, sedation was more often performed in conjunction with physician-assisted dying. In hospitals, these percentages were 10% of all sedated patients for Flanders, 3% for NL, and 1% for the U.K. In home settings, they were 19%, 8%, and 3%, respectively.

Determinants of Continuous Deep Sedation

Multivariate logistic regression analyses (Table 5) showed that, for all countries combined, the likelihood of receiving continuous deep sedation until death was significantly higher for males, younger patients, patients dying of malignant diseases (apart from those dying of diseases of the nervous system), and patients dying in the hospital. Furthermore, Dutch patients were significantly less likely to be sedated than both Flemish and U.K. patients.

Discussion

Summary of Main Findings

Continuous deep sedation until death preceded about 15% of all deaths in Flanders, 8% in NL, and 17% in the U.K.[12–14,23] Our further analysis of the combined data from these studies adds new information about the nature of variations between these countries and the likely causes of this. First, we found differences between settings. The prevalence of continuous deep sedation in hospitals is significantly

Table 5
Determinants of Continuous Deep Sedation in Flanders, NL, and the U.K.

	Beta	SE	Odds Ratios	95% CI
Sex				
Male			1.00	1.00–1.00
Female	−0.07	0.02	**0.93**	**0.90–0.97**
Age[a]				
1–64			1.00	1.00–1.00
65–79	−0.05	0.03	**0.95**	**0.90–1.00**
≥80	−0.26	0.03	**0.78**	**0.74–0.82**
Cause of death				
Malignancies			1.00	1.00–1.00
Cardiovascular	−1.14	0.03	**0.32**	**0.30–0.34**
Respiratory	−0.99	0.04	**0.37**	**0.34–0.40**
Nervous system	−0.02	0.05	0.98	0.89–1.10
Other	−0.50	0.03	**0.61**	**0.58–0.64**
Place of death				
Hospital			1.00	1.00–1.00
Home	−0.62	−0.62	**0.54**	**0.51–0.56**
Other	−0.58	−0.58	**0.56**	**0.54–0.59**
Country				
Flanders			1.00	1.00–1.00
NL	−0.56	−0.56	**0.57**	**0.52–0.63**
U.K.	−0.10	−0.10	0.90	0.79–1.04

Data are weighted % (95% CI). Model summary results: Nagelkerke R square = 0.060; percentage correctly predicted = 91.5%. Nonsudden deaths, all countries together. Missing cases: sex (58) and cause of death (171).
Significant relationships are in bold face.
[a]In the U.K., age group 1–64 was 1–69 years and age group 65–79 was 70–79 years.

lower in NL compared with that in Flanders and the U.K. In the home setting, its prevalence is higher in the U.K. than in the other two countries. Our multivariate analysis for all countries combined shows that males, younger patients, and those dying of malignancies are more likely to receive sedation, but between-country breakdowns of these variables revealed few significant differences between countries. However, there were differences between countries in other characteristics of sedation. In NL, sedation was more often performed with benzodiazepines (sometimes combined with opioids and/or other drugs) and was particularly likely to occur in only the last 24 hours of life. In Flanders, sedation was more likely to be provided in conjunction with physician-assisted dying than in the other countries.

Strengths and Limitations of the Study

This study presents a detailed statistical overview of variations in the use of continuous deep sedation between three European countries. A major strength of our study is the similar terminology and questions used that permit comparability between countries (we have pointed out instances where there were minor question wording differences). By providing the same descriptive definition of the practice (continuous deep sedation until death), we minimized possible differences in how physicians perceived the practice on which they had to report. However, we focused only on one specific type of sedation ("continuous" and "deep" and "until death"), rather than the full range of practices that involve sedation. The large random samples, the acceptable response rates, and the guarantee of anonymity of both physicians and patients also strengthen the validity and reliability of our results.

A limitation concerns the representativeness of the results when comparing samples drawn from death certificates in Flanders and NL and a sample of U.K. physicians recollecting the last death they attended. We corrected for this by weighting the U.K. data by the number of patients each doctor normally attended in a year and calculating CIs accordingly so that the U.K. results could be presented as a proportion of deaths.[30] Because we used a descriptive definition of continuous deep sedation, it is possible that respondents included patients where sedation was an unintended side effect of the drugs given. This may have led to an overestimation of the number of deaths involving continuous deep sedation. Further, in BE, our study was only performed in a specific region (Flanders), so we cannot say if our results can be extrapolated to the whole country. Lastly, our study only provides information from the physician's perspective; its retrospective character might imply a possible recall bias, particularly for the U.K. data, where information from death certificates was not available and had to be recalled from memory and, because of the short questionnaire, in-depth case analyses were impossible.

Comparison With Existing Literature

Wide variation in the prevalence of sedation for patients nearing death has been found by studies in different countries, ranging from 3% to 60%.[10,31–35] Although much of this variation will have been an artifact of the wording of questions referring to this practice, it is plausible that true variation exists, and our surveys have confirmed this. The view that this is a result of large differences in underlying demographic and epidemiological patterns can be rejected. In our study, a comparable distribution across countries was found with regard to sex, age, and cause of death. Another explanation could be that there are differences between countries in the type of patients that are continuously and deeply sedated. However, our study provides little evidence for this hypothesis: in the three countries, sedation was mostly performed with younger patients and patients with malignancies, and intercountry variation in this was minimal.

Our analysis reveals differences in the frequency of continuous deep sedation according to place of death: sedation was less often performed in Dutch hospitals compared with Flanders and the U.K. and more often at home in the U.K. compared with Flanders and NL. Patients with severe symptoms are more likely to die in hospitals; consequently, those patients may require continuous deep sedation more frequently.[36–38] This is supported by our multivariate analysis combining all countries, which showed that patients dying at home had a lower likelihood of sedation at the end of life compared with those dying in hospital. It could be that there are barriers to the use of sedation in

home settings that will only be revealed by more detailed research studies, although such barriers do not seem to affect the U.K., where our results show that continuous deep sedation until death at home is more common.[39,40]

Our analysis also has revealed differences between the countries in how continuous deep sedation was provided. First, benzodiazepines (sometimes combined with opioids and/or other drugs) were most often used for sedation, but this was most common in NL. Other studies have shown benzodiazepines to be the drugs of first choice for providing sedation in palliative care settings.[32,35,40–42] Since the introduction of the National Palliative Sedation guideline in 2005 in NL, there has been an increase from 70% to 90% in the use of benzodiazepines for sedation among Dutch physicians, suggesting a growing compliance with existing guidelines and criteria of due care for sedation.[17,43] In BE, a national guideline was introduced only recently, and after the conduct of our study, and no official guidelines are currently available in the U.K.[22] It also is possible that Dutch physicians' expertise in deciding the indications, and choosing the medication, for providing continuous deep sedation has improved over time. It is possible that Dutch respondents to our survey had a stricter understanding of the concept of "palliative sedation." Unlike Flemish and U.K. respondents, they may have been less willing to report that continuous deep sedation had occurred in situations where morphine was administered, causing drowsiness but without an explicit intention to sedate. The differences in understandings between countries and care settings and how these influence decision making and practice are the focus of the UNBIASED study (**U.K.**–**N**etherlands–**B**elgium **I**ntern**A**tional **SED**ation study), part of the European Association for Palliative Care Research Network.[44]

Second, the shorter duration of sedation in NL deserves comment, as it suggests that continuous deep sedation is used by Dutch physicians as an option of last resort when all other treatments have failed, as is advised in the Dutch guidelines.[17] This also may explain the lower frequency of continuous deep sedation in NL.

Third, continuous deep sedation was most often performed in conjunction with PAD in Flanders, compared with NL and the U.K., for both home and hospital settings. This suggests that the distinction between continuous deep sedation and PAD in Flanders is less clear than in NL, where euthanasia also is legal, or than in the U.K., where PAD is not legal.

Finally, we found in our study that "country" was an important factor in predicting the probability of receiving continuous deep sedation, even when correcting for other variables. This confirms similar results in the literature and suggests that cultural, social, and legal factors, as well as differences in the organization of health service provision, also explain variability in the use and provision of continuous deep sedation in the countries we studied.[10,26,35,36,45–50] It could be that, as a result of euthanasia legislation in NL in 2001 and in BE in 2002, physicians and patients can "choose" between euthanasia and continuous deep sedation until death. In the U.K., the high rate may be a result of the fact that such sedation is perceived to be the only legal "last resort" option for a physician treating a terminal patient with refractory symptoms. An exploratory study in three countries—BE, NL, and the U.K.—also suggests that, especially for U.K. respondents, the patient's clinical condition and context and environment of care—in other words, whether people have the knowledge and expertise to deal with the patient's symptoms—will drive the use of sedation.[49]

Conclusions and Implications for Clinical Practice and Future Research

Our study adds new information about the nature of variation in the prevalence of continuous deep sedation until death in Flanders (BE), NL, and the U.K. We found differences in the frequency of continuous deep sedation according to place of death and the performance of sedation with regard to the use of benzodiazepines (sometimes combined with opioids and/or other drugs), the duration of sedation, and the use of sedation in conjunction with physician-assisted dying. "Country" also was an important factor in predicting the probability of receiving sedation, suggesting that cultural, social, legal, and organizational factors probably play a role. This may have practical implications. There is a need for more detailed intercountry comparative studies to understand these variations and see how they relate to the quality of end-of-life care. The UNBIASED study comprises three linked studies in the U.K., BE, and NL and aims to

explore decision making surrounding the application of continuous sedation until death in contemporary clinical practice and understand the experiences of clinical staff and decedents' informal caregivers of the use of continuous sedation until death and their perceptions of its contribution to the dying process.[44] Until the results of this detailed research on this relatively new practice in end-of-life care are known, existing guidelines for the use of sedatives provide a helpful framework for clinicians to think through the issues involved when making decisions about individual patients.[17,22]

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