

Original Article

Drugs Used for Euthanasia: A Repeated Population-Based Mortality Follow-Back Study in Flanders, Belgium, 1998–2013



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Abstract

Context. According to guideline recommendations, barbiturates and neuromuscular relaxants are the recommended drugs for euthanasia.

Objectives. To describe changes over time in drugs used to perform euthanasia and differences in case characteristics according to the drugs used.

Methods. Repeated population-based mortality follow-back study among physicians attending a large representative sample of deaths in 1998, 2007, and 2013 in Flanders, Belgium.

Results. In 1998, we identified 25 euthanasia cases (1.2% of all deaths), 142 cases in 2007 (2.0% of all deaths), and 349 cases in 2013 (4.6% of all deaths). Use of recommended drugs to perform euthanasia increased from 11.9% of euthanasia cases in 1998 to 55.3% in 2007 and 66.8% in 2013 ($P < 0.001$). In 2013, cases with recommended drugs compared with nonrecommended drugs more often involved requests expressed both orally and in writing (86.8%/14.1%; $P < 0.001$), consultation with colleague physicians (93.8%/69.1%; $P < 0.001$), and administration in the presence of another physician (98.3%/54.3%; $P < 0.001$), and were more often self-labeled by physicians as euthanasia (95.5%/0.9%; $P < 0.001$) and reported to the euthanasia review committee (92.3%/3.8%; $P < 0.001$). Between 2007 and 2013, physicians consistently labeled cases in which nonrecommended drugs were used as palliative sedation (72.8%/78.4%; $P = 0.791$) or alleviation of pain and symptoms (13.2%/15.0%; $P > 0.999$).

Conclusion. Physicians in Flanders are increasingly using the recommended drugs for euthanasia. This suggests that guidelines and training regarding the conduct and pharmacological aspects of euthanasia may have had important effects on the practice of euthanasia. However, the declining but persisting use of nonrecommended drugs requires further attention. *J Pain Symptom Manage* 2018;56:551–559. © 2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Euthanasia, physician-assisted dying, practice guidelines, end-of-life decision making

Introduction

In 2002, euthanasia, that is termination of life by a physician at the patient's explicit request, became a legal possibility at the end of life in Belgium.¹ Strict

due care and procedural criteria are specified in the law to regulate the practice. The Belgian euthanasia law states that euthanasia should be performed by a physician.¹ It does not specify which drugs physicians

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should use to end the patient's life as therapeutic freedom is strongly defended by the medical professional associations. The Belgian professional association for pharmacists has clarified which products and materials are needed to perform euthanasia.² The recommended procedure is to administer a barbiturate overdose, optionally followed by a neuromuscular relaxant to induce respiratory arrest.² Optionally, the physician can administer a benzodiazepine (midazolam) to induce sleep before administering the barbiturate. The Belgian guideline is broadly similar to the Dutch guideline issued by the Royal Dutch Medical Association.³ However, the Dutch guideline states that a neuromuscular relaxant should always be administered, even if the patient seems to be deceased after administering the barbiturate. Other drugs such as opioids and benzodiazepines or combinations of these drugs without the use of a barbiturate and/or a neuromuscular relaxant are explicitly advised against in the Dutch guideline because of the uncertain lethal effect and adverse side effects.^{3,4} Barbiturates are also the preferred drugs in Switzerland and some U.S. states where physician-assisted suicide is legal.^{5,6} In Canada, the most common protocol for euthanasia is midazolam followed by propofol and a neuromuscular relaxant.⁷

The Belgian professional association for pharmacists has additionally provided instructions on the equipment needed to perform euthanasia by infusion or injection.² Information and best practices regarding the euthanasia procedure, including its performance, are also disseminated by the Life's End Information Forum (LEIF) in Flanders, the northern Dutch-speaking part of Belgium. This forum was established in the year following the enactment of the Belgian Euthanasia Law in September 2002.⁸ LEIF is a consultation service that aims to inform, assist, and train physicians in end-of-life care and specifically euthanasia.^{8,9}

Once the physician has assessed all due care criteria and is convinced that euthanasia can be granted for the competent patient, it is important that the correct drugs to perform euthanasia are chosen. Failure to do so may lead to traumatic situations such as an extended time to death or awakening of the patient,^{10,11} causing distress for the patient and the attending family and health care providers. Previous studies have shown that drugs that are advised against, that is, opioids and sedatives, are used to perform euthanasia^{12,13} and that these drugs are used in some euthanasia cases that remain unreported to the euthanasia review committee.¹²

The present study reports on the drugs used for euthanasia in Flanders, Belgium. The aims of this study are 1) to describe which drugs are used to

perform euthanasia, and how this has changed since before the euthanasia law, 2) to describe euthanasia case characteristics (decision-making and administrative characteristics, physicians' perceptions of their act, and reporting) in relation to the types of drugs used to perform euthanasia, and 3) to describe time trends in euthanasia case characteristics in relation to drugs used to perform euthanasia.

Methods

Study Design

We compare data from large-scale population-based mortality follow-back surveys on medical end-of-life decision making conducted in Flanders (the Dutch-speaking northern half of Belgium) in 1998, 2007, and 2013, that is, respectively, four years before, five years after, and 11 years after the introduction of euthanasia legislation in Belgium. All studies are based on a large and representative sample of deaths using the same sampling and data collection method. The Flemish Agency for Care and Health selected a random stratified sample of all death certificates of people aged one year or older within the study period. Attending physicians for these death certificates were requested to complete a questionnaire by mail about the end-of-life care and decision making while consulting the patient's medical file. To guarantee absolute anonymity for participating physicians, a lawyer served as an intermediary between responding physicians, researchers, and the Flemish Agency for Care and Health. The Ethical Review Board of the University Hospital of the Vrije Universiteit Brussel (VUB), the Belgian National Disciplinary Board of Physicians, and the Belgian Privacy Commission approved the mailing and anonymity procedure. The study design, sampling, and mailing procedure are described in detail elsewhere.^{14–17}

A similar study was also performed in 2001, during a period in which the euthanasia debate reached its culmination point, eventually leading to the legalization of euthanasia in 2002.¹⁸ Because of the potential bias related to conducting the study during the euthanasia legalization process, such as socially desirable answers, and the limited number of euthanasia cases ($n = 18$), data for 2001 are not included in the analyses.

Questionnaire

The questionnaire first asked whether the death of the patient had been sudden and unexpected. If the answer was negative, physicians were asked about the medical decisions made at the end of the patient's life with a possible or certain life-shortening effect. We identified cases as euthanasia if the physician

gave an affirmative answer to the following questions: 1) was the death the consequence of the use of drugs prescribed, supplied, or administered by you or another physician with the explicit intention of hastening the end of life or of enabling the patient to end his or her own life? 2) Was the decision made at the explicit request of the patient?

In the 1998 questionnaire, physicians were asked to specify in writing which drugs were used. In 2007 and 2013, physicians were asked to indicate prestructured response categories, which were 1) neuromuscular relaxant (curare or similar drug), 2) barbiturate, 3) benzodiazepine, 4) morphine or other opioid, and 5) other drug, with the possibility to specify the other drug in writing. Multiple answers were possible for this question. Physicians were also asked to indicate who administered the drugs by multiple choice, that is, 1) the patient, 2) you or another physician, 3) a nurse, and 4) someone else, with the possibility to specify in writing. For this question also, multiple answers were possible.

In addition, we asked for the estimated time by which the patient's life was shortened, the manner in which the patient expressed the euthanasia request, whether the decision was discussed with others, how they would label the end-of-life act, whether they reported the act to the euthanasia review committee, and, if not reported to the committee, the reason(s) for not reporting.

Statistical Analysis

Data were weighted to correct for the disproportionate stratification of deaths and adjusted to be representative of all deaths in the period covered by the surveys in terms of age, sex, marital status, province of death, cause of death, and place of death.

We dichotomized the categories in which drugs used to perform euthanasia were categorized, reflecting the recommended drugs to perform euthanasia according to the guideline of the Belgian Professional Association for pharmacists.² The first category, recommended drugs, includes barbiturates and neuromuscular relaxants, barbiturates used alone or with other drugs (excluding neuromuscular relaxants), and neuromuscular relaxants used alone or with other drugs (excluding barbiturates). The second category, nonrecommended drugs, includes benzodiazepines and opioids, benzodiazepines used alone or with other drugs (excluding barbiturates, neuromuscular relaxants, or opioids), opioids used alone or with other drugs (excluding barbiturates, neuromuscular relaxants, or benzodiazepines), and other drugs.

Physician-assisted suicide, that is when patients administer the lethal drugs themselves, is treated as a form of euthanasia by the Belgian Euthanasia Review Committee, although it is not mentioned in the

euthanasia law. Cases of physician-assisted suicide are subject to the same due care criteria as cases of euthanasia. Therefore, cases of physician-assisted suicide were included in the analysis as cases of euthanasia.

We carried out Pearson's Chi-squared tests and Fisher exact tests to analyze differences between recommended and nonrecommended drugs in euthanasia case characteristics. We also carried out Pearson's Chi-squared tests and Fisher exact tests to identify trends in the nature of drugs used to perform euthanasia.

Results

In 1998, we identified 25 euthanasia cases (1.2% of all deaths); in 2007, we identified 142 cases (2.0% of all deaths); and in 2013, we identified 349 cases (4.6% of all deaths) in Flanders, Belgium (Table 1).

Type of Drugs Used to Perform Euthanasia and Time Trends

The use of recommended drugs increased from 11.9% in 1998 to 55.3% in 2007 and 66.8% in 2013 ($P < 0.001$) (Table 2). Barbiturates combined with neuromuscular relaxants were the recommended drugs most often used in 2013 (39.7%).

Table 1
Characteristics of Deaths by Euthanasia in Flanders, Belgium, in 1998, 2007, and 2013

Characteristics	1998	2007	2013
Total number of deaths (unweighted)	1925	3623	3751
Number of euthanasia deaths (unweighted) ^a	25	142	349
Percentage of all euthanasia deaths (weighted)	1.2	2.0	4.6
Sex			
Male	40.4	61.3	51.0
Female	59.6	38.7	49.0
Age (yrs)			
18–64	35.8	37.0	18.9
65–79	29.0	42.6	37.8
80 or older	35.2	20.4	43.2
Cause of death			
Cardiovascular disease ^b	14.1	3.8	14.3
Malignancies	46.1	80.2	57.4
Respiratory disease	11.1	4.7	4.1
Disease of the nervous system	7.6	7.2	7.4
Other disease	21.1	4.0	16.9
Place of death			
At home	48.4	43.1	41.8
Hospital	43.1	51.3	42.5
Care home	8.6	5.6	15.6
Other	0.0	0.0	0.1

Weighted row percentages.

^aNumbers include three cases of physician-assisted suicide in 1998, five cases in 2007, and six cases in 2013. Physician-assisted suicide, that is when patients administer the lethal drugs themselves, is treated as a form of euthanasia by the Belgian Euthanasia Review Committee, although it is not mentioned in the euthanasia law.

^bIncludes cerebrovascular disease.

Table 2
Trends in Drugs Used to Perform Euthanasia, in 1998, 2007, and 2013

Drugs Used	1998	2007	2013	P ^a
Unweighted number of cases	25	142	349	
Recommended drugs ^{2,3}	11.9	55.3	66.8	<0.001
Barbiturates and neuromuscular relaxants	4.8	30.1	39.7	0.009
Barbiturates only or with other drugs (excluding neuromuscular relaxants)	7.1	15.4	20.1	0.258
Neuromuscular relaxants only or with other drugs (excluding barbiturates)	0.0	9.8	7.1	^b
Nonrecommended drugs ³	88.1	44.7	33.2	<0.001
Benzodiazepines and opioids	17.5	20.9	14.8	0.469
Benzodiazepines only or with other drugs (excluding barbiturate, neuromuscular relaxant, or opioid)	9.6	0.5	1.8	^b
Opioids only or with other drugs (excluding barbiturate, neuromuscular relaxant, or benzodiazepine)	61.1	23.3	16.0	<0.001
Other	0.0	0.0	0.5	^b

Weighted column percentages. Missing values: 1998: $n = 5$; 2007: $n = 2$; and 2013: $n = 11$.

^aP-values calculated with Pearson's Chi-squared test.

^bP-value could not be calculated because of low cell frequencies.

Nonrecommended drugs were decreasingly used, from 88.1% of all cases in 1998 to 44.7% in 2007 and 33.2% in 2013. Opioids only or with other drugs (excluding barbiturate, neuromuscular relaxant, or benzodiazepine) were the most often used nonrecommended drugs in 2013 (16.0%).

Decision-Making and Administration Characteristics, Estimated Degree of Life Shortening, Labeling, and Reporting of Euthanasia Cases According to the Type of Drugs Used to Perform Euthanasia in 2013

Where recommended drugs were used, compared with cases where nonrecommended drugs were used, the request for euthanasia was more often expressed both orally and in writing (86.8%/14.1%; $P < 0.001$) and less often only orally (5.7%/80.5%; $P < 0.001$). There was more often discussion with a fellow physician when recommended drugs were used (93.8%/69.1%; $P < 0.001$). Recommended drugs were more often administered by a physician only (93.7%/25.2%; $P < 0.001$) and less often by a nurse only (1.5%/41.5%; $P < 0.001$). A physician was more often present during the administration of recommended drugs (98.3%/54.3%; $P < 0.001$). If recommended drugs were used, the estimated degree of life shortening was less often 24 hours or less (8.3%/21.1%; $P = 0.024$) or one to seven days (33.3%/58.6%; $P = 0.003$), and physicians more often estimated that the patient's life was shortened by more than one week (57.8%/16.7%; $P < 0.001$) (Table 3). In cases with recommended drugs, the physician more often labeled the act as euthanasia (95.5%/0.9%; $P < 0.001$) and less often as palliative sedation (4.3%/78.4%; $P < 0.001$) or alleviation of pain and symptoms (0.0%/15.0%; $P < 0.001$). Euthanasia cases were more frequently reported to the Federal Control and Evaluation Committee when recommended drugs were used (92.3%/3.8%; $P < 0.001$).

Trends in Decision-Making and Administration Characteristics, Estimated Degree of Life Shortening, Labeling, and Reporting of Euthanasia Cases According to the Type of Drugs Used Between 1998, 2007, and 2013

Where recommended drugs were used, in 2013 compared with 2007, euthanasia requests were increasingly expressed both orally and in writing (from 66.9% in 2007 to 86.8% in 2013; $P = 0.026$) and decreasingly only orally (from 24.4% in 2007 to 5.7% in 2013; $P = 0.003$) (Table 4). The presence of a physician during administration of the drugs remained consistent (99.0% in 2007/98.3% in 2013; $P > 0.999$) as well as reporting to the euthanasia review committee (92.0% in 2007/92.3% in 2013; $P > 0.999$).

Where nonrecommended drugs were used, administrative burden (having to report the euthanasia case to the euthanasia review committee) was decreasingly indicated as a reason not to report the case to the committee (from 17.0% in 2007 to 2.5% in 2013; $P = 0.025$). Physicians consistently labeled cases in which nonrecommended drugs were used as palliative sedation (72.8% in 2007/78.4% in 2013; $P = 0.791$) or alleviation of pain and symptoms (13.2% in 2007/15.0% in 2013; $P > 0.999$). The presence of a physician during administration of the drugs remained stable (55.8% in 2007/54.3% in 2013; $P > 0.999$) as well as reporting to the euthanasia review committee (4.5% in 2007/3.8% in 2013; $P > 0.999$).

Discussion

Main Findings

This study found that the recommended drugs, that is barbiturates and/or neuromuscular relaxants, were increasingly used to perform euthanasia, from 11.9% of euthanasia cases in 1998 to 55.3% in 2007 and 66.8% in 2013. The use of nonrecommended drugs, especially opioids and/or benzodiazepines, decreased

Table 3
Decision-Making and Administration Characteristics, Labeling, and Reporting of Euthanasia Cases in Relation to Drugs Used to Perform Euthanasia, 2013

Characteristics	All Cases	Drugs Used to Perform Euthanasia		
		RD	NRD	P ^e
Unweighted number of cases	349	272	64	
Type of request				
Only oral	30.5	5.7	80.5	<0.001
Only in writing	1.2	1.9	0.0	0.549
Oral and in writing	62.8	86.8	14.1	<0.001
Advance euthanasia directive	5.5	5.7	5.4	>0.999
Decision discussed with others ^b				
Another physician	85.6	93.8	69.1	<0.001
Caregiver specialized in palliative care	52.4	53.5	50.3	0.743
Nursing staff	54.9	54.8	52.9	0.869
Relative	81.3	80.9	81.8	>0.999
Person who administered the drugs				
Only physician	71.4	93.7	25.2	<0.001
Only nurse	14.7	1.4	41.5	<0.001
Physician and other person(s) ^c	12.4	4.5	29.0	<0.001
Nurse and other person(s) (excluding physician) ^d	0.6	0.0	2.0	0.327
Only other person(s) ^e	0.9	0.2	2.2	0.327
Physician present during administration	83.7	98.3	54.3	<0.001
Estimated degree of life shortening				
Probably none	1.7	0.6	3.6	0.261
Less than 24 hours	12.5	8.3	21.1	0.024
One to seven days	41.0	33.3	58.6	0.003
More than one week	44.8	57.8	16.7	<0.001
Label given by the physician				
Euthanasia	64.6	95.5	0.9	<0.001
Palliative or terminal sedation	28.5	4.3	78.4	<0.001
Alleviation of pain and symptoms	4.9	0.0	15.0	<0.001
Compassionate life ending	0.8	0.1	2.2	0.337
Other	1.2	0.1	3.5	0.110
Reporting to the euthanasia review committee				
Reported	63.5	92.3	3.8	<0.001
Not reported because ^b				
Not euthanasia according to the physician	30.8	3.8	93.6	0.001
Administrative burden	1.9	1.7	2.5	0.052
Matter between physician and patient	1.7	1.6	2.1	0.052
Possibly not all legal criteria adhered to	0.0	0.0	0.0	>0.999
Possible judicial consequences	1.1	0.6	2.5	0.272

Percentages are weighted column percentages. Missing values for drugs used to perform euthanasia: n = 13.

RD = recommended drugs (barbiturates and/or neuromuscular relaxants); NRD = nonrecommended drugs (opioids, benzodiazepines, or other drugs other than barbiturates or neuromuscular relaxants).

^aP-values calculated with Fisher exact test.

^bMultiple answers possible.

^cOther persons were a nurse and/or the patient.

^dOther persons were a palliative care team.

^eOther persons were the patient with or without a palliative care team.

from 88.1% in 1998 to 44.7% in 2007 and 33.2% in 2013. Cases where the recommended drugs were used more often involved a request that was expressed both orally and in writing, consultation with colleague physicians, and administration in the presence of a physician, and were more often self-labeled by physicians as euthanasia and reported to the euthanasia review committee.

Strengths and Weaknesses of This Study

By taking a population-based approach, we are able to report representative data on euthanasia case characteristics across care settings and diagnoses. In addition, by repeatedly using a similar study design, sampling, and mailing procedure, we can make

reliable comparisons over time. However, our study also has some limitations. The study does not allow an in-depth analysis of the drugs that were administered, for example, information on drug doses was not gathered in all the years studied. Furthermore, as we used a retrospective survey study design, recall bias cannot be excluded. Physicians were however asked to consult the patient's medical file while completing the questionnaire to reduce recall bias. The sensitivity of the survey topic may have introduced the possibility of untruthful or socially desirable reporting, but this is likely negligible given the explicit guarantee of anonymity and the avoidance of the term euthanasia in the survey itself. Finally, as the 1998 sample included a small number of euthanasia

Table 4
Trends in Decision-Making and Administration Characteristics, Labeling, and Reporting of Euthanasia Cases in Relation to Drugs Used to Perform Euthanasia, in 1998, 2007, and 2013

Characteristics	All Cases				Recommended Drugs ^a				Nonrecommended Drugs ^b			
	1998	2007	2013	<i>P</i> ^c	1998	2007	2013	<i>P</i> ^c	1998	2007	2013	<i>P</i> ^c
Unweighted number of cases	25	142	349		2	87	272		18	53	64	
Type of request												
Only oral	<i>d</i>	50.1	30.5	0.005	<i>d</i>	24.4	5.7	0.003	<i>d</i>	84.2	80.5	0.779
Only in writing	<i>d</i>	6.4	1.2	0.025	<i>d</i>	8.7	1.9	0.109	<i>d</i>	3.8	0.0	0.356
Oral and in writing	<i>d</i>	43.1	62.8	0.010	<i>d</i>	66.9	86.8	0.026	<i>d</i>	11.0	14.1	0.739
Advance euthanasia directive	<i>d</i>	0.5	5.5	0.061	<i>d</i>	0.0	5.7	0.339	<i>d</i>	1.1	5.4	0.550
Decision discussed with others ^e												
Another physician	48.9	77.8	85.6	<0.001	100	97.4	93.8	0.680	60.5	52.5	69.1	0.109
Caregiver specialized in palliative care	<i>d</i>	50.0	52.4	0.779	<i>d</i>	65.1	53.5	0.190	<i>d</i>	31.3	50.3	0.121
Nursing staff	30.9	54.1	54.9	0.085	59.8	54	54.8	>0.999	38.7	54.5	52.9	>0.999
Relative	61.6	77.4	81.3	0.106	100	78.9	80.9	>0.999	79.7	76.8	81.8	0.587
Person who administered the drugs												
Only physician	54.6	69.2	71.4	0.248	100	94.5	93.7	>0.999	64.8	37.3	25.2	0.213
Only nurse	6.7	19.1	14.7	0.459	0.0	0.0	1.4	>0.999	10.1	43.1	41.5	>0.999
Physician and other person(s) ^f	14.0	10.6	12.4	0.888	0.0	4.5	4.5	>0.999	21.1	18.5	29	0.444
Nurse and other person(s) (excluding physician) ^g	0.0	0.0	0.6	—	0.0	0.0	0.0	>0.999	0.0	0.0	2.0	>0.999
Only other person(s) ^h	24.8 ⁱ	1.0	0.9	<0.001	0.0	1	0.2	>0.999	4.0	1.1	2.2	>0.999
Physician present during administration	68.6	80.1	83.7	254	100	99	98.3	>0.999	85.9	55.8	54.3	>0.999
Estimated degree of life shortening												
Probably none	3.6	1.7	1.7	0.684	0.0	0.0	0.6	>0.999	5.4	3.8	3.6	>0.999
Less than 24 hours	18.3	9.7	12.5	0.679	0.0	4.0	8.3	0.452	23.3	17.1	21.1	0.585
One to seven days	60.1	44.1	41.0	0.265	0.0	36.3	33.3	0.689	57.5	55.4	58.6	0.823
More than one week	18.0	44.5	44.8	0.029	100	59.7	57.8	>0.999	13.7	23.6	16.7	0.567
Label given by the physician												
Euthanasia	<i>d</i>	54.3	64.6	0.192	<i>d</i>	92.6	95.5	>0.999	<i>d</i>	4.7	0.9	0.356
Palliative or terminal sedation	<i>d</i>	34.1	28.5	0.443	<i>d</i>	4.1	4.3	>0.999	<i>d</i>	72.8	78.4	0.791
Alleviation of pain and symptoms	<i>d</i>	6.1	4.9	0.750	<i>d</i>	0.5	0.0	>0.999	<i>d</i>	13.2	15.0	>0.999
Compassionate life ending	<i>d</i>	0.4	0.8	>0.999	<i>d</i>	0.8	0.1	>0.999	<i>d</i>	0.0	2.2	>0.999
Other	<i>d</i>	5.1	1.2	0.062	<i>d</i>	2.0	0.1	0.253	<i>d</i>	9.3	3.5	0.343
Reporting to the euthanasia review committee												
Reported	<i>d</i>	53.7	63.5	0.194	<i>d</i>	92	92.3	>0.999	<i>d</i>	4.5	3.8	>0.999
Not reported because ^e												
Not euthanasia according to the physician	<i>d</i>	36.1	30.8	0.189	<i>d</i>	1.1	3.8	0.236	<i>d</i>	83.5	93.6	0.135
Administrative burden	<i>d</i>	9.5	1.9	0.030	<i>d</i>	4	1.7	0.547	<i>d</i>	17	2.5	0.025
Matter between physician and patient	<i>d</i>	5.2	1.7	0.241	<i>d</i>	3.9	1.6	>0.999	<i>d</i>	7.1	2.1	0.552
Possibly not all legal criteria adhered to	<i>d</i>	6.1	0.0	0.014	<i>d</i>	6.3	0.0	0.055	<i>d</i>	6.2	0.0	0.136
Possible judicial consequences	<i>d</i>	2.1	1.1	>0.999	<i>d</i>	1	0.6	>0.999	<i>d</i>	3.8	2.5	>0.999

Percentages are weighted column percentages. Missing values for drugs used to perform euthanasia: 1998: n = 5; 2007: n = 2; and 2013: n = 11.

^aRecommended drugs: barbiturates and/or neuromuscular relaxants.

^bNonrecommended drugs: opioids, benzodiazepines, or other drugs other than barbiturates or neuromuscular relaxants.

^c*P*-values calculated with Fisher exact test (type of request, label given by physician, reporting to the euthanasia review committee) or Pearson's Chi-squared test (decision discussed with others, person who administered the drugs, physician present during administration, estimated degree of life shortening).

^dData for 1998 are not available as these questions were not included in the survey.

^eMultiple answers are possible.

^fOther persons were a nurse, the patient, and/or the patient's relative.

^gOther persons were a palliative team.

^hOther persons were a palliative care team and/or the patient.

ⁱThese are four cases in which the palliative care team and one case in which the patient administered the drugs.

cases, the possibility of Type II errors, that is false negatives, cannot be excluded.

Meaning of the Findings and Comparison With Other Studies

We found that the recommended drugs for performing euthanasia, that is barbiturates and/or neuromuscular relaxants, were increasingly used after the introduction of euthanasia legislation in 2002. Before euthanasia legislation, drugs that are considered unsuitable for euthanasia and that are therefore advised against, especially morphine, were used in most cases. After legalization of euthanasia, recommended drugs, that is barbiturates and/or neuromuscular relaxants, were increasingly used. Numbers from the Federal Control and Evaluation Committee for Euthanasia on reported cases show the same trend of recommended drugs being increasingly used to perform euthanasia.^{19,20} This suggests that since the introduction of euthanasia legislation, physicians have become increasingly familiar with recommended euthanasia procedure. Dissemination to physicians of best practices for euthanasia, for instance by LEIF,⁸ and providing training and information to clinicians through media dissemination and exchanges of experiences among professionals in a context that is increasingly open to the topic of euthanasia may have played a significant role in the increase in adoption of the guidelines. Population-based studies in The Netherlands, where euthanasia was also legalized in 2002, have also found that the recommended drugs for euthanasia are increasingly used and that most cases of euthanasia are undertaken with barbiturates and/or neuromuscular relaxants.^{21,22} Recommended drugs are however more frequently used in The Netherlands (in 80% of euthanasia or physician-assisted suicide cases in 2010²¹) than in Flanders, Belgium. This may be related to a longer experience and open societal and medical debate about good euthanasia practice, going back to as early as 1987 when the first guideline on the medicotechnical aspects of euthanasia was issued in The Netherlands, before the practice was formally legalized.³

Despite the observed decrease in nonrecommended drugs to perform euthanasia, one-third of cases identified in this study in 2013 still involved the use of nonrecommended drugs, mainly opioids or benzodiazepines, to intentionally hasten death on patient request. Some physicians may overestimate the actual lethal effect of these drugs in persons at the very end of life.^{4,23–25} Another possible explanation is that some physicians use drugs that are not associated with the recommended euthanasia procedure but with palliative sedation as a strategy to reduce cognitive dissonance, that is the mental discomfort experienced by a person with conflicting attitudes,

as some clinicians find palliative sedation emotionally less burdensome to perform than euthanasia.²⁶ Also, physicians may intend to hasten death without using the established procedures that make it an obvious euthanasia case but by increasing medication for sedation or pain and symptom control to avoid lengthy procedures, due care requirements, or the administrative burden of reporting to the review committee. In these cases, the requirements for due care are significantly less often adhered to than in cases in which recommended drugs were used: there was more often only an oral request, a colleague physician was less often consulted, and the euthanasia was more often carried out in the absence of a physician.

Furthermore, these cases are generally not reported to the committee and thus not reviewed, mainly because physicians did not consider the case as euthanasia. Studies in The Netherlands also show that nonreporting of euthanasia is strongly related to the type of drugs used.²⁷ These nonreported cases are usually considered as palliative sedation or intensified alleviation of pain and symptoms by the attending physicians. Flemish physicians seem to use a fairly narrow definition of euthanasia based on the drugs used and legal procedures. What is not performed with these drugs or is not in accordance with the legal procedures, is not euthanasia in their eyes, but rather a gray zone that they label as palliative sedation. Our findings corroborate previous studies identifying this gray zone.^{12,21,27–29} Although some framework papers make a strict distinction between euthanasia and palliative sedation in terms of physicians' intention and the outcome of the act,^{30,31} previous research showed that this distinction is not always clear in clinical practice^{32–37} and that some physicians administer sedatives with the intention of hastening death.^{38,39}

In half of all euthanasia cases in 2013, the decision to perform euthanasia had been discussed with a palliative care expert. This does not preclude the possibility that palliative care services had been involved outside the euthanasia decision-making procedure. Previously, we have found that palliative care services were involved in 71% of deaths with a euthanasia request.⁴⁰ When no palliative care services had been involved, this had been in more than half of the cases because the existing care already sufficiently addressed the patient's palliative and supportive care needs. Nevertheless, involvement of palliative care experts may increase compliance with guidelines regarding drugs for euthanasia.

Implications and Recommendations

The obsolete practice in which benzodiazepines and/or morphine are used to intentionally end a patient's life on patient request requires adequate

attention. Despite an increase in euthanasia being performed with drugs recommended by euthanasia guidelines, physicians still use drugs that are advised against, mainly opioids, to hasten death on explicit patient request. These cases remain unreported to the euthanasia review committee because physicians do not consider them to be euthanasia.

Continuation and further expansion of initiatives aimed at improving health professionals' skills regarding euthanasia performance are recommended. Further education of physicians on euthanasia procedures and the effects and side effects of opioids and sedatives is needed to avoid euthanasia being performed in a way that may be harmful to patients and their relatives and beyond societal control. To further encourage physicians to report their cases to the euthanasia review committee and to use the recommended drugs for euthanasia and thus improve quality of euthanasia performance, a strong signal is needed from the medical community, for example, through official advice from the National Belgian Disciplinary Board of Physicians. Future studies should focus on the euthanasia practice with nonrecommended drugs, physicians' motives to intentionally hasten death with nonrecommended drugs, and possible complications associated with nonrecommended euthanasia practice.

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