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Physicians' opinion and practice with the continuous use of sedatives in the last days of life

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**Title:** Physicians' opinion and practice with the continuous use of sedatives in the last days of life

**Running title:** The continuous use of sedatives in the last days of life

**Key message:** This questionnaire study among physicians caring for terminally ill patients showed that many considered the continuous use of sedatives acceptable to relieve physical and psycho-existential suffering in the last days of life. Respondents regarded the practice as less acceptable in patients with a longer life expectancy.

**Key words:** questionnaire study, palliative sedation, deep sedation, continuous use of sedatives, palliative care, end of life care

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**Abstract**

Context: There are few international studies about the continuous use of sedatives (CUS) in the last days of life.

Objectives: We aim to describe the experiences and opinions regarding CUS of physicians caring for terminally ill patients in seven countries.

Methods: Questionnaire study about practices and experiences with CUS in the last days of life among physicians caring for terminally ill patients in Belgium (N=175), Germany (N=546), Italy (N=214), Japan (N=513), the Netherlands (N=829), United Kingdom (N=114) and Singapore (N=21).

Results: The overall response rate was 22%. Of the respondents, 88-99% reported that they had clinical experience of CUS in the last 12 months. More than 90% of respondents indicated that they mostly used midazolam for sedation. The use of sedatives to relieve suffering in the last days of life was considered acceptable in cases of physical suffering (87-99%). This percentage was lower but still substantial in cases of psycho-existential suffering in the absence of physical symptoms (45-88%). These percentages were lower when the prognosis was at least several weeks (22- 66% for physical suffering and 5-42% for psycho-existential suffering). Of the respondents, 10% or less agreed with the statement that CUS is unnecessary because suffering can be alleviated with other measures. A substantial proportion (41-95%) agreed with the statement that a competent patient with severe suffering has the right to demand the use of sedatives in the last days of life.

Conclusion: Many respondents in our study considered CUS acceptable for the relief of physical and psycho-existential suffering in the last days of life. The acceptability was lower regarding CUS for psycho-existential suffering and regarding CUS for patients with a longer life expectancy.

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## Introduction

Physicians who care for terminally ill patients often witness unbearable suffering in their patients. Sedatives may be considered as a last resort when this suffering cannot be relieved by standard treatment options. In particular, palliative sedation represents a treatment of last resort to relieve suffering in dying patients.(1)(2)(3)(4)(5) However, there is a lack of standardization regarding palliative sedation in the literature. What are the indications for sedation? How should sedation be performed? When can sedation be considered acceptable practice?(6)(7)(8)(9)

There are many terms for the use of sedatives to relieve the suffering of terminally ill patients, including 'palliative sedation', 'continuous sedation', 'deep sedation', 'terminal sedation' and 'end of life sedation'.(6)(10)(11) The depth of sedation varies from superficial to deep, and the duration of sedation varies from intermittent to continuous until the end of life.(8)(12)(13) There is much debate on the use of sedatives, which is often complicated by a lack of consensual definitions. Empirical studies have described heterogeneous practice involving the use of sedatives for terminally ill patients in different countries and subpopulations.(4)(14)(15)(16) To date, few studies have been conducted to describe medical practices and opinions of physicians in an international context.(17)(18) The aim of this study was to explore practices and opinions regarding continuous use of sedatives (CUS) of physicians caring for terminally ill patients in eight resource-rich countries: Belgium, Germany, Italy, Japan, the Netherlands, Singapore, the United Kingdom, and the United States.

## Methods

### Design:

We designed a questionnaire study in eight countries to gain insight into the medical practices and opinions of physicians regarding CUS in the last days of life. Questionnaires were distributed among 8550 physicians in Belgium (Flanders region, n=555), Germany (n=1091), Italy (n=1083), Japan (n=734), the Netherlands (n=4000), Singapore (n=37), the United Kingdom (n=850), and the United States (n=200) between November 2018 and August 2019. Questionnaires were electronic, except for in the Netherlands and Japan where questionnaires were distributed by post. We attempted to maximize the response rate by introducing the topic at the start of the questionnaire, by the short length of the questionnaire, by personalizing the questionnaire per respondent, and by sending a reminder. Physicians received two reminders in Japan and the United States. No financial incentive was used.

#### Definition of sedation:

We established the definition to be used in the questionnaire by discussing the terms and practices that are used in the participating countries in two face-to-face meetings, and by several subsequent rounds of email contact among the authors. It was important that the definition was acceptable and recognizable in all participating countries, applied to a broad range of patients, including those with and without capacity. We chose to use a descriptive definition: the continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life. "Continuous use" was defined as either a continuous subcutaneous/intravenous infusion or a scheduled repeated injection with the intention of producing a continuous effect.

#### Selection of participants:

Target physicians for this study were physicians caring for terminally ill patients. The national research teams decided about whom and how to optimally recruit participants due to the very different organizational structures of palliative care in the participating countries. In Belgium, Germany, Italy, Japan, the United Kingdom, and the United States, where palliative care is a clinical specialty or subspecialty, palliative care physicians were invited via the member lists of the national associations of palliative medicine. In Belgium, additionally, all physicians who had followed a palliative care training in the last five years prior to completion of the questionnaire were included. In the Netherlands, where there is no specific palliative care discipline, target physicians were random samples of general practitioners, geriatricians, and medical specialists. In Singapore, all physicians of major palliative care units were invited.

#### Development of the questionnaire:

Since no validated questionnaires to survey physicians' experiences and attitudes regarding CUS were available, we developed our own questionnaire using expert opinion. Authors firstly reached a consensus on the definition of CUS. After consensus on the definition of CUS, we identified important themes and knowledge gaps about CUS in the literature. These themes concerned the type of medication, how sedation should be performed, the involvement of the patient and/or their family in the decision-making process, the goal of sedation, CUS to relieve psycho-existential suffering, CUS for patients with a life-expectancy of at least several weeks, and routine withdrawal of artificial hydration during CUS. (11)(19)(20)(21)(22)(23)(24)

Questions were developed by two face-to-face meetings, and by several subsequent rounds of email contact among the authors. The initial English version of the questionnaire was translated into Dutch, German, Italian, and Japanese. A pilot study was conducted in all countries with three physicians who were involved in the care of dying patients. Physicians in our pilot were asked to fill out the questionnaire, and were interviewed afterwards to identify if the questionnaire was applicable in their country, and to identify if the questionnaire included important themes considering CUS in each participating country. This pilot test resulted in minor adjustments to the English questionnaire. The final version was translated into Dutch, German, Italian, and Japanese.

The questionnaire contained 32 questions and consisted of three parts (supplement 1). The first part enquired about physicians' backgrounds including their age, religion, self-identified specialty, work place, work experience and involvement in the care of dying patients in the last 12 months. The second part addressed physicians' practices, including their experiences with providing CUS for terminally ill patients, their medication use, their goals and intentions when providing CUS, and patient and family involvement. Answering options on frequencies were never, rarely, sometimes, often, and always. Questions considering the goal of sedation were not part of the questionnaire in Singapore. The third part of the questionnaire covered physicians' opinions regarding 12 statements about CUS, with the use of 5-point Likert scales from strongly disagree to strongly agree.

#### Review by ethics committee:

The study protocol was approved by ethics committees in Belgium, Germany, the United Kingdom, Japan and Singapore. Approval of the study protocol by an ethics committee was not required according to national policies in Italy and in the Netherlands and therefore not obtained. (25)(26) Ethical approval for the United States respondents was also not obtained because the questionnaire was administered by the Japanese team and this was a minimal risk study involving only healthcare professionals.

#### Data collection and data analyses:

Data were collected between March-December 2019. Data were imported into an SPSS template in each country and merged into a final dataset. Descriptive analyses were performed (i.e., calculating number and percentages per country). Statistical comparisons were not performed due to heterogeneity of respondents in different countries. Percentages were corrected for missing values for those variables that had 5% missing values or less. Responses concerning physicians' medical practices were collapsed

into two categories: 'often' and 'always' vs. others. Responses concerning physicians' opinions were collapsed into two categories: 'agree' and 'strongly agree' vs. others. Results of respondents who returned empty questionnaires, and of respondents who did not fill in any questions on their medical practices or opinions on CUS were excluded from analysis. For the responses of physicians who reported that they had never provided CUS, questions concerning medical practices were excluded from further analysis. Statistical analyses were performed using IBM SPSS Statistics version 25.0.

## Results

A total of 8550 questionnaires were distributed and 2543 were returned. A total of 102 questionnaires where respondents did not fill out any questions about their practices or their experiences were not eligible for further analyses. Because of the low number of participants from the United States (n=29) together with the low response rate (15%), we decided to exclude these results from further analyses, resulting in 2412 eligible questionnaires. The response rates were 13% in the United Kingdom (n=114), 15% in Germany (n=546), 20% in Italy (n=214), 21% in the Netherlands (n=829), 32% in Belgium (n=175), 57% in Singapore (n=21), and 71% in Japan (n=513); 22% overall (N=2412).

By country, the median age of respondents varied between 40-55 years, and median work experience between 16-28 years (Table 1). In line with our recruitment procedures, most German, Italian, Singaporean, and British respondents were palliative care physicians. Most Belgian respondents were general practitioners (56%), and most Dutch respondents were clinical geriatrics / elderly care physicians (27%) or general practitioners (20%). In all countries except for Japan, most respondents considered themselves Christian or non-religious. In Japan most respondents considered themselves as Buddhist or as non-religious. The median number of dying patients for whom respondents were involved in the last 12 months varied from 10 in Belgium up to 100 in the United Kingdom.

Table 2 presents respondents' experiences with the continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life per country. In all countries, most respondents had at least once provided CUS as a means to alleviate severe suffering in the last hours to days of life. The percentages were 82% for Belgian, 95% for German, 99% in Italian, 95% for Japanese, 97% for Dutch, 95% for Singapore, and 94% for British respondents.

In all countries, most respondents indicated that midazolam was the most frequently used medication for sedation, ranging from 91% in the United Kingdom up to 100% in Singapore. Opioids (with the intent to provide sedation) were mentioned by more than 25% of respondents in Belgium, Germany, and Italy. Levomepromazine/chlorpromazine was reported to be used as a sedative by 85% of British respondents, and haloperidol by 47% of Italian respondents. For all countries, 74% or more of the respondents indicated that they usually started low and gradually increased the dosage of the medications until the desired effect was reached. Fewer respondents indicated that they usually started high in order to reach the desired effect rapidly ( 10% in Japan and the United Kingdom; 20-32% in the other countries).

When asked about intention when providing CUS in the last hours to days of life (Figure 1), in all countries nearly all respondents indicated this was often or always to relieve suffering. Between 30% and 49% indicated their intention was often or always to decrease the patient's consciousness (except respondents from the United Kingdom, 9%). Fewer respondents expressed the intention of inducing unconsciousness. Shortening the dying process was rarely mentioned as an intention by respondents in any country, except in Belgium (12%). Table 2 further indicates that most (70-86%) respondents considered the goal of CUS as often/always achieved when the patient was comfortable but not necessarily unconscious. The percentages of the respondents who considered the goal of sedation was to induce unconsciousness was 17%, except for Italy and Belgium (32%).

Figure 2 shows that in all countries most (60-89%) respondents stated that the patient was often/always involved in decision-making. These percentages ranged from 91% to 100% for family involvement.

Figure 3 illustrates respondents' opinions about the acceptability of CUS for patients with varying symptoms and life expectancies per country. In all countries, for patients in the last hours to days of life, more than 87% of respondents considered CUS an acceptable medical practice to alleviate severe physical suffering. This percentage decreased to 45%-88% in case of severe psycho-existential suffering in the absence of physical symptoms. These percentages were lower for patients who were expected to live for at least several weeks. Agreement ranged from 22- 66% in case of physical suffering and from 5-42% in case of psycho-existential suffering in the absence of physical symptoms.

Table 3 presents respondents' agreement with a set of statements. In all countries, more than 60% of respondents agreed that a competent patient with severe suffering has the right to demand CUS in the



last hours to days of life, except for British respondents (41%). Relatively few respondents (17%) thought that CUS in the last hours to days of life shortens the duration of the dying process, except for German respondents (31%). In all countries 10% of the respondents agreed with the statement that CUS in the last hours to days of life is not necessary, as suffering can always be relieved with other measures. Most respondents (more than 70%) indicated that dying during sleep through CUS could be a good death, except for Japanese respondents (31%).

Figure 4 indicates that more than 75% of the Belgian, Dutch, German and Singapore respondents considered routine withdrawal of artificial hydration an acceptable practice for patients with a life expectancy of hours to days; these percentages were lower for Japanese, British and Italian respondents (34-52%). The percentages decreased substantially for patients who were expected to live for at least several weeks.

## **Discussion**

In our questionnaire study we described practices and opinions regarding CUS of physicians in seven countries spanning two continents.

### Strengths and limitations of the study

One of the major strengths of this study was the large number of participating physicians (more than 2400), across seven countries, all experienced in the care of dying patients. Our questionnaire used a clear definition of CUS and underwent pilot testing and modification before being used. However, there were some significant limitations to our study. In the absence of a pre-existing validated questionnaire to ascertain attitudes and practices of CUS we developed a study-specific questionnaire. We developed our study-specific questionnaire based on expert opinion and previous literature.<sup>(11)(19)(20)(21)(22)(23)(24)</sup> The use of a non-validated questionnaire could be considered as a limitation. As a questionnaire based-study we relied on respondents' self-reports about CUS rather than on objective evidence about what practices actually occurred. Despite anonymity, it is possible that respondents did not always actually report their views or practices. Our study had a low response rate in several of the participating countries and a relatively low numbers of participants, particularly in Singapore, the United Kingdom and the United States. Because no data were collected from non-respondents, we were not able to examine factors contributing to this low response rate. Because palliative care is provided by different clinicians across the participating countries, diverse recruitment

strategies were used in different countries and as a result the characteristics of respondents in different countries varied substantially. Another limitation is that the results may not be directly generalizable to other countries that are less resource rich. Lastly, we did not provide a definition of psycho-existential suffering. Because of these limitations, the results of this exploratory study need confirmation in subsequent studies.

#### Analysis and comparison with the literature

There are many ways in which physicians influence the circumstances or timing of a patient's death. A relatively new phenomenon in the ethical discussion on end-of-life decisions is palliative sedation through the continuous use of sedatives (CUS). Often, such a decision is accompanied by the decision to forgo the provision of artificial nutrition and hydration. The combination of these two decisions has made the moral status of CUS the subject of fierce ethical debates and led to a number of conditions being made in guidelines. (22)(27)(28)(29)

Internationally, there are different perspectives towards the acceptability of withholding artificial hydration during CUS. The framework of the European Association for Palliative Care for the use of sedation emphasizes that withholding artificial hydration and providing palliative sedation are two separate decisions at the end of life and that these decisions should be taken and communicated separately.(13) At the same time the British quality standard *Care of dying adults in the last days of life* emphasizes that dehydration can lead to thirst and delirium, and may sometimes result in death, and therefore recommends to continue or to start artificial hydration for terminally ill patients, including those receiving sedation.(30) In our study, there was a consistent view (regardless of country) that withdrawal of hydration/nutrition was more acceptable when the prognosis of the patient is shorter. Furthermore, while guidelines often put limits on life expectancy (13)(27)(28), in Belgium, Germany, Italy and the Netherlands a substantial proportion of respondents (42-66%) considered CUS as an acceptable medical practice to relieve severe physical suffering in patients with a life expectancy of several weeks.

In our study, a substantial proportion of respondents (45%-88%) considered CUS to relieve severe psycho-existential suffering in the absence of physical suffering in the last hours to days of life to be an acceptable practice. These results seem in line with the findings of a systematic review that found that the frequency of continuous deep sedation seemed to have increased over time, possibly partly because

of an extension of indications for sedation, from mainly physical symptoms to include non-physical symptoms as well.(21) In addition, a survey among Canadian palliative care physicians showed also that a third of these respondents provided continuous sedation for existential distress in the absence of physical symptoms.(31) A considerable number of respondents in our study agreed with the statement that a competent patient has the right to demand CUS. A previous study of Robijn et al. showed that in Belgium, the percentage of deaths in which sedation was used on the request of a patient had increased from 10% to 15% between 2007 and 2013.(1) A qualitative study among health care practitioners in Belgium, the Netherlands, and the United Kingdom showed that physicians in the United Kingdom typically discussed the possible use of sedation with patients and their relatives, but that they took the decision themselves, whereas in Belgium, patients more often initiated the conversation and requested the sedation and the role of the physician was more limited to evaluating if medical criteria were met. In the Netherlands, physicians emphasized the making of an "official medical decision", informed by the wish of the patient.(32) This exploratory study suggests several areas where there might be a difference in practice in use of sedatives in the last days, within and between countries. There was a wide range in reported frequency of the use of opioids, levomepromazine/chlorpromazine, and haloperidol for sedation. The appropriateness of these medications as sedative drugs should be further investigated. Also, there were diverse opinions regarding the statement that CUS cannot sufficiently alleviate suffering even when patients become unresponsive. To what degree patients receiving sedatives actually achieve symptom relief is a focus of controversy, and future studies are needed to understand how the effects and potential adverse events of CUS can be measured.(33)(34)(35)

### Conclusions and implications

Insight into the practices and opinions of physicians caring for terminally ill patients regarding CUS is an important first step towards a better understanding of the current practices in the participating countries, and to support an informed debate. In the studied countries, many respondents considered CUS acceptable for the relief of physical suffering in the last days of life. Our finding that for a substantial proportion of respondents CUS is not only considered acceptable for the relief of physical, but also for psycho-existential suffering, and by a somewhat lower proportion of respondents also for patients with a life-expectancy of at least several weeks, seem in line with recent reports that suggest that the indications for the use of CUS may have widened over time, and that CUS may have lost its status as being a treatment of "last resort". Future studies should explore the expectations and experiences in clinical practice of clinicians, patients, and relatives with CUS in different countries. More

research is also needed to better understand how we can assess suffering in patients undergoing CUS, to measure whether CUS is sufficient assurance of comfort to maintain it as a proportional answer to the relief of unbearable suffering of terminally ill patients, and to develop effective interventions to relieve suffering in the most distressed.

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**Table 1. Baseline characteristics of the respondents**

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Country	Belgium		Germany		Italy		Japan		The Netherlands	
	N	%	N	%	N	%	N	%	N	%
<u>No. respondents</u>	175		546		214		513		829	
<u>Age (years)</u>										
Median	48		53		52		55		47	
<u>Work experience as physician (years)</u>										
Median	20		25		21		28		19	
<u>Gender</u>										
Female	114	65	275	51	106	50	102	20	416	50
Male	61	35	269	49	108	51	406	80	411	50
<u>Clinical specialty</u>										
Palliative medicine	19	11	273	50	198	93	334	65	0	0
General practice/ Family medicine	98	56	38	7	5	2	23	5	165	20
Internal medicine	6	3	87	16	0	0	18	4	93	11
Radiotherapy	1	1	14	3	0	0	3	1	0	0
Pulmonology	8	5	36	7	0	0	13	3	93	11
Cardiology	1	1	34	6	0	0	1	0	66	8
Anesthesiology	8	5	4	1	2	1	32	6	0	0
Geriatrics	13	7	4	1	5	2	4	1	227	27 <sup>A</sup>
Oncology	14	8	1	0	2	1	21	4	41	5
Neurology	4	2	1	0	0	0	0	0	69	8
Surgery	1	1	1	0	0	0	39	8	2	0
Other	2	1	53	10	2	1	24	5	71	9
<u>Institution (multiple options possible)</u>										
Hospital	63	36	297	54	21	10	399	78	443	53
Nursing home/Elderly care facility	26	15	29	5	5	2	18	4	192	23
Inpatient hospice	0	0	47	9	99	46	158	31	33	4
Community palliative care services	32	18	216	40	85	40	6	1	0	0
Home practice/ Family practice	106	61	121	22	2	1	86	17	168	20
Other	3	2	53	10	2	1	7	1	43	5
<u>Religion</u>										
Christianity	96	55	411	76	162	76	47	9	353	43
Islam	0	0	4	1	2	1	0	0	9	1
Buddhism	0	0	3	1	4	2	137	27	3	0
Judaism	0	0	0	0	0	0	0	0	4	1
No religion	77	44	117	22	46	22	304	61	443	54
Other	2	1	8	2	0	0	14	3	14	2
<u>Number of patients in whose dying process the physician was involved in the past 12 months<sup>A</sup></u>										
Median	10		80		95		50		13	

A. In the Netherlands these physicians were clinical geriatrics and elderly care physicians

B. Physicians who stated that they had ever provided continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life.

**Table 2. Physicians' experiences with the continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life (percentages indicate physicians' agreement with statement about the continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life (percentages indicate strongly agreed with the statement))**

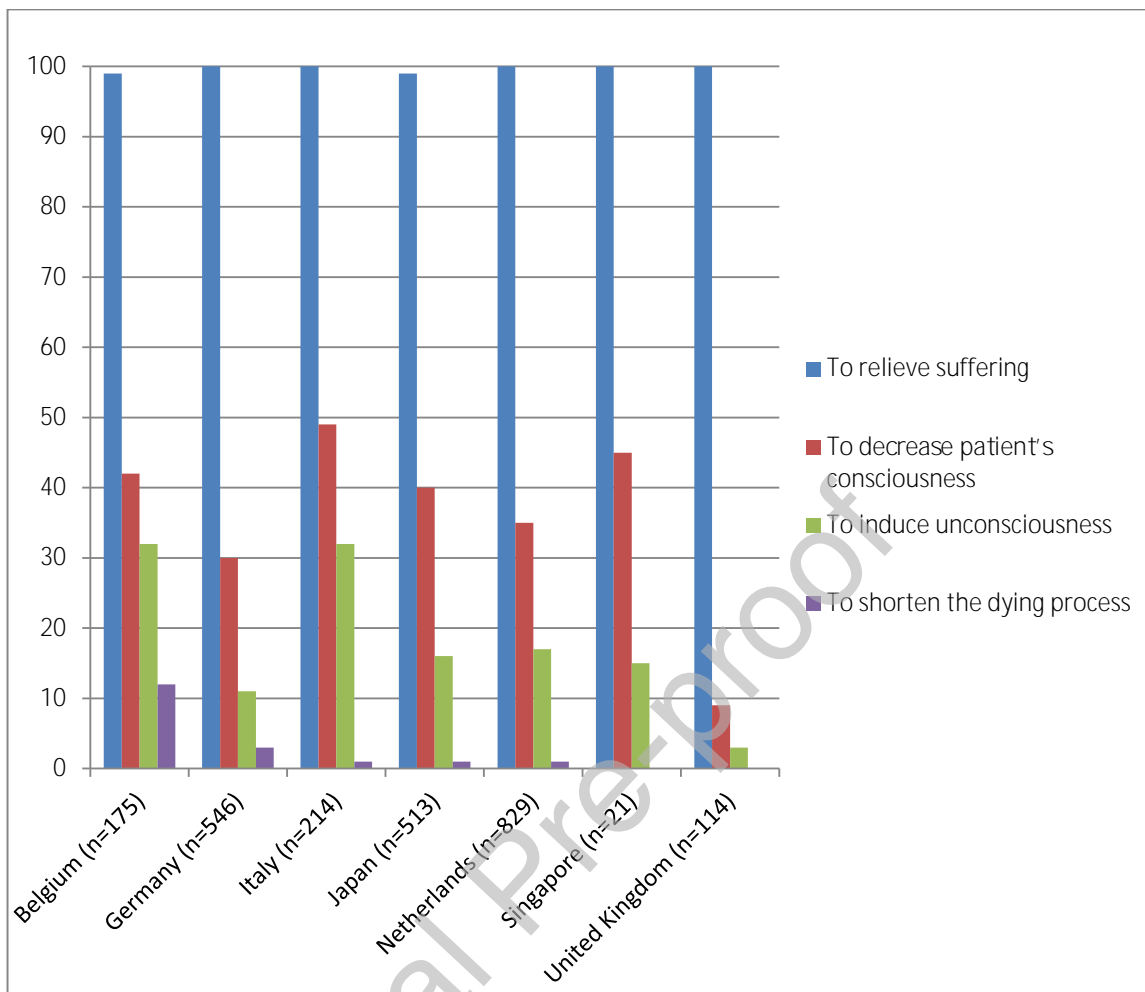
Country	Belgium		Germany		Italy		Japan		Netherlands		Singapore		United Kingdom		Singapore	UK
	N	%	N	%	N	%	N	%	N	%	N	%	N	%		
No. respondents <sup>A</sup>	143		519		212		487		809		20		107		N	%
Number of patients who were provided with the continuous use of sedatives as a means to relieve suffering in the last hours to days of life in the last 12 months <sup>B</sup>			175		546		214		513				829		21	
None	15	11	47	9	2	1	58	12	89	11	1	5	11	11		
1-5 patients	82	58	207	40	21	10	220	45	358	45	12	60	27	26		
6-10 patients	17	12	101	20	31	15	103	21	172	22	5	25	17	17		
>10 patients	28	20	157	31	158	75	106	22	174	22	2	10	48	47		
Medication used for the continuous use of sedatives (multiple options possible) <sup>B</sup>																
Midazolam	132	94	490	94	200	94	466	95	781	98	20	100	97	97		
Propofol	8	6	58	11	2	1	9	2	26	3	2	11	1	1		
Haloperidol	15	11	60	12	99	47	78	16	51	6	0	0	24	24		
Barbiturates	8	6	21	4	9	4	65	13	7	1	0	0	19	19		
Levopromazine/Chlorpromazine	8	6	124	24	56	26	34	7	58	7	8	44	85	85		
Opioids (with the intent to provide sedation)	37	27	285	55	91	43	82	17	127	16	1	6	6	6		
Other	13	9	61	12	11	5	24	5	18	2	0	0	3	3		
Dosage of medication <sup>B</sup>																
I start low and gradually increase the dosage of the medications until the desired effect is reached	102	75	396	81	167	79	427	88	568	74	17	85	92	93		
I start sufficiently high in order to reach the desired effect rapidly	35	26	102	21	42	20	48	10	235	32	4	21	2	2		
The goal of the continuous use of sedatives is achieved <sup>B</sup>																
When the patient is comfortable (but not necessarily unconsciousness)	108	79	354	70	175	83	411	84	673	86	NA	NA	78	79		
When the patient is unconsciousness	98	72	208	41	144	69	126	27	419	54	NA	NA	22	22		

- A. Physicians who stated that they had ever provided continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life.
- B. Physicians that answered the statement with often or always

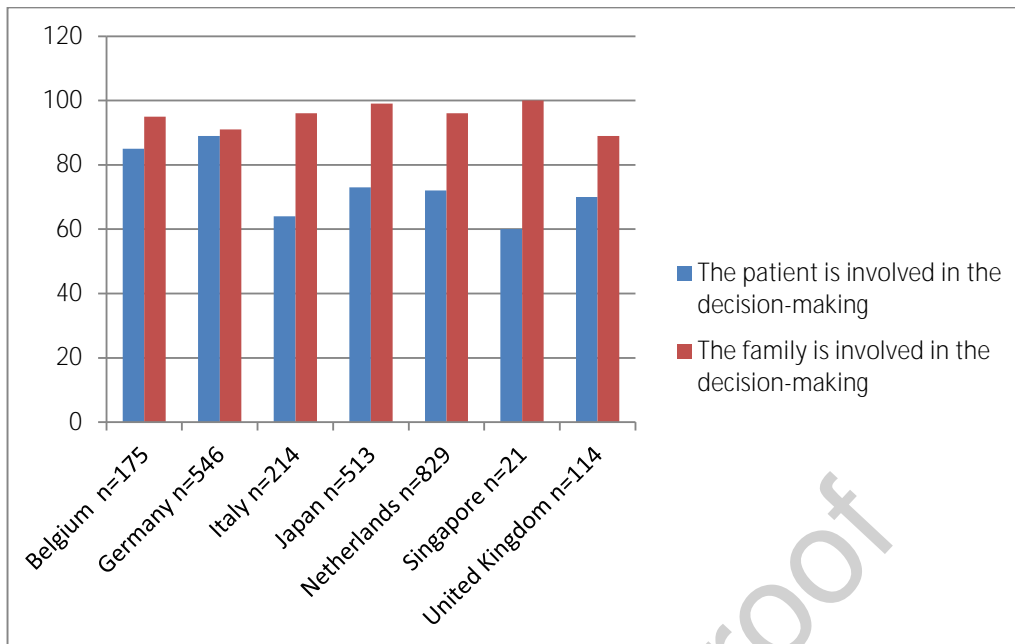


a competent patient with severe suffering has the continuous use of sedatives in the last hours to	147	89	454	83	201	94	485	95	747	91	12	60	4
us use of sedatives as a means to alleviate severe last hours to days of life is not necessary, as suffering relieved with other measures.	7	4	14	3	10	5	40	8	22	3	2	10	8
us use of sedatives in the last hours to days of life ation of the dying process.	25	15	167	31	8	4	41	8	141	17	1	5	4
inical practice the continuous use of sedatives in the s of life can be difficult to distinguish from euthanasia.	28	17	99	18	11	5	114	22	63	8	0	0	1
us use of sedatives in the last hours to days of life ly alleviate suffering in all patients, even when unresponsive.	41	25	331	61	88	41	257	50	288	35	8	40	4
leep through the continuous use of sedatives can be a	143	87	487	90	174	81	157	31	758	92	14	70	7

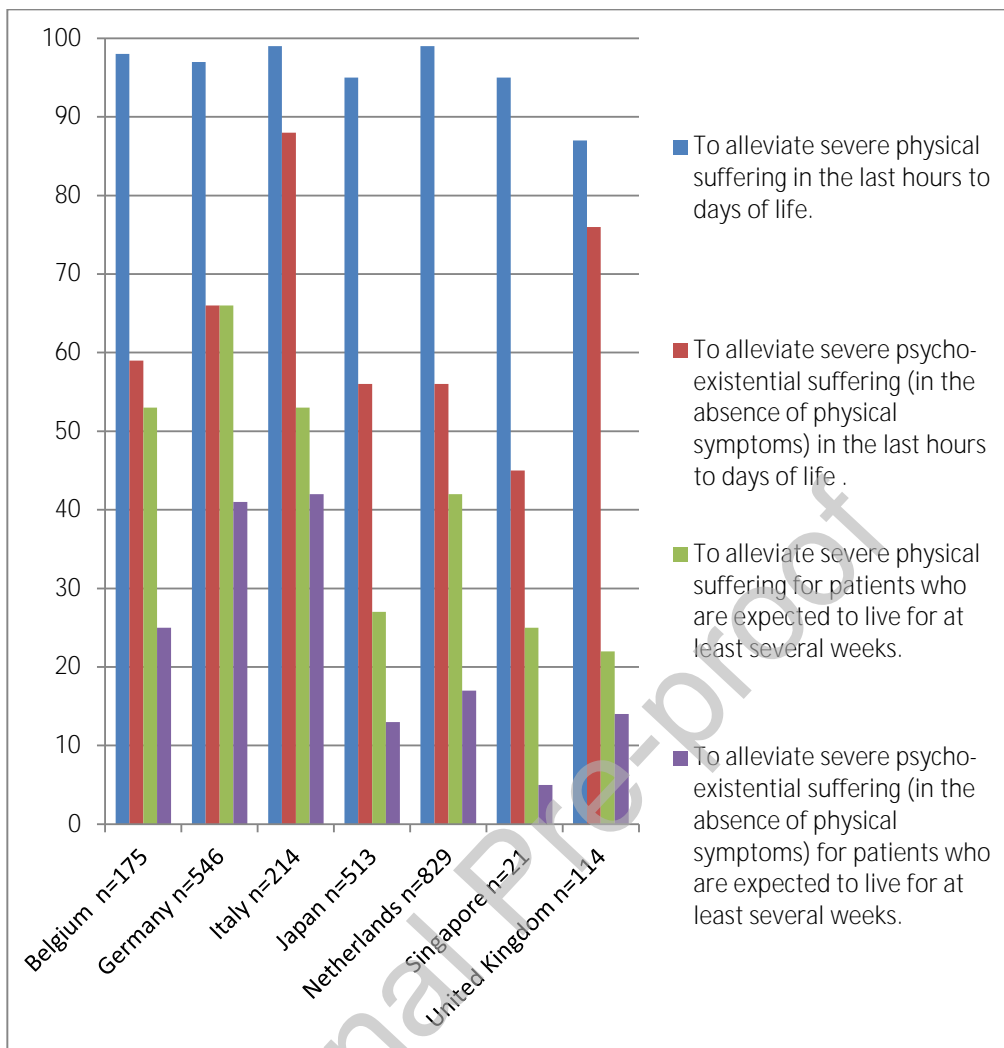
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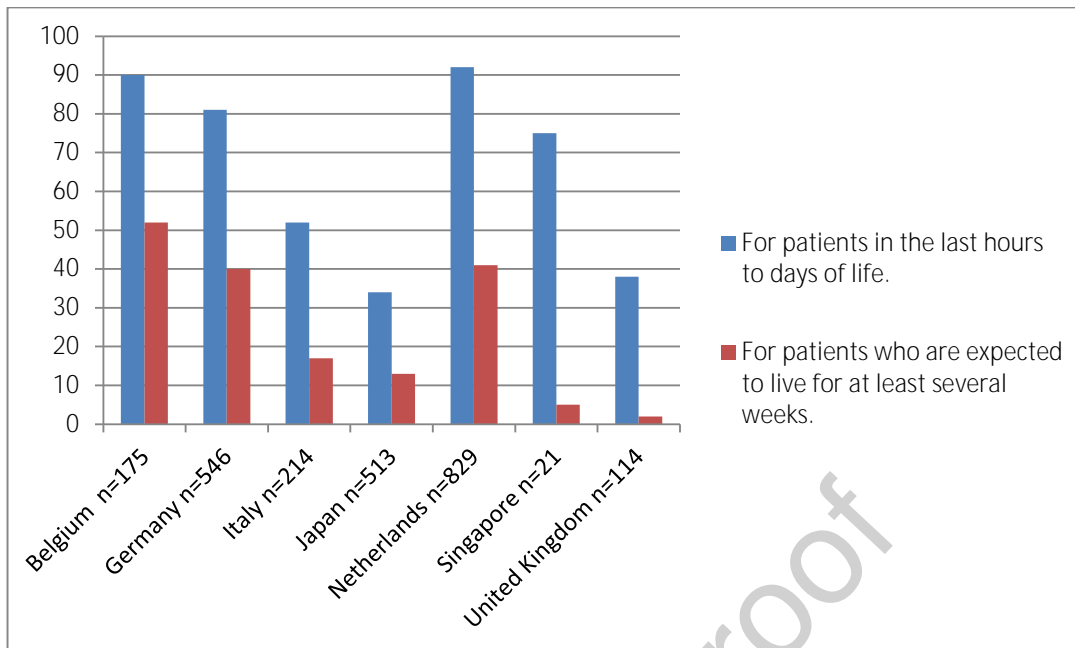
**Figure 1. Percentages of physicians who answered often or always the indicated answer to the statements "What is your intention when you provide the continuous use of sedatives in the last hours to days of life"**



**Figure 2. Percentages of physicians who often or always involved patients or families in the decision-making when providing the continuous use of sedatives as a means to alleviate severe suffering in the last hours to days of life**



**Figure 3. Percentages of physicians who (strongly) agreed with the statement that they would consider the continuous sedation use of sedatives as an acceptable medical practice in the respective situation.**



**Figure 4. Percentages of physicians who (strongly) agreed with the statement that they would consider routine withdrawal of artificial hydration while providing the continuous use of sedatives to alleviate suffering as an acceptable medical practice, in the respective situation.**