CONTINUOUS SEDATION UNTIL DEATH

Experiences of health care professionals
in Belgium, the Netherlands and the United Kingdom

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CONTINUE SEDATIE TOT AAN HET LEVENSEINDE

Ervaringen van zorgverleners in België, Nederland en het Verenigd Koninkrijk

Doctoral dissertation

Proefschrift

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Department of Family Medicine
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Voor papa, overleden na een jarenlange strijd tegen kanker

Voor mama, omdat zij al die jaren voor hem gezorgd heeft

en hem een waardig levenseinde gegeven heeft

Different stars (Trespassers William)

From the movie: A Love Song for Bobby Long

So you'd sing a lullaby to get me to sleep
So it's no surprise my eyes are never heavy
For I've not seen you in the flesh for so long
That I'm not sure we would know each other at all

Oh the weight it must be light wherever you are
And I know you don't think twice wherever you are

So I will hum alone, too far from you
All that I say now is nothing to you
We will lie under different stars
I am where I am and you're where you are

Oh the weight it must be light wherever you are
And I know you don't think twice wherever you are
And I'd ask if you're all right wherever you are
And do you think of me, you might, wherever you are

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Chapters 1-7 are based on the following publications or manuscripts:

Chapter 1 – Anquinet L, Rietjens JAC, Van den Block L, Bossuyt N, Deliens L. General practitioners' report of continuous deep sedation until death for patients dying at home: a descriptive study from Belgium. Eur J Gen Pract 2011;17:5-13.

Chapter 2 – Anquinet L, Rietjens JAC, Vandervoort A, van der Steen JT, Vander Stichele R, Deliens L, Van den Block L. Continuous deep sedation until death in nursing home residents with dementia: a case series. J Am Geriatr Soc 2013;61:1768-1776.

Chapter 3 – Raus K, Anquinet L, Rietjens J, Deliens L, Mortier F, Sterckx S. Factors that facilitate or constrain the use of continuous sedation at the end of life by physicians and nurses in Belgium: results from a focus group study. J Med Ethics 2012 (in press).

Chapter 4 – Anquinet L, Raus K, Sterckx S, Smets T, Deliens L, Rietjens JAC. Similarities and differences between continuous sedation until death and euthanasia – professional caregivers' attitudes and experiences: a focus group study. Palliat Med 2013;27:553-561.

Chapter 5 – Anquinet L, Rietjens JAC, Seale C, Seymour J, Deliens L, van der Heide A. The practice of continuous deep sedation until death in Flanders (Belgium), the Netherlands and the U.K.: a comparative study. J Pain Symptom Manage 2012;44:33-43.

Chapter 6 – Anquinet L, Rietjens JAC, Mathers N, Seymour J, van der Heide A, Deliens L, on behalf of UNBIASED. Descriptions of general practitioners and nurses of their collaboration in continuous sedation until death at home. In-depth qualitative interviews in three European countries (submitted).

Chapter 7 – Anquinet L, Rietjens JAC, van der Heide A, Bruinsma S, Janssens R, Deliens L, Addington-Hall J, Smithson WH, Seymour J, on behalf of UNBIASED. Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life (submitted).

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Part I

Introduction

CONTINUOUS SEDATION UNTIL DEATH: AN INTRODUCTION

Death and dying are phenomena that have intrigued and frightened many throughout history. Nonetheless, death is a certainty that is shared by all people worldwide. Where, when and how someone dies however differs considerably. Unlike a century ago where most people died of acute infectious diseases, modern dying is more prolonged with chronic, progressive and degenerative illnesses such as cancer and cardiovascular disease as the leading causes of death in the world nowadays (1). Currently, approximately 70% of all deaths happen 'non-suddenly and expectedly' after a more protracted dying trajectory involving some end-of-life care (2;3). End-of-life care involves for almost one in two patients a medical decision at the end of life that probably or certainly hastens the patient's death (4;5). Medical decisions at the end of life have been hotly discussed in many countries for many years (5). A relatively new practice in the medical, ethical and societal debate on medical decisions at the end of life is 'continuous sedation until death'. Continuous sedation until death is one of the last resort options for terminally ill patients when severe suffering can no longer be relieved by normal medical treatments or palliative care. It may take away the patient's perception of suffering by continuously lowering the patient's consciousness until death by using medication with a sedative effect (6-8). In the following paragraphs, we will go further into detail on the variety of terms and definitions used for continuous sedation until death, the available guidelines and recommendations for its use, what is already known about the practice of continuous sedation until death, and the aims of this dissertation.

Terminology and definition

'Sedation' (9), 'end-of-life sedation' (10), 'controlled sedation' (11), 'sedation for intractable distress of a dying patient' (12) and 'palliative sedation therapy' (13) are some of the ways the practice of sedation at the end of life is referred to. Two terms that are widespread but criticized by some are 'terminal sedation' and 'palliative sedation' (14;15). A critique of both terms concerns the neutrality of the adjective used to describe 'sedation' (14). Terminal sedation on the one hand may have the connotation that sedation is used for a terminally ill patient at the end of life, but might suggest that sedation is used to 'terminate' the patient's life, which is considered not to be the aim (14;16). Palliative sedation on the other hand is often used as an 'umbrella' term for all types of sedation at the end of life, varying in depth (mild to deep) and duration (intermittent to continuous) (6;7). 'Palliative' may have the connotation that this type of sedation is a normal medical practice and part of palliative care (6;7). Yet it is an accepted term that is most frequently used in guidelines and research papers (6-8). However, some say that this term might be used as a 'euphemism', concealing some of the cases in which sedation is being used to hasten the patient's death (14;17).

Other authors go much further by using terms like 'euthanasia in disguise' or 'slow euthanasia', suggesting that sedation inevitably leads to the patient's death, although more slowly (18;19). However, both terms fell out of favour because of their potential to be misinterpreted as causing and intending the patient's death (20).

In line with the range of terms found in the literature, a continuum of narrow to broad definitions has been proposed for this practice. Although there does not exist one clear-cut and universally agreed upon definition, the definitions share common ground, including 'lowering or taking away the patient's consciousness' (17). Narrow definitions may include several normative due care criteria for the use of sedation, focusing on very specific practices (14). These normative definitions may be useful for health care professionals in real life practice because they describe the ideal standard practice of sedation, and affirm how this practice should or ought to be performed in practice. For example, Claessens et al. describe palliative sedation as *'the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve*

one or more refractory symptoms' (15). This definition is however not suited for research aims because it excludes all cases in which the same act (sedation) was performed but deviated from standard directives (14). In order to include all possible options of this practice and to allow separate medical and ethical discussions on the due care criteria for the use of sedation, a broad and descriptive definition should be obtained in research (14;17;21).

In this dissertation, the descriptive and more neutral term 'continuous sedation until death' is used. In some articles, we refer to the most far-reaching and controversial type of sedation, namely continuous *deep* sedation until death. We have defined continuous sedation until death as *'the practice where sedation, that is, the lowering of the patient's consciousness, is administered continuously until the time of death'*.

Guidelines and recommendations

Several local, regional and national sedation guidelines have been developed worldwide to outline the indications and proper performance of sedation at the end of life, to educate physicians, and to improve its quality (22-24). They are usually based on pre-existing guidelines, literature and consensus among (inter)national palliative care experts from different fields, and set standards for best practice and optimal care (6-8;25). The Royal Dutch Medical Association published a nationwide guideline in the Netherlands in 2005 and revised it in 2009 (6). In Belgium in 2010, a guideline was presented by the Federation for Palliative Care Flanders and revised in 2012 (7). The European Association for Palliative Care (EAPC) published in 2009 a framework of recommendations to guide the development of procedural guidelines for the use of sedation in palliative care (8). A summary of the key recommendations of the Belgian, Dutch and EAPC sedation guidelines is presented in Box 1. When referring to '(sedation) guidelines' in the remainder of the Introduction, we refer to these Belgian, Dutch and EAPC sedation guidelines.

Box 1. Key recommendations of the Belgian, Dutch and EAPC sedation guidelines.

Sedation is indicated for patients with (one or more) intractable or 'refractory' symptoms, causing the patient unbearable suffering.
Sedation should only be considered if the patient is in the very terminal stages of his/her illness with a limited life expectancy of hours or days at most.
In case of a patient with decisional capacity, sedation should be discussed with the patient and preferably with the patient's significant family members. If the patient lacks decisional capacity and there is no advance directive, a legally recognized proxy must be consulted by the physician about what the patient would have wanted.
The decision about the administration of artificial food and fluids is independent of the decision about sedation itself. It should be individually decided through comprehensive evaluation of the patient's wishes and the estimated benefits/harms in light of the treatment aim. However, in principle, there is no artificial administration of food and fluids in the case of continuous sedation until death.
Whenever possible, the attending physician must be present at the initiation of sedation.
Midazolam is the drug of choice; the use of morphine as a sedative is advised against. Morphine should only be given or continued (alongside sedatives) to relieve pain and/or dyspnoea.
Sedation should be applied proportionally, that is, the level of sedation (or reduction of consciousness) should be the lowest necessary to provide adequate relief of suffering.
(An) appropriate expert(s) with specialist knowledge (e.g. psychiatrists, anesthetists, pain specialists, oncologists and specialist nurses) should be consulted in good time when a physician has doubts regarding his/her own expertise or has difficulty balancing the different considerations involved in deciding whether to start sedation.
The aim of sedation should be the relief of the patient's suffering and not the hastening of the patient's death.

Two key recommendations, the presence of refractory symptoms and the patient's short life expectancy, deserve some further reflection here and will also be further examined in depth in this dissertation. According to the sedation guidelines, continuous sedation until death is indicated for patients suffering from so-called refractory symptoms. A symptom is or becomes 'refractory' when none of the treatments are effective anymore or are no longer fast-acting enough, and/or come with unacceptable side-effects (6-8). The most common refractory symptoms described in the literature include mainly physical symptoms, such as severe pain, agitated delirium and dyspnoea (6). According to the guidelines, psychological and existential suffering may also be among the reasons for using sedation but this is considered more controversial (15;26). Unlike physical symptoms, it is more difficult to assess whether this type of suffering is truly refractory. There are no well-established assessment tools available to assess its refractory nature and the reporting of psychological and existential suffering is subjective and idiosyncratic (8;27). According to the guidelines however, psychological and existential suffering mainly go together with the patient's poor physical condition and severe physical suffering and are rarely the only indication for sedation (6;7). A survey among Dutch physicians found that depression, existential suffering and anxiety were amongst the indications for sedation mentioned for respectively 30%, 29% and 13% of the patients (28). According to British physicians, intractable psychological suffering was among the reasons for sedation in 25% of sedated patients (29). Little in-depth insight exists however in how physicians deal with this psychological and existential suffering before resorting to the use of continuous sedation until death for terminally ill patients.

Regarding the patient's short life expectancy, sedation guidelines recommend that continuous sedation until death should only be considered if the patient is in his/her last phase of life with a limited life expectancy of hours or days at most (6-8). The patient's limited prognosis has been recommended because sedation guidelines also suggest the withholding or withdrawal of artificial food and fluids in cases in which the patient is no longer able or willing to take food and fluids before the use of sedation (6-8). Sedation guidelines suggest that, by following both recommendations, it will be unlikely that sedation will have a life-shortening effect. This also applies when following the recommendation that sedation should be performed proportionally (the dosages and combinations of medication should be administered in proportion to the patient's symptom burden because a surplus of medication may also possibly have a life-shortening effect), and that the aim of sedation should be the relief of the patient's suffering and not the hastening of the patient's death (6-8). In this way, sedation guidelines distinguish continuous sedation until death from active ending of life, like euthanasia, which is the administration of drugs by someone other than the patient with the explicit intention of ending the patient's life at the patient's explicit request (30).

Current debate and research however, questions whether these differences between continuous sedation until death and euthanasia as demarcated by sedation guidelines are also reflected in medical practice, and thus whether sedation and euthanasia are always mutually exclusive (31). On the one hand, a Dutch study among physicians reporting on their most recent patient who had received terminal sedation and their most recent patient who had received euthanasia clearly found marked differences between the practice of sedation and the practice of euthanasia in clinical practice (31;32). Patients receiving euthanasia had always been actively involved in the decision-making process, whereas this was only the case for about half of the patients receiving sedation. Relatives had in those cases almost always been involved. Patient requests for sedation were more often based on physical and psychological symptoms, whereas a sense of loss of dignity was more often a reason for requesting euthanasia. Barbiturates had almost always been administered in cases of euthanasia, and benzodiazepines in cases of sedation. In cases of euthanasia, the physician had always the explicit intention of hastening the patient's death. This was the case in only a small number of sedation cases. The authors suggested that in most of the cases, sedation and euthanasia are indeed two distinguishable practices (31). On the other hand, that same Dutch study and several other studies showed that there might sometimes be interface or even overlap between both clinical practices, for

instance when sedation is used with the explicit intention of hastening the patient's death or is estimated to have a life-shortening effect (28;33-35). Further studies are however needed to research this issue in more depth.

CONTINUOUS SEDATION UNTIL DEATH IN AN INTERNATIONAL PERSPECTIVE

Continuous sedation until death is used across different countries although with different frequencies (15). Prevalence estimates of the use of palliative sedation range from 2% to 60% (15;36-38). International comparisons of results regarding continuous sedation until death are however difficult due to differences in the terminology and definitions applied, methodology used, patient population and research setting (15;26;39-41). Therefore in 2001, a large-scale cross-national death certificate study was simultaneously set up in six European countries: Belgium, Denmark, Italy, the Netherlands, Sweden and Switzerland, with a similar study design (37;41). Continuous deep sedation until death was practiced in all studied countries and settings, and for patients dying from all kinds of diseases. In all six countries, sedation was more frequently applied in males, patients younger than 80 years, patients with cancer and patients dying in a hospital. Its prevalence ranged from 2.5% (Denmark) to 8.5% (Italy) of all deaths. For Belgium, the Netherlands, Switzerland and Sweden, its prevalence was estimated to be 8.2%, 5.7%, 4.8% and 3.2% respectively (37). A similar variability between the countries in the prevalence of other medical decisions at the end of life (euthanasia, physician-assisted suicide, ending of life without an explicit patient request and non-treatment decisions) was found (41). The authors suggested that the variation in frequencies of these practices may to a large extent have been determined by cultural and legal factors (40;41).

Follow-up research on continuous deep sedation until death using comparable study designs as the European study in 2001 was conducted in, among other places, the Netherlands (2005 and 2010) and in Belgium (2007) and showed an increase in the incidence of sedation. In Belgium, in 2007, its incidence was estimated to be 14.5% of all deaths (33). In the Netherlands in 2005, this was 8.2% and increased to 12.3% in 2010 (34;42). In the United Kingdom, which wasn't included in the European study in 2001, its prevalence was 16.5% in 2008 (43). In-depth cross-national studies that address why sedation is frequently and increasingly being used over countries and years are lacking. As suggested by the European study in 2001, it may be possible that for the practice of continuous sedation until death, true variation exists between the countries, and that cultural, social, organizational and legal factors influence the use, provision and quality of this practice.

Recently, a qualitative interview study was conducted among physicians from the Netherlands and the United States of America which are two countries with different ethical and clinical contexts, and different regulations regarding sedation at the end of life (44). For instance, in the United States of America, there are no guidelines regarding palliative sedation, except for a position statement regarding its use by the National Hospice and Palliative Care Organization published in 2010 (45). The study revealed differences between the respondents from both countries with regard to the way they justified their use of sedation and how openly they discussed it with the patient and the patient's family. The authors attributed these differences to the influence of different ethical and legal frameworks in both countries (44). A quantitative study in Israel, South Africa and Spain in specialized palliative care settings (hospices or palliative care units) found differences between the countries regarding the patient's symptom distress, the intention to use sedation and the use of sedatives, and also related these differences among others to cultural and psychosocial influences (46). Further in-depth understanding on the clinical characteristics of continuous sedation until death, the circumstances in which it is provided and its contribution to the quality of dying across different countries, allowing in-depth insight into country-specific factors, seem to be needed.

CONTINUOUS SEDATION UNTIL DEATH IN BELGIUM, THE NETHERLANDS AND THE UNITED KINGDOM

In this dissertation, we focus on the practice of continuous sedation until death in three European countries, Belgium, the Netherlands and the United Kingdom, within the framework of the UNBIASED study (UK Netherlands Belgium International Sedation Study). Crossing national boundaries to study the practice of sedation in these three countries is highly interesting because of several perceived societal, legal and organizational similarities and differences regarding end-of-life care between the countries. Conducting research within this international research consortium allows us to share and disseminate knowledge on the contentious practice of continuous sedation until death, and to encompass and learn from differences (and similarities) between our studied countries.

All three are northwestern European countries with high palliative care standards (47). According to several studies and rapports, Belgium, the Netherlands and the United Kingdom are classified with the highest scores regarding palliative care development and integration within their health care system (47-50). Their high ranking may be among others due to their relative wealth, good health care system and focus on palliative care development and integration within the system (47;49). Furthermore, they all have a longstanding research tradition in end-of-life care. Interestingly, Belgium and the Netherlands hold a unique position compared to the United Kingdom regarding their law on euthanasia. Euthanasia was legalized in the Netherlands in 2001 and in Belgium in 2002 (51). In the United Kingdom, euthanasia is illegal. A beneficence approach, or 'acting in the patient's best interests', is more dominant in end-of-life care decision-making in the United Kingdom, whereas a greater emphasis exists on patient autonomy in Belgium and the Netherlands (39). In the Netherlands and Belgium, guidelines for the use of sedation have been available since 2005 and 2010 respectively, but not in the United Kingdom (6;7). In the United Kingdom however, several tools have been developed within the National Health System End of Life Care Programme to guide health care professionals in their care for patients at the end of life (52). One of these key tools is the 'Liverpool Care Pathway for the Dying Patient', developed in the 1990s in the United Kingdom (52;53). This framework supports multidisciplinary teamwork and good communication with the patient and the patient's family (52). It provides guidance on different aspects of care required for patients in the last hours or days of life, including the discontinuation of medically futile treatments, the adequate management of common, and sometimes intolerable, end-of-life symptoms, and the anticipatory prescription of medication (52-54).

End-of-life care settings in Belgium, the Netherlands and the United Kingdom can be grouped into two categories: home and inpatient setting. Common inpatient settings in the three countries are the hospital setting, care and nursing homes and (palliative) day centers. In care homes, elderly residents receive basic nursing but are still able to do most of the activities of daily life. Elderly people in nursing homes are often disabled (e.g. residents with progressive dementia) and are dependent from multidisciplinary and complex care and monitoring (55). Hospices are mainly available in the Netherlands and the United Kingdom, and palliative care units in Belgium. Both are specialist residential units for a limited number of terminal patients (50;56). 'Home' is the preferred place where most people in the three countries would want to receive end-of-life care and eventually would want to die if faced with advanced cancer. This is the case for 83% of people in the Netherlands, 72% in Belgium, and 63% in England (57). In the Netherlands, most patients with cancer actually died at home (45%). Patients with cancer in Belgium and England however mostly died in the hospital (61% and 50% respectively; 31% in the Netherlands). In Belgium, 28% of patients with cancer died at home, and in England 22% (58).

In the above mentioned end-of-life care settings, palliative care is provided by different services. However, palliative care is to a large extent organized differently in each country, and different names are sometimes given to more or less similar services (50;59). At home in Belgium, the Netherlands and the United Kingdom, palliative care is primarily the responsibility of the general practitioner (60-62). General palliative care is provided by the home care

team (or 'primary health care team' or 'district nursing team' in the United Kingdom), including the general practitioner and nurses ('community and district nurses' in the United Kingdom). Informal carers and/or volunteers may also be involved (63-65). Multidisciplinary palliative home care teams are involved, on the general practitioner's request to inform, support and advise general home care teams. This team mainly consists of a physician and nurses, but may also include other health care professionals such as a physiotherapist or a psychologist (49). In the Netherlands, health care providers can additionally consult palliative care consultation teams by phone. These multidisciplinary teams consist of health care professionals from different care settings, trained in palliative care (66). Palliative care is also delivered in care homes by the resident's former general practitioner, nurses, family and/or volunteers. There is a difference between the countries regarding palliative care provided in nursing homes, though. In Belgium, nursing home residents are still supervised by their general practitioner, but health care professionals with specialized palliative care training such as the coordinating and advisory physician and the palliative care reference nurse of the nursing home can be involved in the provision of palliative care (67). In the United Kingdom, a similar palliative care structure exists: palliative care is provided by the resident's general practitioner and specially trained staff (50). The nursing homes in the Netherlands however have been suggested to have reached the highest level of development in Northern Europe (50). (Palliative) care is not only provided by nursing staff, but also by well trained medical, paramedical and psychosocial staff (55). Unique is the involvement of nursing home physicians who have completed an officially recognized specialist training program (68). Palliative support teams (sometimes called 'palliative consulting teams or consultants' in the Netherlands and 'hospital specialist palliative care teams' in the United Kingdom), made up of physicians, nurses and paramedics specially trained, are mobile teams in hospitals that provide palliative care to patients on different hospital wards (50;63). Palliative care units and hospices are run by palliative care physicians, nurses, paramedics and volunteers who provide palliative care (50;56).

In the three countries, physicians and nurses have a central role in providing palliative care and continuous sedation until death (35). The final responsibility and decision for the use of continuous sedation until death lies with the physician, after consultation with the (competent) patient and/or the patient's family (6-8). The physician should discuss the medical indications for the use of sedation with the nursing staff and should be present when sedation is initiated so that s/he is able to intervene when necessary (6-8). S/he should make agreements with the nurses regarding the monitoring of continuous sedation until death and should regularly visit the patient during the use of sedation (6-8). As the professionals who see the patient most frequently, nurses also play an important role during the process of sedation (35;69). They usually inform and talk with the patient and the patient's family about continuous sedation until death, they observe the patient's symptoms, they often indicate the use of sedation to the physician and they sometimes initiate and monitor sedation until the patient's death (35;69-71). However, in-depth studies regarding physicians' and nurses' experiences of being involved in the use of continuous sedation until death are lacking.

RESEARCH AIMS

This dissertation will address two central aims: first, to study the practice of continuous sedation until death in Belgium and secondly, to put the practice of continuous sedation until death in an international perspective and compare it with the Netherlands and the United Kingdom. The following research questions will be addressed:

1. What are the characteristics of patients receiving continuous sedation until death and of the decision-making process and its performance in different care settings in Belgium, the Netherlands and the United Kingdom? (Chapters 1, 2, 3, 4, 5 and 7)

2. How does the practice of continuous sedation until death in Belgium relate to the existing international recommendations for the use of sedation? (Chapters 1, 2, 3, 5 and 7)

3. How do general practitioners and nurses describe their collaboration, roles and responsibilities during the process of continuous sedation until death at home in Belgium, the Netherlands and the United Kingdom? (Chapter 6)

4. How is psychological and existential suffering being dealt with before resort to the use of continuous sedation until death and how is use of continuous sedation being decided in Belgium, the Netherlands and the United Kingdom? (Chapter 7)

5. How do physicians and nurses perceive differences and similarities between the practice of continuous sedation until death and the practice of euthanasia in Belgium? (Chapters 1, 2, 4 and 5)

METHODS

Four different studies were used for this dissertation. All studies were retrospective and had a mixed methods design (The SENTI-MELC study), a quantitative design (The Dying Well with Dementia study and The death certificate and questionnaire study) or a qualitative design (The UNBIASED study). Ethical approval was always obtained. In all studies but one (The SENTI-MELC study), we studied data from Flanders, the Dutch-speaking part of Belgium. In The SENTI-MELC study, we also studied data from Brussels and the Walloon provinces in Belgium. As we will discuss the practice of continuous sedation until death from an international perspective in this dissertation, we have adopted the term 'Belgium' instead of 'Flanders' in the following paragraphs.

The SENTI-MELC registration and interview study

The SENTI-MELC study (Sentinel Network study Monitoring End-of-Life Care) was set up in Belgium in 2005 to monitor end-of-life care of different patient groups in different care settings (72). Data were gathered by the Belgian Sentinel Network of General Practitioners, a reliable surveillance system that monitors the health of the entire population on a regular and continuous basis since 1979 (72;73). In 2005, the Network covered 1.75% of the total Belgian population and was representative of all Belgian general practitioners in terms of age, gender and geographical distribution (74). During two years (2005-2006), sentinel general practitioners were asked to report weekly, using a standardized registration form, about all deaths of patients in their practice, aged one year or older at the time of death, and who had died non-suddenly and expectedly as judged by the general practitioner. The study resulted in a representative sample of 1690 non-sudden deaths. The study protocol of the quantitative registration study is published elsewhere (72). Subsequently, general practitioners were invited every two months to participate in a face-to-face interview about the end-of-life care that had been provided to the registered patients that met the above mentioned inclusion criteria and had died at home or in a care home (61;72). In this dissertation, we have studied data of 28 interviews conducted with general practitioners who had reported that the patient had been continuously and deeply sedated until death. We refer to Part II, Chapter 1 for more information on the methodology of this study.

The Dying Well with Dementia Study

A cross-sectional study was conducted in Belgium in 2010 to study the quality of end-of-life care and quality of dying of nursing home residents with dementia. The nursing home administrator screened anonymously for eligible residents who had died in the nursing home or in another setting in a period of three months, meeting the criteria 1) 'category Cdementia' (being completely care dependent for washing, dressing, eating, toileting, continence and transferring and moving, plus being disoriented in time and space), or 2) disorientation in time and space (≥3 or having 'almost daily a problem with disorientation in time and space') from the Belgian Evaluation Scale for Activities of Daily Living (BESADL, adapted Katz scale) (75;76). Further, the general practitioner or a nurse must have indicated that the resident 'had dementia' or 'was diagnosed with dementia'. The nursing home administrator, the general practitioner, the nurse and the relative most involved in the care for the resident completed a structured questionnaire surveying socio-demographic characteristics, health status, clinical complications and quality of dying. The health care professionals received the questionnaire accompanied by an information letter at most three months after the resident's death. Relatives received the letter and questionnaire at the earliest two weeks after the resident's death. 205 deceased residents with dementia from a representative sample of 69 nursing homes meeting the inclusion criteria were identified. The study protocol of this study has not been published yet. In this dissertation, we have studied general practitioner questionnaires supplemented with data from the nurse and relative questionnaires of 11 residents who had been kept in deep sedation or sleep continuously until death according to the general practitioner. We refer to Part II, Chapter 2 for more information on the methodology of this study.

The death certificate and questionnaire study

Surveys on end-of-life decisions were conducted in Belgium in 2007 and the Netherlands in 2005. In both countries, stratified at random samples of death certificates of Belgian and Dutch residents aged one year or older at the time of death were drawn. This resulted in representative samples of 3623 and 5239 death certificates in respectively Belgium and the Netherlands. For each sampled death, the attending physician was sent a questionnaire. The death certificate method could not be used in the United Kingdom because of privacy legislation (77); there, a random sample of medical practitioners with different specialties was drawn in 2007-2008 from Binley's database (www.binleys.com), a regularly updated national database describing the medical workforce (43). This resulted in a representative sample of 2842 physicians. Each was sent a questionnaire about their last patient to die in the last year. In all countries, the questionnaire contained structured questions about the end-of-life decision-making process in the case concerned (78). The methods of the studies are described elsewhere (43;78;79). In this dissertation, we studied the physician questionnaires of patients who had been continuously and deeply sedated until death. The three databases were merged and data was weighted so that comparison between the countries was possible. We refer to Part II, Chapter 5 for more information on the methodology of this study.

The UNBIASED study

The UNBIASED study (UK Netherlands Belgium International Sedation Study) was conducted in Belgium, the Netherlands and the United Kingdom to explore medical practitioners' and relatives' experiences with and perceptions of continuous sedation until death. The UNBIASED study consisted of an exploratory phase in 2010-

2011, to set the following case study phase in 2011-2012 into a broader context of understanding. The study protocol is available elsewhere (80).

The exploratory phase included focus groups with health care professionals in Belgium. Two focus groups with physicians and two with nurses were held to gain insight into the attitudes and experiences of professional caregivers from different care settings (home and hospital: oncology ward and palliative care unit/palliative support team) regarding continuous sedation in end-of-life care. In all, four to nine participants who had been involved in the use of continuous sedation until death took part in each focus group. In total, eight physicians and 13 nurses took part in the focus groups. A topic guide and three vignettes were used to guide the discussion. We refer to Part II, Chapters 3 and 4 for more information on the methodology of this study.

The case study phase in the three countries took the form of an in-depth retrospective interview study with the physician, nurse and relative most involved in the care for a cancer patient aged over the age of 18 for whom sedating medications were administered continuously until the time of death. Cases were included from three settings to enable maximum variation: home, hospital and specialized palliative care setting (palliative care units in Belgium; hospices in the Netherlands and the United Kingdom). Cases with and without specialist palliative care involvement in hospital and home settings were included. In total, 22 cases were included in the United Kingdom, 27 in Belgium and 35 in the Netherlands, and 57 physicians, 73 nurses and 32 relatives were interviewed. The interviews were semi-structured and supported by the use of a topic guide that had been piloted in the exploratory focus groups. Interviews focused on recollections of the patient's care and the use of continuous sedation until death in particular. In this dissertation, we studied physician and nurse interviews from all countries in the home setting in Chapter 6 (Part III) and physician interviews from all care settings in Chapter 7 (Part III).

Table 1. Overview of parts, chapters and data used.

	PART II – CONTINUOUS SEDATION UNTIL DEATH IN BELGIUM				PART III – CONTINUOUS SEDATION UNTIL DEATH IN BELGIUM, THE NETHERLANDS AND THE UNITED KINGDOM		
STUDY	**Chapter 1**	**Chapter 2**	**Chapter 3**	**Chapter 4**	**Chapter 5**	**Chapter 6**	**Chapter 7**
SENTI-MELC study	2005-2006 Mixed methods Questionnaires and interviews						
Dying Well with Dementia Study		2010 Quantitative Questionnaires					
Death certificate and questionnaire study					BE: 2007; NL: 2005; UK: 2007-2008 Quantitative Death certificate data and questionnaires		
UNBIASED study			2010 Qualitative Focus groups	2010 Qualitative Focus groups		2012 Qualitative Interviews	2012 Qualitative Interviews

OUTLINE OF THIS DOCTORAL DISSERTATION

Following this introduction (Part I), Part II is concerned with the study of the practice of continuous sedation until death in Belgium. The characteristics of patients receiving continuous sedation until death, the decision-making process and the performance of sedation for patients who died at home are described in Chapter 1, and for residents with dementia who died in nursing homes in Chapter 2. Chapter 3 reports on physicians' and nurses' perceptions of factors that could facilitate and constrain their decision to use continuous sedation until death. Chapter 4 sheds light on physicians' and nurses' perception of similarities and differences between the practice of continuous sedation until death and the practice of euthanasia.

Part III deals with the practice of continuous sedation until death in Belgium, the Netherlands and the United Kingdom. Chapter 5 describes the characteristics of patients receiving continuous sedation until death, the decision-making process and its performance in different care settings in the three countries. Chapter 6 examines how general practitioners and nurses describe their collaboration, roles and responsibilities during the process of continuous sedation until death at home, and Chapter 7 examines how physicians deal with psychological and existential suffering before resorting to the use of continuous sedation until death, and how the use of sedation is decided upon. Differences between Belgium, the Netherlands and the United Kingdom are studied in Chapter 5, Chapter 6 and Chapter 7.

Part IV consists of reflections on the (methodological) strengths and weaknesses of the study designs, a general summary and discussion of the main findings, and recommendations for future research and implications for health practice.

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Part II

Continuous sedation until death in Belgium

Chapter 1

General practitioners' report of continuous deep sedation until death for patients dying at home: a descriptive study from Belgium

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ABSTRACT

Background

Palliative sedation is increasingly used at the end-of-life by general practitioners (GPs).

Objectives

To study the characteristics of one type of palliative sedation, 'continuous deep sedation until death', for patients dying at home in Belgium.

Methods

SENTI-MELC, a large-scale mortality follow-back study of a representative surveillance network of Belgian GPs was conducted in 2005-2006. Out of 415 non-sudden home deaths registered, we identified all 31 cases of continuous deep sedation until death as reported by the GPs. GPs were interviewed face-to-face about patient characteristics, the decision-making process and characteristics of each case.

Results

Twenty-eight interviews were conducted (response rate 28/31). Nineteen patients had cancer. Nineteen patients suffered persistently and unbearably. Pain was the main indication for continuous deep sedation (15 cases). In six cases, the patient was competent but was not involved in decision making. Relatives and care providers were involved in 23 cases and 18 cases, respectively. Benzodiazepines were used in 21 cases. During sedation, 11/28 of patients awoke, mostly due to insufficient medication. In 13 cases, the GP partially or explicitly intended to hasten the patient's death.

Conclusion

Continuous deep sedation until death, as practiced by Belgian GPs, is in most cases used for patients with unbearable suffering. Competent patients are not always involved in decision making while in most cases, the patient's family is.

INTRODUCTION

In the last phase of life, patients wish to be comfortable and free from suffering (1). When symptoms remain uncontrollable despite optimal palliative care, palliative sedation, i.e. reducing the patient's consciousness and thus the awareness of suffering, can be used as an option of last resort (2;3). Palliative sedation can vary from mild to deep sedation and can be used intermittently or continuously. The most far-reaching type of palliative sedation is continuous deep sedation until death.

European studies showed that the frequency of continuous deep sedation until death varies between 2.5% of all deaths in 2001-2002 (Denmark) and 16.5% of all deaths in 2007-2008 (United Kingdom) (3;4). In Belgium in 2007, its incidence was estimated to be 14.5% of all deaths (5). This is a striking increase compared with 2001, when 8.2% of all deaths followed the use of continuous deep sedation until death. Studies from the Netherlands also demonstrated a similar increase (6).

The practice of continuous deep sedation until death has become the subject of much medical, ethical and societal debate focusing on the indications for and adequate performance of this practice (7-9). Although in a few countries, nationwide (10;11) or local (12-14) guidelines have been developed for the use of continuous deep sedation, no such guidelines are currently available in Belgium. Recently, the European Association for Palliative Care (EAPC) published a framework of recommendations for the use of sedation in palliative care comparable with earlier published international recommendations (7;15). The bottom-line of these recommendations is that sedation can be considered when the patient is suffering unbearably from refractory symptoms. The disease should be advanced and without prospect of improvement, with death expected within hours or days. When possible, the patient and/or their family should be actively involved in the decision making and benzodiazepines should be the drugs of first choice. The purpose of continuous deep sedation until death should be symptom relief and not the hastening of death.

Although most studies on the use of continuous deep sedation are performed in high care settings like hospitals or palliative care units (3;5;6;16), sedation is also carried out at home by the general practitioner (GP) (6;16-19). This is a care context, with fewer available technological treatments and a stronger focus on the continuity of care, especially with respect to the management of end-of-life care (20). A recent study has shown that the increase in the use of continuous deep sedation was most noticeable in home deaths in Belgium, from 3.7% in 2001 to 9.8% in 2007 (5).

This study aims to achieve more insight into the clinical characteristics of the patient, the decision-making process and the characteristics of continuous deep sedation until death at home, from the perspective of the GPs. We also investigated whether this practice is in conformity with existing recommendations (7;15).

METHODS

Study design

We used data from the mortality follow-back SENTI-MELC study, conducted in 2005-2006 to monitor end-of-life care in general practice in Belgium (21;22). Data were gathered by the Belgian Sentinel Network of General Practitioners, a reliable surveillance system that monitors the health of the entire population. It provides information, representative of all Belgian GPs, and covers 1.75% of the total Belgian population (23). The Ethical Review Board of the Brussels University Hospital of the Vrije Universiteit Brussels approved the protocol of the study (21).

Selection of study subjects

This study focuses on one specific subtype of palliative sedation that is considered to be the most far-reaching subtype, *continuous deep sedation until death*. In the quantitative registration study, GPs reported weekly about all deaths of patients in their practice using a standardized registration form. Out of a total of 2690 registered (sudden and non-sudden) deaths, we identified all deceased patients who 1) were aged one year or older at time of death, 2) died 'non-suddenly and not totally unexpectedly' as judged by the GP, 3) died at home, and 4) were continuously and deeply sedated until death. GPs involved in the cases meeting these inclusion criteria, were selected for an interview study about the end-of-life care they had provided at home. Details of the registration study are published elsewhere (21). Out of a sample of 415 non-sudden home deaths, 272 cases were eligible for the interview study. In 52 cases, no valid interview was held so a quasi-control group of 192 non-sedated patients could be obtained, consisting of all non-sudden home deaths about which a valid interview with the GP could be held.

Interview procedure

The selected GPs were contacted by telephone by an independent party and invited for a face-to-face structured interview. The interviews were face-to-face and structured, quantitative with qualitative elements. They contained mostly closed questions (in which the interviewer could tick boxes), and some open-ended questions for which the interviewer was instructed to literally write down the answer of the GP. Furthermore, the interviewer could note additional information or remarkable statements given by the GP; these comments were often paraphrased by the interviewer.

The interview took place within two months after the patient's death and lasted on average one hour. Three interviews could not be held for methodological reasons: one interview could not be held because the maximum of one interview per GP every two months was reached, one case was identified as a case of continuous deep sedation only after closing the interview period and in the last case, the interviewed GP was not the attending physician in the last week of the patient's life.

Patient anonymity and GP confidentiality were preserved by the use of strict procedures. Before each interview, the interviewers gave the GPs a closed envelope containing patient information, prepared by an independent party, to make sure their answers related to the correct patient. GPs also used anonymous codes to refer to the patient in the registration form so patient names were never identifiable to the interviewers or other research group members. The interviews were not audio taped and in all data files, the identity of the GP was permanently deleted.

Measurements

For this study, we used the information obtained from questions about the patient's clinical characteristics, the decision-making process, the performance and the potential life-shortening effect of the sedation in each interview, from the GPs' perspective. The patient's socio-demographic information was obtained from the registration form. Where possible, quantitative data was supplemented with additional (qualitative) paraphrases from the GPs.

Two researcher (L.A. and J.A.C.R.) then compared this information with five key recommendations made in different guidelines on palliative sedation (7;15), i.e. 1) whether the situation was medically hopeless, 2) whether the suffering

was unbearable and persistent, 3) whether there was active involvement in the decision making of patient and/or family, 4) whether benzodiazepines were used, and 5) whether there was an intention to hasten death.

Outcomes and statistical analysis

All closed-ended questions were analyzed using SPSS 17.0 and described in tables. X^2-tests, Fisher's Exact tests and Mann-Whitney *U*-tests were used to identify differences between sedated and non-sedated patients. For the variable 'treatment goal', when there were multiple answers, we classified the additional goal under the main goal. The main goal of treatment always focused on the most 'curative' treatment. So 'cure and life-prolonging' was recoded into 'cure' and 'life-prolonging and comfort/palliation' into 'life-prolonging'.

Answers to the open-ended questions and the additional paraphrases of GPs remarks were entered in Excel and were possible, coded into relevant categories by two researchers, (L.A. and J.A.C.R.). The tables were then scrutinized to identify results that could be further explained and strengthened by the paraphrases. Wherever information was available, two researchers selected appropriate paraphrases (L.A. and J.A.C.R.).

RESULTS

Study population characteristics

220 registered non-sudden home deaths were included in the interview study. In respect of the 31 cases of continuous deep sedation until death at home, 28 interviews were held (response rate 28/31).

Sixteen of all patients who were sedated continuously and deeply until death were men. Twenty-one patients were aged <80 years. Nineteen had cancer, two had a cardiovascular disease, two had a pulmonary disease, two had a nervous system disease and three patients had another disease. Thirteen patients had been ill for more than six months, 24 had been diagnosed more than six months before death. The most frequently reported physical symptoms distressing the patient to a large extent in his/her last week of life were lack of energy (n=11) and pain (n=11). As for psychological symptoms, these were sadness (n=13), worrying (n=10) and agitation (n=10).

Compared with non-sedated patients (n=192), sedated patients were more often younger than 65 years, had been ill for less than one month, were less distressed by lack of energy, and were more distressed by pain (*P*-values <0.05).

Symptoms and prognosis

In all 28 cases in which the GP decided to sedate the patient, the GP judged that there was no chance of improvement of the patient's medical situation. GPs considered the suffering of the patient to be persistent and unbearable in 19 cases. Of the nine remaining patients, six patients suffered 'quite a lot' to 'very much' from a combination of physical and psychological symptoms such as pain, dry mouth, lack of energy, difficulty breathing, drowsiness, feeling sad, worrying and feeling nervous in their last week of life. In the three other cases, the physical and psychological symptoms were less present.

The number of patients receiving treatment aimed at comfort/palliation increased when they were nearing death: from nine patients two to three months before death to 27 patients in the last week of life.

Decision-making process

In two cases, data on the decision-making process were missing (Figure 1). The decision to sedate the patient deeply was discussed with the patient in 12/26 cases and in 23 cases with the patient's relatives (Figure 1). Ten patients had requested continuous deep sedation according to the GP. In 16 cases, there was an explicit request by the patient's relatives e.g.: case 8: 'the family asked to calm the patient down'.

In six cases, the patient was competent, but not involved in the decision-making process. There was discussion with relatives in all but one of these cases. Reasons for not discussing the decision to sedate with a competent patient were in three cases that the physician thought that it was better for the patient not to discuss, e.g. case 13: 'the patient did not realize that the end was near, it was not easy for the patient to reconcile himself/herself to the situation'; that there was no explicit request from the patient, that the patient preferred to leave the decisions up to the physician, that the patient's wishes had been clear for years and that the physician had to react quickly to the distress of the patient.

Physicians discussed the decision to sedate the patient in two cases with a colleague physician, in 15 with a nurse and in one case with both. Pain was the most frequently reported indication for continuous deep sedation (n=15) (Table 1), e.g. case 3: 'the pain was unmanageable'.

Performance and evaluation of continuous deep sedation

Continuous deep sedation was induced in 21 of the 28 cases with benzodiazepines. In eight cases, artificial nutrition and/or hydration were administered during sedation. The most frequently reported reason for limited administration of nutrition and/or hydration was patient comfort (n=5), e.g. case 8: 'to avoid a dry mouth'.

During continuous deep sedation, 11 out of 28 patients woke up, mostly due to insufficient medication (n=8) or to communicate with the family (n=3). Other explanations were 'to administer food and fluid' (case 4) and that the family did not want a deep sedation (case 8).

According to the GP's appraisal, seven patients did not die a (very) gentle death: 'it was a painful struggle; the patient could not really be sedated deeply, woke up and had oxygen deficiency' (case 1). The patients who did not die a gentle death suffered more frequently persistently and unbearably, had a higher likelihood to wake up after the onset of the sedation, had less often discussed the use of sedation with the GP, and had less often a wish for euthanasia than patients who died a gentle death. However, these differences are not statistically significant.

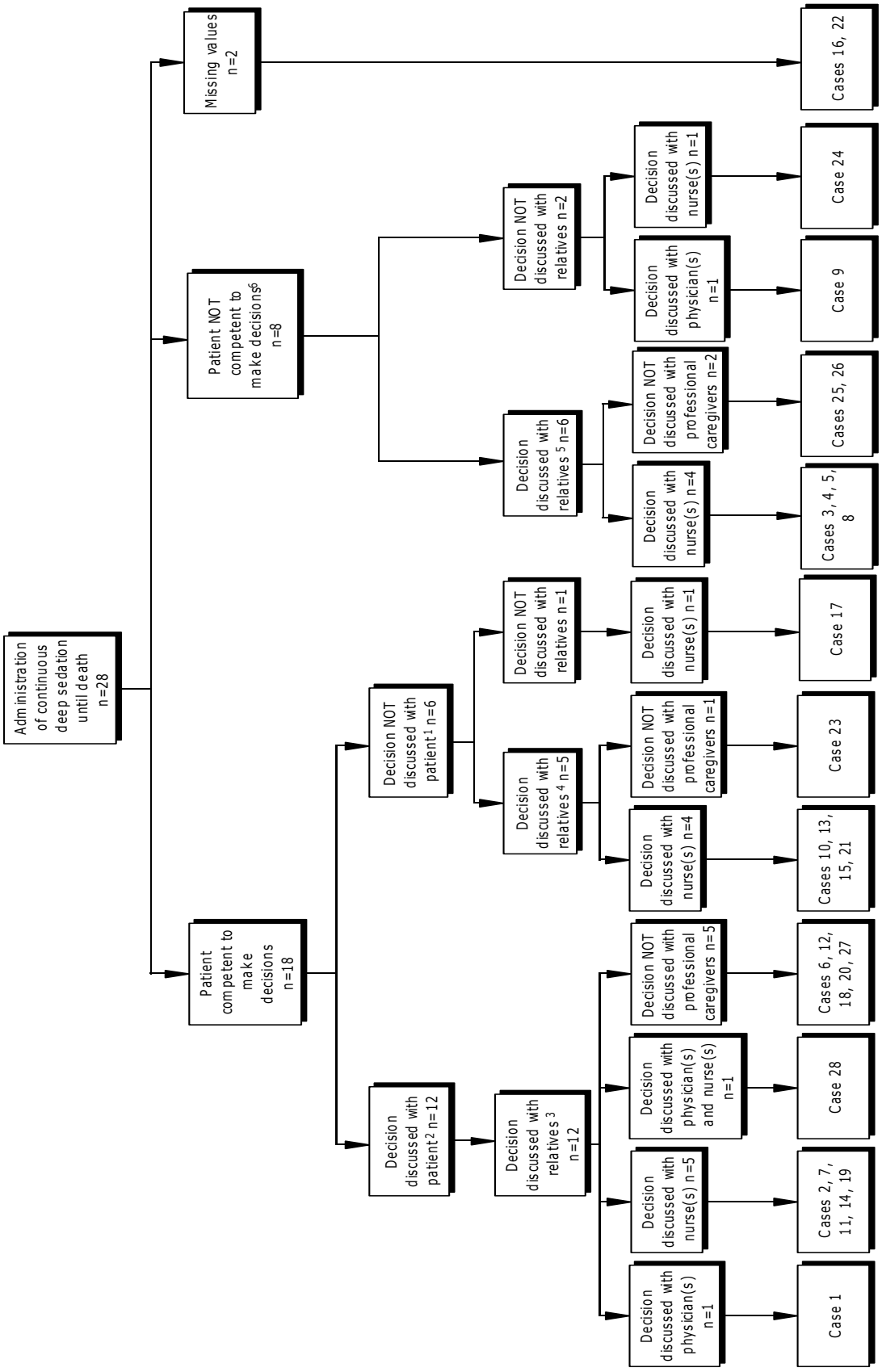

Figure 1. Continuous deep sedation until death: the decision-making process (n=28). [1] Reason(s) for not discussing: the proposed act was obviously the best for the patient (n=2), discussion would have done more harm than good (n = 1), other (n=8). [2] Request for continuous deep sedation until death from the patient: n=10. [3] Request for continuous deep sedation until death from the patient's relatives: n=7. [4] Request for continuous deep sedation until death from the patient's relatives: n=4. [5] Request for continuous deep sedation until death from the patient's relatives: n=4. [6] Reason(s) for not discussing: patient was incompetent (n=2), patient was unconscious or subcomatose (n=4), patient had dementia (n=3).

Table 1. Characteristics of continuous deep sedation until death.

	n=28	%
Indications for continuous deep sedation until death*		
Pain	15	54
Agitation	7	25
Dyspnea	4	14
Other†	13	46
Types of drugs used for inducing continuous deep sedation until death		
Benzodiazepines only	9	32
Benzodiazepines in combination with opioids and/or other drugs	12	43
Opioids only	4	14
Opioids and other drugs (excl. opioids)	3	11
Administration of artificial nutrition or hydration during continuous deep sedation until death		
Limited amount of artificial nutrition and/or hydration‡	8	29
No artificial nutrition and hydration	20	71
Duration of continuous deep sedation until death		
0-24 hours	13	46
1-7 days	13	46
>1 week	1	4
Unknown	1	4
Patient woke up during continuous deep sedation until death		
Yes	11	39
No	17	61
Reason(s) for waking up*		
Insufficient effect of medications	7	25
Possibility of contact with family	4	14
Other	3	11
Physicians' appraisal of patient's quality of dying		
(Very) gentle death	20	71
Neutral	1	4
Not (very) gentle death	7	25

* Multiple answers possible.

† Other reported indications for deep sedation are: fear (of pain or death) n=3 (11), (nocturnal) restlessness n=2 (7), conventional treatment/preventive n=1 (4), epilepsy n=1 (4), existential reasons n=1 (4), hopeless situation n=1 (4), to do something n=1 (4), nervousness n=1 (4), patient was already somnolent n=1 (4).

‡ Purpose of limited administration of nutrition and/or hydration n=7 (25)*: Comfort of the patient n=2 (7), symptom control n=1 (4), infusion n=1 (4), other n=5 (18), unknown n=3 (11).

Patients' wishes for euthanasia and physicians' intentions

Eight patients had previously expressed a wish for euthanasia (Table 2), 'you are going to help me if it does not go well, aren't you? I want life to remain valuable, if not, then I want you to put an end to it' (case 1). In two out of these eight cases, the GP had partly the intention to hasten the patient's death. In three cases, the GP had the explicit intention to shorten the patient's life. Six GPs perceived the use of continuous deep sedation to be similar to euthanasia (n=2) or life-ending without explicit patient request (n=4): 'depending on what is asked each time, you end up in a sort of euthanasia situation. You want it to go well' (case 28).

Table 2. The potential life-shortening effect of continuous deep sedation until death.

	Patient's request for euthanasia		
	All n=28* (%)	**Yes n=8 (%)**	**No n=19 (%)**
Intention of hastening death			
No intention to hasten death	14 (50)	3 (38)	11 (58)
Partly with the intention to hasten death	7 (25)	2 (25)	5 (26)
Explicit intention to hasten death	6 (21)	3 (38)	3 (16)
Use of sedation also perceived as life ending act by GPs†			
Perceived as euthanasia	2 (7)	2 (25)	0
Perceived as ending life without and explicit patient request	4 (14)	0	4 (21)

* Patient's request for euthanasia: n=1 (4) unknown.

† 22 cases (79) were not perceived as life-ending acts.

Comparison with recommendations

Finally, we compared our GPs' practices as found in our study with five key recommendations for the use of continuous deep sedation: 1) the medical situation should be without prospect of improvement, 2) the suffering should be unbearable and persistent, 3) the decision to deep sedation should be discussed with a competent patient or an incompetent patient's family, 4) benzodiazepines should be administered, and 5) the GP should have no intention to hasten the patient's death (7;15). In five cases, the GP acted in accordance with all five recommendations for the use of continuous deep sedation, in nine cases four recommendations were met, in 13 patients, three criteria were met and in one case only two recommendations were met.

DISCUSSION

Summary of main findings

Our study describes the practice of continuous deep sedation until death at home in Belgium in 2005-2006 from the perspective of the general practitioner. For all patients, the medical situation was without prospect and 19/28 patients suffered persistently and unbearably. Six GPs had not consulted a competent patient but 23/26 had consulted the patient's family. Other care-providers were involved in 18/26 cases in the decision making. In three-quarters of the cases, benzodiazepines were used to induce sedation and in eight cases artificial nutrition and/or hydration were administered. Eleven of the 28 patients awoke after the onset of continuous deep sedation. Eight patients had previously expressed a wish for euthanasia. Thirteen out of 28 GPs partially or explicitly intended to hasten the patient's death.

Strengths and limitations of the study

Our study is the first to provide detailed insight into the practice of sedation at home in Belgium. A major strength is the case-specific information obtained from 28 sedation cases, selected from a large representative sample of non-sudden deaths and gathered by a reliable nationwide surveillance network of GPs. The research procedures were of high quality due to quality control measures. Furthermore, anonymity was preserved for the patient and confidentiality

for the GP (22). However, our sample size is small and results have to be interpreted carefully. Possible recall and an interviewer bias could not be excluded entirely, but were limited as much as possible by weekly registrations and interviews within two months of the patient's death.

Indications

In our study, continuous deep sedation was used in 11/28 cases for patients younger than 65 years, which conforms with other studies (6;16;17;24;25). The most frequently mentioned indication for sedation in our study was pain. While this finding is in line with some other studies (8;16;17;19), a review of 17 studies, conducted in several settings, reported that a syndrome of delirium and agitation was the most frequently mentioned indication for sedative use (25). Most GPs have adequate knowledge of pain control for common problems in general practice, but might not always be fully aware of good management techniques for specific cancer pain (26). This may explain to some extent the ongoing presence of pain at the end of life in several of these cases.

In 9/28 cases, the GP considered the suffering of the patient not to be persistent and unbearable. However, suffering is a long-debated and complex concept. A Dutch study found that patients and physicians not always agree on the nature and extent of unbearable suffering (27). Unbearable suffering is considered to be subjective and thus difficult to assess by the physician (28). This points to the need for more research about the concept of suffering in relation to the practice of continuous deep sedation until death.

Decision-making process

While it is generally recommended to include competent patients in the decision making (11;15), six GPs in our study did not discuss the use of sedation with competent patients, only with their family members. GPs gave several reasons why they did so. Some thought that it was better for the patient, others indicated that they thought that the patient preferred to leave the decisions up to the physician, or that they felt that the patient's wishes had been clear for years to the GP. This is in line with studies showing that some physicians think that sharing full information is too heavy a burden for the patient (29) or that not all patients want detailed information about their situation (30). Nevertheless, adequate patient-centred communication entails timely discussion of how and to what extent the patient wishes to be involved in the decision making (31), and it is unclear to what extent the GPs in our study have explored patients' wishes for involvement sufficiently and initiated advance care planning timely. Further research should address this in more detail. Further, in our study, GPs consulted other health care providers in 18/26 cases, possibly because they are less accessible in the home situation (16).

Medication

GPs in our study used benzodiazepines in three-quarters of all cases. It is commonly advised that benzodiazepines should be the drugs of first choice and that using only opioids may be counterproductive (9;25). Our findings are comparable with the literature, although two recent Dutch studies reported higher levels of benzodiazepines (6;18). Although the GPs in our study indicated that they had performed continuous deep sedation until death in all cases, 11/28 patients awoke after the onset of continuous deep sedation, something also found in a study in Japanese

palliative care units (32). In seven cases, this was due to insufficient use of medications, which suggests that GPs' medication policy for the use of sedation could be further enhanced.

Artificial nutrition and hydration

Further, in recommendations, the administration of artificial nutrition and hydration during sedation is not encouraged unless the benefits outweigh the harm (7). In our study, artificial nutrition and hydration was forgone in 20/28 cases (71%). Other studies in home settings report frequencies from 51% (17) to 95% (6); studies in nursing-homes usually report higher frequencies and studies in hospitals lower frequencies (6;17). This points to the need for further evidence regarding the benefits and disadvantages of the administration of artificial nutrition and hydration in patients nearing death.

Continuous deep sedation or euthanasia?

Several recommendations and studies state that continuous deep sedation and euthanasia represent two different clinical practices with different techniques and intentions (7;10;12-15;24). However, our findings suggest that some GPs do not always strictly distinguish between continuous deep sedation and euthanasia and its respective techniques. In 13 cases, the GP indicated to have had a partly or explicit intention to hasten the patient's death. In five of these cases, the patient had requested euthanasia. Other studies mention similar intentions of physicians (5;16;24).

In two cases, the GP perceived the use of continuous deep sedation as euthanasia or in four cases as life-ending without explicit patient request. This shows that for some GPs, there is a lack of clarity about how continuous deep sedation for dying patients and euthanasia are recommended to be used, resulting in a grey zone between the two practices. However, whether GPs use sedation as an alternative to euthanasia as sometimes suggested (33), e.g. because they consider it better care, less distressing to perform or 'easier' to do because it lacks a formal and time-consuming procedure, deserves further study.

Implications for clinical practice and future research

Given the high incidence of continuous deep sedation until death in Belgium and the fact that several GPs did not act in accordance with one or more recommendations, our study showed the need for monitoring the quality of this end-of-life practice, as well as the potential for improvement.

Since the introduction of a nationwide palliative sedation guideline has actually improved the practice of sedation in the Netherlands, implementation of a nationwide guideline in Belgium seems to be advisable (8). Timely communication of the GP with the patient, the patient's family, as well as professional caregivers, might contribute to higher GP awareness of patient's wishes at the end of life. Furthermore, medical training and education about the differences and similarities between the use of sedation and euthanasia in end-of-life care and attention how they should be used in GPs practices seem needed.

In general, further in-depth and international research from multiple perspectives (physicians, nurses and relatives) is needed that adds to our understanding of this practice.

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Chapter 2

Continuous deep sedation until death in nursing home residents with dementia: a case series

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ABSTRACT

Objectives

To describe the characteristics of continuous deep sedation until death and the prior decision-making process among nursing home residents dying with dementia and to evaluate this practice according to features reflecting sedation guideline recommendations.

Design

Epidemiological retrospective study completed with a case series analysis.

Setting

Flemish nursing homes in 2010.

Participants

From a representative sample of 69 nursing homes, all residents who had dementia and had been continuously and deeply sedated until death over a period of three months were selected.

Measurements

Questionnaires to general practitioners (GPs), nurses and relatives most involved in the care of the resident regarding the clinical characteristics of the resident, how sedation was decided upon and performed, quality of care and dying. Advanced dementia was identified using the Global Deterioration and Cognitive Performance Scale. Whether this practice is in conformity with sedation guideline recommendations was also investigated.

Results

Eleven out of 117 deceased residents with dementia (9.4%; 95% confidence interval (CI) = 4.0-14.8) and nine out of 64 residents with advanced dementia (14.1%; 95% CI = 5.3-22.8) were sedated. Two of the 11 sedated residents were not considered to be terminal. Sedation duration ranged from 1 to 8 days. Two received artificial food and fluids during sedation. Five were partly or fully competent at admission and three in the last week. Four had expressed their wishes or had been involved in end-of-life decision making; for eight residents, the GP discussed the resident's wishes with their relatives. Relatives reported that five of the residents had one or more symptoms while dying. Nurses of three residents reported that the dying process was a struggle. For two residents, sedation was effective.

Conclusions

Continuous deep sedation until death for nursing home residents does not always guarantee a dying process free of symptoms and might be amenable to improvement.

INTRODUCTION

People with advanced dementia have been found to suffer substantially from a range of symptoms such as pain, restlessness, difficulties swallowing and anxiety at the end of life (1). When symptoms are uncontrollable and unresponsive to conventional therapies and optimal palliative care, palliative sedation (the deliberate lowering of consciousness) may be administered (2-4). Palliative sedation can vary from mild to deep and can be used intermittently or continuously. The most far-reaching and controversial type of palliative sedation is continuous deep sedation until death (herein referred to as 'sedation') (2;3). The debate about this practice focuses mainly on its indications, appropriate performance and its relationship with life-shortening end-of-life practices such as euthanasia (2;5). Sedation guidelines recommend its use when the individual is experiencing refractory symptoms (2-4). The individual's disease should also be advanced and without prospect of improvement, with death expected within hours or days. Wherever possible, the individual should be actively involved in decision making and give consent for the initiation of sedation. If the individual is no longer capable of expressing his or her wishes, the physician should consult the individual's relative. The purpose of sedation should be symptom relief and not the hastening of death (2-4). Table 1 provides an overview of the main recommendations of the Belgian and Dutch sedation guidelines. Only the Dutch sedation guideline has legal ramifications (6).

In the Flemish region of Belgium, in 2007, sedation was estimated to be used in 14.5% of all deaths. The frequency of sedation in nursing homes was 9.4% in Flanders in 2007 (7), 7.8% in 2007-08 in the United Kingdom (8), and 6.4% in the Netherlands in 2005 (9), but little information is available about the characteristics of this practice in nursing home populations, particularly in individuals with dementia, and whether this practice is performed according to the law of the art. Nevertheless, such knowledge may add to better quality of end of life for the growing number of elderly people with dementia in nursing homes (1). The aim of this study was to describe the clinical characteristics of nursing home residents with dementia in Flanders who are continuously and deeply sedated until death, how sedation was decided upon and performed, and the residents' quality of care and dying. Whether the practice of sedation is in conformity with sedation guideline recommendations is also investigated.

Table 1. Main recommendations of the Belgian and Dutch sedation guidelines.

Continuous sedation is always administered in the final stages of life to patients who are dying and are experiencing unbearable suffering.
Indications for sedation are present when one or more intractable or 'refractory' symptoms are causing the individual unbearable suffering. The physician will have to decide whether a symptom is treatable on the basis of accepted good medical practice, bearing in mind the specific circumstances of an individual in the last stages of life.
The individual's life expectancy should not exceed one to two weeks.
If the patient is capable of making a conscious decision, the individual must agree with sedation; if the individual is no longer competent to make an informed decision, the physician must consult his or her representative.
The attending physician must be present at the initiation of the sedation.
In principle, there is no artificial administration of fluids in the case of continuous sedation.
(An) appropriate expert(s) with specialist knowledge of palliative care should be consulted in good time when a physician has doubts regarding his/her own expertise or has difficulty balancing the different considerations involved in deciding whether to start continuous sedation.
Midazolam is the drug of choice; the use of morphine as a sedative is regarded as counterproductive. Morphine should only be given or continued (alongside sedatives) to relieve pain and dyspnea.
The aim of continuous deep sedation is relieving the individual's suffering and not hastening or postponing death.
Accurate records must be kept of the decision-making process, the way sedation is being administered and the effect of the intervention.
Relatives play an important role when sedation is being considered and while it is being administered. Relatives should be involved in the decision-making process, they can assist in monitoring and caring for the individual, and they should be clearly informed and supported. Furthermore, it is important not only to provide the best possible information and emotional support for

the individual and her family, but also to care for the various professionals involved in the care.

METHODS

Study design and setting

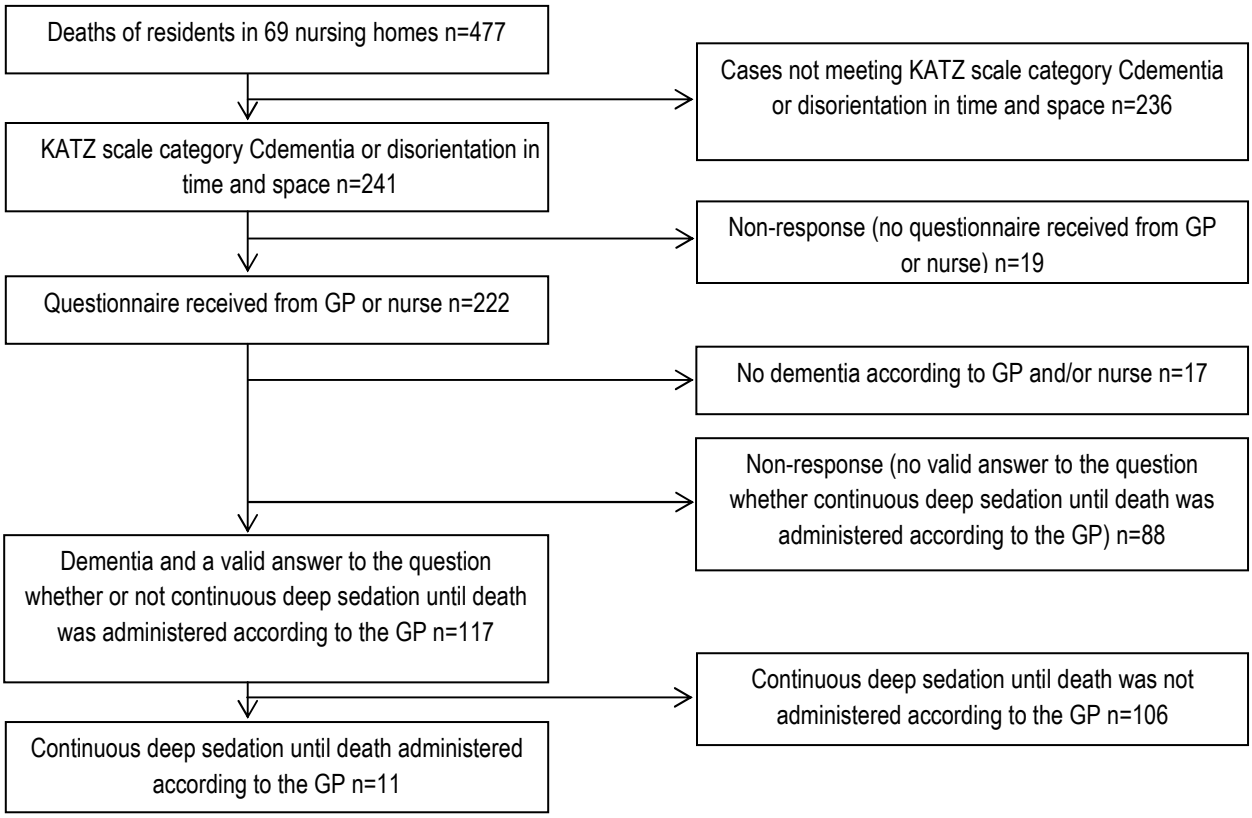
A retrospective cross-sectional study was conducted in 2010 in Flemish (Belgian) nursing homes. The nursing home administrator, the general practitioner (GP), the nurse and the relative most involved in care for the resident completed structured questionnaires.

The goal was to enrol 400 nursing home residents with dementia who lived in one of 80 homes in Flanders and died over a period of three months. For the study to be representative of all nursing homes in Flanders, nursing homes were proportionally and randomly sampled and selected in four strata based on region (five provinces) and then according to bed capacity (≥ or >90 residents) and ownership (public, private nonprofit, private for profit). Other randomly sampled nursing homes replaced institutions that declined to participate to reach the targeted number of nursing homes per stratum; 69 nursing homes (58% response rate) participated.

Study subjects and data collection

The nursing home administrator anonymously listed all residents who had died in the nursing home or in another setting over a period of three months and screened them against inclusion criteria. First, the resident had to meet the criteria for category Cdementia, (being completely dependent for washing, dressing, eating, toileting, continence and transferring and moving, plus being disoriented in time and space), or disorientation in time and space (KATZ scale ≥ 3 or an almost daily problem with disorientation in time and space on a scale from 1 to 4) (10;11). The GP or a nurse must also have indicated that the resident had been diagnosed with dementia. A nursing home administrator identified from the administrative file the resident's GP and the most involved nurse and relative. The GP and the nurse most involved in the care of the resident received an informational letter and a structured questionnaire at most three months after the resident's death and, for relatives, at the earliest two weeks after the resident's death. If the identified nurse was not willing to cooperate, the head nurse filled in the questionnaire. Non-responders (except relatives) received a reminder after three weeks. Response rates were 57.1% for GPs, 88.4% for nurses, 95.0% for nursing home administrators, and 53.0% for relatives; 205 deceased residents with dementia meeting the inclusion criteria were identified (Figure 1). After excluding all cases in which there was no questionnaire from the GP or cases in which the GP had not given a valid answer to the question of whether the resident had been continuously and deeply sedated until death, 117 cases remained.

Figure 1. Flowchart of the selection of nursing home residents dying with dementia who were continuously and deeply sedated until death. GP = general practitioner.



Measurements

Data from the GP questionnaires supplemented with data from the nurse and relative questionnaires were used for this study. The question about sedation, asked to the physician, was: 'Was the individual kept in deep sedation or sleep continuously until death?'. The questionnaires also contained structured and validated instruments, including the Quality of Life in Late-Stage Dementia to assess the resident's quality of dying during the last week of life (12) and the Comfort Assessment in Dying End-Of-Life in Dementia during the last week of life (CAD-EOLD) (13). Items (pain, restlessness, shortness of breath, choking, gurgling, difficulty swallowing, fear, and anxiety) from the CAD-EOLD to describe symptoms that were predominantly present in the last week of life (according to the nurse) and while dying (according to the relative). Fear and anxiety were combined into the symptom fear. Socio-demographic information was obtained from the administrative file. Based on the Cognitive Performance Scale (14) and the Global Deterioration Scale (15) (as scored by the nurse), residents were classified into three groups according to dementia severity one month before death (very severe or advanced dementia, CPS≥5 and GDS=7; severe dementia, CPS≥5 and GDS<7 or CPS<5 and GDS=7; moderate or mild dementia, CPS<5 and GDS<7. The physician questionnaire asked whether the physician 'believed that the individual was (fully, partly or not) competent for decision on preferred medical treatment at any time during admission' and 'during the last week of life'. 'Competent', meant that the individual was capable of expressing his or her wishes. The practice of sedation was evaluated according to five features that reflect sedation guideline recommendations: suffering in the last week of life, life expectancy of less than two weeks, discussion with the resident or his or her relative, withholding or withdrawal of medical and nursing

procedures not strictly necessary during sedation, and effectiveness of sedation. Specific information on the features can be found in the Table 2. Two illustrative case descriptions of residents for whom the practice of sedation followed or did not follow all of the pre-specified features are outlined at the end of the Results section based on the respondents' reported information to show the interplay of variables and to present an overall picture of these practices.

RESULTS

Eleven of 117 deceased nursing home residents with dementia (9.4%; 95% CI = 4.0-14.8) and nine out of 64 residents with advanced dementia (14.1%; 95% CI = 5.3-22.8) were continuously and deeply sedated until death. At the time of death, the 11 residents dying with dementia who had been sedated had a mean age of 82; eight were female. Underlying causes of death were old age (n=4), cancer (n=3), cardiovascular disease (n=1), cerebrovascular disease (n=1) and gastric haemorrhage (n=1) (Table 2). In one case, the cause was missing. Mean length of stay was 2.3 years. Nine residents died in the nursing home, one resident died on a general hospital ward and place of death was missing for one resident.

All eight residents for whom this information was available suffered in the last week of life. According to the nurse, eight of 10 residents for whom symptoms were rated had more than one of the pre-specified symptoms a lot in the last week, most often difficulties swallowing (n=5, resulting in choking for two), fear (n=2), pain (n=2), and restlessness (n=1). Quality-of-life scores in the last week ranged from 22 to 46 (mean 31). Nine of 11 residents had a life expectancy of less than two weeks; these nine residents were considered to be in the terminal phase according to the GP. Sedation was used with varying duration, ranging from one to eight days (mean 3.4 days).

For nine of 11 residents, the feature that the resident or the resident's relative had been involved in decision making was met. According to the GP, five sedated residents were partly or fully competent at admission, three of them in the last week of life. Two of the five residents who were partly or fully competent at admission (three in total) had at some time expressed specific wishes for (or the physician had spoken to them about) possible medical treatments at the end of life. Resident 10 had a written do-not-resuscitate order according to the relative; resident 11 had no written advance directives but do-not-resuscitate; withholding or withdrawal of artificial food, fluids, antibiotics, and other treatments; do-not-intubate; and terminal sedation orders were documented in the resident's medical record according to the GP. Two residents had a written statement of their wishes, asking for the use of sedation or assigning a proxy decision-maker. One resident had both (resident 4), the other resident had the latter (resident 9). For eight residents, the GP had indicated that he or she had discussed the resident's wishes, including the use of sedation, with a relative. Of the remaining three, the wishes of one were known. In two cases, neither the resident nor the resident's relative had been involved in decision making. One of these residents was competent at admission.

During the administration of sedation, two residents received artificial food or fluids; one of these residents was estimated not to be in the terminal phase. In eight of 11 residents, the GP indicated having made a decision to forgo potentially life-prolonging treatments. These non-treatment decisions were, among others, the withholding or withdrawal of food or fluids, antibiotics, and other treatments.

For two of eight residents, sedation was effective. Despite the use of sedation, relatives rated five of eight residents as having one or more symptoms during dying; fear for one; difficulty swallowing for one, and five to seven symptoms, including pain, restlessness, shortness of breath, difficulty swallowing, choking, gurgling, and fear for the

other three. Of eight of the 11 residents that the nurses considered to have died peacefully, relatives had reported one or more symptoms during dying for four. For three residents, the nurse reported that dying was a struggle. For two of these (three in total), the GP had indicated that he or she had made a decision to intensify symptom control with a strong increase of the morphine(-like drug) the day before death. For one resident, the physician reported having performed euthanasia. Eight days of sedation preceded the euthanasia, during which the resident had received artificial food or fluids. The GP had indicated that this resident was partly competent in the last week.

All pre-specified features for the practice of sedation were met in one case, four features in five cases, three features in two cases, and two features in three cases. The practice of continuous deep sedation until death was in accordance with all five of the pre-specified features for resident 7:

Resident 7 was in a severe stage of dementia one month before death. At admission, s/he was partly competent for decisions about which medical treatments s/he wanted. S/he had never expressed specific wishes for and the GP had never spoken with him/her about the medical decisions s/he did or did not want in the last phase of life. However, end-of-life decisions, including the use of sedation, were discussed with the resident's relative. S/he was in the terminal phase in the last week of life. S/he suffered from pain in the last week of life according to the nurse. His/her quality of life was estimated to be rather high. No artificial food and/or fluids were administered during sedation. During death, s/he was free from symptoms according to the relative. S/he died peacefully according to the nurse. S/he died of old age in the nursing home where s/he had stayed for almost three years.

The practice of continuous deep sedation until death was in accordance with two of four pre-specified features for resident 1:

Resident 1 was in an advanced stage of Alzheimer dementia one month before death. At admission, s/he was not competent for decisions about which medical treatments s/he wanted. S/he had never expressed specific wishes for and the GP had never spoken with him/her about the medical decisions s/he did or did not want in the last phase of life. In the last week of life, s/he was not in the terminal phase and his/her quality of life was estimated to be relatively high according to the nurse. Then s/he suffered from a gastric haemorrhage. Prior to possible end-of-life decisions, there had been a discussion with a relative about his/her wishes. S/he was sedated for one day without the administration of food and fluids and received morphine or a morphine-like drug during the last 24 hours that was strongly increased the last day before death. During death however, s/he experienced a broad range of symptoms according to the relative. According to the nurse, the last six hours of his/her death were a struggle. S/he died in the nursing home, where s/he had stayed for 1.1 years.

Table 2. Main Characteristics.

	RESIDENTS											TOTAL
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	
Demographic and clinical characteristics												
Stage of dementia one month before death*	Advanced	Advanced	Advanced	Advanced	Advanced	Advanced	Severe	Advanced	Advanced	Advanced	Moderate	**Advanced:9**
Underlying cause of death†	Gastric haemorrhage	Old age	Old age	Cancer	CeVD	Old age	Old age	CaVD	Cancer	Missing	Cancer	**Old age:4 Cancer:3**
Length of nursing home stay (years)‡	1.1	3.7	0.7	1.6	1.7	6.2	3.0	2.5	2.4	0.3	Missing	**Mean: 2.3y**
Place of death‡	Nursing home	Nursing home	Nursing home	Nursing home	Nursing home	Nursing home	Nursing home	Nursing home	Nursing home	General hospital ward	Missing	**Nursing home:9**
Evaluation of clinical practice												**Total number of cases in which condition was met**
1.Suffering in last week of life§	**Unknown**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**Unknown**	**+**	**Missing**	**8/8**
Symptoms a lot present in last week of life‖,¶	None of the pre-specified	Choking; Difficulty swallowing	Pain; Restless-ness; Fear	Difficulty swallowing	Fear	Choking; Difficulty swallowing; Fear	Pain	Difficulty swallowing; Fear	None of the pre-specified	Difficulty swallowing	Missing	
Quality of life during last week of life‖,**	22	34	43	33	29	26	31	46	24	32	22	**Mean:31**
2.Short life expectancy (<2 weeks)††	**-**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**-**	**+**	**9/11**
Resident was in terminal phase in last week of life	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	**9/11**

Duration of sedation (days)	1	1	5	5	3	Missing	Missing	3	1	Missing	8	**Mean:3.4 days**
3.Discussion with the resident or his/her relative‡‡	**+**	**-**	**-**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**9/11**
Competent at admission?	No	Yes	No	No	No	No	Partly	No	Yes	Yes	Yes	**5/11**
Specific wishes about medical treatments that the resident would (not) want in the last phase of life expressed and/or discussed	No	No	No	Yes	No	No	No	No	No	Yes§§	Yes§§	**3/11**
Resident had a written statement of his/her wishes concerning the use of sedation	Missing	No	No	Yes	No	No	No	No	No	No	No	**1/10**
Resident had a written assigned proxy decision-maker‖‖	Missing	No	No	Yes	No	No	No	No	Yes	No	No	**2/10**
Prior to a possible decision, the wishes of the resident were discussed with a relative	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	**8/11**
Competent in last week?	No	No	No	No	No	No	Yes	No	No	Yes	Partly	**3/11**
4.Withholding/ withdrawal of medical and nursing procedures that are not strictly necessary during sedation¶¶	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**-**	**-**	**9/11**
Administration of artificial food and/or fluids during sedation	No	No	No	No	No	No	No	No	No	Yes	Yes	**2/11**
Non-treatment decision***	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	**8/11**
5. Sedation was effective†††	**-**	**-**	**+**	**Missing**	**Missing**	**-**	**+**	**-**	**-**	**-**	**Missing**	**2/8**

Relatives' perceptions of symptoms a lot present during death¶,||	Pain; Restlessness; Shortness of breath; Choking; Gurgling; Difficulty swallowing; Fear	Fear	None of the pre-specified	Missing	Missing	Restlessness; Choking; Gurgling; Difficulty swallowing; Fear	None of the pre-specified	None of the pre-specified	Difficulty swallowing	Pain; Restlessness; Shortness of breath; Gurgling; Difficulty swallowing; Fear	Missing	
Alleviation of symptoms with a strong increase of the morphine or a morphine-like drug the day before death‡‡‡	Yes	No	No	No	No	Yes	No	Yes	No	No	No but euthanasia	**3/11 Euthanasia: 1/11**
Manner of dying, last 6 hours of life||	Struggle/ agony	Peaceful	Peaceful	Peaceful	Struggle/ agony	Peaceful	Peaceful	Struggle/ agony	Peaceful	Peaceful	Peaceful	**Struggle: 3/11**
Number of conditions that were met per case	**2/4**	**3/5**	**4/5**	**4/4**	**4/5**	**4/5**	**5/5**	**4/5**	**3/4**	**2/5**	**2/3**	

* Stage of dementia according to the Cognitive Performance Scale (CPS) and the Global Deterioration Scale (GDS), according to the nurse. Advance dementia: CPS≥5 and GDS=7; severe dementia: (CPS≥5 and GDS<7) OR (CPS<5 and GDS=7); moderate dementia: CPS<5 and GDS<7.

† CeVD=Cerebrovascular disease; CaVD=Cardiovascular Disease.

‡ According to the nursing home administrator.

§ Suffering in the last week of life: '+' when ≥1 symptoms a lot present in last week of life AND a score of ≥33 on the Quality of Life in Late-Stage Dementia scale during last week of life.

|| According to the nurse.

¶ Presence of pain, restlessness, shortness of breath, choking, gurgling, difficulty swallowing and fear as assessed (a lot present) by the Comfort Assessment in Dying End-of-Life in Dementia Scale (CAD-EOLD). Fear=fear and/or anxiety.

** Quality of Life in Late-Stage Dementia scale during last week of life. Total scores range from 11 points to 55 points with lower scores reflecting a higher quality. Median score=33.

†† Short life expectancy: '+' when resident in terminal phase in last week of life.

‡‡ Decision-making process: '+' when specific wishes about medical treatments that the resident would (not) want in the last phase of life expressed and/or discussed OR prior to a possible decision, the wishes of the resident were discussed with a relative.

§§ Case 10: the patient had a written do-not-resuscitate order which was the GP's decision according the relative, but had no written statements according to the GP and nurse. There were no GP orders documented in the resident's medical record according to the GP and nurse. Case 11: the patient had no written advance directive according to the GP. The following GP orders were documented in the resident's medical record according to the GP: do-not-resuscitate, do not transfer to hospital, withholding/withdrawal of antibiotics, withholding/withdrawal of artificial food and/or fluids, do-not-intubate, withholding/withdrawal of other treatments, and terminal sedation. (There was no questionnaire from the nurse and relative).

|| || According to the relative.

¶¶ Withholding/withdrawal of medical and nursing procedures that are not strictly necessary during sedation: '+' when no administration of artificial food and/or fluids during sedation.

*** Non-treatment decision=treatment not started up or discontinued, taking into account the hastening of the end of life or with the explicit goal to hasten the end of life.

††† Sedation was effective: '+' when none of the pre-specified symptoms were 'a lot present' during death according to the relative AND peaceful manner of dying in the last 6 hours of life was achieved according to the nurse.

‡‡‡ Alleviation of symptoms=the intensification of symptom control, taking into account the hastening of the end of life or partly with the goal to hasten the end of life, with a strong increase of the morphine or a morphine-like drug the day before death according to the physician; Euthanasia=medication administered, with the explicit goal to hasten the end of life.

DISCUSSION

This is the first study to provide in-depth insight into the practice of continuous deep sedation until death for nursing home residents with dementia through case-based analysis. This approach offers unique information about a much debated practice in a population about which little scientific information exists. Multiple perspectives were included to capture a comprehensive picture. The cases presented were selected from a large representative sample with high response rates.

Sedation can be used when an individual suffers unbearably from physical or psychological symptoms at the end of life (3;4). Next to often-reported indications such as pain, dyspnoea, and delirium or agitation (16;17), this study suggests that residents with dementia before sedation also often experience fear and difficulty swallowing, possibly with choking as a consequence. Two residents did not suffer a lot from any of the pre-specified symptoms in the last week of life, although one died as a result of a gastric haemorrhage, which might result in other symptoms. It is a limitation of this study that the GP was not asked whether the individuals suffered symptoms other than the ones in the questionnaire. A Dutch study performed in nursing home residents with cancer or dementia reported similar indications, except for difficulty swallowing and choking, which were not included in the study (17). Relatives reported that several residents experienced a broad range of symptoms during dying, despite the use of sedation. This may indicate that sedation did not always sufficiently relieve suffering, which is in line with a Japanese study in specialized palliative care units, showing that sedation was not effective in symptom palliation in 17% of cases (18). Nurses in the current study, in contrast to relatives, less often seemed to consider the dying process to be a struggle. Relatives may have been present at the bedside more often during the dying phase and thus have observed the dying process more closely, yet sedation is often an emotionally distressing event for relatives, (19;20) and they are often unprepared for and inexperienced with the dying process and the use of sedation in particular, which might have framed their perceptions.

Sedation was used for two residents who were not terminal, which is in conflict with guideline recommendations (3;4). In one other resident, euthanasia was performed after eight days of sedation. For three residents, the GP had indicated that there was a strong increase of morphine(-like drug) in the last day. The physician's duty to relieve suffering may be challenging, especially when symptoms arise or increase even during death. Guidelines also recommend that the competent individuals should be actively involved in decision making (3;4). When individuals are no longer competent, the decision must be discussed with their representative (3;4). The current study shows that decision making regarding sedation mostly involves relatives and that competent residents are not always involved. Four residents had in some way previously expressed their wishes regarding end-of-life decisions through an advance directive, the assignment of a proxy decision-maker, or a conversation with the GP. A Belgian study of GPs found that, before the last month of life, individuals with dementia were involved in end-of-life communication significantly less often (45%) than those dying without dementia (73%) (21). It may be possible that consultation with residents in the current study was uncommon because physicians may not have recognized in time that the resident was in the terminal phase because of the lack of reliable prognostic markers and a predictable death trajectory (1;22-24) or because the physician or the resident may have hesitated to discuss these issues (25-27). In the current study, neither two residents, one of whom was competent at admission, nor their relatives had been involved in decision making. A previous study found that the GP had not involved (competent) individuals or their relatives in all cases before administering continuous deep sedation until death (28).

Care must be taken when interpreting these results because the number of identified subjects was small. Although 69 nursing homes, representative of all nursing homes in Flanders, were included, the fact that only 117 of 205 individuals with dementia were included in this study may we weaken the response rate of 58%. Also, the

retrospective design does not preclude recall bias, although minimizing the time between death and completion of questionnaires and focusing on the last month and week of life limit this. Other limitations of the study are that the nurses were not asked the meaning of 'struggle' in the last six hours, nor were the GPs asked meaning of a 'strong' increase in the morphine(-like) drugs.

In conclusion, this study shows that the current practice of sedation for the nursing home residents with dementia included in the study does not always guarantee a dying process free of symptoms and might therefore be amenable to improvement. The use of sedation was not always restricted to the terminal phase, and relatives were mostly involved in the decision making. Care planning, especially on end-of-life questions, should be begun with residents in an early stage of the illness when they are still competent and with their relatives. In addition, the study suggests the need to inform relatives appropriately about what to expect in the course of sedation because they may perceive symptoms during the individual's death and may be distressed by them (3). Symptom control and sedation depth should be monitored simultaneously and at regular intervals in the course of sedation with the use of sedation monitoring instruments to evaluate whether palliative sedation is applied in an effective manner.

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Chapter 3

Factors that facilitate or constrain the use of continuous sedation at the end of life by physicians and nurses in Belgium: results from a focus group study

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ABSTRACT

Continuous sedation at the end of life (CS) is the practice whereby a physician uses sedatives to reduce or take away a patient's consciousness until death. Although the incidence of CS is rising, as of yet little research has been conducted on how the administration of CS is experienced by medical practitioners. Existing research shows that many differences exist between medical practitioners regarding how and how often they perform CS. We conducted a focus group study to find out which factors may facilitate or constrain the use of continuous sedation by physicians and nurses. The participants often had clear ideas on what could affect the likelihood that sedation would be used. The physicians and nurses in the focus groups testified that the use of continuous sedation was facilitated in cases where a patient has a very limited life expectancy, suffers intensely, makes an explicit request and has family members who can cope with the stress that accompanies sedation. However, this 'paradigm case' was considered to occur only rarely. Furthermore, deviations from the paradigm case were said to be sometimes due to physicians initiating the discussion on CS too late or not initiating it at all for fear of inducing the patient. Deviations from the paradigm case may also occur when sedation proves to be too difficult for family members who are said to sometimes pressure the medical practitioners to increase dosages and speed up the sedation.

INTRODUCTION

It is becoming more and more common that in the care of terminally ill patients, decisions are taken that can potentially have an effect on the patient's time of death (1). One such end-of-life decision is continuous sedation at the end of life (CS) where a physician uses sedatives resulting in the reduction or taking away of a patient's consciousness until death.[1] Various types of continuous sedation exist; sedation can be light (patient can still be woken) or deep (patient is in a coma-like state), and can be induced suddenly (in response to an acute problem) or be the result of a gradual increase of sedative medication (in response to gradually worsening symptoms). Research in Belgium indicates a high (and rising) incidence for CS: in Belgium, the practice was used in 8.2% of all deaths in 2001, and this number rose to 14.5% of all deaths in 2007 (1). Accordingly, medical practitioners deal more and more frequently with patients who are continuously sedated until death, and the practice has, arguably, become part and parcel of palliative care.

Nevertheless, various differences seem to exist in the frequency with which and the reasons why medical practitioners use CS. As regards frequency, for example, CS was used in 16.5% of all deaths in the United Kingdom in 2007-2008 (2), whereas in The Netherlands it was used in 8.2% of all deaths in 2005 (3). Concerning the reasons why CS should be initiated, existing guidelines leave some room for interpretation. One example of a difference in national practices is that in The Netherlands in 2001, in accordance with a Dutch guideline (4), the initiation of CS was requested or consented to by the patient in 59% of cases (5), while in Belgium in 2007, a request for or a consent to continuous sedation was obtained in only 30% of cases (6). This indicates that there might be many factors influencing whether, why and when medical practitioners decide on CS. However, little is known as to what those factors might be and how they influence the medical professionals. Our focus group research attempts to shed light on this issue and to answer the following question: 'What, according to physicians and nurses in Belgium, could make it more or less likely that continuous sedation will be used in a particular case?'. In other words, which factors could facilitate Belgian physicians and nurses in choosing to use continuous sedation, and which factors could constrain them in making such a choice?

METHOD

We asked physicians and nurses about their experiences with and their attitudes towards the practice of continuous sedation at the end of life. The participants in our focus groups were also specifically questioned about situations in which they would consider their involvement with continuous sedation to be psychologically more or less difficult.

Participants

In April 2010, we conducted two focus groups with physicians (n=4 and n=4), and two focus groups with nurses (n=4 and n=9). The participants were selected with the inclusion criterion that they had to have been involved in at least one case of CS in their entire professional career. The participants came from a balanced mix of settings (home care, hospital oncology wards, and hospital palliative care units or palliative support teams).

For the recruitment of the participants, we sent out invitations to physicians and nurses from the home care setting, the hospital oncology setting and the palliative care setting, asking them to participate in our focus group study. Professional registries (of the Belgian National Disciplinary Board of Physicians and the Belgian Society for Medical

[1] Among the other terms that are used to refer to this practice are 'terminal sedation' and 'palliative sedation'.

Oncology) were used to contact many physicians at once. Subsequently, we also contacted particular physicians, whom we know or who have contributed to earlier research of our research group, by e-mail or telephone in order to obtain a balanced mix of settings.

Focus groups

Each focus group was moderated by two moderators with considerable experience in (qualitative) end-of-life care research and moderating focus groups. Also present were observers taking field notes. Before the focus group discussions started, anonymity of data was discussed and informed consent for the electronic recording of the proceedings was obtained. All focus group discussions lasted about 2 hours and were guided by an aide-memoire (i.e., a document containing the key questions to be asked as well as potential sub-questions or prompts) covering several topics: 1) general thoughts on CS, 2) general experiences with the practice, 3) attitudes towards CS, and 4) circumstances in which the participants would consider their involvement in continuous sedation to be more or less problematic.

Data analysis

All focus group discussions were recorded electronically and transcribed verbatim, removing all data that could possibly identify the participants. For analysing the transcribed data, constant comparative analysis was used. Two junior researchers reread the transcripts separately and developed a preliminary coding to identify the most important themes and ideas.

Subsequently, on the basis of this preliminary coding, a coding tree was made and discussed within the research team and served to cluster relevant concepts. There were only minor differences in interpretation between the members of the research team and, after discussion, consensus was always reached. Next, the coding tree was used to go back to the uncoded transcripts to check whether it covered all relevant ideas. Again, this was done separately by the junior researchers, and double-checked by two senior researchers. After some minor adjustments, the coding tree was finalised. The qualitative analysis software used for this research was NVIVO 9.

RESULTS

This section provides an overview of the circumstances and factors that, according to the participants, could affect the likelihood that sedation would be used.

The patient's current state

The state that the patient is in at the time that CS is considered, was mentioned as being important by the focus group participants. A clear facilitator for deciding to use the practice is that the patient is suffering severely and has a short life-expectancy. A good indicator for a short life expectancy was said to be when the patient herself stops taking in food and fluids.

Nurse P: You have to do it in the final phase [of life] and not with patients who are suffering from symptoms but are still eating and drinking. Patients who are still eating and drinking will perhaps live for one or two months.

Physician F: Time must be short, you have to be close to the expected end of life and actually, practically speaking, it boils down to when someone no longer can or wants to drink, so when somebody is no longer taking in fluids. Then we can presume that somebody will die within about fourteen days. Then, for me, it is possible to sedate, to continuously sedate. Otherwise it's never possible, because then you are going to make different decisions.

However, when a patient's suffering was deemed to be existential rather than physical, this could be perceived as a psychological barrier by the focus group participants.

Nurse D: But existential suffering, I find one of the most difficult issues. When you see the patient's suffering and we want to solve it all and then it's easy when the patient is sleeping quietly.

Nurse CL: But whether that's solved with sedation, I'm afraid not. I'm afraid not.

Moderator: What do you mean by that?

Nurse CL: Well, that patients go through their sedation with their suffering continuing. That it happens under a different form, of nightmares and images and such. But I'm afraid they are not relieved from it.

Physician A: So psychological unbearableness, to mention only one example. So for me it's psychologically unbearable but she [the patient] is not vomiting, is not experiencing pain, ... In such cases I would actually find it difficult to start up sedation.

Deliberation and communication

Presence or absence of good communication between all parties involved was mentioned as a factor that could greatly impact on the likelihood that CS would be performed.

Request from the patient

If a clear request from the patient had been made, the participants in the focus groups mentioned they would feel more comfortable in performing CS.

Physician M: People can be conscious and really choose palliative sedation, and that is, I think, a comfortable situation. Also for the patient herself, because she plays a role in the decision and to some extent even determines the moment [sedation is initiated].

Nevertheless, the focus group participants mentioned that a patient request was not always possible, and this was perceived as a barrier, for example when people at the end of life have diminished cognitive capacities.

> **Physician M:** And then you get into a situation where it may no longer be possible to discuss everything. Or metastases in the brain that make people confused, or other causes that make them confused and that sometimes leave you no other option than to use palliative sedation. I find that a less comfortable situation for the physician. I prefer it to be discussed in a straightforward manner, both with the patient and others ...

Another important reason why a request was not always possible, was that patients were not always aware of the existence of continuous sedation, and the physician did not bring it to their attention for the fear of inducing the patient, meaning that the physician did not want to unduly influence the patient to choose CS.

> **Nurse C:** Hardly any patients know of the possibilities of sedation.
>
> **Nurse N:** Indeed.
>
> **Nurse C:** I think few patients will ask the question: 'Now I want to be sedated'. They don't know about the practice.
>
> **Nurse N:** No. They won't ask that question. But our physician insists on that question, not literally a request for sedation, but a patient indicating 'I can't go on', 'I want to sleep' mainly or 'I've had enough', because he is scared that, otherwise, we are going to induce things.

Expectations

In a decision for CS, according to the physicians and nurses in our focus groups, the patient's family is important. For family members it is sometimes very difficult to watch a loved one who is sedated, especially if the sedation extends for a long period of time. It is therefore deemed important always to properly inform the family of what continuous sedation involves and what can be expected to happen to their sedated relative to make sure that they know what to expect. But even when appropriate information has been provided, when medical practitioners feel that a sedation could cause the family distress, this works as a barrier.

> **Physician P**: We certainly do not find it ideal, a palliative sedation, because of the family's expectations and the fact that it can take some time, much longer than the family had imagined. That their father or mother or brother or sister or partner is lying there, unconscious in a coma, but still with physical discomforts and all the care involved ... which is often difficult for the family, and we definitely do not promote this. We really try to ask because we're afraid of the disappointment, the fact that the patient, the family may not be able to cope, that it takes too long. So we try to discourage it more than we suggest it. Definitely not suggest it.

When the family is not adequately informed, according to the participants, this could lead to the family pressurising the medical professionals to speed up their relative's dying process.

> **Physician A:** You have to explain it very clearly to the family because if you don't, you really get into trouble. If you do not say clearly that it can even take a week, if you did not make that clear to the family beforehand, you will encounter some people who become almost aggressive and say 'well it's not easy with my job and I have to be able to plan when the funeral will be and that's when I want it to happen and can't you speed it up?'. You are, quite simply, being pressured by the family. That is why I always say, don't start with sedation if you have not made everything very clear to the family beforehand.

Existence and use of guidelines

Some nurses stated that the existence of guidelines made the use of CS easier for some physicians.

> **Nurse MT:** But in a euthanasia procedure it is required that a physician consults with the nursing team and the family, while for a palliative sedation there are no procedures, there are no guidelines. So precisely this profile of very dominant hierarchical physicians matches very well with a palliative sedation, because there, they are master and commander and they don't have to consult anyone.
>
> **Moderator:** So that's a completely different framework than the one surrounding euthanasia?
>
> **Nurse MT**: That's right, that kind of physician and their choice of not performing euthanasia, but instead initiating palliative sedation and quietly increasing the dosage, we call that a 'sans papiers'[2] in our team. There's no procedure, there's no registration and it's all OK, the problem is solved.

Attitudes of medical practitioners involved in continuous sedation

The focus group participants considered the attitudes of physicians and nurses towards sedation and euthanasia to be a factor that could work as a facilitator to the use of the practice.

> **Nurse N:** So in our ward, euthanasia is not possible. That's the physician's choice, whether we support it or not. But from time to time we have a patient with [a request for] euthanasia and then that always gets turned into a sedation.

Sometimes certain attitudes could also function as a barrier.

> **Nurse CL**: I think life is important, but consciousness, for goodness sake, that's almost even more important and we should not easily interfere with that.

Possibility of alternatives

An important indication to initiate CS was said to be that no alternatives were possible. The physicians in the focus groups stressed that sedation could only be considered when it was the very last option.

> **Physician A:** When you feel you have reached the end with other medication and other means, you stand with your back against the wall as a physician ... you can't offer anything else and you see that your patient is suffering immensely and this is your last way of making it dignified for her and her family.

Some nurses, however, questioned how this 'last resort' should be interpreted. They argued that even in cases where there are no medical alternatives, there might still be non-medical alternatives.

> **Nurse C**: And I have some questions about that. I think tackling the anxiety with medication is a possibility, but I think there are other options besides that. Sometimes, perhaps, making patients feel you are supporting them more, together with the family. Also guiding the family and giving support together to a dying person: spiritual guidance, psychological guidance, massages, presence, relaxation. There are, I think, other options.

[2] 'Without papers' - an expression normally used to refer to illegal immigrants.

Moderator: You mean non-medical solutions?

Nurse C: Non-medical solutions.

Nurse M: Presence in all its forms, by involving yourself with people.

Nurse CL: And that might be much more effective than a sedation, the fact that someone is standing behind you or beside you.

Nurse C: Yes.

DISCUSSION

This study analyses the insights and experiences of 21 medical professionals, from a balanced mix of settings, with CS. In view of the nature of our research methods, we would caution against a generalisation of our results to CS practice as a whole or even to CS practice in Belgium. However, at the same time we believe our results represent more than simply reflections from a small group of caregivers. Thanks to the fact that we used experienced moderators and included participants from a balanced mix of setting, our study provides several valuable insights into which factors are likely to influence physicians in their choice for or against administering CS.

In their reflections on what facilitates or constrains them in the use of continuous sedation, physicians and nurses gave a lot of attention to patients' needs as well as to their wishes.

First, all the nurses and physicians in our focus groups agreed that not every patient who asks for CS should receive it. Certain criteria have to be met: 1) the patient must have a short life-expectancy and 2) must be suffering intensely. Medical practitioners are therefore more likely to use CS when they are convinced that the patient is in a state where she needs it. This could perhaps partly explain why sedation is most often used very shortly before death. Research in Belgium indicates that in 56% of sedation cases, sedation lasted less than 48 hours (6).

Second, according to the physicians and nurses in our study, the use of CS is not only facilitated by patients' perceived needs, but also by a clearly expressed patient wish to be continuously sedated until death. So it seems that physicians and nurses are most comfortable in using sedation on patients who are clearly perceived to need CS *and* explicitly ask for it. This might be called the 'paradigm case', where, according to the participants, a choice for sedation is most likely.

However, the nurses and physicians in our focus groups also had a lot of questions regarding this paradigm case. As regards patient needs, it was often unclear when a patient actually needed CS, since, unlike with patient *wishes*, whether a patient *needs* CS is assessed by a physician, implying that different physicians may reach different decisions. For some nurses, purely existential suffering could be regarded as equal to physical suffering and could therefore sometimes be an indication for CS, whereas some physicians were more reluctant to use continuous sedation in these cases. Other nurses questioned whether patients who were said to need sedation might in fact be better helped with non-medical alternatives such as presence and/or spiritual guidance. Even though our focus group participants were aware of the Dutch national guideline which provides that continuous sedation should only be

initiated as a last resort and for refractory symptoms[3], a judgment is still necessary as to whether in a specific case the patient's symptoms are indeed refractory or whether continuous sedation is indeed the only available option, hence an element of subjectivity is unavoidable. In 2010, after the focus groups were held, a Belgian guideline for continuous sedation was published (7). Like its Dutch counterpart, the Belgian guideline requires a physician's judgment by stressing that CS should only be used in patients with a short life expectancy and unbearable suffering from a refractory symptom that may be physical, purely existential or a combination of both, and that, if possible, there should be a request or consent from the patient or her legal representative.

Patients were said to request CS rarely. One of the main reasons that was given, was that patients were often not aware of the existence of CS. At the same time, physicians were hesitant to mention the practice first for fear of unduly influencing the patient to choose CS. This then creates the rather awkward situation that a physician is waiting for the patient to request a practice she doesn't even know about. This may lead to sedation not being discussed, or discussed only very late in the disease trajectory when the patient is suffering severely and obtaining her consent has become problematic or even impossible, thereby deflecting decision making to a third party (8). As mentioned above, available research indicates that, in Belgium in 2007, a request was made by the patient in only 10% of all continuous deep sedation (CDS)[4] cases, and in another 20%, while there was no request, the patient had consented to CDS (6).

Another factor that was mentioned by our focus group participants as being of great importance, was the patient's family. Data from Belgium indicate that, while patients are often not involved in the decision to use continuous sedation (due to incompetency or other reasons), family members are involved most of the time, making them an important third party (6). This was confirmed in the focus groups. In some cases, it was said, families will exert pressure on the medical team to increase the dosage and to speed up the sedated patient's death, making the medical practitioners feel very uncomfortable. This is interesting since, in the absence of a patient request or consent, one might expect the family members to help determine what the patient would have wanted if she were competent, bringing the difficult cases as close as possible to the paradigm case.

Thus it seems that even though there is a paradigm case in which, according to the physicians and nurses in our focus groups, continuous sedation is clearly indicated, and in which its use is perceived as comfortable, this paradigm case might be the exception rather than the rule. Moreover, deviations from the paradigm case may often be due to the physicians themselves, when they are unwilling to initiate a conversation about continuous sedation or when they initiate it too late. For incompetent patients, the family is frequently involved in decision making, but after the sedation has been initiated, families were said to often be a hindrance when they put pressure on the medical team to speed up the process.

Accordingly, there might be reasons for medical professionals to try to approach this paradigm case as closely as possible, since such cases pose the least problems. This means placing more emphasis on patient consent, as recommended in a Belgian guideline published in 2010. In The Netherlands, a guideline on continuous sedation that also stresses patient request or consent was published in 2005 and, after its introduction, patient involvement in decision making rose (9). One might hope the same will happen in Belgium, although it should be noted in this regard that the Dutch guideline has legal ramifications, whereas, the Belgian guideline does not (10). When patient involvement is impossible, the best way to approximate patient consent is to involve the patient's family to determine what the patient would have wanted.

[3] By which are meant symptoms that are unresponsive to available treatment or for which available treatment has unacceptable side-effects.

[4] This research focused only on deep continuous sedation.

Finally, another interesting finding that emerged from our focus groups, even though the moderators did not mention the topic of euthanasia, was that some physicians consider continuous sedation to be an alternative to euthanasia. One of the nurses used the term 'sans papiers' to refer to a case where sedation is used as a way to shorten life, while at the same time avoiding all the requirements of due care that are obligatory when performing euthanasia, as well as the obligation to report, and thus avoiding scrutiny. Another nurse indicated that in her ward, CS is even used on patients who have made a clear request for euthanasia. This confirms again that the issue of the relation between continuous sedation at the end of life and euthanasia is not merely debated in academic literature (11;12), but is also an important topic for physicians and nurses in their daily practice. This raises serious questions, since one of the reasons for legalising euthanasia in Belgium was that legalisation, together with an obligation to report, would make a practice which, before, was hidden, visible and susceptible to scrutiny. Some of the participants in our focus groups had many reservations about whether CS should be initiated without a patient request or with patients who have a longer life expectancy, but were less concerned about whether CS should be used as an alternative to euthanasia.

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Chapter 4

Similarities and differences between continuous sedation until death and euthanasia – professional caregivers' attitudes and experiences: a focus group study

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ABSTRACT

Background

According to various guidelines about continuous sedation until death, this practice can and should be clearly distinguished from euthanasia, which is legalized in Belgium.

Aim

To explore professional caregivers' perceptions of the similarities and differences between continuous sedation until death and euthanasia.

Design

Qualitative data were gathered through focus groups. Questions pertained to participants' perceptions of continuous sedation. The focus groups were recorded and transcribed verbatim. Analyses were conducted by a multidisciplinary research team using constant comparison analyses.

Setting/Participants

We did four focus groups at Ghent University Hospital: two with physicians (n=4 and n=4) and two with nurses (n=4 and n=9). The participants could participate if they were ever involved in the use of continuous sedation until death.

Results

Although the differences and similarities between continuous sedation until death and euthanasia were not specifically addressed in the questions addressed in the focus groups, it emerged as an important theme in the participants' accounts. Many caregivers elaborated on the differences between both practices, particularly with regard to patients' preferences and requests, decision making, and physicians' intentions. However, some stated that the distinction between the two sometimes becomes blurred, especially when the sedating medication is increased disproportionally or when sedation is used for patients with a longer life expectancy.

Conclusions

The differences and similarities between continuous sedation until death and euthanasia is an issue for several Flemish professional caregivers in their care for unbearably suffering patients at the end of life. Although guidelines strictly distinguish both practices, this may not always be the case in Flemish clinical practice.

INTRODUCTION

In Belgium, numerous palliative care structures and services have been developed to provide high-quality care for terminally ill patients (1). Yet it is possible that patients in the final phase of their life suffer persistently and unbearably from refractory symptoms, that is, symptoms unresponsive to available treatment. According to various guidelines, in such cases, continuous sedation until death can be considered (2;3). Continuous sedation refers to the practice where sedation, that is, the lowering of the patient's consciousness, is administered continuously until the time of death (4). Continuous sedation can vary from mild to deep sedation (2;3;5;6). In the Flemish region of Belgium in 2007, its incidence was estimated to be 14.5% of all deaths (7). In the Netherlands, in 2005, continuous sedation was given in 8.2% of all deaths and in the United Kingdom, in 2008, in 16.5% of all deaths (8-10).

Various guidelines state that continuous sedation at the end of life can only be performed when the patient has a very limited life expectancy (2;3). Further, they stress that continuous sedation should be distinguished from euthanasia - that is, the intentionally ending of life by administering medication at the explicit request of a patient -, explaining that continuous sedation is a way of proportionally alleviating the patients' refractory suffering and does not aim at the death of the patient (11). In Belgium as well as in the Netherlands, given the fact that euthanasia is legalized (11;12), the guidelines regarding sedation address the issue of the differences between continuous sedation and euthanasia. A nationwide Palliative Sedation guideline has been introduced in 2005 (and revised in 2009) in the Netherlands (2). In Belgium however, a guideline was introduced only recently (December 2010) and after we conducted our study (3). The goal of our study was to explore the attitudes and experiences of physicians and nurses in Flanders with the practice of continuous sedation until death. We therefore conducted focus groups. The focus groups were conducted at the preliminary stage of a larger international interview study (the UNBIASED study - UK Netherlands Belgium International Sedation Study), aiming at exploring clinical decision making surrounding the use of continuous sedation until death and understanding the beliefs, perceptions and experiences of (in)formal caregivers regarding this practice (4).

In this article, we focus on the following research question: 'What do Flemish physicians and nurses perceive as similarities and differences between the practice of continuous sedation until death and the practice of euthanasia?'.

METHODS

Focus groups with professional caregivers were held in Flanders, Belgium, in April 2010. The main aim of the focus groups was to gain insight into the attitudes and experiences of professional caregivers regarding continuous sedation in end-of-life care.

Participants and setting

Physicians and nurses could participate in the focus groups if they had ever been involved in the use of continuous sedation until death. In order to obtain a broad range of multidisciplinary views and experiences, we included physicians and nurses from the home-care setting as well as the hospital setting (oncology ward and palliative care unit/palliative support team) in Flanders.

The participants were recruited in several ways. Contact information of potential participants was obtained through professional registries (the National Council of Physicians and the Belgian Society of Medical Oncology), the Federation for Palliative Care in Flanders, professional contacts of members of the research team, and physicians

who had already participated in previous studies of our research group. Invitations were sent by e-mail and through post. Follow-up phone calls were done by L.A. after 1 week.

Two focus groups were held with physicians and two with nurses. In all, 4-9 participants took part in each focus group. See Table 1 for their characteristics.

Table 1. Characteristics of focus group participants.

	Physicians (n=8)		**Nurses (n=13)**	
	Focus group 1 (n=4)	**Focus group 2 (n=4)**	**Focus group 1 (n=4)**	**Focus group 2 (n=9)**
Sex				
Male	1	3	1	4
Female	3	1	3	5
Age (Years)				
30-39	0	1	0	0
40-49	2	0	1	5
50-59	2	2	3	3
60-69	0	0	0	1
≥70	0	1*	0	0
Setting				
Oncology ward	1	0	0	2
Palliative care unit	2	2	3	3
Home†	1	2	1	4
Experience with continuous sedation				
Yes	2	4	4	9
In the last year‡	3	3-4§	1-4‖	1-30‖
In the professional career‡	5§	2-50§	10-15§	3-15§,‖
No	2	0	0	0

* 85 years, retired.

† In the home-care setting, physicians included general practitioners, whether or not part of a palliative home-care team. Nurses in the home-care setting were always member of a palliative home-care team.

‡ The number of times physicians or nurses have had experience with continuous sedation until death.

§ Missing: focus group 1 physicians (in the professional career: n=1); focus group 2 physicians (in the last year: n=1; in the professional career: n=1); focus group 1 nurses (in the professional career: n=2); focus group 2 nurses (in the professional career: n=3).

‖ Unknown: focus group 1 nurses (in the last year: n=1); focus group 2 nurses (in the last year: n=1; in the professional career: n=1).

Procedures

The focus groups were held at Ghent University Hospital and lasted about 2 hours. They were led by experienced moderators (L.D. and J.R., S.S. and J.R. or S.S. and R.D. (Prof. Dr. Reginald Deschepper, anthropologist and member of the End-of-Life Care Research Group)). Notes were made by two observers (L.A. and K.R.). All participants gave their informed consent to the audio taping of the discussions. The moderators used a topic guide, consisting of open questions and a brief set of prompts (Box 1). This topic guide covered several themes: 1)

experiences of the participants with various types of sedation at the end of life, 2) attitudes regarding continuous sedation, and 3) the medical situations in which continuous sedation is perceived to be more easy or difficult. Three vignettes were used to guide the discussion (Box 2). In each vignette, the presented patient had terminal breast cancer and suffered unbearably from untreatable physical symptoms despite receiving palliative care. The cases varied according to the patient's life expectancy (a few days vs. 3-4 weeks), the performance of continuous sedation (deep sedation from the start vs. titration of sedation according to symptoms) and the duration of the sedation (3 days vs. 1 week). Socio-demographic characteristics were obtained from all participants (Table 1).

Box 1. Topic guide of the focus groups with physicians and nurses.

Introduction
Part I: types of sedation (= kinds of sedation according to depth and duration of sedation)
1. Which types of sedation do you use for patients in their last phase of life? How do you define these?*
Prompts: depth of sedation (deep, mild), duration of sedation (intermittent, continuous) and terms used.
Part II: understandings of and experiences with continuous sedation until death – vignettes
Vignettes of cases of continuous deep sedation until death are presented via Powerpoint. Questions per vignette:
1. Which term best describes this act? Why?
2. Would you act in the same way? Why (not)?
3. Do you have any experience with other situations or circumstances in which patients are continuously sedated until death?
Prompts: situations in which the patient was suffering from non-physical symptoms in which sedation was used as an alternative for euthanasia, or in which sedation was performed on request of the patient who wanted to die sleeping.
Part III: situations in which the use of sedation is more easy or more difficult
1. Are there situations in which the use of continuous sedation until death is more easy or more difficult for you?†
Closing; answering questions; thanking the participants

* The questions for nurses were as follows: 'In which types of sedation for patients in their last phase of life have you been involved? How would you define these? How have you been involved in the performance of continuous sedation for a patient in her last phase of life?'.

† The question for nurses was as follows: 'Are there situations in which your involvement in the performance of continuous sedation until death is more easy or more difficult for you?'.

Box 2. Hypothetical clinical cases of continuous sedation.

Case 1
Patient A is a 72-year-old woman with metastatic breast cancer. She suffers from severe pain and anxiety. She is fatigued and getting out of bed is becoming more and more difficult for her. Her life expectancy is estimated at **a few days**. A morphine drip proves insufficient relieve the pain and anxiety. There are no curative or life prolonging treatment options available anymore and the patient is receiving palliative care. The patient indicates to her physician that she can't go on like this. She has a deep desire to sleep. It is decided to alleviate the patient's suffering as much as possible by administering midazolam until death. It is also decided not to administer artificial nutrition or hydration any more. **Midazolam is administered to bring the patient into a deep sleep. The patient no longer reacts any more to physical stimuli or when spoken to. The patient dies 3 days after the start of Midazolam.**
Case 2
Case 2 is similar to case 1 except that **the doses of Midazolam are matched to the severity of the symptoms. The patient lies there very peacefully, she is sleepy but still reacts when spoken to. The patient dies 3 days after the start of Midazolam.**
Case 3
Case 3 is similar to case 1 except that **the patient has a life expectancy of 3 to 4 weeks. The patient dies 1 week after the start of Midazolam.**

Data analysis

The recordings of the focus groups were transcribed verbatim and all data that could identify the participants were removed to preserve anonymity. We performed constant comparative analyses. First, all transcripts were read several times by a multidisciplinary team of researchers (J.R., S.S., L.A., K.R. and L.D.). We identified the differences and similarities between continuous sedation and euthanasia as a major theme. We re-read all text fragments concerning this theme, and discussed, designed and agreed upon a coding tree. All the text fragments were coded independently by L.A. and K.R., and the codes were independently checked by J.R. and S.S. Differences in coding between the researchers were minimal, and a consensus was always reached. Qualitative analysis software (NVIVO 9) was used to organize the data. Finally, quotes were selected by L.A., K.R., J.R. and S.S. and translated by S.S. working with a native speaker.

RESULTS

Differences between continuous sedation and euthanasia

Many participants reflected about the differences they perceived between continuous sedation and euthanasia, particularly in relation to patients' preferences and requests, decision making and physicians' intentions.

Preferences and requests

Both physicians and nurses stressed the importance of good communication between everyone involved when they are confronted with a terminally ill patient who experiences great suffering and who indicates that he or she cannot bear it anymore. They considered it important to clarify the patient's wishes with respect to end-of-life decision making. Physicians and nurses in our study indicated that they are rarely confronted with an explicit patient request for continuous sedation. In most cases, the patient's request was formulated in general terms, asking the physician to do something to relieve severe suffering. In contrast, patients requesting euthanasia were reported to generally use more specific formulations.

Several caregivers indicated that they discussed with the patient whether his or her wishes for the end of suffering included a desire for continuous sedation or a desire for euthanasia.

> **Physician A; Home:** When a patient says: 'I don't want to experience it anymore'. Well, that can be achieved with sedation or with euthanasia; does he want to sleep or does he want to die? So anyway, you need to talk about both.

> **Nurse A; Home:** First, we start by clarifying a request from a patient. If a patient says 'I don't want to experience the end anymore', then it is absolutely not clear to me what that patient wants. Does that man or woman want euthanasia or sedation? […] Once we have some insight as to what that patient is requesting, we then raise this issue with the attending physician, usually the general practitioner. Sometimes we [the physician and the nurse] listen to the patient's request separately and then check with each other whether we have heard the same. Because for us, there is a strong distinction between putting someone to sleep and killing somebody by lethal injection.

The participants attributed the fact that continuous sedation was usually not requested in specific terms mostly to the fact that unlike the practice of euthanasia, this practice is not (well) known to the general public.

> **Nurse B; Home:** I think there are few patients who would ask: 'now I want to be sedated'. They don't know the practice. I would say that the request [for continuous sedation] often comes from the family and caregivers, but very rarely from the patient.

Yet, sometimes, the patient's request for continuous sedation until death was very clear.

> **Nurse C; Home:** But there are also people who consciously choose not to have euthanasia, but who do indicate: 'if I experience symptoms that cannot be alleviated anymore, then I want sedation'.

After caregivers explained the differences between continuous sedation and euthanasia, patients often seemed to have different preferences for one practice or the other.

The respondents explained that some patients expressed a preference for continuous sedation over euthanasia because of spiritual reasons or also out of concern for his or her family. In the latter, the patient had a euthanasia request but had withdrawn this request.

> **Nurse D; Palliative support team:** And for various reasons, which could be spiritual, or with people who say 'I don't want euthanasia, but I don't want to suffer either, so when the time comes, please make sure that I am asleep'.

> **Physician B; Palliative support team:** For example, it can happen that a patient does want euthanasia, but knows that his wife, for instance, has difficulties with that. Such patients will say 'no, in that case, do something like sedation', simply out of respect or concern for their family, which would have a hard time coping afterwards [if euthanasia had been chosen].

In some cases, however, patients preferred euthanasia to continuous sedation because of the frightening thought of being unconscious for several days.

> **Physician A; Home:** And then there are patients who say 'yes, but if you put me to sleep and my body may have to lie here for another week or two …', then they recoil and some of them say 'in that case, give me euthanasia'.

For the physician, the possibility to comply with the patient's request for continuous sedation or euthanasia becomes more difficult when a discussion about these decisions is raised too late either by the physician or by the patient, or when no clear consensus can be reached between physician and patient.

> **Physician A; Home:** Those are the situations that we encounter most frequently in practice. Someone ends up in a hopeless situation, with no clear consensus having been reached with the patient in advance about the possibility of performing euthanasia, of performing a technique to shorten life. Sometimes this argument [that there was no clear consensus] is abused by colleagues of ours […] who have kept postponing [any discussion with the patient about

> euthanasia] and then of course, the patient ends up with her back against the wall and then the patient asks for euthanasia, but until then, they weren't listening to their patient and then they say 'yes, but now it is too late, because I can't arrange that [euthanasia] in such a short time'.

> **Physician B; Palliative support team:** What I sometimes experience is that [patients] know their end is getting near, and euthanasia, no no, that is not discussed or requested. And then suddenly, the symptoms become so unbearable and then they say: 'yes but in fact, I want euthanasia'. But then you [the physician] are confronted with an acute situation and then you can't perform euthanasia anymore, because you need your own safety [in terms of respecting the legal requirements]. […] In such circumstances we move to palliative sedation because we say from a legal point of view we are not allowed to perform euthanasia, but we see that it is no longer bearable for the patient and it isn't medicine to leave the patient in an unbearable state, so the only thing we can do is initiate palliative sedation. Then we explain to the patient as well as to the family: […] this is no longer bearable for the patient, we can't bear to see this any longer, the only thing we can do now is put the patient to sleep, but in a way that the rest of the process will follow a natural course, and how long that will take, well we don't know.

Not all patients had specific preferences for one practice or the other when the differences between both practices were explained to them. As illustrated by a physician:

> **Physician A; Home:** That often happens in practice in my experience, that when you talk to people about the possibilities [at the end of life], patients will often reply: 'just act for the best and make sure I don't suffer'. Of course, this is not the same as having a patient say: 'I want euthanasia'.

Decision making

Both physicians and nurses mentioned to be reluctant to use continuous sedation for patients with a longer life expectancy, whereas this was not necessarily regarded as a problem for patients requesting euthanasia.

> **Physician A; Home:** For euthanasia, the patient can still have a life expectancy of weeks, months, or even years. You can have cancer patients who may still have months to live […]. In these cases, we would not perform palliative sedation.

Concerning the actual decision making, some nurses in our focus groups stated that compared with cases of euthanasia, physicians less often included nurses in the decision making regarding continuous sedation.

> **Nurse F; Oncology:** In our hospital I have observed that when we talk about euthanasia, it is always discussed by the team. […] And everyone can give their input, whereas when we are talking about palliative sedation, the decision is often taken by the physician […]. When we talk about euthanasia, we [nurses] are involved in the decision making, so it is strange that when palliative sedation is at issue, not a single nurse on the ward finds it odd that she is not involved.

A nurse explained that this may have to do with a lack of official procedures and guidelines for continuous sedation, combined with an unwillingness of certain physicians to consult others in their decision making:

Nurse A; Home: The euthanasia procedure provides that a physician should consult with the nursing team and with the family, whereas for palliative sedation, there are no procedures, there are no guidelines. So it is precisely the profile of very dominant and hierarchical physicians that matches very well with palliative sedation, because there they hold absolute sway and they don't have to consult with anyone. So it is true that there is a certain kind of physician who chooses not to perform euthanasia, but performs palliative sedation instead: 'we will quietly increase the dose'. In our team we call those patients a 'sans papier' [i.e. an undocumented person, a term used for illegal aliens]. You don't have a procedure, you don't have to report anything, and it's all okay and the problem is solved.

Intention

Finally, many physicians and nurses drew a clear distinction between continuous sedation and euthanasia with regard to the intention involved. They explained that sedation aims to control refractory symptoms, whereas in the case of euthanasia one has the intention to end the patient's life.

Nurse E; Palliative support team: Everyone is always talking about an intention. Thus, sedation does not have the intention to kill, but to control refractory symptoms, whereas euthanasia has the intention to kill.

Physician C; Palliative support team: You don't initiate sedation to shorten [a patient's] life, that is never an intention of … [palliative sedation].

Physician A; Home: Indeed, that is precisely the reason why you have to perform it in the last phase and not for patients who are suffering from symptoms but who are still eating and drinking. Patients who continue to eat and drink, may live for another month or two.

Physician B; Palliative support team: [W]hen you start palliative sedation, [the] comfort of your patient […] is your only intention.

When the distinction between continuous sedation and euthanasia may become blurred

Although the majority of the respondents considered continuous sedation and euthanasia as different practices at the end of life, some stated that the distinction between the two may become blurred, conceptually or ethically.

Nurse F; Oncology: I'm always struggling with this. The transition. When do we talk about euthanasia, and when about sedation?

Nurse G; Home: No, euthanasia, that is clear … that is very clear.

Nurse F; Oncology: I don't know, for me it is not so clear. I find it a bit eh …

Nurse G; Home: Euthanasia is really […] where someone is […] giving a lethal injection at the request of the patient. Whereas sedation is just keeping someone asleep until maybe death follows.

Physician B; Palliative support team: Whether you perform sedation or euthanasia, ethically speaking that is the same for me… I would cover myself and take the same measures and follow the same procedures for sedation as I would for

> euthanasia. When performing sedation, a physician should not delude herself into thinking 'since it is sedation I am administering, there cannot be any problems'. I would want to rely on various people's advice that sedation is indeed appropriate in the case at hand, before initiating it. From an ethical point of view, it is exactly the same action … initiating a euthanasia or a sedation is the same, ethically speaking.

According to the respondents, the distinction between continuous sedation and euthanasia diminishes or may even disappear when medication is increased disproportionally. Some participants described that the intention shifted to the ending of life.

> **Nurse H; Palliative care unit:** What I have observed in the context of my work in the [palliative] support team is that usually, from the start, a thorough sedation was given. Sedation was frequently started with the understanding: 'if the patient is still here tomorrow, then we will double [the dose]'. That was commonplace. So in fact they often ended life, even if this was not the initial intention of the sedation. [The underlying reasoning seemed to be:] since the patient is not awake anymore, what is the point of letting her lie here for days?

> **Nurse A; Home:** That is one of the sore points. There is a strong temptation to increase the dose until the sedation is no longer proportional to the refractory symptoms, and then you are probably shortening life.

> **Nurse I; Home:** [I] think: 'darn, we are doing it [increasing the dose] and it happens all the time in practice'. And that is very difficult for me. What do you have to do about the team? How can the team cope with the fact that yesterday the pump was on such and such a dose but today it is at a higher dose.

> **Nurse J; Palliative support team:** If it is agreed in advance that we will increase, increase, increase the dose until the patient dies, then what is happening is not attempting to control the symptoms and allowing the patient to die. The intention then is to end life.

A physician described another situation in which sedation might shorten life, namely when sedation is induced for patients with a longer life expectancy.

> **Physician A; Home:** But if one performs it too early in the course of a disease, then one is shortening life.

DISCUSSION

Although the differences and similarities between continuous sedation until death and euthanasia were not specifically addressed in the questions in the focus groups, it emerged as an important theme in the accounts of the participants. Our study describes the similarities and differences between both practices as perceived by physicians and nurses in Flanders, Belgium. Sometimes the term euthanasia was used by both groups as an umbrella term, also including acts of life ending without a request of the patient. Many participants perceived differences between continuous sedation and euthanasia, particularly with regard to preferences and requests, decision making, and intention. However, some participants stated that the distinction between the two is sometimes blurred or even non-existent, especially when medication is increased disproportionally or when sedation is induced too early.

Our study is one of the few studies that provide in-depth insight into physicians' and nurses' attitudes and experiences regarding the practice of continuous sedation until death. Our study benefitted from the use of focus groups allowing us to explore knowledge, views and beliefs about two end-of-life practices that are subjects of medical and ethical discussion. Through focus groups, it is also possible to obtain multiple perspectives about the same topic of research by inviting participants from different backgrounds and settings. However, this research method entails some limitations. In view of the small numbers of participants and the fact that these participants do not constitute a representative sample, our findings cannot be generalized to the whole population of physicians and nurses. Furthermore, focus groups are not fully anonymous since opinions and experiences are shared with the group as a whole. The sensitivity of the topic of our focus groups might have led to socially desirable answers by the participants and participants being more reluctant to state their true opinions. We have tried to overcome this issue as much as possible by stressing confidentiality. Finally, respondents' terminology did not always correspond with the definitions of the researchers, nor with those of the Belgian Euthanasia Law, and the term 'euthanasia' sometimes also referred to acts of life ending without a request of the patient. This should be taken into account when interpreting our findings.

Euthanasia was legalized in Belgium in 2002 after more than a decade of intense societal debate galvanized by an opinion on euthanasia from the Belgian Advisory Committee on Bioethics as well as 3 years of debate in parliament (11). This end-of-life practice has increasingly been brought to the attention of caregivers and the general public, also by way of the media, and to this day, it remains an important issue of public debate (13). According to our participants, patients requesting euthanasia generally used more specific formulations, whereas continuous sedation was less often or less explicitly addressed by patients. It is possible that the practice of continuous sedation until death is less well known among patients and their environment. Furthermore, it may also relate to the fact that a key condition for euthanasia is that the patient should make an explicit request, while such a request is not a prerequisite for the use of continuous sedation until death (although guidelines state that its use should be discussed with a competent patient or his or her representatives). Despite the fact that patients' and families' wishes were not always expressed clearly or specifically, the participants in our study stated that they deemed it important to clarify these wishes and preferences through ample communication and discussion.

Besides the importance of discussing such far-reaching end-of-life decisions with the patient, consultation and discussion with other caregivers is deemed important too. For euthanasia, the physician must consult with a second independent physician as well as with the nursing team if applicable (12). Various guidelines on sedation state that the members of the team involved in the care for the patient should be actively involved in decision making (2;3). If a physician doubts his or her own expertise concerning continuous sedation or finds it difficult to decide whether or not to initiate continuous sedation, the physician should seek specialist palliative care advice. Nurses in our study reported to be less often involved in decision making for continuous sedation than for euthanasia. This is in line with the findings from another Belgian study: Inghelbrecht et al. (14) found that there was no communication between the nurse and the physician about continuous deep sedation in 17.6% of the sedation cases.

Although the majority of the respondents in our study considered continuous sedation and euthanasia as different practices at the end of life, some stated that the clear distinction between continuous sedation and euthanasia diminishes or may even disappear when medication is increased disproportionally or when sedation is induced too early. Some respondents described that in such instances, the physicians' intention is or shifts to life ending. The focus group participants thus often considered the intention with which the action is performed as well as the outcome pivotal in distinguishing continuous sedation from euthanasia, which is in line with the argumentation developed in Materstvedt (15). The finding that some respondents did not always find sedation and euthanasia to be

always clearly distinguishable is also in line with other studies. In a study of Rietjens et al. (16), some American nurses had difficulties with working on a 'fine line' between sedation and euthanasia. According to them, sedating a patient diminishes the patient's capacity to eat and drink, and as such will contribute to their death. A study concerning general practitioners of Anquinet et al. (17) revealed that 2 out of 28 physicians perceived the use of continuous deep sedation as similar to euthanasia. This was the case when the patient had previously made a request for euthanasia. Other studies have also shown that physicians sometimes also administer sedatives when they intend to end life (7;18). An international study of Anquinet et al. (8) that compared the practice of continuous deep sedation in Belgium, the Netherlands and the United Kingdom, found that in several cases, physicians who had indicated that they had performed continuous deep sedation until death also indicated that they had done so to end the patient's life. However, these studies do not report on the types and dosages of drugs administered during the performance of continuous deep sedation until death. Because it is known from studies about the effect of morphine on patients' life expectancy that physicians might overestimate the life-shortening effect of such medications (19) these studies should be interpreted cautiously.

Guidelines distinguish the use of continuous sedation until death from drug-induced ending of life (this is referred to as euthanasia in the case of an explicit patient request) by referring to the physicians' intention as well as to the outcomes of the physicians' acts, therefore referring to similar concepts as our focus group respondents. More specifically, the guidelines state that the physician's intention while applying continuous sedation should be to relieve suffering through the lowering of consciousness, while the physician's intention while applying euthanasia is to relieve suffering through the ending of life by the administration of a lethal dose of medication (2;3). They further state that 'the physician's act should reflect this intention, meaning that the dosages and combinations of medication should be administered in proportion to the specific suffering of the patient that the physician wants to alleviate' (3). In addition, the guidelines say that 'there is no evidence that sedation, if carried out in accordance with good medical practice, does shorten life, while euthanasia certainly does' (2). Therefore, they state that sedation can only be used for patients with a life expectancy of at most a few days to one week (Belgian guideline), or to two weeks (Dutch guideline), because otherwise patients would die as a result of the sedation, that is, through dehydration, since both guidelines recommend to withdraw the administration of artificial hydration when this is considered to be medically futile (2;3).

We want to point to two caution remarks here. First, on the basis of our qualitative data, we cannot draw conclusions on the frequency of physicians' use of sedation with the intention or the outcome of shortening life. Second, there is ample ethical debate and no clear consensus about the differences and similarities between sedation and euthanasia, and several authors claim different borders (15;20). In this article, we describe the experiences and attitudes of our focus group respondents. Having that said, it is clear that the situations described by the respondents are clearly not always in line with guideline recommendations (2;3). This might, in part, be explained by a lack of knowledge about the circumstances in which sedation can be used as well as the way it should be performed properly. The Belgian sedation guideline has been published in September 2010, after the performance of our focus group study. Moreover, it is possible that physicians perceive continuous sedation as part of regular medical treatment and therefore, for example, do not feel obliged to talk the decision for sedation through, for example, with nurses involved in the care for the patient or palliative care expert teams.

Our findings may have some practical implications. Safeguards with regard to decision making on continuous sedation may be necessary for clinical practice. The practice of continuous sedation and its appropriate performance should be included and extensively discussed in medical training for physicians as well as for nurses, and guidelines could also play an important role in achieving these goals. In addition, future in-depth research should be concerned

with what types and dosages of medications are being used in continuous sedation, the indications for such treatment, and should address the issue of the potential life-shortening effect of such sedative medicines. Our qualitative data on the differences, but most important, on the similarities between continuous sedation and euthanasia as perceived by professional caregivers may be relevant to other countries, also countries where euthanasia is illegal. In those countries, professional caregivers might experience similar struggles as the respondents in our study. It would be interesting to explore in further international research whether our findings could be extrapolated to other countries in general and to countries without a euthanasia law more specifically. Finally, in-depth and international research from multiple perspectives (also relatives) should also be encouraged to provide a better understanding of the practice of continuous sedation until death.

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Part III

Continuous sedation until death in Belgium, the Netherlands and the United Kingdom

Chapter 5

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 to 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 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.

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 for 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), the Netherlands (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 to 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 (Netherlands) 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 the Netherlands (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: '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: '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: '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. Patient's socio-demographic 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).

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%).

Table 1. Characteristics of deaths.

	Flanders	**NL**	**U.K.**
Number of deaths per year*	54,880	130,870	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†			
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‡			
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§			
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 non-response. 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).

* Flanders, data are for 2007; the Netherlands, data are for 2005; the United Kingdom, data are for 2008.

† 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.

‡ Cerebrovascular disease is included in cardiovascular diseases for Flanders, NL and the U.K.

§ 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.

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 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%).

Table 2. Frequency of continuous deep sedation.

	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).

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.

Table 3. Characteristics of patients who received continuous deep sedation.

	Hospital			Home		
	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*						
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†						
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).
* In the U.K., age group 1-64 was 1-69 years and age group 65-79 was 70-79 years.
† U.K. cause of death: weighted by specialty only.

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 U.K., but reached only statistical significance for NL compared with Flanders. For the home setting, these proportions were 89% (Netherlands) vs. 72% (Flanders) and 81% (U.K.) and for 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.

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.

Table 4. Characteristics continuous deep sedation.

	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 (excl. 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)
> 1week	10 (7-16)	11 (6-18)	8 (3-12)	9 (5-18)	4 (2-8)	8 (0-15)
In conjunction with PAD*	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 the U.K. (455).
Missing cases: U.K. hospital (n): Medication (29), Duration (29).
* For Flanders, NL, and the U.K., PAD includes euthanasia, physician-assisted suicide and life shortening not on request.

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.

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*				
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 bold.

* In the U.K., age group 1-64 was 1-69 years and age group 65-79 was 70-79 years.

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 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%-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 to patients 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 in 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 focuses of the UNBIASED study (U.K.-Netherlands-Belgium International Sedation 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 – Belgium, 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).

Conclusion 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 between 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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Chapter 6

Descriptions by general practitioners and nurses of their collaboration in continuous sedation until death at home. In-depth qualitative interviews in three European countries

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Submitted

ABSTRACT

Background

One palliative care approach that is increasingly being used at home for relieving intolerable suffering in terminally ill patients is continuous sedation until death. Its provision requires a multidisciplinary team approach, with adequate collaboration and communication. However, it is unknown how general practitioners (GPs) and home care nurses experience being involved in the use of sedation at home.

Aim

To present case-based GP and nurse descriptions of their collaboration, roles and responsibilities during the process of continuous sedation until death at home in Belgium, the Netherlands and the United Kingdom.

Design

In-depth qualitative interviews.

Setting/Participants

25 GPs and 26 nurses closely involved in the care of 29 adult cancer patients who received continuous sedation until death at home.

Results

We found that in Belgium and the Netherlands it was the GP who typically took the final decision to use sedation whereas in the United Kingdom it was predominantly the nurse who both encouraged the GP to prescribe anticipatory medication and decided when to use the prescription. Nurses in the three countries reported that they commonly perform and monitor sedation in the absence of the GP which they reported to experience as *'emotionally burdensome'*.

Conclusion

We have found variety between the countries studied regarding the decision making and provision of continuous sedation until death at home. These differences may among others be due to different organizational contexts in the three countries such as the use of anticipatory medication in the United Kingdom.

INTRODUCTION

Continuous sedation until death (from here onwards referred to as 'sedation') is often used as a last resort option for relieving intolerable refractory (i.e. untreatable) symptoms of terminally ill patients at the end of life in which the patient's consciousness is lowered until the time of death (1-4). Previous international research has shown that sedation is commonly used in different countries and that systematic differences occur in its practice between countries (5-8). It has been suggested that different cultural, legal, and organizational contexts may underlie this variation (5;7;8). To explore qualitatively and to seek to explain these differences in reported practices of sedation between different countries, the UNBIASED study (UK Netherlands Belgium International Sedation Study) has been set up in Belgium, the Netherlands and the United Kingdom (9). This study is part of the UNBIASED study and focuses on the reports of physicians and nurses in the home setting.

Due to a strong governmental emphasis on primary health care and the wishes of many patients to be cared for at home as long as possible in all three countries, general practitioners (GPs) may increasingly encounter people with refractory symptoms necessitating sedation (10-13). For supporting GPs in their practice of sedation, guidelines on sedation were developed in the Netherlands in 2005 and in Belgium in 2010 (2;3). In 2009, the European Association for Palliative Care (EAPC) published a framework of recommendations for the use of sedation (4). No sedation guidelines exist in the United Kingdom. For patients who wish to remain at home in the last few days or weeks, it is good practice for the GP to prescribe anticipatory medication to ensure that there is no delay in responding to a symptom if it occurs (14). The anticipatory medication that is prescribed in advance consists of sedatives alongside other commonly used drugs at the end of life often referred to as the 'just in case' four core end-of-life medications which are kept in the patient's home (15). It has been suggested that British nurses have a key role in activating these anticipatory prescriptions although literature research into this issue is scarce (16).

In the countries studied, palliative care is primarily the responsibility of the GP (17-19). For daily care, GPs can be supported by home care teams. Palliative support teams, which are often multidisciplinary (including a physician, nurses, a psychologist and/or a physiotherapist), can be called by the GP to offer advice and support at the bedside or by telephone (17-20). Although most GPs value highly their central role in providing palliative care, some may find it challenging. GPs in a qualitative study reported that they experienced barriers in providing adequate palliative care such as a lack of time to arrange home care and to fulfill their tasks, a lack of knowledge about medical treatments, particularly for symptom control and suboptimal communication, coordination and collaboration with other health care professionals (21;22). As the professionals who see the patient most frequently, home care nurses also have a central role in providing palliative care (23). Similarly to GPs, they find palliative care rewarding but often challenging due to a lack of staff, time and formal support and a heavy workload and stress (23). Belgian and Dutch home care nurses have reported that they are less often involved by physicians in the decision-making process concerning interventions such as sedation than are nurses working in institutions (24-27). On the other hand, they are frequently involved in the performance and monitoring of these interventions (24-26). Consequently, several authors have raised questions regarding the responsibilities of nurses at home (24-26).

There is a lack of qualitative in-depth studies of the complex realities of sedation at home from a double perspective, i.e. from the GP and the nurse. Therefore, in our qualitative in-depth interview study, we investigated descriptions by GPs and nurses of their collaboration, roles and responsibilities during the process of sedation at home in Belgium, the Netherlands and the United Kingdom.

METHODS

In the UNBIASED study, in-depth interviews were held with physicians, nurses and decedents' relatives in Belgium, the Netherlands and the United Kingdom in 2011-2012 in hospitals (oncology wards), palliative care units (in Belgium) or hospices (in the United Kingdom and the Netherlands), and at home. We refer to the published UNBIASED study protocol for a full description of the methods used (9).

Study design, setting and participants

In this paper, we report perspectives from GPs and nurses in the home care setting in the three countries. GPs and nurses were invited to take part in a face-to-face interview if they had recently taken a key role in the care of a patient 1) older than 18, 2) who had died of cancer, and 3) who had been continuously sedated until death. Senior clinical staff identified eligible decedents and nominated GPs and nurses involved in their end-of-life care. GPs and nurses were invited through an information sheet and letter explaining the purpose of the study. GPs and nurses in the three countries were interviewed about no more than three patients.

Procedures

All GPs and nurses gave their informed consent to the audio taping of the interview. At the beginning of each interview, socio-demographic information was obtained about the interviewee and the patient (via the GP in the three countries or the nurse in the United Kingdom). Patient anonymity was preserved. Participants could use the patient records if necessary to support them in their recollection. The interviews were semi-structured and supported with the use of aide-memoires which focused on participants' recollections of the decedent's care and the use of sedation in particular. Interviewees were asked to describe the reasons for the use of sedation, how the decision-making process evolved and how sedation was performed. Finally, we asked them about their general ideas and attitudes regarding the use of sedation.

Data analysis

All recordings of the interviews were transcribed verbatim and participant confidentiality was guaranteed. The Belgian and Dutch interviews were translated into English by a professional translation bureau and checked for accuracy. All interviews were read by L.A. and J.A.C.R. and the main themes concerning GPs' and nurses' collaboration, role and responsibilities during the process of sedation at home were identified. The interviews were reread and quotes were selected and classified under the matching main themes. The selection and classification was done by L.A. and checked by J.A.C.R. The development of the analysis was discussed with all co-authors in telephone meetings. Finally, quotes per main theme were selected by L.A. and J.A.C.R. for publication and approved by all researchers.

RESULTS

We explored 29 cases of patients with cancer (11 BE; 10 NL; 8 UK) who had been continuously sedated until death at home with 25 GPs (9 BE; 10 NL; 6 UK) and 26 nurses (11 BE; 8 NL; 7 UK). In 28 cases, both a GP and a nurse had been involved in the patient's care at home (11 BE; 9 NL; 8 UK). In one Dutch case, no nurse had been involved

according to the GP because the patient's family took care of the patient until the patient's death. In 24 (9 BE; 9 NL; 6 UK) of these 28 cases we were able to interview both the GP and the nurse most involved. Characteristics of the deceased patients, GPs and nurses can be found in Table 1.

A home care team had been involved in 24 cases (10 BE; 6 NL; 8 UK) and a specialist palliative home care team in 20 cases (7 BE; 9 NL; 4 UK). In two Belgian cases, GPs reported that a specialist palliative home care team had not been involved but that they themselves were specialized in palliative care.

In the interviews, GPs and nurses in the three countries reported on their collaboration, roles and responsibilities during the decision-making process, performance and monitoring of sedation at home.

Table 1. Characteristics of patients, physicians and nurses.

	Patients n=29	**Physicians* n=25**	**Nurses* n=26**	**Cases with both perspectives n=24**
Country				
Belgium	11	9	11	9
Netherlands	10	10	8	9
United Kingdom	8	6	7	6
Age				
≤40	2	2	6	n/a
41-50	1	6	8	
51-60	3	9	7	
61-70	8	2	0	
71-80	10	0	0	
>80	5	0	0	
Not stated	0	6	5	
Sex				
Male	12	14	2	n/a
Female	17	11	23	
Not stated	0	0	1	
Specialism				
Primary care/care home	n/a	23	10	n/a
Palliative home care team		2	15	
Not stated		0	1	
Diagnosis				
Abdominal/stomach	1	n/a	n/a	n/a
Bladder/renal	1			
Colo-rectal	2			
Brain/glioblastoma	1			
Breast	4			
Gynaecological	1			
Facial maxillary/oesophageal	1			
Gall bladder/pancreatic	3			
Leukaemia/myelofibrosis/myeloma	2			
Lung/mesothelioma	8			
Melanoma	1			
Peritoneal	2			
Prostate	2			

* More than one could have been interviewed.

Decision-making process of the use of sedation until death

In the three countries, GPs and nurses said that nurses often coordinated the care at home. They also described how nurses supported the patient and the patient's family when there were emotional issues towards the end of the patient's life.

> **GP, BE, case 7:** Those nurses played a very, shall I say yes covering role, a coaching role. They take over a lot [of the tasks].

> **Nurse n°2, UK, case 1:** I remember my role [as a palliative care nurse] being more related to the emotional side of things. I didn't have much contact with the patient or the district nurses towards the end of his/her life because they were coordinating things by then and the patient had a syringe driver in situ so they were going in every day and, as a specialist nurse, unless there are specific emotional or symptom issues, we would liaise with the community team and they know they can contact me for advice but I wouldn't necessarily be visiting regularly because the district nurses were going in daily and things were controlled.

The nurses in the studied countries also often explained that they had an explanatory role, informing the patient and the family about what one can expect towards the end of life. In some cases, nurses reported that they informed patients and their families about the possibilities at the end of life, such as sedation and euthanasia in Belgium and the Netherlands, and the use of anticipatory medication in the United Kingdom.

> **Nurse, BE, case 8:** We give the possibilities [decisions at the end of life]. And then there are also the nurses from the palliative home care team who were more specific [about it] and who had more time to go deeper into it, as in 'what do the various options precisely entail'.

> **Nurse n°2, UK, case 1:** I [a palliative care nurse] do a lot of explanation with the family as to what they [anticipatory medication] are and when they're used.

According to the Belgian and Dutch respondents, the option of sedation was mostly discussed by the GP with the patient and the patient's family, and the GP also discussed it in a few cases with the nurses or the palliative team.

> **GP, NL, case 1:** The decision [to sedate] lies with me because you cannot just perform palliative sedation in any situation.
>
> **Interviewer:** And who else was involved in the decision making?
>
> **GP, NL, case 1:** If you take a decision about dying, I want to have the conversation in the first instance only with the patient. Then I have a second conversation with the most involved relative. What I also always say is that the decision [to sedate] is never my own decision. I also involve the palliative care team, and I also let them decide.

Nurse, NL, case 1: It [sedation] is not our decision, it is really a decision between the GP and the patient, who [the GP] then decides to start with it.

Interviewer: And you yourself were present at that conversation.

Nurse, NL, case 1: At the moment when the GP discussed sedation with the patient today, I was present. Not before.

Interviewer: And who else was present during that conversation?

Nurse, NL, case 1: The patient's wife.

In Belgium and the Netherlands, it was usually the GP who took the final decision to use sedation and reported themselves as having overall responsibility, even where the nurses suggested when sedation should be begun or increased the sedative medication within prescribed parameters.

Nurse, BE, case 7: I think that the indication of that decision often lies with the nurse. But the GP always decides. The GP is the one who says: 'the syringe driver will or will not be placed', but I think we indicate the moment. Especially the nurses, because we are the ones who are most often with the patient day by day.

Nurse, BE, case 9: The doctor is still the one responsible, that's good because in the end it is the nurse who puts in the pump and increases the medication.

The role of the nurses in the decision-making process was, according to most of them, to advocate the patient's perspective and needs and affirm the GP's decision to sedate.

Nurse, NL, case 1: The doctor really takes the decision, we only suggested that the patient also had told us that he/she can't take it anymore and we just supported him/her. We see it as well, not that I'm saying to the doctor: 'you should do that now' because we are not doctors, it doesn't work like that.

Nurses and GPs from the United Kingdom described a rather different decision-making process about the use of sedation compared with those from Belgium and the Netherlands. In their description, two separate decisions need to be taken: the decision to prescribe anticipatory medication, and the decision to use this medication. Several British GPs and nurses reported that it is often the nurse who encourages the GP to prescribe the anticipatory medication and then takes the responsibility for deciding when to use prescribed medication for the patient.

Interviewer: And what about the district nurses - do they come sometimes and say to you, 'I think…'

GP, UK, case 5: Yeah, they're generally quite good and they generally will suggest if they think that somebody's at the stage of needing a syringe driver, and they probably deal with it a lot more than we [GPs] do really.

Nurse n°2, UK, case 5: I think the district nurses have really got to terms with the use of anticipatory drugs and, whereas I used to have conversations with GPs where I would recommend that they prescribe anticipatory drugs and they would then say to me, 'What do you recommend I prescribe?'.

A few British nurses and GPs reported that GPs were very wary and afraid of prescribing or administering medication because of possible implications for themselves.

GP, UK, case 5: I don't think sedation is over-used. Perhaps in occasions, as doctors, we maybe should have thought about putting drivers in sooner than later.

Interviewer: And why do you think that we tend to wait and hang on a little bit?

GP, UK, case 5: Sometimes I think it's just worrying about being too aggressive and making somebody too sedated and how the family might react to that. You always worry about, you give that dose of morphine and then they stop breathing that second and then it just looks like you've done it. If there was no family you might do things a bit differently if you felt that you wouldn't have eyes scrutinizing you.

Nurse n°2, UK, case 1 and 5: I think it's very difficult to sort of marry up the GP's responsibility for prescribing that sedation with the patient's wishes, as in the case of the patient who wanted to be sedated. It is difficult to go back to the patient and say, 'I know you don't want to be awake… but you've got to be.' I mean, obviously I would never say, 'the doctor won't prescribe it…because s/he's worried about the implications on him/her,'.

British nurses described how they sometimes suggested what medication should be used for sedation, although several of them reported this should be a team decision.

Nurse n°2, UK, case 1 and 5: It's often the district nurse making that decision and going to see the GP and saying, 'time for a syringe driver'. And it depends on the GP and their knowledge and experience, but quite often we're suggesting what they put in it as well.

Nurse, UK, case 3: I've noted that in the county sometimes nurses will go their own way, which I think is a huge thing. I strongly believe it should be a double-up nursing situation. If you're making that decision and you feel that it's appropriate to start a syringe driver, I would still always ring the out-of-hours GP, even though it's written up, and discuss it. I think it's got to be a team decision.

In a few cases in the United Kingdom, the decision to administer anticipatory medication was described as a joint decision between the nurse and the GP with the final responsibility lying with the GP.

GP, UK, case 6: So it [administering medication] is always a collaborative decision making in some respect. The final sort of responsibility probably lies with me, but in fact the actual decision's been made with nursing input, and in fact the patients and staff and the relatives' wishes as well.

Interviewer: Who made that decision?

Nurse, UK, case 6: We make it together with the GPs. There's a basic set of drugs written up that cover the base symptoms. It's just deciding when to or if you need to start them.

Interviewer: And was that a nursing decision to start them?

Nurse, UK, case 6: Well, it's a joint decision between the nurses and the GP.

Performance of sedation until death

After the decision was made to use (anticipatory) medication, respondents in the three countries described how it was mainly the nurse who started up the syringe driver and administered the medication, mostly in the absence of the GP.

> **Interviewer:** Was the GP also present at the time of the connection of the pump?
>
> **Nurse, NL, case 5:** Well here in X [place] that is almost never the case. I worked in Y [another place] before and there it was a must; we would say to the GP: 'if you are not there then we won't start the sedation'. But that is not common here.

According to some Belgian and Dutch nurses, GPs lack knowledge about placing a syringe driver. Also, starting sedation is a technical act and several nurses said that they are more skilled at it than GPs.

> **Interviewer:** Is it also usually the doctor who starts the sedation, or is that left to the nurse?
>
> **Nurse, BE, case 1:** Yes, the nurse usually does that with someone from the palliative home care team.
>
> **Interviewer:** And administering the medication in the pump – is that also done by the nurse?
>
> **Nurse, BE, case 1:** Yes. We know what should go in there and we do that. The doctors don't start up the syringe driver. They actually don't really know that driver. And if there is a problem at night then we are also the ones who go because doctors usually don't know that.

In a Dutch case, the GP said that s/he didn't find his/her presence necessary at the start of sedation because the nurse had plenty of experience. The nurse from that same case said that s/he found the presence of the GP desirable although the GP was mostly not present.

> **Interviewer:** Have you been present at the start of sedation?
>
> **GP, NL, case 6:** No, I've discussed it with the nurse who was going to administer it, and whether s/he wanted me to be there. But well, I think it's not necessary, because they have plenty of experience and everything was said and done and discussed. So yeah, I don't need to be present at the start of sedation I think.
>
> **Interviewer:** And you were there yourself, at the start of the sedation, you connected the pump.
>
> **Nurse, NL, case 6:** Yes.
>
> **Interviewer:** How does that exactly work? Is there for example a doctor always present as well?
>
> **Nurse, NL, case 6:** No a doctor isn't always present, it is desirable that the GP is there, but that's usually not the case. No, there is usually no doctor present.

Another Dutch nurse explicitly said that s/he had appreciated the GP's presence while s/he had started up the sedation.

> **Nurse, NL, case 4:** Well I'm the one who connected the pumps, inserted the needles. What I found very positive by the way, was that the GP was present when connecting the pump. This is very desirable but it's actually almost never done.
>
> **Interviewer:** Oh I think that is special to hear, that it wasn't, let's say, that standard that the GP stayed?

Nurse, NL, case 4: Yes, I have said it to the GP as well, that his/her presence is very nice. For the family too, because they have been so long with the GP. It's just closing a piece of care, I think it's very neat.

In a few cases in Belgium and the Netherlands, the GP had started up the sedation.

Interviewer: Were you actually present yourself at the start of the sedation?

GP, NL, case 8: Yes I have been present, but I can imagine there might be situations where it'll be different, I don't know.

Interviewer: Okay, but in any case, you were present for this patient.

GP, NL, case 8: Yes.

Nurse, NL, case 8: The GP just gave the injection.

Interviewer: And does it always go like that, or do you as a nurse do that too?

Nurse, NL, case 8: We do it as well, but that first injection is usually done by the doctor, yes always actually.

Monitoring of sedation until death

In general, the monitoring of sedation until the patient's death was not often discussed by physicians and nurses during the interview in any of the countries. According to some GPs and nurses in all countries, this was mostly the nurse's task.

Interviewer: So obviously you're saying that the Macmillan nurses were involved…I presume the district nurses were involved as well?

GP, UK, case 4: Yeah, district nurses obviously. The syringe driver was being looked after by the district nurses.

Several Belgian, Dutch and British nurses talked about the responsibility that they, and colleagues with less experience of syringe drivers, experienced during sedation. A British nurse said that, although they are trusted by GPs to take decisions regarding giving anticipatory medication, nurses may also struggle with the dilemma of actually administering the medication; some reported an emotional burden relating to uncertainty about whether the medication had hastened the patient's death.

Nurse n°2, UK, case 1 and 5: Actually, once the doctors have written the medication up, it's up to the nurses to decide when it's given and to monitor it and contact the doctor if it's not working or if the patients are needing it frequently. And I remember a very sort of difficult situation with someone with terminal agitation who was very near to death, and that dilemma: 'Will this sedation actually kill them?'. But they need it because they're not settled and they're a danger to themselves, but it's still that sort of emotional burden on the nurse, sort of like, 'Do I give it?'. And I suppose in doubt you ask the doctor but we're trusted enough to make the decision.

Nurses perceived responsibility especially when the GP lacked sufficient knowledge and left the start up and monitoring of sedation to the nurse.

Nurse n°1, UK, case 1: GPs rely on us virtually for all the information because they just don't know the patients or the families. I wish that GP's had more education. They often do not even know how to write a script and we have to tell them. They tend to write up the largest doses straight away and we will say 'No, I think we should start with a small dose'. They should do out and visit the patient before prescribing. Not all of them do that, and this is a big responsibility on us, especially nurses with less experience of syringe drivers. It all comes from experience.

DISCUSSION

Summary

Our study provides insight into GPs' and nurses' views and descriptions of their collaboration, roles and responsibilities during the decision-making process, performance and monitoring of end-of-life sedation at home. We found that it was the GP who mostly took the final decision to use sedation in Belgium and the Netherlands whereas in the United Kingdom, many nurses reported that they encouraged the GP to prescribe the anticipatory medication and then decided themselves when to use the prescription for the patient. Most nurses in all three countries reported that they had themselves performed and monitored sedation until death, often in absence of the GP. Several nurses reported that they felt burdened by the responsibility of performing and monitoring sedation in cases where the GP was not present or lacked knowledge about sedation.

Strengths and weaknesses

By conducting interviews with GPs and nurses in three European countries we were able to obtain detailed, diverse and in-depth knowledge on the collaboration between health care professionals during the practice of sedation at home. A major strength of our qualitative study is the cross-national comparison between Belgium, the Netherlands and the United Kingdom, which enabled us to identify and explain possible differences in the practice of sedation in these countries. Another strength is that we combined the perspectives of both GPs and nurses involved in the care for of the same patient during sedation at home. This allowed us to compare how they had experienced their collaboration during this medical practice. Although our results cannot be generalized to the whole population of GPs and nurses due to the relatively small numbers of cases and interviews, we believe that our findings may provide new insights that may be extrapolated to similar clinical situations.

Comparison with existing literature

Belgian and Dutch interviewees in our study reported that it was mostly the GP who took the final decision for the use of sedation. This is in agreement with sedation guidelines that state that the GP most involved in the patient's care bears responsibility for determining the indications the decision making for sedation (2-4). Nurses reported however that they were not always involved in this process by the GP. This finding follows several quantitative studies that found that home care nurses are less often involved in decision making than their colleagues in institutions (25;27;28). Unlike institutions where physicians and nurses work within the same teams and attend daily multidisciplinary team meetings to review patient cases, GPs and nurses at home usually work separately and do not often see one another at the patient's bedside (27;29;30). In contrast we found that in the United Kingdom, nurses reported how they encouraged GPs to prescribe anticipatory medication and often took the decision about when to

use the prescription. This proactive and leading role of nurses in decision making about the administration of anticipatory medication for symptom control has been described in other British studies (31;32).

Nurses in the three countries reported that they initiated and monitored sedation until the patient's death, often in absence of the GP. These practices seem not to be uncommon as they are also reported in other studies among nurses on sedation at home (24;25). Several respondents in our study suggested that GPs often lack knowledge about the technical performance of sedation, and sometimes about the dosages of medication that should be used. This is supported by qualitative and quantitative studies reporting that GPs perceived their own lack of knowledge and technical competence about symptom control as barriers to providing good palliative care and were less aware of the drugs that may be used in syringe drivers (12;21). As GPs are confronted with patients with unbearable symptoms needing sedation less often than are specialists in a hospital, they may not have adequate knowledge about its use and its performance (5;12). Also, nurses may have greater experience with drugs and syringe drivers, and GPs in our study may therefore have left the administration of sedation to them for (33).

Several studies however have raised questions with respect to nurses' responsibilities and emotional distress when administering sedation on their own (24;25;31;34). In these studies, 'emotional distress' was understood to mean among other things ambivalent feelings, ethical dilemmas and concerns, and struggles regarding this practice (34;35). Our findings support the idea that some nurses find the performance of sedation *'burdensome'* and feel responsible, especially when GPs leave its initiation and monitoring to them and lack sufficient knowledge regarding its use. Nurses said that they sometimes 'struggle' with the 'dilemma' of actually administering the medication and the *'emotional burden'* of wondering whether the medication has hastened the patient's death. As nurses may find it challenging to question their GPs' decisions openly or to discuss their feelings, it may be possible that GPs are not always aware of the responsibility and burden perceived by nurses when complying with GP orders (31;36).

Implications for policy, practice and research

We believe that open communication between GPs and nurses regarding their roles and responsibilities during the use of sedation combined with increased multidisciplinary teamwork may further improve this practice at home. Further in-depth research is needed on the unique roles and responsibilities of nurses regarding the decision to use sedation (in the United Kingdom by using the anticipatory prescriptions) and the performance and monitoring of sedation. When formulating suggestions for policy regarding the use of sedation, we suggest keeping in mind that cultural, legal, and organizational differences may exist between countries and may affect end-of-life care.

In conclusion, our study reveals how respondents perceived that the final decision on the use of sedation in Belgium and the Netherlands was often taken by the GP whereas in the United Kingdom it was often the nurse who took the decision to use an anticipatory prescription. These differences may among others be due to different organizational contexts in the three countries. Furthermore, nurses in all three countries reported that they had often initiated and monitored sedation until death in absence of the GP and that they often experienced this as burdensome.

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Chapter 7

Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life

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Submitted

ABSTRACT

Objective

The use of continuous sedation until death for terminally ill cancer patients with unbearable and untreatable psychological and existential suffering remains controversial, and little in-depth insight exists into the circumstances in which physicians resort to it.

Methods

Our study was conducted in Belgium, the Netherlands and the United Kingdom in hospitals, palliative care units/hospices, and at home. We held interviews with 35 physicians most involved in the care of cancer patients who had psychological and existential suffering and had been continuously sedated until death.

Results

In the studied countries, three groups of patients were distinguished regarding the origin of their psychological and existential suffering. The first group had preexisting psychological problems before they became ill; the second developed psychological and existential suffering during their disease trajectory; and the third presented psychological symptoms that were characteristic of their disease. Before they resorted to the use of sedation, physicians reported that they had considered an array of pharmacological and psychological interventions that were ineffective or inappropriate to relieve this suffering. Necessary conditions for using sedation in this context were for most physicians the presence of refractory symptoms, a short life expectancy, and an explicit patient request for sedation.

Conclusions

Physicians in our study used continuous sedation until death in the context of psychological and existential suffering after considering several pharmacological and psychological interventions. Further research and debate is needed on how and by whom this suffering at the end of life should be best treated, taking into account patients' individual preferences.

INTRODUCTION

Continuous sedation until death (from here onwards referred to as 'sedation') is considered to be a last resort option to relieve unbearable and untreatable (refractory) symptoms experienced by terminally ill cancer patients (1-3). It is defined by sedation guidelines as the deliberate lowering of consciousness, continuously until the patient's death (1-3). Sedation guidelines indicate that wherever possible, the patient (and/or the patient's family) should be actively involved in decision making and give consent for the initiation of sedation. The purpose of sedation should be symptom relief and not the hastening of death (1-3).

One of the key controversies about the practice of sedation concerns its use for patients who have psychological and existential suffering at the end of life (4;5). While the literature lacks uniform terms and definitions of these concepts, a common component includes non-physical suffering such as an overwhelming sense of meaningless, hopelessness, (death) anxiety, panic, depression, sadness, anhedonia, guilt, and/or lack of any interest (6-9). Psychological and existential suffering is not uncommon among end-stage cancer patients: depression and anxiety rates range from respectively 3-77% and 13-79% (10). Prevalence rates of cancer patients' reported hopelessness or demoralization, and losing one's will to live or desire for death range from respectively 7-41% and 2-26% (11). As delirium may interfere with the recognition and control of physical and psychological symptoms, its presence should be ruled out or treated appropriately (12).

Sedation for psychological and existential suffering is considered controversial for a number of reasons. Unlike physical symptoms, it is more difficult to assess whether this suffering is truly refractory due to its subjective nature and a lack of well-established assessment tools (3;5;13). The European Association for Palliative Care (EAPC) recommends in its framework for the use of palliative sedation that psychological and existential distress should be confirmed by mental health care professionals after trials of appropriate therapy such as for instance intermittent sedation. Only after repeated trials of intermittent sedation, continuous sedation could be considered (3). These recommendations are in line with the Belgian and Dutch sedation guidelines (1;2).

A few quantitative studies have addressed the issue of using sedation for the relief of psychological and existential suffering of severely ill patients. According to Dutch physicians, existential suffering, anxiety and depression were amongst the indications for sedation mentioned for respectively 29%, 13% and 30% of the patients (14). British physicians reported that in 25% of the cases in which their patient had been continuously and deeply sedated, sedation had been given because of the patient's intractable psychological suffering (whether or not in combination with other reasons) (15). In addition, a few case studies addressing this issue concluded that sedation is a useful but controversial method for treating psychological and existential suffering at the end of life but that further research is needed on the causes of and therapeutic options for this suffering (13;16-18).

There is little in-depth insight in the circumstances in which physicians resort to the use of sedation for terminally ill patients with psychological and existential suffering. We performed comparative qualitative, case-based studies in three European countries with different legal, policy and service delivery frameworks. We aimed to give insight into physicians' considerations about and descriptions of the use of sedation for cancer patients who had psychological and existential suffering at the end of life.

METHODS

This qualitative interview study is part of the larger UNBIASED study in which in-depth interviews were held with physicians, nurses and relatives in Belgium, the Netherlands and the United Kingdom in 2011-2012 in hospitals (oncology wards), palliative care units (in Belgium) or hospices (in the United Kingdom and the Netherlands), and at home. We refer to the published study protocol for a full description of the methods used (19).

Study design, setting and participants

This paper concerns the physician interviews in the three countries. Physicians were invited to take part in a face-to-face interview if they had recently taken a key role in the care of a patient 1) aged over the age of 18, 2) who had died of cancer, and 3) who had been continuously sedated until death. We did not ask physicians how the process of continuous sedation was monitored. Senior clinical staff identified decedents who met the inclusion criteria and nominated physicians. Physicians in the three countries were interviewed about no more than four patients. If more than one physician was involved, the other involved physician was also interviewed if possible.

Procedures

All physicians gave their informed consent to the audio taping of the interview. At the beginning of each interview, patient and physician socio-demographic information was obtained via the physician. Patient's anonymity was preserved. The interviews were semi-structured, supported with the use of aide-memoires which focused on physicians' recollections of the decedent's care and the use of sedation in particular, and their general attitudes regarding sedation.

Analysis

All recordings of the interviews were transcribed verbatim, and all data that could identify the physicians were removed to preserve anonymity. The Belgian and Dutch interviews were translated into English by a professional translation bureau and checked for accuracy. One researcher (L.A.) selected all physician interviews in which the physician reported on the use of sedation for patients with psychological and existential suffering. This was checked by a senior researcher (J.A.C.R.). All interviews were read by L.A. and J.A.C.R. and main themes were identified. A coding tree was designed and agreed upon, based on the main themes. The interviews were reread and quotes were selected and classified under the matching main themes by L.A. and J.A.C.R. The development of the analysis was discussed with all co-authors in telephone meetings. Qualitative analysis software (NVIVO 9) was used to organize the data. Finally, quotes per main theme were selected by L.A. and J.A.C.R. for publication and approved by all researchers.

RESULTS

For the present study, we explored 39 cases of patients with cancer who had psychological and existential suffering according to the physician (18 BE; 12 NL; 9 UK), involving 35 physicians (13 BE; 11 NL; 11 UK). Characteristics of patients and physicians can be found in Table 1. In this results section, we report on physicians' descriptions of the

various types and origins of patients' suffering before sedation; the health care professionals and relatives involved and interventions used to manage psychological and existential suffering before sedation; and conditions identified by physicians as necessary for the initiation of sedation.

Table 1. Characteristics of patients and physicians.

	Patients n=39	**Physicians* n=35**
Country		
Belgium	18	13
Netherlands	12	11
United Kingdom	9	11
Care setting		
Hospital	10	7
Home	14	13
PCU/Hospice	15	15
Age		
<40	2	10
41-50	0	10
51-60	9	8
61-70	9	2
71-80	14	0
>80	5	0
Not stated	0	5
Sex		
Male	20	19
Female	19	16
Specialism		
Primary care	n/a	12
Palliative home care team		2
Hospital		2
Palliative support team hospital		5
Palliative care/hospice care		14
Diagnosis		
Abdominal/stomach	2	n/a
Bladder/renal	4	
Colo-rectal	6	
Brain/glioblastoma	1	
Breast	2	
Gynaecological	3	
Facial maxillary/oesophageal	2	
Gall bladder/pancreatic	2	
Leukaemia/myelofibrosis/myeloma	2	
Lung/mesothelioma	8	
Melanoma	2	
Peritoneal	1	
Prostate	1	
Sarcoma	1	
Unknown primary	2	

* More than one physician could have been interviewed.

Types of suffering

Physicians in the studied countries described a broad range of symptoms that patients experienced before they were sedated. Physical symptoms included mainly pain, dyspnea, (terminal) agitation, cachexia or fatigue. Psychological symptoms included: panic, anxiety, depression or sadness, and paranoia. Existential suffering included demoralization, despondency, sense of dependency, having difficulties being on the decline, loss of will to live, hopelessness, being 'battle-weary', being [mentally] exhausted and death anxiety.

Based on the physicians' accounts, we identified a continuum of patients who, at one end, suffered mainly from physical symptoms, over patients who suffered from a combination of psychological, existential and physical symptoms, to patients who suffered predominantly psychologically and existentially.

> **UK, General Practitioner, case 37:** Quite a lot of her distress was psychological because she didn't want the children to see her ill [and] to know that she was ill. She developed intractable headache, intractable vomiting and some sort of gradual fixed extension of her neck that we think was metastases at the back of her neck.

Several physicians suspected that the presence of some physical symptoms were related to and may have increased the psychological and existential suffering, and vice versa.

> **UK, Palliative care physician n°2, case 32:** The patient had a lot of problems with anxiety and pain which were very difficult to control all the way along. So there was felt to be quite a large psychological element to it. He was very anxious about his pain and therefore his anxiety made the pain worse and vice versa.

In patients who suffered predominantly psychologically and existentially, physical symptoms were also part of the clinical picture but were sufficiently alleviated.

> **Interviewer:** So the pain was well controlled but the fatigue…
>
> **Belgium, Oncologist, case 19:** It actually was his psychological burden… He could no longer continue.

We could not identify different patterns between the countries in perceived presence of psychological, existential and physical symptoms.

Origin of psychological and existential suffering

The origin of patients' psychological and existential suffering varied in the opinion of physicians. We distinguished three pathways. The first pathway concerned patients who already suffered from psychological problems such as depression, anxiety or mourning for the death of their partner before they became (terminally) ill.

> **Belgium, Oncologist, case 7:** At admission, there was another symptom that we didn't know about from before. There was a pronounced problem of fear, that lady took antidepressants, so throughout her life she had been depressed.

Patients to whom the second pathway applied developed psychological and existential suffering during their disease trajectory as a reaction to their decline and approaching of death. In this second group, there were two subgroups with regard to the patients' way of coping with their approaching end. Patients of the 'resigned' subgroup usually appeared to have accepted that they were going to die soon and were often described to have had 'enough of it'.

> **Belgium, Oncologist, case 5:** The patient asked the question and took the decision. 'I want to sleep, I do not want to wake up anymore'. He was just totally bedridden, he couldn't do anything anymore, he had no quality of life and he also had a very bad life expectancy. He just had enough.

The 'resistance' subgroup did not appear to have accepted that they were ill or dying and were described as angry, anxious, in panic, not wanting to be dependent on others and finding it hard to accept that their health was declining.

> **Netherlands, Palliative care physician, case 29:** The pain was well controlled, but the man had a fear of going to bed, because if he went to bed he could die. He was very afraid of that. He was really fighting it.

The third pathway concerned patients whose psychological symptoms were described as a direct result of their disease. Examples are patients who suffered from a neurological deficit due to a brain tumour, with aggressive behavior, agitation or confusion as a consequence. They were often not (fully) competent anymore according to the physicians.

> **Belgium, Palliative care physician, case 3:** Sedation was used for obvious symptoms of fear, paranoia in the context of a central tumour with severe communication disorders.

Management of psychological and existential suffering

Physicians in the three countries described how they had managed the patient's psychological and existential suffering before using sedation. They described three groups of carers that were involved and who had used several psychological as well as pharmacological interventions.

The first group of carers consisted of general health care professionals such as the physician himself/herself, other physicians and nurses. A pharmacological intervention described was the administration of medication such as anxiolytics, antidepressants, or benzodiazepines (in smaller dosages).

> **UK, General Practitioner n°1, case 38:** We give people diazepam in exactly the same way that we would use diazepam for acute anxiety and psychological distress in people who weren't terminally ill.

Sometimes, intermittent sedation had been used by physicians as a 'time-out'.

> **UK, Palliative care physician, case 34:** Talking and communicating is one side of it but you can't be there all the time and the patient just wants some time out. We sometimes talk about it in those terms with the patient: 'When things are getting really on top of you, an injection that will put you to sleep, might just help you get over that really bad period. That will give you a sleep for four, six hours, but then when you wake up we can see how things are then.' And patients and doctors often refer to that as giving somebody Midazolam [a sedative] for time out.

Not all physicians had used medication to alleviate the suffering. One of them explained that drug treatment for psychological symptoms needs several weeks to take effect, while the patient only had days to live. The physician added that drug treatment of psychological symptoms in terminally ill patients may meet additional effectiveness problems, for example when the liver fails to metabolize medications.

> **Netherlands, Oncologist, case 21:** The problem was that a drug treatment for depression needs at least several weeks to take effect. And because her liver was not working, you cannot give her medication. So her depression was not treatable with medication.

Sometimes, psychological interventions such as talking and spending extra time with the patient had been applied.

> **UK, Palliative care physician n°3, case 31:** He was a gentleman who the team probably spent more time than average with, because he was anxious we tried using more conservative measures. Sometimes just talking things through with patients can be quite effective.

Some other physicians stated that nurses tended to be more involved in the psychological management than they themselves.

> **UK, Palliative care physician, case 39:** They [the nurses] tend to do maybe a bit more of the psychological and social issues. Although, clearly there's a big overlap and we all do a bit of everything. But that's the way we tend to divide it up.

Furthermore, psychological interventions were not by all physicians deemed suitable for all patients, for instance because the patient needs to have sufficient energy, should be competent, mustn't be too exhausted and should want to get involved.

> **Belgium, Palliative care physician, case 18:** As a doctor you can reasonably estimate what can still be done and what can't. And to what extent the patient still wants, and still brings up the energy to get started with something. Because for a psychologist, or a consultant, the patient must indeed certainly still have a clear capacity of thinking and not be too tired.

The second group of carers who was involved in the management of the patient's psychological and existential suffering included mental health care professionals. These concerned psychiatrists, psychologists, psycho-oncologists, counselors and pastors. Their main involvement concerned, according to the respondents, talking to the patient (or the patient's family).

> **UK, Palliative care physician, case 31:** The other people we involved were the psychiatrist, because he'd had depression and he'd been depressed for some time before he became ill. He'd also seen the psycho-oncologist when he came in, and [she/he] just talked to him.

Sometimes, a psychiatrist had been called in by the physician to determine the refractory nature of a psychological symptom.

> **Netherlands, Oncologist, case 21:** In extensive consultations with the psychiatrists we determined that the depression was refractory because we had no options to treat it.

However, not all physicians reported on the involvement of a specialist and some said explicitly that they had not done so.

> **Belgium, Palliative care physician, case 18:** The moral counsellor, that's something we seldom use, this is a Catholic hospital. They're there, but they [psychologist and moral counsellor] are not involved that much, unless the patient really wants it.

The third group were the patient's relatives. They were described as talking to and supporting the patient.

> **Belgium, General Practitioner, case 10:** I had the impression that we were lucky that the informal care provided by the family was very good, that it made the patient very calm.

Similar types and treatments of psychological and existential suffering, and groups of carers involved in these treatments were reported by physicians in all three countries.

Conditions for the use of sedation

Several physicians described that for them, a condition for the initiation of sedation for psychological and existential suffering was the presence of refractory symptoms.

> **Netherlands, Oncologist, case 21:** Frankly, we were a bit happy that the lady had refractory symptoms. Initially we said sedation is not possible, because we do not have refractory symptoms.

Moreover, the presence of *physical* refractory symptoms was an important condition to perform sedation for most, but not all, physicians.

> **Netherlands, Oncologist, case 21:** Terminal restlessness, delirium, dyspnoea and pain. These are the most common reasons for someone to sedate. I had never experienced using sedation for refractory depression, and I think in our unit it is also unprecedented.

Some said that they would be reluctant to sedate for mainly psychological and existential suffering, and some said that in the case of psychological symptoms, they would wait until some refractory physical symptoms arise.

> **Interviewer:** You said that those physical problems must also increase before you start with the sedation?
>
> **Belgium, Palliative care physician, case 18:** Yes. Purely based on psychological symptoms is a lot harder, the physical deterioration must most certainly be there as well.

Yet, the refractory nature of symptoms was not for all physicians a necessary condition for the use of sedation.

> **Netherlands, Palliative care physician, case 20:** I just couldn't put my finger on what it was. It was behaviour that was not possible to correct, in which she lingered, where she was frightened. I'm not sure whether it was a delirium, or behavioural disorders that can occur from the stroke. My colleague said: you're really with your back up against a wall here. You do not really have a refractory symptom, but by God you have no idea what else you could possibly do about this. Do you have to interpret the guidelines so broadly? That sometimes makes it difficult.

Similar results were found in each of the studied countries.

Another condition that was frequently described in the three countries was a patient's short life expectancy.

> **Interviewer:** What are the criteria [for the use of sedation] you uphold?
>
> **Netherlands, Palliative care physician, case 19:** First that's a life expectancy of less than two weeks. I usually keep to a week, because death needs to be close by.

This condition was more present in the accounts of Dutch and British physicians, compared to what Belgian physicians reported.

A last condition according to several physicians was the patient's explicit request for the use of sedation or request to be asleep and not wake up anymore.

> **Belgium, Palliative care physician, case 18:** So [among the indications for sedation are] a [short] prognosis, […] and a second point of course is that the patient asks for it [sedation].

DISCUSSION

This study provides insight into physicians' experiences with continuous sedation until death in the context of psychological and existential suffering, physicians' reported management of this suffering, and conditions identified by physicians as necessary before resorting to sedation at the end of life.

Our study benefited from the use of in-depth face-to-face interviews, allowing us to explore physicians' experiences with and perspectives on a highly debated subject. However, our results cannot be generalized in a statistical way to the whole population of physicians or to physician specialty in particular due to the relatively small number of cases and interviews. Instead, our findings may provide insights that may be transferrable to similar clinical cases and contexts. Additionally, our data gathered by interviews is dependent on the subjective experience and interpretation of both the physician and the interviewer. Although our retrospective design does not preclude recall bias, this is limited in most of the cases by minimizing the time between the patient's death and the interview with the physicians to two months. In a few cases, this was longer than two months and the risk of recall bias could have been larger in these cases.

Physicians in the three countries had used sedation for a continuum of patients who were mainly suffering from physical symptoms to patients predominantly suffering psychologically and existentially. The patients' psychological and existential suffering could have been present before the patient became (terminally) ill, or developed and worsened during the patient's disease trajectory. As stated by the respondents and confirmed by literature, the existence of (unrelieved) physical symptoms may have led to the psychological and existential suffering and vice versa (8).

In the accounts of the physicians, the various manners in which they had attempted to relieve the patient's psychological and existential suffering and the considerable efforts that this often took were central. In several of our case studies, in addition to being near the patient and building a trusting relationship, physicians had involved mental health care professionals and they often had administered medication or intermittent sedation to relieve suffering before using continuous sedation. Similar interventions were reported by physicians in a Japanese study in palliative care units for terminally ill cancer patients suffering from refractory psycho-existential issues before sedation (7). In the literature, a number of psychotherapeutic interventions have been proposed, such as cognitive-behavioural therapy, group therapy, existential therapy, and psycho-education, but research does not seem to support the value of one approach over others in cancer patients (9;20).

Nevertheless, our study shows that pharmacological and psychological interventions may not be effective nor appropriate for all patients. Physicians reported that pharmacological therapies other than sedation were considered but were precluded by the patient's short life expectancy or liver failure. It is supported by the literature that drug therapy takes time to have effect and that drug metabolism may be altered and decreased due to organ failure in terminally ill patients (21;22). Recently however, there has been renewed interest, especially in the United States, in the use of psychostimulants for treating depression in physically ill patients. Although the evidence base is still limited, its use has been recommended due to its potential to enhance mood, energy and arousal within hours (23).

Also, antipsychotics may help reduce delirium symptoms as well as psychological symptoms (24). Intravenous Ketamine, an analgesic, has also been shown to contribute to the rapid treatment of depressive symptoms in palliative patients (25).

A main condition for the initiation of sedation for psychological and existential suffering was for most physicians the presence of refractory symptoms. This conforms with sedation guideline recommendations (1-3). There was often reluctance among physicians in the studied countries to sedate for mainly psychological and existential suffering. Another study also found physicians to be less in favour of or opposed to using sedation to unconsciousness for existential suffering (26). Physicians in our study explained that they were reluctant to use sedation in these cases for personal reasons and that they would wait for the appearance of co-existing refractory physical symptoms. It is also possible that physicians are reluctant to use sedation for psychological and existential suffering because this suffering may fluctuate as death approaches and is usually amenable to pharmacological and psychological treatments such as the Dignity Model intervention designed for patients at the end of life (27;28). This reluctance may heighten the risk of not exploiting enough the potential for interventions. Further, for the physicians in our study, the patient's short life expectancy and an explicit request to be asleep and not to wake up again were deemed as important. No differences were found between the studied countries, except that the patient's short life expectancy as a condition for the use of sedation seemed of less importance for Belgian physicians. This does not conform with sedation guideline recommendations (1-3). Possibly, these physicians primarily focused on adequate symptom relief regardless of the patient's short life expectancy.

In conclusion, physicians in our study resorted to the use of continuous sedation until death for cancer patients with psychological and existential symptoms after considering several pharmacological and psychological interventions and involving health care professionals. Extensive debate and research on when, how and by whom psychological and existential suffering at the end of life should be best treated is urgently needed, taking into account the individual differences between patients regarding their preferences and wishes, and health care status (9). Studies should focus on how mental health care can be most effectively incorporated into routine medical care and especially palliative care, taking into account patients' individual preferences (29;30). As several studies have shown that existential distress such demoralization and hopelessness is linked to terminally ill patients' desire for death, ethical debate should focus on whether and under which circumstances a far reaching medical practice such as continuous sedation until death is a desirable response to psychological and existential suffering at the end of life (31,32)..

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Part IV

General discussion and conclusions

INTRODUCTION

The central aims of this dissertation are to study the practice of continuous sedation until death in Belgium, and to put this practice in an international perspective by comparing it with the Netherlands and the United Kingdom. The main study findings will be discussed in this section. We will address the strengths and weaknesses of the study designs we have used in this dissertation, followed by an overview of the most important results and an in-depth interpretation and discussion of these findings. We will conclude Part IV by formulating recommendations and implications for clinical practice, and suggestions for future research.

STRENGTHS AND WEAKNESSES OF THE STUDY DESIGNS

The SENTI-MELC registration and interview study

In Chapter 1, we used data from a mixed methods retrospective study via the Belgian Sentinel Network of General Practitioners to study the practice of continuous deep sedation until death at home in Belgium. As extensively discussed elsewhere, the SENTI-MELC study has several major strengths (1;2). First, general practitioners are well-placed to provide reliable information on health-related issues and practices at the end of life in the home care setting. They play a key role in the Belgian healthcare system: general practice is highly accessible and most inhabitants have their own general practitioner (3). They often provide and coordinate the patient's care at home, and have a central role in providing palliative care for many of their patients (1;2). The general practitioners involved in the Belgian Sentinel Network of General Practitioners are representative of all practicing general practitioners in Belgium. They participate on a voluntarily basis which may, among other things, explain the low yearly turnover rates (2;4). Another strength is that we selected cases of continuous deep sedation until death at home from a sample of non-sudden deaths, representative for all non-sudden deaths in Belgium in 2005-2006 (2).

However, the SENTI-MELC study has some drawbacks that should be mentioned. During the two-year study period, we identified 31 patients who had received continuous deep sedation until death and we were able to interview the general practitioner responsible for 28 of these patients (Chapter 1). This rather small number of cases thus urges us to stress the carefulness with which one has to interpret our results. Further, because we used structured interviews containing mostly closed questions, in-depth exploration of the general practitioner's experiences and perspectives was not possible and the qualitative (narrative) interview material was rather scarce and superficial. Also, general practitioners had to report on care provided by themselves and they could have given socially desirable answers during the interview, especially regarding a far-reaching practice such as continuous deep sedation until death. However, in order to minimize this potential social desirability bias, we asked general practitioners about the processes of care instead of the outcomes of care (1). Finally, recall bias could not be entirely excluded despite the use of quality control measures such as weekly registrations and interviews within two months after the patient's death (1).

The Dying Well with Dementia Study

To study the practice of continuous deep sedation until death in nursing home populations, particularly in dementia patients, we used data from the retrospective Dying Well with Dementia study (Chapter 2). This is the first population-based study that focuses on dementia patients' received end-of-life care in Belgium from multiple perspectives

(general practitioner, nurse and relative most involved in the patient's care) (5). Other major strengths of the study are the high response rates of both the participating nursing homes and care providers, and the random cluster sampling procedure that resulted in a representative sample of 69 nursing homes (5). Further, the sample of nursing home residents with dementia was selected by using a two-step screening protocol, including validated scales and health care professionals' expert judgment, to both minimize the risk of excluding false negatives (patients with dementia) and including false positives (patients without dementia) (5).

However, some limitations should be mentioned. From a representative sample of 205 residents with dementia, we could only include 117 because of selective non-response (no valid answer to the question whether the general practitioner had administered continuous deep sedation until death). From these residents, 11 had been continuously sedated until death. This small number of cases makes generalization of our results difficult. A recall bias could not, due to the retrospective design, entirely be excluded, although this was limited by focusing on the resident's last month of life, and by minimizing the time between the resident's death and the completion of the questionnaire. We also had to rely on reports from others than the residents themselves (5).

The death certificate and questionnaire study

In Chapter 5, we performed secondary analyses based on the death certificate studies among physicians in Belgium and the Netherlands, and questionnaire studies among physicians in the United Kingdom. The use of the death certificate method has repeatedly been shown to be highly reliable in estimating incidences of medical decisions at the end of life using large random sample sizes, representative for an entire population or time period (6). A major strength of the study is that patients' and physicians' anonymity is safeguarded by a complex mailing procedure and the involvement of a lawyer bound by confidentiality (7). Further, the questionnaire used is validated and entails the same set of key questions from questionnaires used in previous European studies, allowing comparison with these studies. By linking this questionnaire to data from the death certificates, associations can be made between the patient's socio-demographic characteristics and decision making and care at their end of life. In relation to our study on continuous deep sedation until death, a major strength of this method is the possibility to sample official death certificates of a region or country allowing international comparison (7). Also, the questionnaire used in the questionnaire study in the United Kingdom is based on the questionnaire from the death certificate studies, used among others in Belgium and the Netherlands, and entails similar questions (with minor question wording differences) (8). More specifically, the same descriptive definition of continuous deep sedation until death is used in both questionnaires which minimizes possible differences in how physicians perceive the practice on which they report in the three countries (9).

There are some limitations in both methods, though. A limitation that specifically concerns this study is the impossibility of using death certificates in the United Kingdom due to privacy legislation and therefore, its implications for the representativeness of the results for the United Kingdom. In Belgium and the Netherlands, the death case was the unit of measurement of the death certificate study whereas in the United Kingdom, this was the physician recollecting his/her last death attended. We corrected for this by weighting the data from the United Kingdom by the number of patients each physician normally attends per year. The UK method also entailed a higher risk of recall or memory bias among British physicians because information from death certificates was not available and had to be recalled from memory. Also, the time between death and reporting could have been much longer for British physicians than for Belgian and Dutch physicians, reporting on deaths that occurred at least two months and at most six months before the physicians had received the questionnaire (9). Further, in Belgium, we only had access to data

from death certificates from Flanders, and not from the Walloon provinces. As such, our results and conclusions may not be valid for the French-speaking part of Belgium. Also, due to the questionnaire's limited length and complexity, we were not able to get detailed insight into the whole process of continuous deep sedation at the end of life. However, it allowed us to obtain a descriptive overview to form the background for further in-depth qualitative study.

The UNBIASED study

The UNBIASED study is the first study to take a qualitative perspective on the use of continuous sedation until death from different perspectives (physicians and nurses), in different settings (home, hospital and specialized palliative care setting), and in different European countries (Belgium, the Netherlands and the United Kingdom). This international collaboration brought together a team of specialists from different disciplines (psychologists, sociologists, ethicists, public health researchers and clinicians) and different national contexts to gain a deeper understanding of such a complex and contentious practice (10).

The UNBIASED study combines two qualitative methods: focus groups in an exploratory phase of the study, and individual in-depth interviews in the subsequent case study phase. This strategy has the advantage of achieving a more comprehensive understanding of continuous sedation until death by first identifying a broad range of experiences and perspectives in focus group discussions, and then adding more depth by exploring specific perceptions and experiences in face-to-face interviews (11;12). We will discuss the strengths and limitations of both methods in more depth.

Chapters 3 and 4 report on the results of focus groups held with physicians and nurses in Belgium. By using focus groups, we elicited participants' multiplicity of views, beliefs and knowledge about and experiences with the practice of continuous sedation until death. Multiple perspectives about the same topic were obtained by inviting participants from different backgrounds and settings. Because we used focus groups at a preliminary stage of a larger interview study, we could ask health care professionals about their ideas and views on the feasibility of this interview study, and on potential questions of interest that we could include in our future interviews. Although group interaction, a crucial feature of focus groups, could have facilitated the discussion about this sensitive practice, it may also have the potential to lead to socially desirable answers by the participants and to participants being more reluctant to state their true opinions (11;13). We have tried to overcome this as much as possible by stressing confidentiality and by organizing separate focus groups for physicians and nurses. Moreover, the latter had the advantage that participants, especially nurses, could speak more freely because of issues relating to structural inequality in the physician-nurse relationship (14). Also, experienced moderators led the focus groups who helped the participants feel at ease, facilitated group interaction, ensured that everyone participated and got a chance to speak, and kept the focus groups focused (13;15).

Chapters 6 and 7 report on results from the case study phase of our study. The case study approach has been described in the literature as highly suitable for exploring and investigating practically and ethically complex phenomena such as continuous sedation until death in their real-life context involving multiple perspectives (16). Therefore, potential cases of deceased adult cancer patients who received continuous sedation were purposively sampled and identified by using standardized criteria, and semi-structured interviews were held with the most involved physicians and nurses in Belgium, the Netherlands and the United Kingdom (10). By sampling cases of 'continuous' sedation, a broad range of cases of interest were included in our study, varying in depth and length of continuous sedation. By including cases from a variety of settings in our study, we were able to compare the practice

of continuous sedation until death in these settings, between but also within the studied countries. Also, we sampled cases in each country until a point of data saturation was reached. This means that sufficient depth as well as breadth of information on the practice of continuous sedation until death could be achieved (17). The semi-structured interviews were guided by a topic guide (one topic guide for each group of interviewees) containing comparable key questions across the three countries and some country-specific questions to be covered during the interview. Using interviews enabled us to collect rich and detailed accounts of interviewees' knowledge, attitudes, and experiences pertaining to the practice of continuous sedation until death (18). Using semi-structured interviews in particular allowed us to ensure the fluidity of the interview and flexibility regarding the sequence of topics that were discussed while covering the same topics in each country. Also, it allowed us to be sensitive to the language that was used by the interviewee and to explore it in depth (18). We tried to reduce recall bias by interviewing physicians and nurses as soon as possible after the patient's deaths. To decrease the workload and to obtain as much variation as possible, participants were not interviewed about more than four patients. Also, the terminology and definition that we used for continuous sedation until death in our qualitative studies (focus groups and interviews) differed from that in our quantitative studies. However, by too rigidly standardizing our studies, we might have missed the breadth of the practice of sedation. Nonetheless, we should keep in mind that our results should be carefully interpreted.

MAIN FINDINGS

In Part I (Introduction), five research questions were formulated regarding the practice of continuous sedation until death in Belgium, the Netherlands and the United Kingdom. In this section, the main findings to each of those research questions are concisely formulated.

What are the characteristics of patients receiving continuous sedation until death and of the decision-making process and its performance in different care settings in Belgium, the Netherlands and the United Kingdom?

Based on the data from the death certificate and questionnaire study (Chapter 5) we found that 15% of decedents in 2007 in Belgium were continuously and deeply sedated until death. These decedents were often younger than 80 years and died mostly from cancer or cardiovascular diseases. There was an equal distribution of men and women receiving continuous deep sedation until death. Belgian physicians had mostly used benzodiazepines (sometimes combined with opioids and/or other drugs) rather than opioids (alone or in combination with other drugs excluding benzodiazepines) to induce continuous deep sedation until death. Most sedated people in Belgium died within one week after the onset of continuous deep sedation until death. Some Belgian physicians had performed continuous deep sedation until death in conjunction with physician-assisted dying (euthanasia, physician-assisted suicide, and life shortening without an explicit patient request).

In Belgium, people receiving continuous deep sedation until death in the hospital died significantly more often from cardiovascular (29% versus 13% respectively) and respiratory diseases (15% versus 0% respectively), whereas those sedated at home significantly more often died from malignancies (30% versus 78% respectively) (Chapter 5), as also supported by our findings in Chapter 1. Sedated residents with dementia were however more often female (8/11), older than 80 years (mean age of 82 years), and were mostly in an advanced stage of dementia one month before death (9/11) (Chapter 2). With respect to signs and symptoms, before the onset of continuous deep sedation until death, people at home frequently physically suffered to a large extent from a lack of energy and pain, and psychologically from sadness, worrying and agitation in their last week of life (Chapter 1). Nursing home residents

with dementia suffered 'a lot' in their last week of life from rather different symptoms such as difficulties swallowing, fear, pain, and restlessness. In cases where the physician had used sedation in the context of psychological and existential suffering, people suffered from a broad range of physical, psychological and existential symptoms such as pain, dyspnea, (terminal) agitation, panic, anxiety, depression, demoralization, despondency and hopelessness (Chapter 7). According to the general practitioners in Chapter 1, the most frequent indications for administering continuous deep sedation until death were pain (15/28), agitation (7/28) and dyspnoea (4/28).

Regarding the decision-making process of continuous sedation until death in Belgium, we found that several patients were lacking in capacity before the use of continuous deep sedation until death and were not involved in decision making. This concerned eight of 26 patients at home, and eight of 11 residents with dementia in nursing homes (Chapters 1 and 2). However, not all competent patients were always involved in decision making regarding continuous deep sedation until death (home: 6/18; nursing homes: 1/3). In all our studies, we found that the physician had mostly involved the patient's family in decision making about continuous deep sedation until death (home: 23/26 cases; nursing homes: 8/11) (Chapters 1 and 2). Barriers and facilitators in the decision-making process were discussed in Chapters 3 and 4. The final decision to use continuous sedation until death may, according to the physicians and nurses in our focus group study, be facilitated when the patient is suffering unbearably, has a short life expectancy, makes an explicit request for its use, and has relatives who would not get distressed during sedation until death. Other facilitators are the availability of a sedation guideline, a positive attitude towards sedation until death in the health care professional and continuous sedation until death as the option of last resort to relieve the patient's suffering. Factors that would make it more difficult to decide for the use of sedation until death would exist when the patient is suffering existentially, has a longer life expectancy or cannot make an explicit sedation request anymore, when the discussion about sedation is raised too late either by the physician or by the patient or when no clear consensus can be reached between physician and patient, and when the patient's family cannot cope with the stress accompanying sedation and pressurizes the health care professional to speed up the patient's dying process.

Regarding the performance of continuous deep sedation until death in Belgium, we found that (a limited amount of) artificial food and/or fluids were only in a small number of cases administered during sedation until death, mostly for the patient's comfort according to the physician (Chapters 1 and 2). Compared with Belgium, Dutch physicians had significantly more often used benzodiazepines (sometimes combined with opioids and/or other drugs) than opioids alone to induce continuous deep sedation until death. Also in the Netherlands, continuous deep sedation was significantly more likely to last for less than 24 hours compared with Belgium and the United Kingdom (Chapter 5).

How does the practice of continuous sedation until death in Belgium relate to the existing international recommendations for the use of sedation?

In several of our studies, we gathered information regarding sedated patients' clinical characteristics, characteristics of the decision-making process, the performance and effectiveness of continuous sedation until death. These features may reflect the following guideline recommendations for the use of sedation until death: 1) the patient should suffer unbearably and persistently from refractory symptoms, 2) the patient should have a short life expectancy, 3) the competent patient or the incompetent patient's family should be actively involved in decision making, 4) benzodiazepines should be the drugs of choice, 5) sedation should be applied proportionally, and 6) the aim of sedation should be the relief of the patient's suffering. We evaluated to what extent the practice of sedation until death as performed by health care professionals in our studies reflects these sedation guideline recommendations.

However, it should be remarked that we did not ask health care professionals directly whether the patient's symptoms were refractory and whether sedation was performed proportionally.

In Chapter 1, 19 (of 28) patients who received continuous deep sedation until death at home suffered unbearably and persistently from physical as well as psychological symptoms according to the general practitioner. In Chapter 2, eight (of eight) residents with dementia also physically and psychologically suffered 'a lot' in their last week of life according to the nurse. In Chapter 7, which dealt with the use of sedation for psychological and existential suffering, one group of patients suffered from a combination of psychological and existential and severe physical symptoms, whereas the other group of patients suffered predominantly from psychological and existential symptoms according to the physicians. In the latter group, physical symptoms were also part of the clinical picture but were reported to be sufficiently alleviated.

In Chapter 2, most residents with dementia met the criterion of 'having a short life expectancy'. Nine (of 11) residents with dementia were considered to be in the terminal phase according to their general practitioner before they received continuous deep sedation until death. Several health care professionals reported in our studies that they considered the patient's short life expectancy to be a facilitator for deciding to use sedation until death (Chapters 3 and 7). For some physicians, the patient's life expectancy was of less importance in the decision making about continuous sedation in case of psychological and existential (sometimes combined with physical) suffering (Chapter 7).

The recommendation that the competent patient should be actively involved in the decision-making process was not always met. In Chapter 1, six of 18 competent patients were not involved and in Chapter 2, one of three (partly) competent residents. The recommendation that the patient's family should be involved when the patient is incompetent was mostly met (home: 6/8; nursing homes: 6/8) (Chapters 1 and 2).

In Chapters 1 and 5, the recommendation that benzodiazepines (sometimes combined with opioids and/or other drugs) should be used to induce continuous deep sedation until death was met in 55% of the cases in the hospital and 72% of the cases at home (Chapter 5), and in 21 of 28 cases at home (Chapter 1). The guideline also recommends the withholding or withdrawal of medical and nursing procedures that are not strictly necessary during continuous deep sedation until death. In 20 (of 28) patients dying at home in Chapter 1 and nine (of 11) nursing home residents with dementia in Chapter 2, patients did not receive artificial food and/or fluids during sedation until death.

Another recommendation says that sedation should be applied proportionally, that is, the level of sedation (or reduction of consciousness) should be the lowest necessary to provide adequate relief of suffering. Although we did not study the proportionality with which continuous sedation until death had been applied in a direct way, we do have information regarding the patient's waking up during sedation, the patient's symptoms during dying and the patient's quality of dying. In Chapter 1, most patients who received continuous deep sedation did not wake up during sedation until death (17/28) and had had a (very) gentle death (20/28) according to the general practitioner. In Chapter 2, three (of eight) relatives had not perceived any of the pre-specified symptoms during their relative's dying, and eight (of 11) residents had died peacefully according to the nurse.

A final recommendation that we were able to assess was that the physician should not act with an intention to hasten the patient's death when administering continuous sedation until death. In both chapters 1 and 2, we found some cases that did not meet this recommendation. In Chapter 1, in seven and six of all cases, respectively, the general practitioner indicated that s/he had partially or explicitly the intention to hasten the patient's death when performing

continuous deep sedation until death. In four (of 28) cases, the general practitioner perceived the use of continuous deep sedation to be similar to life-ending without explicit patient request. In Chapter 2, the general practitioner reported having performed euthanasia for one (of 11) resident with dementia who was continuously and deeply sedated until death. In Chapter 5, Belgian physicians had reported that they had performed continuous deep sedation until death in conjunction with physician-assisted dying (euthanasia, physician-assisted suicide, and life shortening without an explicit patient request).

How do general practitioners and nurses describe their collaboration, roles and responsibilities during the process of continuous sedation until death at home in Belgium, the Netherlands and the United Kingdom?

In Belgium, the Netherlands and the United Kingdom, general practitioners and nurses in our interview study in Chapter 6 said that nurses often had a coordinating, supporting, informing and explanatory role regarding the care at home for the patient and the patient's family. In Belgium and the Netherlands, it was mostly the general practitioner who discussed the use of continuous sedation until death with the patient and the patient's family and who typically took the final decision to use it. Belgian and Dutch nurses' roles in the decision-making process were mostly advocating the patient's wishes and affirming the general practitioner's decision to use continuous sedation. In the United Kingdom however, it was reported by several general practitioners and nurses that it was predominantly the nurse who has both the role to encourage the general practitioner to prescribe anticipatory sedative medication as well as to decide when to use these prescriptions. Some British respondents said that general practitioners may be afraid and cautious of prescribing or administering anticipatory sedative medication because of the perceptions patients, family and colleagues may have about the general practitioner during the patient's care at the end of life.

After the decision was being made to use the (prescribed anticipatory) sedative medication, nurses in the three countries reported that they commonly administered the medication, mostly in the absence of the general practitioner. Some Belgian and Dutch nurses reported that general practitioners may lack knowledge about placing a syringe driver for administering the medication, and that nurses are more skilled in the technical act of performing continuous sedation until death. In some cases in Belgium and the Netherlands, the general practitioner was present during the initiation of sedation or had started up the sedation according to several respondents. The monitoring of the patient's sedation until death was also reported by most respondents in the studied countries to be the nurse's task. Several nurses in the three countries reported that they tended to experience the performance and monitoring of continuous sedation until death to be 'emotionally burdensome', especially in absence of the general practitioner or when the general practitioner lacked sufficient knowledge about continuous sedation until death.

How is psychological and existential suffering being dealt with before resorting to the use of continuous sedation until death and how is use of continuous sedation being decided in Belgium, the Netherlands and the United Kingdom?

Based on the accounts of physicians from Belgium, the Netherlands and the United kingdom in our interview study in Chapter 7, we identified a continuum of patients who, at one end, suffered mainly from physical symptoms, over patients who suffered from a combination of psychological, existential and physical symptoms, to patients who suffered predominantly psychologically and existentially. The origin of the patients' psychological and existential suffering varied according to the physicians and could be classified in three categories: patients with preexisting

psychological problems before they became ill such as depression or anxiety; patients who developed psychological and existential suffering during their disease trajectory as a reaction to their decline and approaching of death; and patients who presented psychological symptoms that were described as a direct result of their disease such as aggressive behavior, agitation or confusion. Some patients who developed psychological and existential suffering during their disease trajectory accepted that they were going to die soon and were described to have had 'enough of it' whereas other patients from that category were more resistant, did not appear to have accepted that they were ill or dying and were mostly angry or in panic.

To manage the patient's psychological and existential suffering before using continuous sedation until death, physicians in the three countries described three groups of carers that had been involved and several psychological as well as pharmacological interventions they had used. The first group of carers consisted of general health care professionals such as the physician himself/herself, other physicians and nurses. Most physicians reported that they had used several pharmacological interventions such as intermittent sedation, and psychological interventions such as talking and spending extra time with the patient. Physicians reported that both pharmacological and psychological interventions were not always effective nor appropriate to use for terminally ill patients. The second group of carers included mental health care professionals such as psychiatrists, psychologists, psycho-oncologists, counsellors and pastors. They mainly were involved in psychological interventions, and sometimes, a psychiatrist had specifically been called in by the physician to determine the refractory nature of a psychological symptom. These carers were however not always involved. The third group were, according to the physicians, the patient's relatives. They were also involved in psychological interventions such as talking to and supporting the patient.

Three conditions identified by most physicians in the three countries as necessary for using continuous sedation for the relief of patients' psychological and existential suffering, were the presence of (physical) refractory symptoms, the patient's short life expectancy, and the patient's explicit request for the use of continuous sedation until death, or request to be asleep and not wake up anymore. For the presence of predominantly psychological and existential suffering, some physicians said that they would be reluctant to use continuous sedation until death and some others said that in this case they would wait until some refractory physical symptoms would arise.

How do physicians and nurses perceive differences and similarities between the practice of continuous sedation until death and the practice of euthanasia in Belgium?

According to the physicians and nurses in our focus group study in Chapter 4, the differences between the practice of continuous sedation until death and the practice of euthanasia related to 1) the patient's preferences and requests, 2) the decision-making process, and 3) the physician's intention. Both physicians and nurses said that patients explicitly request euthanasia, whereas this is rarely the case for continuous sedation. Also, the reasons for the patient's preference for one practice or the other may differ. Some respondents reported that patients prefer sedation over euthanasia for spiritual reasons or out of concern for their family, whereas others prefer euthanasia because of the frightening thought of being unconscious for several days. Regarding the actual decision making, some nurses stated that they are less often involved by the physician in the decision-making process regarding sedation than in euthanasia. Also, respondents reported to be more reluctant to use continuous sedation until death than euthanasia for a patient with a longer life expectancy. Finally, physicians and nurses explained that the physician's intention when performing continuous sedation should be the alleviation of refractory symptoms, whereas in euthanasia, the physician has to aim to end the patient's life.

Although the majority of physicians and nurses in our focus group study clearly distinguished continuous sedation until death from euthanasia, some stated that the distinction between the two practices may become blurred or may even disappear when medication is increased disproportionally or when sedation is induced for patients with a longer life expectancy (Chapter 4). This was also found in Chapter 1, where 13 (of 28) general practitioners reported that they had performed continuous deep sedation until death with the (partial or explicit) intention to hasten the patient's death. In two cases in which the patient had previously expressed a wish for euthanasia, the general practitioner had an explicit intention to hasten the patient's death when performing sedation until death and had perceived its use to be similar to euthanasia (Chapter 1). Continuous sedation until death had also been used by the physician in conjunction with euthanasia (or physician-assisted dying) in one (of 11) case in nursing homes (Chapter 2), and in 10% and 19% of the cases of sedation until death in respectively the hospital and at home in Belgium (Chapter 5).

GENERAL DISCUSSION

Continuous sedation until death for refractory symptoms and severe suffering at the end of life

Since ancient times, ill and suffering patients have been cared for (19). With the discovery of anesthetics in the 19th century and exponential advances in medicine in the 1990s, we have seen a revolution in the care of terminally ill patients (19;20). However, as a reaction to the prevailing focus on curative treatment for the dying and a growing dissatisfaction with the medicalization of the end of life in the 1950s, palliative care and palliative medicine have developed rapidly since the 1960s (21;22). It was the work of Dame Cicely Saunders in the United Kingdom and colleague Elisabeth Kübler-Ross in the United States that provided health care professionals and society with a holistic view of terminally ill patients' needs regarding dying and death (19). Saunders' concept of 'total pain' went beyond its physical component to encompass psychological, existential and social dimensions (23). Although palliative care has been closely related to oncology in its initial period with a major emphasis on cancer pain relief, its approach and focus has nowadays been broadened to different diseases and symptoms (21). Also, the attention to adequate symptom control at the end of life in general has increased in the medical world and beyond (21). Many health care professionals perceive it as their clinical and ethical responsibility and duty to help their patients to die with dignity and free of suffering (24).

In 1990 however, a prospective study among terminally ill cancer patients reported that some symptoms at the end life may remain unbearable and uncontrollable despite optimal palliative care efforts (25). This was one of the first studies that made mention of the concept of 'sedation at the end of life' to control these intractable symptoms. From then on, the practice of continuous sedation at the end of life and its potential to alleviate terminally ill patients' suffering increasingly became the subject of medical, ethical and societal debate and empirical research, as is witnessed by the increasing number of scientific publications since the early 1990s (26). The increasing attention given to the practice of continuous sedation (for instance in the media), among other reasons through the development and launch of sedation guidelines, may also have influenced the common (and increasing) use of this practice across different countries and settings (27). We found in our studies that continuous sedation had mostly been initiated for patients who were suffering unbearably and persistently from several physical and/or psychological symptoms (Chapters 1, 2 and 7). Beside commonly reported physical and psychological symptoms in our studies such as pain, dyspnea, (terminal) agitation, fear, and sadness, nursing home residents with dementia also often suffered from other symptoms such as difficulties swallowing, possibly with choking as a consequence. It has been shown in the literature that problems of swallowing are common in patients with advanced dementia and may arise from the cognitive alterations in the patient's brain (28). In addition, in the accounts of physicians in our study and

confirmed by literature, prolonged suffering caused by uncontrolled physical symptoms may lead to psychological and existential symptoms and vice versa (29). These results suggest that in a considerable number of terminal patients, physicians may not always be able to control distressing symptoms by means of common symptom management treatments (for instance the use of opioids), and that this sometimes may lead to new symptoms or an increased severity of already existing symptoms. In these cases, physicians may have no choice but to use a far-reaching practice such as continuous sedation until death. Notwithstanding physicians' responsibility to relieve their terminally ill patients' suffering, taking the decision to use continuous sedation until death may be difficult and distressing in some cases.

One such situation in which it may be emotionally, ethically and morally challenging for health care professionals to decide about the use of sedation until death may be the presence of (severe) psychological and existential suffering at the end of life (Chapters 3 and 7). Whereas the use of continuous sedation until death is increasingly accepted for physical symptom control, it remains a controversial practice for the relief of predominantly psychological and existential suffering (30). Also among several sedation guidelines there is no consensus as to whether or not sedation until death should be used in response to primarily psychological and existential suffering (31-34). The Belgian, Dutch and EAPC guidelines however remark that, since the prerequisite of an imminent death should also be met, the patient can be expected to be in a poor physical condition and will in most cases suffer from refractory physical symptoms as well. According to these guidelines, this makes it very unlikely that there will be many cases in which the patient suffers *only* psychologically and existentially (32-35). Nonetheless, these 'rare' cases in which the patient mainly suffers psychologically and existentially (and in which physical suffering may be absent or under control) do occur in clinical practice as described in Chapters 2 and 7, and many physicians have shown hesitance in using sedation in these cases by saying that they would wait for the appearance of co-existing refractory physical symptoms before resorting to continuous sedation until death (Chapters 3 and 7). Due to, among other reasons, the lack of a clear definition of this (existential) suffering, its subjective and dynamic nature, a lack of assessment tools for determining its refractory nature, a lack of (consensus on) well-established strategies for its management, and a lack of training among physicians in psychological and existential end-of-life issues, physicians may have felt distressed themselves when witnessing this suffering and may have felt unable to assess and alleviate this suffering (30;36;37). From the perspective of the patient however, it seems undesirable to let him/her suffer unbearably and persistently from psychological and existential issues until s/he may (and this may not always be a certainty) develop additional *physical* suffering. From the perspective of the physician however, these results demonstrate their high reluctance to use a medical practice (continuous sedation until death) for a predominantly psychological or existential problem that may be beyond their expertise. This may need further debate and study.

Nevertheless, our qualitative interviews showed that some physicians use or may be willing to consider the use of continuous sedation until death for patients who predominantly suffer from psychological and existential symptoms, even for patients with a longer life expectancy, as confirmed by literature (Chapter 7) (38). What drove these physicians to decide on the use of this far-reaching practice? As for the physicians in our study who were willing to use sedation until death for patients with a longer life expectancy, they indicated that they perceived it as their responsibility to primarily focus on adequate symptom relief regardless of the patient's prognosis (Chapter 7). This argument was also found in another qualitative study among physicians (38). Further, physicians in our study indicated that they resorted to the use of continuous sedation because several pharmacological and psychological interventions they (and other care givers) had used before sedation were ineffective or inappropriate. This was mostly because of a lack of time for the drugs to be effective, due to the inability of the patient's body to absorb the drugs, or due to the patient's lack of energy, competence or willingness to be involved in these interventions (Chapter 7). As such, these cases appeared to have fulfilled the guideline condition that sedation should only be used as an

option of last resort when other treatments fail (32-34). The fact that some terminal patients couldn't benefit anymore from certain interventions because there wasn't enough time left, or because of the patient's poor physical condition, may however raise some questions. Were the care providers involved and the interventions started up in time by the physician? And if not, why was this not the case? Moreover, should the patient's psychological care actually be the responsibility of the physician? And how can physicians be better equipped to deal with these situations? These questions cannot be answered based on results from our studies, but they may nonetheless be relevant for further debate and research. For instance, we already know from the literature that advanced cancer patients are frequently confronted with psychological and existential suffering and that a lot of these needs go underdiagnosed and undertreated (29;36;39-41). This may be due to, among other things, physicians' lack of understanding of this suffering, a lack of knowledge, skills, time and confidence in the effectiveness of addressing these issues, and a lack of specialized health care professionals' involvement (42-44). Although a number of health care professionals believe that the in-depth psychological and existential care of terminally ill patients should not be their responsibility, they believe that they should at least be open for and willing to recognize and listen to patient's psychological and existential concerns (45;46). Also, patients may benefit from the involvement of interdisciplinary palliative care services, early in the course of their disease. Early multidisciplinary palliative care has been shown to have a considerable effect on the patient's quality of life, relief of (physical and psychological and existential) symptoms and mood (47;48).

When a physician eventually decides to use continuous sedation until death for refractory symptoms, another challenging situation may arise, that is, when sedation until death appears unsuccessful in alleviating the patient's intractable suffering at the end of life (49;50). Sedation guidelines advise that the level of sedation should be proportional to the level of the patient's suffering (32-34). To ensure that the patient's suffering is alleviated, the depth of sedation may vary from mild to deep sedation in clinical practice (51). Although the proportionality with which the medication was administered wasn't studied in a direct way, we found cases in our studies in which the patient's suffering at the end of life didn't appear to be sufficiently alleviated by continuous (deep) sedation until death. In some cases, the patient's relative had reported having observed a broad range of symptoms during the patient's dying phase (Chapter 2). Also, some patients woke up unexpectedly during continuous deep sedation until death, mostly due to the insufficient effect of medications, and/or their dying had been reported by physicians and nurses to be not (very) gentle or a struggle (Chapters 1 and 2). Some physicians in our studies reported that they had also used euthanasia for their sedated patient (Chapters 2 and 5), which may be an indication that sedation may not always have the desired or aimed for effect of relieving the patient's suffering in a small number of cases (52-55). Accurately assessing the patient's distress and awareness of this suffering may be challenging for general health care professionals although several means are available to help them monitor the patient's level of consciousness at the end of life. Health care professionals may among others base their judgment on clinical assessment (e.g. observation, or calling out the patient's name and monitoring the response) and sedation assessment scales (e.g. the Ramsay Sedation Scale or the Richmond Agitation – Sedation Scale) (35;56;57). However, these tools are not always fully validated in palliative care patients or may be invasive (35;58). Further systematic research should be performed on the use of less invasive procedures and the validation of existing clinical tools for the evaluation of adequate symptom control and depth of continuous sedation until death while taking health care professionals' judgment into account (50;58). Yet, as is also reported in the literature and found in Chapter 1, 'waking up' during continuous sedation may not always be perceived as problematic by the patient, the patient's family and the physician but may have its reasons, such as to have contact with the family (51;54;59). Some patients would prefer to maintain their intellectual capacities rather than to reach complete symptom relief (with the loss of consciousness as a consequence) (59). Also, literature reports on physicians who prefer to start with mild sedation (in contrast to physicians in favor of deep sedation from the start) because they highly value preserving the patient's consciousness

during continuous sedation until death as long as possible (51). This shows that the patient's waking up is something that may occur during sedation and that shouldn't always be distressing for the patient and the family, although patients and their family should be well informed and prepared in advance about the patient's possible waking up, especially at the start of sedation when the physician determines the proportional dose of medication to the patient's degree of suffering (51).

Continuous sedation until death and euthanasia

The Belgian, Dutch and EAPC sedation guidelines take as a premise that continuous sedation until death, unlike euthanasia, is a normal medical practice and stress that both clinical practices should be clearly distinguished from each other (32-34). They recommend several criteria of due care for the practice of sedation to support this premise, and as such to preclude the practice of continuous sedation until death from having a life-shortening effect. The findings in this dissertation contribute to the existing empirical literature which shows that in many cases this distinction is clearly experienced, yet it also shows that a clear distinction between the practice of continuous sedation until death and the practice of euthanasia as presumed by sedation guidelines is not always tenable in clinical practice (60-62).

To distinguish continuous sedation until death from euthanasia, sedation guidelines recommend that the patient should have a life expectancy of hours or days at most at the start of continuous sedation until death (in order to prevent the withholding/withdrawal of artificial food and fluids from having a life-shortening effect), that sedation until death should be performed proportionally and that the aim of sedation should be the relief of the patient's intractable suffering (32-34). Although most physicians and nurses in our focus group study confirmed that the distinction between continuous sedation until death and euthanasia may become blurred when sedation is used for patients with a longer life expectancy (Chapter 4), some physicians in our studies reported that not all of the patients were terminal in their last week of life and considered the patient's short life expectancy as a less important decisive criterion when deciding about continuous sedation until death (Chapters 2 and 7). Previous research among Dutch physicians showed similar findings (38;53;63). Further, most health care professionals in our study confirmed that the distinction between both practices diminishes or may even disappear when medication is increased disproportionally and that the physician's intention then is, or shifts from alleviating suffering, to ending life (Chapter 4). Although we didn't study the proportionality with which the medication was administered in a direct way, we found that some physicians had administered continuous sedation until death to (partly or explicitly) hasten the patient's death, and/or had perceived this practice as euthanasia in the case of an explicit patient request for euthanasia (Chapter 1). Also, some physicians reported that they had actively ended the sedated patient's life (Chapters 2 and 5). A life-shortening intention of the physician when performing continuous sedation until death was also found in several other studies (53;60;62-64).

Across different studies in different settings and countries in our dissertation, it seems that the practice of continuous sedation until death and the practice of euthanasia may border or overlap in some cases in clinical practice. However, although physicians reported that they might have shortened or even actively ended the patient's life while using sedation, there is discussion whether physicians can always accurately estimate this. Previous studies showed that physicians consider estimating a terminally ill patient's life expectancy as difficult, and demonstrated that they have a tendency to overestimate the patient's survival (38;65-67). It may be possible that they believed that the sedation had a life-shortening effect, while the patient's actual life expectancy was in fact shorter and life shortening less likely. Further, literature shows that physicians often overestimate the life-shortening effect of certain medication

(e.g. opioids) while clinical studies have found no evidence for this effect, at least on group level (68). Also, several authors state that intentions are difficult to verify. They are considered not to be black and white but highly personal, complex and multilayered (69-71). However, the concept of intention is often used by physicians themselves to distinguish both practices and to justify their own actions (72;73). Also, intention is a crucial part of the definition of euthanasia and therefore it is a relevant factor in distinguishing euthanasia from sedation (74). Nonetheless, despite these remarks, it is clear from our results that physicians and nurses report that continuous sedation until death and euthanasia seem to border or overlap in some cases, at least in clinical practice. The fact that in countries such as Belgium and the Netherlands, where both a law on euthanasia and a sedation guideline exist, cases in the 'grey zone' still seem to occur, may be a possible indication that reality in clinical practice is very complicated for health care professionals confronted with severe suffering (75). Also, although it might be important to know whether the physician actually shortened the patient's life when performing continuous sedation until death for legal reasons, among others, as well as other consequences like the physician's own mental well-being or proper communication with the patient's family, it is also important that the debate is not narrowed down to this point. It should also keep other issues in mind, such as the question of whether we shouldn't focus more on the patient's quality of dying during continuous sedation until death and how to assure the patient a 'good death'.

Similarities and differences between Belgium, the Netherlands and the United Kingdom regarding the practice of continuous sedation until death

The frequency of continuous sedation until death in Belgium, the Netherlands and the United Kingdom varies: its use is significantly lower in the Netherlands than in Belgium and the United Kingdom (respectively 8%, 15% and 17%) (Chapter 5). Also, variation exists in reported practice of continuous sedation between the three countries (76). In the UNBIASED main paper (2013, manuscript submitted for publication), most Belgian health care professionals described their practice of continuous sedation as often deep from the start, whereas Dutch respondents commonly reported on the practice of sedation as titrated against the patient's symptoms (76). British health care professionals experienced a continuum of sedation practice, starting with the administration of 'prn' or 'as needed' doses of anticipatory sedative medication to the provision of deep sedation in exceptional cases (76). Further, in our quantitative analysis, we found differences in how continuous sedation until death was provided with regard to the medication used, the duration of sedation until death and its performance in conjunction with a decision to actively end the patient's life (Chapter 5). In the three countries, benzodiazepines (sometimes combined with opioids and/or other drugs) were most often used for continuous sedation until death but this was most common in the Netherlands (Chapter 5). Also, most patients in the three countries died within one week of the onset of continuous sedation until death, but in the Netherlands compared with Belgium and the United Kingdom, most patients died within 24 hours (Chapter 5). Finally, we found that Belgian physicians more often performed continuous sedation until death in conjunction with active life ending compared with the Netherlands and the United Kingdom (Chapter 5). Also, sedation until death was less often performed in hospitals in the Netherlands (11% of all deaths in Dutch hospitals) compared with the United Kingdom (17% of all deaths in British hospitals) and Belgium (20% of all deaths in Belgian hospitals). On the other hand, sedation was more often used at home in the United Kingdom (19% of all deaths at home in the United Kingdom) compared with Belgium (10% of all deaths at home in Belgium) and the Netherlands (8% of all deaths at home in the Netherlands) (Chapter 5). Our qualitative interview study among physicians and nurses in the three countries revealed differences in health care professionals' reported decision-making process of continuous sedation until death at home. According to most of our Belgian and Dutch respondents, the final decision on the use of sedation was typically taken by the general practitioner after discussion with the patient and the

patient's family. In the United Kingdom however, it was predominantly the nurse who both encouraged the general practitioner to prescribe anticipatory sedative medication and decided when to use the prescription (Chapter 6). Our dissertation further elaborates on these findings and enables the formulation of additional hypotheses to guide further understanding of the practice of continuous sedation until death in Belgium, the Netherlands and the United Kingdom.

Differences in health care professionals' attitudes towards the existence and consultation of guidelines or frameworks may explain the lower numbers of continuous sedation until death in the Netherlands and the differences in performance of continuous sedation until death in Belgium, the Netherlands and the United Kingdom. It has been found in several studies that the majority of Dutch physicians report that they are aware of the general recommendations of the Dutch sedation guideline and that their practice also mostly reflects these recommendations (53;76;77). In contrast with Belgium where a sedation guideline has only recently been published and in the United Kingdom where no sedation guideline is available, it appears that Dutch physicians might have built up relevant expertise over the years in deciding the right timing and choosing the appropriate medication for the use of continuous sedation until death. Also, it is possible that Dutch physicians have a stricter understanding of the concept of sedation until death, and that they might only report on cases of continuous sedation that comply with sedation guideline recommendations. Cases of sedation that fall outside the sedation guidelines may then possibly be less often labeled as continuous sedation until death in the Netherlands compared with Belgium and the United Kingdom (9). These hypotheses may be supported by findings from the UNBIASED main paper (2013, manuscript submitted for publication) regarding Dutch practitioners' use of sedation guidelines to frame their sedation practice, and findings from the literature regarding the heightened compliance with sedation guideline recommendations in the Netherlands since the introduction of the Dutch sedation guideline in 2005 (76;77). At the same time however, since the introduction of the Dutch sedation guideline, frequency of sedation until death is rising in the Netherlands, possibly due to increasing attention in the media and its increased acceptance as a normal medical practice (78). This may need further research.

The differing attitudes of health care professionals regarding the possibility of sedation to hasten death or the perception of sedation as an alternative to euthanasia probably explains our finding that Belgian practitioners more often performed sedation in conjunction with active life ending than do Dutch and British practitioners. It is possible that Belgian practitioners have rather different views towards hastening of death and to using sedation as an alternative to euthanasia. This hypothesis follows the finding from the UNBIASED main paper (2013, manuscript submitted for publication) that several Belgian practitioners tended to accept a possible life-shortening effect of sedation somewhat more than Dutch and British practitioners. Most British practitioners avoided and most Dutch practitioners didn't perceive a possible life-shortening effect of sedation (76). Additionally, it is possible that bringing about a peaceful dying process is for several Belgian physicians of overriding importance, regardless of whether their intervention affects the time of the patient's death (79). In the UNBIASED main paper (2013, manuscript submitted for publication), most Belgian respondents also perceived continuous sedation and euthanasia to be alternatives that could be chosen by patients, whereas this perception appeared less strongly in the Dutch accounts. Among British respondents, there was little mention of euthanasia (76).

Differences in how Belgian, Dutch and British health care professionals describe their practice of continuous sedation until death may explain the differences found in our study in their reported decision-making process of continuous sedation until death at home. It has been shown that Belgian and Dutch health care professionals reported they perceive continuous sedation until death as a separate medical decision, whereas British health care professionals perceived the decision making of sedation as a prolonged process (76). It may be possible that the actual starting

point of continuous sedation until death is not very clear-cut in the United Kingdom for health care professionals. Further, the unique responsibility of nurses in the United Kingdom compared with Belgium and the Netherlands regarding the use of anticipatory prescriptions has also been shown in a previous study and may affect patient care (76;80).

Differences in the organization of the health care system in Belgium, the Netherlands and the United Kingdom may also contribute to the cross-national variation in place of death in sedated patients. Primary care holds a strong position in Dutch and British health care systems with 'gate keeping' general practitioners as key actors who only refer patients to secondary care if necessary (81;82). Palliative care consultation teams and specialist nursing palliative care teams (such as the Macmillan nurses and the Marie Curie Nurses) are highly available in the Netherlands and the United Kingdom, respectively, to inform, support and advise health care professionals involved in complex palliative care, which may be the case when using continuous sedation until death (82-86). These teams might help improve the quality of palliative care at home and prevent the referral of terminally ill patients to secondary care (83). In Belgium on the contrary, patients have direct access to medical specialists in hospitals due to an 'open access' health care system (87). Palliative care is highly accessible and more widespread in Belgian hospitals, witness among others the higher ratio of inpatient palliative care beds and palliative support teams in hospitals (85;86). Further, it is known from the literature that a predominant culture of open communication exists between physicians and patients in the Netherlands (88-90). It may be possible that Dutch general practitioners are more aware of the patient's wish to die at home at all circumstances, or at least, not to be transferred to the hospital.

Variation in the practice of continuous sedation until death was also explained in the UNBIASED main paper (2013, manuscript submitted for publication) by Belgian, Dutch and British health care professionals' different attitudes towards the preservation of the patient's consciousness during sedation until death (76). In the United Kingdom, practitioners sought to ensure that consciousness and interaction with the patient's environment could be preserved for as long as possible. In Belgium, once a decision was taken to start sedation, several practitioners stressed the need to ensure that the patient stayed asleep in order to honour their request for sedation. Dutch physicians reported a more mixed picture (76). The latter is confirmed by a Dutch qualitative study which found different stances among physicians in relation to the depth of sedation until death, namely starting with either mild or deep sedation (51).

Understanding how and explaining why the practice of continuous sedation until death varies between Belgium, the Netherlands and the United Kingdom is highly complex and several factors seem to be interwoven, influencing clinical practice. We have tried to formulate some lines of reasoning that should be further explored in depth. Nonetheless, our results demonstrate that the reported practice of continuous sedation until death, a decision at the end of life that is strongly influenced by cultural, organisational, and legal factors, may vary between countries. This finding follows the results from a large questionnaire study among six European countries (91). Additionally, it may be possible that our findings reflect at least to some extent variations in conceptualization of the practice of sedation between countries. From our findings, it also seems unfeasible to strive for a uniform practice, with a uniform and international guideline across countries. We therefore encourage the use of the European Association for Palliative Care's presented 10-point framework when developing sedation guidelines in different countries, because it leaves space for country-specific interpretations and accents (34).

RECOMMENDATIONS

Implications and relevance for policy and clinical practice

Our dissertation demonstrates that adequately alleviating the severe suffering of terminally ill patients may be challenging for health care professionals in different settings and countries. In general, a multidisciplinary team approach of continuous sedation until death is preferable, whereby the need for timely communication with the patient and family, as well as multidimensional assessment and treatment of symptoms should be emphasized (44;55). In practice, health care professionals and patients should be encouraged to start up discussion about the patient's wishes regarding the use of continuous sedation until death in good time, especially in patients with dementia. Our findings and the literature demonstrate that competent patients are not always involved in decision making (92).

Our findings also indicated some overlap between the practice of continuous sedation until death and the practice of euthanasia. Whether all these reported cases in our study reflect true hastening of death cannot be concluded from our results, but it nonetheless demonstrates the need to increase health care professionals' knowledge about how and when each practice should be used in clinical practice through training courses, workshops and seminars. Further encouraging the development and implementation of guidelines for the use of sedation at the end of life may also be beneficial for reducing overlap, given the positive experiences in the Netherlands with the introduction of the national sedation guideline in 2005 (53;77). Yet, studies are needed to evaluate implementation and monitor its effects. When developing such sedation guidelines, policy makers should take country-specific organizational, cultural, and legal influencing factors into account. The European Association for Palliative European Association for Palliative Care's recommended framework may be used as a guidance (34).

Further, physicians should involve specialist palliative care practitioners and services in good time to provide adequate end-of-life care. General practitioners in particular may benefit from support by a multidisciplinary palliative care team, as we found several cases of continuous sedation until death that were not performed in accordance to sedation guidelines recommendations at home and in nursing homes. Also when predominantly psychological and existential suffering at the end of life is an issue, it would be helpful, although should not be mandatory, for general health care professionals to consult and involve colleagues who are expert in palliative and mental health care. As several practitioners in our study reported feeling uncomfortable when confronted with this type of suffering, more clarity and guidance seems needed on how general health care professionals may deal with this type of suffering at the end of life.

Recommendations for future research and debate

The findings in this dissertation have also revealed several new areas of research and themes for debate. First, differences in frequency and characteristics of the practice of continuous sedation until death between countries should be further monitored, quantitatively as well as qualitatively. Also, the practice of continuous sedation until death is developing rapidly, which necessitates careful monitoring over time to further enhance our understanding.

Further, our UNBIASED study could benefit from duplication in other countries and cultures to study the country-specific cultural, legal and organizational factors influencing quality of end-of-life care and continuous sedation until death. Moreover, future research should also focus on the practice of continuous sedation until death in patient populations other than cancer patients. The findings in our explorative study among patients with dementia give

sufficient reason for further research. Also, to get a complete picture of the practice of continuous sedation until death, patient perspectives should be incorporated in future studies, albeit this is very complex.

Furthermore, the effectiveness of continuous sedation until death and the factors contributing to the patient's (in)adequate symptom control, quality of dying, and relatives' satisfaction should be further explored. Qualitative longitudinal prospective research could be used, including different perspectives, settings and countries to allow in-depth analysis of experiences regarding the practice of continuous sedation until death between and within countries. Also, research regarding the efficacy of continuous sedation until death should combine health care professionals' assessments, existing sedation scales and medical imaging techniques to assess the sedated patient's distress during sedation to assure the patient a symptom-free death (50). This research can be further used to validate existing scales in a palliative care population and to give clinical assessment and sedation scales a more solid evidence base (35;50). There is also something to be said for the development of quality indicators for the practice of continuous sedation until death to measure and improve the performance of this practice, but also to inform health care professionals about their own practice (93). These outcomes could be further used as a basis for development and improvement of health care professionals' education and training tuned to adequate sedation practice in different clinical settings.

Finally, there is a need for intervention research regarding optimal psychological and pharmacological interventions to relieve the predominantly psychological and existential suffering of patients earlier in the course of the patient's disease trajectory (94).

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Nederlandstalige samenvatting

DEEL I - INLEIDING

Continue sedatie tot aan het levenseinde kan een laatste uitweg bieden wanneer ernstig lijden bij terminale patiënten niet langer verlicht kan worden door middel van normale medische behandelingen of palliatieve zorg. Het is een medische handeling waarbij de patiënt zijn/haar waarneming van ernstig lijden verminderd of weggenomen wordt door het bewustzijn van de patiënt door middel van medicatie met een sederend effect doelbewust en continu te verlagen tot aan het levenseinde. De indicaties voor en een juiste uitvoering van sedatie aan het levenseinde zijn omschreven in verscheidene sedatierichtlijnen, gepubliceerd door onder andere de Koninklijke Nederlandsche Maatschappij tot bevordering der Geneeskunst (KNMG) in Nederland in 2005 (en herzien in 2009), de Federatie Palliatieve Zorg Vlaanderen in België in 2010 (en herzien in 2012), en de 'European Association for Palliative Care' (EAPC) in 2009. Een samenvatting van de belangrijkste aanbevelingen van de Belgische, Nederlandse en EAPC richtlijnen zijn weergegeven in kader 1. Twee kernaanbevelingen die verder in dit proefschrift bestudeerd zullen worden, zijn de aanwezigheid van refractaire symptomen en de korte levensverwachting van de patiënt. De richtlijnen geven aan dat sedatie tot aan het levenseinde ingezet kan worden voor patiënten die ondraaglijk lijden aan één of meerdere 'refractaire' of 'onbehandelbare' symptomen die zowel van fysische, psychische als existentiële aard kunnen zijn. Het gebruik van continue sedatie tot aan het levenseinde is echter controversieel wanneer het hoofdzakelijk psychisch en existentieel lijden betreft. Verder geven de richtlijnen aan dat de levensverwachting van de patiënt kort moet zijn vooraleer continue sedatie tot aan het levenseinde opgestart kan worden. De richtlijn raadt ook aan om het kunstmatig toedienen van vocht en voeding te staken of niet meer op te starten wanneer de patiënt niet langer wil of in staat is om zelf vocht en voeding tot zich te nemen voorafgaand aan de sedatie. De medicatie dient proportioneel toegediend te worden en de sedatie heeft het verlichten van lijden als doel, niet het bespoedigen van het overlijden van de patiënt. De richtlijnen suggereren dat wanneer deze aanbevelingen opgevolgd worden, een levensverkortend effect van sedatie onwaarschijnlijk is. Op deze wijze onderscheiden sedatierichtlijnen continue sedatie tot aan het overlijden van actieve levensbeëindiging zoals euthanasie. Euthanasie is het toedienen van middelen door iemand anders dan de patiënt met het uitdrukkelijke doel om het levenseinde van de patiënt te bespoedigen, op uitdrukkelijk verzoek van de patiënt.

Kader 1. Belangrijkste aanbevelingen van de Belgische, Nederlandse en EAPC sedatierichtlijnen.

Sedatie kan aangewezen zijn voor patiënten met (één of meerdere) onbehandelbare of 'refractaire' symptomen die leiden tot ondraaglijk lijden van de patiënt.
Sedatie kan enkel overwogen worden wanneer de patiënt zich in de allerlaatste terminale fase van zijn/haar ziekte bevindt, met een levensverwachting van hooguit uren of dagen.
Sedatie moet steeds besproken worden met een wilsbekwame patiënt en wenselijk ook met de meest betrokken naaste(n). In het geval de patiënt wilsonbekwaam is en in afwezigheid van een wilsverklaring, moet de arts de wettelijk vertegenwoordiger van de patiënt consulteren over de wensen van de patiënt.
De beslissing om al dan niet vocht en voeding kunstmatig toe te dienen moet onafhankelijk van de beslissing tot sedatie genomen worden. Deze beslissing dient in functie van het behandeldoel genomen te worden en dient individueel beslist te worden na evaluatie van de wensen van de patiënt en een inschatting van de voor- en nadelen. In principe wordt bij continue sedatie tot aan het overlijden geen vocht en voeding kunstmatig toegediend.
De behandelend arts dient, indien mogelijk, aanwezig te zijn bij de start van sedatie.
Midazolam is het medicijn dat de voorkeur geniet; het gebruik van morfine als sedativum wordt beschouwd als een kunstfout.
Morfine dient alleen toegediend of voortgezet te worden (naast sedativa) om pijn of benauwdheid te verlichten.
Sedatie dient proportioneel toegediend te worden, dat wil zeggen dat die mate van bewustzijnsdaling dient te worden bereikt die nodig en voldoende is voor de gewenste mate van symptoombestrijding.
Deskundigen (bijvoorbeeld psychiaters, anesthesisten, pijnspecialisten, oncologen en gespecialiseerde verpleegkundigen) moeten tijdig geraadpleegd worden wanneer de arts twijfelt aan zijn/haar deskundigheid betreffende sedatie of over beslissing

om sedatie al dan niet op te starten.
Sedatie heeft het verlichten van lijden als doel en niet het bespoedigen van het overlijden van de patiënt.

Uit verschillende internationale studies blijkt dat continue sedatie tot aan het levenseinde in verschillende landen toegepast wordt, hoewel met variërende frequenties (2%-60%). Naast factoren die de vergelijking tussen internationale studies bemoeilijken, zoals verschillen in gebruikte terminologie, definities, methodologie, bestudeerde patiëntenpopulatie en onderzoekssetting, suggereren een aantal studies dat de variatie in frequentie ook voor een aanzienlijk deel verklaard kan worden door landspecifieke culturele, juridische en organisatorische factoren. Om inzicht te krijgen in deze beïnvloede landspecifieke factoren is verder diepgaand internationaal onderzoek nodig naar de klinische kenmerken van continue sedatie tot aan het overlijden, de omstandigheden waarin het toegediend wordt en de bijdrage van deze praktijk aan de kwaliteit van sterven.

Wij bestudeerden in dit proefschrift de praktijk van continue sedatie tot aan het levenseinde in drie Europese landen, België, Nederland en het Verenigd Koninkrijk, in het kader van de UNBIASED study (UK Netherlands Belgium International Sedation Study). Een vergelijkende studie in deze drie landen is hoogst interessant en leerrijk aangezien deze landen zowel culturele, juridische en organisatorische gelijkenissen als verschillen ten aanzien van levenseindezorg vertonen.

Het proefschrift begint met een inleiding en een overzicht van de onderzoeksvragen en de gebruikte onderzoeksmethoden (**Deel I**). Het proefschrift heeft twee centrale doelstellingen: ten eerste het bestuderen van de praktijk van continue sedatie tot aan het levenseinde in België, en ten tweede het plaatsen van de praktijk van continue sedatie tot aan het levenseinde in een internationaal perspectief en vergelijken met Nederland en het Verenigd Koninkrijk. De volgende onderzoeksvragen zullen behandeld worden:

1. Wat zijn de kenmerken van de patiënten die continue sedatie tot aan het overlijden hebben toegediend gekregen, het besluitvormingsproces en de uitvoering van sedatie in de verschillende zorgsettings in België, Nederland en het Verenigd Koninkrijk? (Hoofdstukken 1, 2, 3, 4, 5 en 7)

2. Hoe verhoudt de praktijk van continue sedatie tot aan het overlijden in België zich ten aanzien van bestaande internationale aanbevelingen voor het gebruik van sedatie? (Hoofdstukken 1, 2, 3, 5 en 7)

3. Hoe beschrijven huisartsen en verpleegkundigen hun samenwerking, rollen en verantwoordelijkheden tijdens het proces van continue sedatie tot aan het overlijden in de thuissetting in België, Nederland en het Verenigd Koninkrijk? (Hoofdstuk 6)

4. Hoe wordt psychologisch en existentieel lijden behandeld alvorens continue sedatie tot aan het levenseinde toe te dienen en hoe wordt besloten tot het gebruik van continue sedatie in België, Nederland en het Verenigd Koninkrijk? (Hoofdstuk 7)

5. Welke verschillen en gelijkenissen percipiëren artsen en verpleegkundigen tussen de praktijk van continue sedatie tot aan het levenseinde en de praktijk van euthanasie in België? (Hoofdstukken 1, 2, 4 en 5)

Vier verschillende retrospectieve studies werden gebruikt om deze vragen te beantwoorden: (1) de mixed-methods SENTI-MELC registratie en interviewstudie met huisartsen, (2) de kwantitatieve Dying Well with Dementia Study met artsen, verpleegkundigen en nabestaanden, (3) de kwantitatieve sterfgevallenstudie met artsen, en (4) de

kwalitatieve UNBIASED focusgroepen- en interviewstudie met artsen en verpleegkundigen. De verschillende studies en methoden worden in de desbetreffende hoofdstukken uitvoerig beschreven. Ethische goedkeuring werd steeds bekomen. In alle studies behalve één (de SENTI-MELC studie), bestudeerden we gegevens uit Vlaanderen, het Nederlandstalige gedeelte van België. In de SENTI-MELC studie bestudeerden we ook data uit Brussel en Wallonië. Aangezien we in dit proefschrift de praktijk van continue sedatie tot aan het levenseinde bespreken vanuit een internationaal perspectief, hebben we ervoor geopteerd om de term 'België' in plaats van 'Vlaanderen' te gebruiken in de volgende paragrafen.

DEEL II – CONTINUE SEDATIE TOT AAN HET LEVENSEINDE IN BELGIE

Hoofdstuk 1 beschrijft de kenmerken van patiënten die continue diepe sedatie tot aan het levenseinde hebben toegediend gekregen, het besluitvormingsproces en de uitvoering van sedatie bij patiënten die thuis in België stierven. In 2005-2006 werden er 31 door huisartsen gerapporteerde gevallen van continue diepe sedatie tot aan het levenseinde in de thuissetting geïdentificeerd. Er werden 28 interviews afgenomen van huisartsen.

We vonden dat de meerderheid van de patiënten een man was (16/28), jonger was dan 80 jaar (21/28), kanker had (19/28), en ondraaglijk en aanhoudend leed voorafgaan aan de sedatie (19/28). De medische situatie van de patiënt werd in alle gevallen door de huisarts beoordeeld als uitzichtloos. Pijn was de voornaamste indicatie voor continue diepe sedatie (15/28). Zes wilsbekwame patiënten werden door de huisarts niet betrokken bij de besluitvorming, terwijl familieleden (23/26) en zorgverleners (18/26) dat meestal wel waren. Continue diepe sedatie werd meestal opgestart met benzodiazepines (21/28). 20/28 patiënten kregen tijdens continue diepe sedatie geen kunstmatige toediening van voeding en vocht. Tijdens continue diepe sedatie ontwaakten 11 van de 28 patiënten, veelal door onvoldoende medicatie (n=7) of om contact te hebben met de familie (n=4). Volgens de huisartsen stierven 20 van de 28 patiënten een zachte dood. In 13 gevallen gaf de huisarts aan dat hij/zij deels of expliciet de bedoeling had om het overlijden van de patiënt te bespoedigen. In vijf van deze gevallen had de patiënt om euthanasie gevraagd.

Hoofdstuk 2 beschrijft de kenmerken van rusthuisbewoners met dementie die continue diepe sedatie tot aan het levenseinde hebben toegediend gekregen, het besluitvormingsproces en de uitvoering van sedatie in België. In 2010 werden er over 69 rust- en verzorgingstehuizen 11 rusthuisbewoners geïdentificeerd die volgens de huisarts en/of de verpleegkundige aan dementie leden en die volgens de huisarts continu en diep gesedeerd geweest zijn tot aan het levenseinde. We bestudeerden de gegevens uit vragenlijsten van de huisarts, aangevuld met gegevens uit vragenlijsten van de verpleegkundige en de naaste die het meest betrokken waren in de zorg voor de bewoner.

We vonden dat er bij negen van de 11 gesedeerde bewoners met dementie sprake was van gevorderde dementie. De bewoners waren hoofdzakelijk vrouwen (8/11), ouder dan 80 jaar (gemiddelde leeftijd: 82 jaar), en stierven volgens de huisarts voornamelijk door ouderdom (4/11) of kanker (3/11). 8/8 bewoners leden in hun laatste week van het leven. Volgens de verpleegkundigen hadden 8/10 bewoners één of meerdere van de vooropgestelde symptomen 'vaak' in de laatste week. Frequent gerapporteerde symptomen waren slikmoeilijkheden, angst, pijn, en rusteloosheid. 9/11 bewoners werden in de laatste week van het leven als terminaal beschouwd door de huisarts. Bij opname waren vijf bewoners volgens hun huisarts deels of volledig wilsbekwaam. Drie van hen waren dat volgens hun huisarts nog steeds in de laatste week. Vier bewoners hadden ooit specifieke wensen geuit over een medische behandeling die zij al dan niet wilden in de laatste levensfase en/of hadden hier ooit met hun huisarts over gesproken. Twee (van 11) hadden een schriftelijke wilsverklaring van hun wensen waarin zij ofwel verzochten om sedatie ofwel een derde persoon de volmacht hadden gegeven om beslissingen te nemen in het geval de bewoner

incompetent zou worden. Eén bewoner had beide, een andere bewoner had enkel een derde persoon volmacht gegeven. Voor acht bewoners had de huisarts de naaste van de bewoner betrokken in overleg over de wensen van de bewoner. In twee gevallen was de bewoner noch de naaste betrokken in overleg. Eén van deze bewoners was wilsbekwaam bij opname. De duur van sedatie varieerde van 1 tot 8 dagen. Tijdens sedatie kregen twee bewoners nog kunstmatig vocht en voeding toegediend. Naasten van vijf bewoners rapporteerden dat de bewoner één of meerdere van de vooropgestelde symptomen 'vaak' had tijdens het stervensproces. Eén bewoner was angstig, één bewoner had slikmoeilijkheden, en de overige drie bewoners leden volgens de naasten aan vijf tot zeven symptomen waaronder pijn, rusteloosheid, kortademigheid, slikmoeilijkheden, verslikken, rochelen en angst. Verpleegkundigen van drie bewoners rapporteerden dat het stervensproces van de bewoner een strijd was. In twee van deze drie gevallen had de huisarts een beslissing genomen om de symptoomcontrole te verdiepen waarbij er een sterke verhoging van morfine of een 'morfineachtig' middel was de dag voor het overlijden. In één geval rapporteerde de huisarts dat hij/zij naast continue diepe sedatie ook euthanasie had uitgevoerd. De euthanasie werd voorafgegaan door acht dagen van sedatie, waarbij de bewoner nog vocht en voeding kunstmatig toegediend kreeg.

Hoofdstuk 3 rapporteert over factoren die het gebruik van continue sedatie tot aan het levenseinde volgens artsen en verpleegkundigen in België vergemakkelijken of bemoeilijken. In 2010 hielden we 4 focusgroepen (n=2 met artsen en n=2 met verpleegkundigen) waarin we artsen en verpleegkundigen uit verschillende settings (thuissetting, oncologieafdelingen en palliatieve eenheden) vroegen naar hun ervaringen met continue sedatie.

De deelnemers beschreven verschillende factoren die hun gebruik van continue sedatie kunnen beïnvloeden. Ten eerste is de huidige fysieke toestand van de patiënt belangrijk. Artsen en verpleegkundigen rapporteerden dat voor een patiënt die ernstig (fysisch) lijdt en een korte levensverwachting heeft, de kans op het gebruik van continue sedatie toeneemt. In het geval van psychisch lijden zijn artsen en verpleegkundigen meer terughoudend om te beslissen tot sedatie. Ten tweede gaven artsen en verpleegkundigen aan dat ze zich meer comfortabel zouden voelen om te beslissen tot sedatie wanneer de patiënt een expliciet verzoek doet voor continue sedatie tot aan het levenseinde. Een expliciet verzoek is echter niet altijd mogelijk volgens de deelnemers. Dit was volgens hen enerzijds omwille van verminderde cognitieve vaardigheden bij de patiënt of omdat patiënten niet altijd op de hoogte zijn van het bestaan van sedatie en artsen het niet onder hun aandacht (durven) brengen. Anderzijds werd volgens de deelnemers de communicatie met patiënt en familie bemoeilijkt door onrealistische verwachtingen van de patiënt of familie. Ten derde en vierde werden de beschikbaarheid en het gebruik van sedatierichtlijnen en de (positieve) attitude van hulpverleners ten aanzien van continue sedatie tot aan het levenseinde door de deelnemers aanzien als factoren die hun besluitvorming vergemakkelijkten. Tot slot was het voor de deelnemers gemakkelijker om te besluiten tot het gebruik van sedatie indien er geen andere alternatieven meer beschikbaar waren dan continue sedatie om het lijden van de patiënt te verlichten.

Hoofdstuk 4 rapporteert bevindingen uit dezelfde focusgroepen gehouden met artsen en verpleegkundigen in Hoofdstuk 3. Dit hoofdstuk beschrijft de verschillen en gelijkenissen die artsen en verpleegkundigen in België percipiëren tussen de praktijk van continue sedatie tot aan het levenseinde en de praktijk van euthanasie.

Verschillende deelnemers bemerkten verschillen tussen beide praktijken. Een eerste verschil had betrekking op de wensen en voorkeuren van de patiënt. Bij continue sedatie werd er volgens de deelnemers minder vaak een expliciet verzoek gesteld door de patiënt, terwijl dit altijd het geval was bij euthanasie. Een verzoek voor sedatie werd volgens de deelnemers veelal beschreven in algemene, vage termen, waarbij de arts gevraagd werd om 'iets te doen' om het lijden te verlichten. Daarenboven hadden sommige patiënten volgens de deelnemers een duidelijke voorkeur voor de ene, dan wel de andere praktijk. Een tweede verschil tussen beide praktijken kon volgens de deelnemers gevonden worden in de manier waarop de beslissing genomen wordt. Sommige verpleegkundigen rapporteerden dat zij in het

geval van continue sedatie minder vaak betrokken worden in de besluitvorming door de arts dan in het geval van euthanasie. Tot slot is volgens de deelnemers ook de intentie waarmee de arts de ene dan wel de andere praktijk uitvoert verschillend. Volgens hen heeft sedatie het controleren van refractaire symptomen als doel, terwijl men bij euthanasie de intentie heeft om het leven van de patiënt te beëindigen. Hoewel de meerderheid van de deelnemers continue sedatie en euthanasie als twee verschillende praktijken aan het levenseinde beschouwden, vonden sommigen dat beide praktijken soms kunnen grenzen aan, of soms zelfs overlappen met, mekaar. Dit is volgens de deelnemers het geval wanneer de medicatie disproportioneel opgehoogd wordt, en wanneer continue sedatie opgestart wordt bij patiënten met een langere levensverwachting. In beide gevallen bestaat dan volgens de respondenten de mogelijkheid dat sedatie een levensverkortend effect heeft.

DEEL III – CONTINUE SEDATIE TOT AAN HET LEVENSEINDE IN BELGIE, NEDERLAND EN HET VERENIGD KONINKRIJK

In **Hoofdstuk 5** onderzochten we in België, Nederland en het Verenigd Koninkrijk, in zowel de ziekenhuis- als thuissetting, de frequentie van continue diepe sedatie tot aan het levenseinde, de kenmerken van patiënten die continue diepe sedatie hebben toegediend gekregen, en andere kenmerken van deze praktijk vanuit het perspectief van de arts.

We vonden een significante en substantiële variatie in de prevalentie van continue diepe sedatie tot aan het levenseinde tussen de verschillende landen: continue diepe sedatie werd significant minder gebruikt in Nederland (8% van alle sterfgevallen) dan in België (15% van alle sterfgevallen) en het Verenigd Koninkrijk (17% van alle sterfgevallen). In ziekenhuizen komt continue diepe sedatie beduidend minder voor in Nederland (11%) dan in de andere twee landen (Verenigd Koninkrijk: 17%; België: 20%), terwijl het in thuissituaties net vaker voorkomt in het Verenigd Koninkrijk (19%) in vergelijking met België (10%) en Nederland (8%). We vonden geen verschillen tussen de landen en settings betreffende de kenmerken van overleden patiënten in het algemeen, en kenmerken van overleden patiënten die continu en diep gesedeerd geweest zijn tot aan het overlijden. We vonden echter wel verschillen betreffende de kenmerken van de praktijk van sedatie zelf. In Nederland wordt sedatie vaker uitgevoerd met benzodiazepines (soms gecombineerd met opioïden en/of andere medicatie) en vooral tijdens de laatste 24 uur van het leven. In België wordt continue diepe sedatie tot aan het overlijden meer uitgevoerd in combinatie met actieve levensbeëindiging in vergelijking met de twee andere landen. Onder actieve levensbeëindiging valt euthanasie, hulp bij zelfdoding en levensbeëindiging zonder expliciet verzoek van de patiënt. Tevens vonden we dat de kans op het toegediend krijgen van continue diepe sedatie hoger is voor mannen, jongere patiënten, patiënten die overlijden aan kanker en patiënten die overlijden in het ziekenhuis. Het 'land' waartoe de patiënt behoort is eveneens een belangrijke voorspellende factor voor het gebruik van continue diepe sedatie.

In **Hoofdstuk 6** rapporteren we over de beschrijvingen die huisartsen en verpleegkundigen in België, Nederland en het Verenigd Koninkrijk gaven van hun samenwerking, rollen en verantwoordelijkheden tijdens het besluitvormingsproces, de uitvoering en opvolging van continue sedatie tot aan het levenseinde in de thuissetting. Hiervoor bestudeerden we 25 semigestructureerde interviews met huisartsen en 26 met verpleegkundigen die nauw betrokken waren in de zorg voor 29 kankerpatiënten die continue sedatie thuis toegediend kregen.

Huisartsen en verpleegkundigen uit België, Nederland en het Verenigd Koninkrijk rapporteerden dat verpleegkundigen vaak een coördinerende, ondersteunende, en informerende rol hebben ten aanzien van de zorg voor de patiënt en de familie in de thuissetting. In België en Nederland is het volgens de respondenten vooral de

huisarts die het gebruik van continue sedatie overlegt met de patiënt en de familie, en ook meestal de definitieve beslissing neemt om continue sedatie te gebruiken. In het Verenigd Koninkrijk daarentegen werd door de respondenten beschreven dat het voornamelijk de verpleegkundige is die enerzijds de huisarts aanmoedigt om noodmedicatie (waaronder sedativa) voor te schrijven, en anderzijds beslist wanneer deze voorschriften gebruikt moeten worden. Nadat de beslissing gemaakt is om de sedativa toe te dienen, zijn het voornamelijk de verpleegkundigen die de medicatie toedienen, meestal in afwezigheid van de huisarts. Dit werd gerapporteerd door verschillende verpleegkundigen uit de drie landen. Volgens sommige Belgische en Nederlandse verpleegkundigen ontbreekt het sommige artsen aan kennis over het plaatsen van een spuitdrijver, en zijn verpleegkundigen vaak meer geschoold in deze technische handeling. Het opvolgen van de sedatie is volgens verschillende respondenten uit de drie landen ook de taak van de verpleegkundige. Een aantal verpleegkundigen beschreef het uitvoeren en opvolgen van continue sedatie tot aan het levenseinde als emotioneel belastend, vooral in afwezigheid van de huisarts of wanneer de huisarts onvoldoende kennis heeft over continue sedatie.

Hoofdstuk 7 gaat in op de bedenkingen en ervaringen van artsen uit België, Nederland en het Verenigd Koninkrijk over en met het gebruik van continue sedatie tot aan het levenseinde voor kankerpatiënten die voornamelijk psychologisch en existentieel lijden aan het levenseinde. We bestudeerden 35 semigestructureerde interviews met artsen die betrokken waren in de zorg voor 39 kankerpatiënten die volgens de arts psychologisch en existentieel leden.

Op basis van de beschrijvingen van de artsen identificeerden we een continuüm met aan het ene uiteinde patiënten die voornamelijk leden aan fysische symptomen, over patiënten die leden aan een combinatie van psychologische, existentiële en lichamelijke klachten, tot aan het andere uiteinde patiënten die voornamelijk psychologisch en existentieel leden vooraleer zij continu gesedeerd werden tot aan het levenseinde. De oorsprong van het psychologisch en existentieel lijden van de patiënten varieerde volgens de artsen. We konden drie categorieën onderscheiden: patiënten met reeds bestaande psychologische problemen vooraf hun ziekte, patiënten waarbij het psychologisch en existentieel lijden zich ontwikkelde tijdens het ziektetraject als reactie op hun ziekte en naderende levenseinde, en patiënten waarbij het psychologisch en existentieel lijden een direct gevolg was van hun ziekte, zoals bijvoorbeeld patiënten die leden aan een neurologisch deficit zoals een hersentumor met agressief gedrag, agitatie of verwarring als gevolg.

Om dit psychologisch en existentieel lijden te verlichten beschreven de artsen uit de drie landen dat zij drie groepen van zorgverleners betrokken hadden en dat zowel farmacologische als psychologische interventies gebruikt werden. De eerste groep zorgverleners bestond uit algemene zorgverleners zoals de behandelend arts, andere artsen en verpleegkundigen. De meeste artsen meldden dat zij verschillende farmacologische interventies waaronder intermittente sedatie hadden toegepast, maar ook psychologische interventies, zoals praten met en extra tijd doorbrengen bij de patiënt, voordat zij continue sedatie tot aan het levenseinde hadden toegediend. Deze interventies waren echter niet altijd voldoende effectief of geschikt voor de patiënt. De tweede groep zorgverleners bestond uit geestelijke gezondheidszorgverleners zoals psychiaters, psycho-oncologen, counselors en predikanten. Zij waren volgens de artsen vooral betrokken bij de psychologische interventies. Soms werd een psychiater ingeroepen door de arts, specifiek om vast te stellen of het psychologisch symptoom refractair was. Deze zorgverleners werden echter niet altijd betrokken. Een derde groep ‘zorgverleners’ betrof de familie van de patiënt. Zij waren voornamelijk betrokken bij de psychologische interventies, zoals praten met en ondersteunen van de patiënt.

Artsen uit de drie landen identificeerden drie belangrijke voorwaarden voor het gebruik van continue sedatie tot aan het levenseinde voor patiënten met voornamelijk psychologisch en existentieel lijden. Deze waren de aanwezigheid

van refractaire symptomen, een korte levensverwachting van de patiënt en een uitdrukkelijk verzoek van de patiënt voor het gebruik van continue sedatie tot aan het levenseinde of een verzoek om te slapen en niet meer wakker te worden.

DEEL IV – ALGEMENE DISCUSSIE EN CONCLUSIES

In **Deel IV** reflecteren we over de sterke punten en beperkingen van onze gebruikte studies en geven we een samenvatting van de gevonden resultaten. Vervolgens wordt dit deel besloten met een interpretatie van onze belangrijkste bevindingen en aanbevelingen voor de klinische praktijk, beleid en vervolgonderzoek.

Continue sedatie voor refractaire symptomen en ernstig lijden aan het levenseinde

We vonden dat continue sedatie door zorgverleners gebruikt wordt voor patiënten die zowel ernstig fysisch als psychologisch en existentieel lijden aan het levenseinde. Vaak gerapporteerde fysische en psychische symptomen vooraf sedatie in onze studies zijn pijn, kortademigheid, (terminale) agitatie, angst en verdriet. Rusthuisbewoners met dementie ondervinden volgens verpleegkundigen ook vaak hinder van andere symptomen zoals slikproblemen die volgens de literatuur het gevolg zijn van cognitieve veranderingen in de hersenen van de demente patiënt. Volgens de artsen in onze studies en bevestigd door de literatuur, kan langdurig lijden ten gevolge van ernstige fysische symptomen leiden tot het ontstaan van of de versterking van reeds bestaand psychologisch en existentieel lijden en omgekeerd. Deze resultaten suggereren dat artsen niet altijd in staat zijn om ondraaglijke en aanhoudende symptomen bij een aantal terminale patiënten te bestrijden door middel van gebruikelijke symptoombehandelingen zoals het toedienen van opioïden. In deze gevallen kan continue sedatie tot aan het overlijden een laatste oplossing bieden.

Hoewel het gebruik van continue sedatie tot aan het levenseinde voor fysische symptomen in toenemende mate aanvaard is, blijft het een controversiële praktijk voor het verlichten van voornamelijk psychologisch en existentieel lijden aan het levenseinde. Niet alle artsen in onze studie bleken echter terughoudend om continue sedatie op te starten voor patiënten die voornamelijk psychologisch en existentieel leden en een langere levensverwachting hadden. Dit kan betekenen dat het voor deze artsen van doorslaggevend belang is om deze patiënten rustig en zacht te laten overlijden, ongeacht een mogelijk levensverkortend effect van sedatie. Daarenboven bleek uit de beschrijvingen van de meeste artsen dat zij continue sedatie opgestart hadden nadat verschillende farmacologische en psychologische interventies onvoldoende effectief of geschikt waren, en zij dus sedatie hadden ingezet als allerlaatste redmiddel om het lijden van de patiënt te verlichten. Eenmaal continue sedatie opgestart was, vonden we in onze studies enkele gevallen waarin het lijden van de patiënt onvoldoende verlicht leek te zijn. Zo werden enkele patiënten nog wakker tijdens continue diepe sedatie, hadden verschillende nabestaanden nog symptomen waargenomen tijdens het stervensproces van de patiënt, en beoordeelden de zorgverleners het stervensproces van enkele patiënten als een strijd. Deze bevindingen nopen tot voldoende opvolging van sedatie tot aan het overlijden en het meten van het bewustzijn van de patiënt door middel van klinische observatie, sedatie meetschalen, en andere technieken. Echter, wakker worden tijdens continue sedatie hoeft niet altijd als problematisch beschouwd te worden. Dit kan soms wenselijk en zelfs verkieslijk zijn voor de patiënt, zijn/haar familie en de behandelende arts. Tijdig en voldoende overleg met alle betrokken partijen is hierbij van cruciaal belang.

Continue sedatie tot aan het levenseinde en euthanasie

Tevens draagt dit proefschrift bij aan de bestaande empirische literatuur over de relatie tussen de praktijk van continue sedatie tot aan het levenseinde en de praktijk van euthanasie. De Belgische, Nederlandse en EAPC sedatierichtlijnen stellen dat continue sedatie tot aan het levenseinde, in tegenstelling tot euthanasie, een normale medische praktijk is en benadrukken dat beide klinische praktijken duidelijk van mekaar onderscheiden moeten worden. In het merendeel van de gevallen in onze studies vonden we dat zorgverleners een duidelijk onderscheid maakten tussen beide klinische praktijken. Zorgverleners rapporteerden dat er verschillen waren tussen beide praktijken in de wensen en voorkeuren van de patiënt, het besluitvormingsproces en de intentie van de arts. Toch vonden we dat dit onderscheid tussen beide praktijken zoals vooropgesteld door verschillende sedatierichtlijnen niet altijd op die manier werd ervaren in de klinische praktijk. Zo rapporteerden enkele artsen dat sommige patiënten een langere levensverwachting hadden (waardoor de sedatie mogelijk levensbekortend kon zijn als er voeding en vocht werd onthouden; dit laatste was vaak het geval in onze studies), dat zij een expliciete intentie hadden om het levenseinde van de patiënt te bespoedigen of dat zij het leven van de patiënt actief beëindigd hadden, en vonden we aanwijzingen voor het feit dat de sederende medicatie mogelijks disproportioneel toegediend werd. Deze bevindingen dienen echter genuanceerd te worden omdat ander onderzoek laat zien dat de inschatting van de prognose door artsen niet altijd accuraat is, dat artsen vaak het levensverkortende effect van bepaalde medicatie (zoals opioïden) overschatten, en dat intenties moeilijk objectief te meten zijn. Hoewel het belangrijk is om te weten of de arts daadwerkelijk het leven van de patiënt verkort heeft door middel van continue sedatie tot aan het levenseinde, onder andere omwille van mogelijke juridische maatregelen, lijkt het ons ook belangrijk om het debat over sedatie niet te verengen tot enkel dit punt. Het lijkt ons aanbevolen om ons, naast dit debat, ook te richten op (onderzoek en debat over) de kwaliteit van sterven van de patiënt tijdens continue sedatie, en hoe we de patiënt een goede, symptoomvrije dood kunnen garanderen.

Verschillen en overeenkomsten tussen België, Nederland en het Verenigd Koninkrijk betreffende de praktijk van continue sedatie tot aan het levenseinde

Tenslotte toont de literatuur en bevestigen onze resultaten dat continue sedatie tot aan het levenseinde significant minder vaak toegepast wordt in Nederland in verhouding tot België en het Verenigd Koninkrijk (respectievelijk 8%, 15% en 17% van alle sterfgevallen). Daarenboven blijkt uit de UNBIASED hoofdpublicatie (2013, EAPC abstract) dat de praktijk van continue sedatie tot aan het levenseinde zoals gerapporteerd door zorgverleners verschilt tussen deze drie landen. In deze studie beschreven Belgische zorgverleners dat zij diepe sedatie van bij aanvang toedienden, terwijl Nederlandse zorgverleners continue sedatie titreerden tegen de symptoomlast van de patiënt. Britse zorgverleners beschreven een continuüm, gaande van het toedienen van dosissen sedativa die net voldoende zijn om het lijden van de patiënt te verlichten tot het toedienen van diepe sedatie in enkele uitzonderlijke gevallen. Daarnaast vonden we in onze kwantitatieve analyses verschillen betreffende de gebruikte medicatie voor sedatie, de duur van sedatie en de uitvoering van sedatie samen met een beslissing om het levenseinde van de patiënt actief te beëindigen. Ook werd sedatie tot aan het overlijden minder vaak uitgevoerd in ziekenhuizen in Nederland en vaker in de thuissetting in het Verenigd Koninkrijk. In onze kwalitatieve studies vonden we verschillen in het gerapporteerde besluitvormingsproces voor continue sedatie tot aan het levenseinde.

In de discussie van dit proefschrift formuleren we mogelijke hypothesen voor onze bevindingen. Deze hypothesen centreren rond de verschillende attitudes van zorgverleners betreffende het gebruik en het bestaan van sedatierichtlijnen, de verschillende attitudes van zorgverleners betreffende de mogelijkheid van sedatie om het

overlijden te bespoedigen, de verschillen in de organisatie van de gezondheidszorg in de drie landen, en de verschillende attitudes van Belgische, Nederlandse en Britse zorgverleners ten aanzien van het behoud van het bewustzijn van de patiënt tijdens continue sedatie.

Begrijpen hoe en verklaren waarom de praktijk van continue sedatie tot aan het levenseinde verschilt in België, Nederland en het Verenigd Koninkrijk blijkt complex te zijn en verschillende factoren lijken de klinische praktijk te beïnvloeden. Desalniettemin tonen onze resultaten dat de gerapporteerde praktijk van continue sedatie tot aan het levenseinde, een praktijk die sterk beïnvloed wordt door culturele, organisatorische en juridische factoren, kan variëren tussen landen. Vanuit onze bevindingen lijkt het daarom moeilijk haalbaar om te streven naar een uniforme praktijk van sedatie, met een uniforme en internationale richtlijn.

Aanbevelingen

In het algemeen bevelen we voor de klinische praktijk een multidisciplinaire teambenadering aan waarbij op een holistische manier gekeken wordt naar symptomen en deze ook desbetreffend behandeld worden. Aangezien de uitvoering van continue sedatie tot aan het overlijden in onze studies in de thuissetting en rust- en verzorgingstehuizen niet altijd in overeenstemming was met aanbevelingen van de sedatierichtlijnen, lijkt het ons dat in het bijzonder huisartsen voordeel kunnen halen uit de ondersteuning door een multidisciplinair palliatief team omdat zij nog vaak solistisch werken. Ook moedigen we zorgverleners aan om met patiënten en familie tijdig in dialoog te gaan over de wensen en voorkeuren van de patiënt met betrekking tot continue sedatie aan het levenseinde. De overlap die we vonden in enkele gevallen tussen de praktijk van continue sedatie tot aan het levenseinde en de praktijk van euthanasie wijst op de noodzaak om door opleiding de kennis van zorgverleners inzake beide praktijken te vergroten. Overigens lijkt het ook raadzaam om sedatierichtlijnen verder te ontwikkelen, te implementeren en te evalueren om zo mogelijks de bestaande overlap tussen sedatie en euthanasie in de praktijk te verkleinen. Bij de ontwikkeling van dergelijke richtlijnen doen beleidsmakers er goed aan om landspecifieke organisatorische, culturele en juridische beïnvloedende factoren in rekening te nemen. Aangezien verschillende zorgverleners in onze studies zich ongemakkelijk voelden wanneer zij geconfronteerd werden met voornamelijk psychologisch en existentieel lijden aan het levenseinde, raden we zorgverleners aan om tijdig deskundigen, gespecialiseerd in geestelijke gezondheidszorg, te consulteren.

Tot slot doen we enkele aanbevelingen voor toekomstig onderzoek. Ten eerste zouden de verschillen tussen landen in frequentie en kenmerken van de praktijk van continue sedatie tot aan het levenseinde verder kwantitatief en kwalitatief opgevolgd moeten worden. Ook is het blijvend opvolgen van de praktijk van continue sedatie gewenst. Verder zou het interessant zijn om de UNBIASED studie in andere landen, culturen en patiëntenpopulaties te repliceren. Om een volledig beeld te krijgen van de praktijk van continue sedatie dient ook het patiëntenperspectief in toekomstig onderzoek opgenomen te worden. De effectiviteit van continue sedatie tot aan het overlijden en de factoren die bijdragen aan (in)adequate symptoomcontrole, de kwaliteit van sterven van de patiënt en de tevredenheid van familieleden dienen ook verder onderzocht te worden. Kwalitatief longitudinaal prospectief onderzoek zou hiervoor gebruikt kunnen worden, met inbegrip van verschillende perspectieven, settings en landen. Daarenboven is het wenselijk om kwaliteitsindicatoren te ontwikkelen voor de praktijk van sedatie om de kwaliteit en de uitvoering ervan te meten en te verbeteren, maar ook om zorgverleners inzicht te geven in hun eigen handelen. Tenslotte is verder onderzoek nodig naar geschikte psychologische en farmacologische interventies om ondraaglijk psychologisch en existentieel lijden van de patiënt al eerder tijdens het ziektetraject te verlichten.

Curriculum vitae of Livia Anquinet

CURRICULUM VITAE LIVIA ANQUINET

Livia Anquinet was born on 17 December 1985 in Anderlecht, Belgium, as the only child of Ludwig Anquinet and Martine Biltereyst.

She attended high school at the Sint-Godelieve Institute in Sint-Martens-Lennik where she graduated in Sciences-Mathematics (2003). At the Vrije Universiteit Brussel in Brussels, she obtained her Master of Science degree in Clinical Psychology (2008) and followed a Teacher Training (2009).

In February 2009, she started working as a junior researcher on a PhD project on continuous sedation until death, supervised by Prof. Dr. Luc Deliens and co-supervised by Prof. Dr. Judith A.C. Rietjens, at the Vrije Universiteit Brussel & Ghent University End-of-Life Care Research Group.

She currently works as coordinator of Werkgroep Verder, an organization for the bereaved by suicide, and follows a systemic psychotherapy training.

Livia Anquinet werd geboren op 17 december 1985 te Anderlecht, België, als enig kind van Ludwig Anquinet en Martine Biltereyst.

Zij behaalde haar diploma Wetenschappen-Wiskunde aan het Sint-Godelieve-Instituut te Sint-Martens-Lennik (2003). Zij studeerde verder aan de Vrije Universiteit Brussel waar zij haar Master Klinische Psychologie behaalde (2008) en de Specifieke Lerarenopleiding volgde (2009).

In februari 2009 startte zij als junior onderzoeker op een doctoraatsproject omtrent continue sedatie tot aan het levenseinde onder supervisie van Prof. Dr. Luc Deliens en cosupervisie van Prof. Dr. Judith AC Rietjens bij de Vrije Universiteit Brussel & Universiteit Gent Onderzoeksgroep Zorg rond het Levenseinde.

Zij werkt momenteel als coördinator van Werkgroep Verder, een organisatie voor nabestaanden na zelfdoding, en volgt een opleiding in systeempsychotherapie.

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