Towards the improvement of continuous sedation until death in nursing homes

Lenzo Robijn

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Promotors:	Prof. dr. Kenneth Chambaere (Vrije Universiteit Brussel)
	Prof. dr. Luc Deliens (Ghent University)
Co-promotors:	Dr. Judith Rietjens (Erasmus MC Rotterdam)
	Prof. dr. Peter Pype (Ghent University)

Doctoral Jury Committee:

Chair:	Prof. dr. Koen Pardon (Vrije Universiteit Brussel)
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	Dr. Jeroen Hasselaar (Radboud UMC Nijmegen)
	Dr. Roeline Pasman (VU University Medical Center Amsterdam)

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LIST OF ABBREVIATIONS

CSuD	Continuous sedation until death
PS	Palliative Sedation
CDS	Continuous deep sedation
MRC	Medical Research Council
CRA	Coordinating advisory physician
GP	General practitioner
NH	Nursing Homes
ELD	End-of-life decision

Chapters 2-7 are based on the following publications:

Chapter 2:

Robijn L, Cohen J, Rietjens J, Deliens L*, Chambaere K*. Trends in Continuous Deep Sedation until Death between 2007 and 2013: a repeated nationwide survey. PLoS One. 2016;11(6):e0158188. [2016 SCI impact factor 2.806; journal ranking Q1; ranking n°15/64 in Multidisciplinary Sciences].

Chapter 3:

Robijn L, Chambaere K, Raus K, Rietjens JA, Deliens L. Reasons for continuous sedation until death in cancer patients: a qualitative interview study. European Journal of Cancer Care. 2017;26(1): e12405. [2017 SCI impact factor 2.409; journal ranking D1; ranking n°5/118 in Nursing].

Chapter 4:

Robijn L, Seymour J, Deliens L, Korfage I, Brown J, Pype P, van der Heide A, Chambaere K, Rietjens J, on behalf of the UNBIASED consortium. The involvement of cancer patients in the four stages of decision-making preceding continuous sedation until death. A qualitative study. Palliative Medicine. 2018;32(6):1055-1077. [2018 SCI impact factor 4.956; journal ranking D1; ranking n°15/185 in Public, Environmental & Occupational Health].

Chapter 5:

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Chapter 7:

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PART I

General introduction

CHAPTER 1

Background, research questions and outline of this dissertation

1.1. Continuous sedation until death: a general introduction

There is no getting away from the fact that death happens. However, the dying experience and the way we deal with death and dying have changed considerably in our society during the last century.[1–3] Acute deaths due to infectious diseases have been gradually replaced by more prolonged dying trajectories with chronic, progressive and degenerative illnesses such as cancer and cardiovascular disease at the leading cause of death in the world nowadays.[4–6] In many cases, death is not merely the result of the natural course of a lethal disease but is often preceded by medical decision-making.[7–9] Such decision-making may concern the use of medical treatment to prolong or end the life of seriously ill patients.[4,8,10] However, there is increasing recognition that prolonging life is not always the most appropriate goal of medicine at this stage of life and that other goals such as preserving quality of life and alleviating suffering are equally, if not even more important.[8,11]

Some people approaching death experience devastating symptoms such as intractable pain, dyspnoea and delirium that cannot be alleviated despite intensive medical and palliative treatment.[12,13] This leaves health care professionals, patients and relatives with a last-resort treatment, continuous sedation until death, which entails the use of sedative drugs to induce a state of unconsciousness until death, with the added effect that it takes away the person's experience of symptoms.[13,14] Findings from surveys of physicians suggest that continuous sedation is a frequently used practice across all care settings where people die estimated to involve between 2.5% and 18.2% of all deaths in Europe[13,15–17] and 10% in the United States.[1318] In the following paragraphs, we will go 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, the aims of this dissertation and methods used.

1.1.1. Terminology and definition: what's in a name?

Continuous sedation can be administered with various degrees of consciousness as a result.[19] Continuous sedation should , all guidelines agree, generally be administered proportionally to the severity of a patient's symptoms.[20–23] As mentioned by Raus[23] it implies that symptoms that cause a lower degree of suffering will therefore permit a patient to be more lightly sedated to a level at which the patient is still capable of communicating about his/her experiences making it making it easier for physicians to adjust the sedatives proportionally to the symptoms.[23–26] On the other hand more severe symptoms might require a more drastic form of continuous sedation, namely continuous deep sedation where a patient is sedated to a coma-like state accompanied by a loss of all ability to communicate and is said to have no experiences any more: neither negative or positive experiences.[23,27–31] Assessing whether sedation is too deep (i.e. the patient is sedated more heavily than necessary) or too shallow (i.e. the patient is still experiencing suffering) then becomes difficult because one can only rely on observers' assessments.[14,23,25,26,30]

While it is commonly argued that the adoption of a single, clear-cut and well-defined term for the use of continuous sedation until death, and a clear definition for the practice would greatly improve the quality of practice[13] and comparability of studies that investigate the practice of sedation, there are still large variations in the terms and definitions currently used.[7,32] One widely used term is 'palliative sedation', which is often employed as a broad term to refer to many types of sedation at the end of life,[14,28,33] including light as well as deep sedation, and continuous as well as intermittent sedation.[12,14,28,34] Although commonly used, this term has been according to Raus et al.[14,23] accused of being overly suggestive and euphemistic, concealing some of the cases in which sedation is being used to hasten the patient's death.[14,35] By including the word 'palliative', the term seems to impose its own justification as an acceptable part of medicine and palliative care, in linguistics known as 'semantic prosody'.[14,23,36] The suggestion then seems to be that, when using this practice, doctors intend to palliate suffering rather than, for example, to shorten life.[14,23,35] Although sedation is a part of palliative care and it may be true (but would need to be

argued) that sedation is ethically acceptable, it has been argued including by Raus et al.[14,23] that it seems improper to include elements of moral justification in the term used to label the practice.[14,23]

Several other terms with different connotations are also being used, for example 'terminal sedation', 'sedation for intractable distress in the imminently dying', 'end of life sedation', 'total sedation', 'controlled sedation', 'palliative sedation therapy' and 'proportionate sedation'.[33] These terms have also been criticized according to Raus and Sterckx[14] for being non-neutral. For example, the authors indicate that the term 'terminal sedation' has been criticized for focusing too much on the end-point of sedation (i.e. the death of the patient) rather than on the presumed purpose of the process (i.e. the palliation of suffering).[14,23,37] This may according to these authors suggest that the practice has to do with 'terminating' life or that seeking death is an integral part of successful sedation.[14,23,37] While other commentators according to Raus and Sterckx[14] actually prefer this term to any of the alternatives because they perceive it as being descriptive and as stressing an essential element of sedation – that it is in fact an end-of-life practice.[23,38,39]

In addition to the large number of terms used to refer to the practice, there is also wide variety in how these terms are defined.[40] According to one review, there are over 50 variant definitions in the literature.[41] Broadly speaking, the definitions fall into two types: those which include criteria of due care and those which are predominantly descriptive.[7] 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"*.[19] This definition mixes descriptive language with criteria of due care: the use of sedating medications, proportionality, the patient being terminally ill and the presence of refractory symptoms.[14,29] However, by incorporating normative elements within a definition, moral discussions become obfuscated and the question is raised as to what to call cases in which sedation was performed but in which other medications, indications or patients were involved.[14]

In this dissertation we will use the descriptive and more neutral term 'continuous sedation until death', occasionally abbreviated to 'continuous sedation', referring to "*the practice whereby one administers sedative drugs resulting in the continuous reduction or taking away of a patient's consciousness until death follows*".[14] As argued above, this is a rather broad definition and captures many different types of continuous sedation. Though these different types carry the same label, they should be according to Raus et al.[23] clearly distinguished as they differ in ethically relevant ways. Some moral issues are present in many such types, while others are unique to one specific type of sedation.[23]

1.1.2. Continuous sedation: (not) just normal medical practice

There are many ways in which doctors influence the circumstances and/or the timing of a patient's death. Some of these are accepted as normal medical practice, for instance, when a disproportional treatment is forgone.[23,35,42] Others are considered acceptable only under strict conditions, others unacceptable, such as non-voluntary active euthanasia.[29,35,43] Doctors have a fundamental ethical responsibility to ease suffering, particularly when intolerable and in those close to death.[44–46] Symptom burden for patients at the end of life is high[47] and thus there will be occasions where continuous sedation can be justified on the grounds of necessity.[44] It could be therefore reasonable to consider continuous sedation until death as 'normal' treatment, partly because its aim is not to shorten life and because the regulations governing it have been laid down in professional guidelines.[23,48] However, some commentators imply that continuous sedation until death is not so normal.[23,27,49] First, its non-life shortening nature is contested.[23,31] Second, even when no life shortening is at issue, it deprives patients in their very last days of the possibility to communicate, to say goodbye or having meaningful experiences, and many patients and their relatives consider being conscious until death as extremely important.[50–52]

According to Raus,[23,45] several commentators consider continuous sedation to be more like non-treatment decisions or the alleviation of pain and symptoms than like euthanasia or physician-assisted suicide, and thus to be justified according to the doctrine of double effect (DDE).[45,53,54]

The DDE is one of the most commonly cited justifications for continuous sedation at the end of life, and more broadly, for symptom alleviation in general.[23] Briefly, this states that a harmful effect of treatment (relieve of intractable suffering), even one resulting in death, is permissible providing that it was not intended, arose as a side-effect of a beneficial action and that the harmful effect (whether life-shortening or consciousness-reduction or both) was not the means of achieving the beneficial effect.[2345] Its use involves the judgement of intention and has been criticised on that account as two or even more intentions can go hand in hand. For instance, treatment can be aimed at alleviating suffering as well as shortening life.[55] In 1993, Quill already pointed out that '*multi-layered intentions are present in most, if not all, end-of-life decisions*'.[56] A qualitative study performed by Rietjens et al. among physicians from the Netherlands and the USA showed that respondents mentioned different and sometimes multiple intentions for their use of sedation.[57] Besides alleviating severe suffering, most Dutch respondents justified its use by stating that it does not hasten death, while most American respondents indicated that it might hasten death but that this was justifiable as long as that was not their primary intention. Thus, intention is a multi-interpretable and multi-layered concept, unfit to distinguish normal from exceptional medical treatment.[23,48,49]

In a study that described the practice of continuous deep sedation in Flanders, Belgium in 2007, 13% of physicians partly had the intention to hasten death in 13% of cases and had the explicit intention to hasten death in 4%.[58,59] While some argue that it should be clearly distinguished from euthanasia, others argue that it may resemble euthanasia without the legal supervision or even consider it to be 'slow euthanasia'.[23,43,60,61] There are also indications that, in countries where euthanasia is legal, continuous sedation is sometimes used as an alternative to euthanasia by physicians who struggle with euthanasia, for example because of religious objections, or wish to avoid the legal procedures involved with euthanasia in jurisdictions in which it is permitted.[61–63]

1.1.3. Guidelines and recommendations

Several local, regional and national generic guidelines and frameworks have been developed worldwide to outline the indications and proper performance of sedation at the end of life, to educate medical practitioners, and to improve quality in practice.[64–66] 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.[65,67] In 2009, the European Association for Palliative Care (EAPC) published a framework of recommendations for the use of sedation in palliative care to guide policy and facilitate the development of high-quality local procedural guidelines (see Table 1) based on the existing guidelines and literature and extensive peer review.[68,69] It states that prudent application of this approach requires due caution and good clinical practice and that problematic practices and inattention to potential risks can lead to harmful and unethical practice.[64,68–70]

Table 1. Ten-item framework EAPC[68]

- Recommend pre-emptive discussion of potential role of sedation in end-of-life care and contingency planning.
- Describe the indications in which sedation may or should be considered.
- Describe the necessary evaluation and consultation procedures.
- Specify consent requirements.
- Indicate the need to discuss the decision-making process with the patient's relative.
- Present direction for selection of the sedation method.
- Present direction for dose titration, patient monitoring and care.
- Guidance for decisions regarding hydration and nutrition and concomitant medications.
- The care and informational needs of the patient's relatives.
- Care for the medical professionals.

The Royal Dutch Medical Association published a nationwide guideline in the Netherlands in 2005 and revised it in 2009.[71] In Belgium, a guideline was issued by the Federation for Palliative care Flanders in 2010.[72] These guidelines sought to define 'palliative sedation' (including continuous sedation), to set rules for indications and contraindications, and to give recommendations for medication and practical procedures.[73–75] These guidelines define 'palliative sedation' as '*the deliberate lowering of a patient's level of consciousness in the last stages*

of life'. [71,72] It distinguishes between two types of sedation: continuous sedation until death; and temporary or intermittent sedation. The main premise of the guideline is according to Janssens et al.[49] that, unlike euthanasia, continuous sedation is a normal medical practice.[49] A summary of the main recommendations of the guidelines is presented in Table 2.[68,71,72]

Table 2. Key recommendations of the Belgian, Dutch and EAPC sedation guidelines[68,71,72]

- Continuous sedation until death should always be administered in the final stages 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 patient unbearably suffering. The physician will have to decide whether a symptom is treatable or not based on accepted good medical practice, bearing in mind the specific circumstances of a patient in the last stages of life.
- The patient's life expectancy should not exceed one to two weeks.
- 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 is no longer competent to make an informed decision 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 considering the treatment aim. However, in principle, there is no artificial administration of food and fluids in the case of continuous sedation until death.
- (An) appropriate expert(s) with specialist knowledge (e.g. psychiatrists, anaesthetists, 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 sedation is aimed at the relief of the patient's suffering and not at hastening or postponing death.
- 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.
- The attending physician must be present at the initiation of the sedation.
- Midazolam is the drug of choice. The use of morphine as a sedative is regarded as bad practice, morphine should only be given or continued (alongside sedatives) to relieve pain and/or dyspnoea.

1.1.4. Clinical aspects of continuous sedation: gaps between principle and practice

Beyond the conceptual and ethical dilemmas, controversy also seems to have reached clinical practice, with discussions being raised about the conditions under which continuous sedation should be performed and how it should be performed.[28,76] Some studies show that continuous sedation until death is not always performed in accordance with the relevant guidelines or recommendation and that clinicians are not well acquainted with generally recommended indications, leading to uncertainty whether, when and how to start.[15,58,77] We will discuss some of the main problems in practice below that will also be further examined in depth in this dissertation.

Guidelines generally state that indications for continuous sedation are present when one or more intractable or 'refractory' symptoms are causing the patient unbearable suffering.[68,71,72,78] A symptom is, or becomes, 'refractory' if none of the conventional modes of treatment is effective or fast-acting enough, or if these modes of treatment are accompanied by unacceptable side-effects.[79] This already contains two difficulties. First, estimating whether a symptom is actually refractory required sufficient knowledge in pain and symptom management as well as in palliative care.[69] We know from the literature that even basic palliative care knowledge appears to be suboptimal in many cases.[80,81] According to the European Association for Palliative Care (EAPC) framework for the use of sedation in palliative care, injudicious use of sedation occurs in '*situations in which before resorting to sedation, there is a failure to engage with clinicians who are experts in the relief of symptoms despite their availability*'.[68,69] However, consultation with experts prior to continuous sedation appeared to be rather rare.[82,83] Rietjens and colleagues reported that specialist palliative care services were consulted in only one-fifth of all palliative sedation cases.[15,84] As mentioned above, these symptoms should cause the patient unbearable suffering, which could only be experienced by dying persons themselves. A systematic review of the literature showed that the majority of papers listed only physical symptoms as the reason for sedating a patient, the most important being delirium, dyspnoea and pain.[19,48,85] A minority of

studies mentioned psycho-existential suffering as well as physical suffering as being a reason for sedating a patient, even though this was only true for a minority of patients.[7,86–88] Most frequently mentioned were anxiety, mental anguish and psycho-existential suffering (without elaboration).[19,85,86] A Dutch study of Swart et al.[85] showed that the indication for sedation typically originates from physical symptoms and non-physical symptoms 'adding up' to a situation in which a patient in the last phase of life suffers unbearably.[85]

Another precondition for the use of continuous sedation is the expectation that death will ensue in the reasonably near future – that is, within one or two weeks.[23,49,71] Despite its limitations, the prognosis of survival is still essential information at the end of life. If sedation is initiated too late, the patient's refractory symptoms may not be relieved adequately.[89,90] If it is initiated to early, it may result in extremely difficult situations and does not guarantee that the patient will die from her disease before she dies from the dehydration involved in continuous sedation without artificial nutrition and hydration.[91] It should be noted that it may be difficult to estimate life expectancy accurately.[35] Clinicians have a tendency to overestimate life expectancy: it has been shown that survival time of patients is typically 30% shorter than predicted by physicians, but that the accuracy of prediction increases as death approaches.[92] Studies have shown that continuous sedation is rarely performed when life expectancy is more than two weeks at the start of sedation.[84] According to the study of Chambaere et al.[58] this was the case in 2.7% of all Flemish sedation cases in 2007.[58] A Dutch study of Rietjens et al. [93,94] showed that the life expectancy at the start of continuous sedation was estimated to be less than two weeks in 97% of cases.[93,94] Based on retrospective reports from Dutch physicians, they found that 38% of patients died within 24 hours, whereas 96% of patient died within one week.[93,94]

Also, monitoring of the depth and dosages is often not done. Monitoring of continuous sedation is generally regarded as essential to ensure that the patient is comfortable and odes not receive too much or too little sedation, and that adverse effects can be recognized and acted on.[67] However, there is currently no consensus on the optimal level of sedation necessary for the relief of

suffering, nor the ideal method to assess the level of consciousness.[95] In practice, palliative care physicians often rely on a number of observational scales based on the patient's ability to react to different stimuli.[30,67] The questions remains whether the current assessments based on these observational scales are accurate and whether it can be excluded that even though they appear unconsciousness, are still aware of their situation and still experiencing discomfort. A study performed by Swart et al.[34] investigated Dutch physicians' considerations about the depth of continuous sedation. They found two approaches towards the depth of continuous sedation: starting with mild sedation and only increasing the depth if necessary; and deep sedation right from the start.[34] Physicians who choose either mild or deep sedation appear to be guided by the same objective of delivering sedation in proportion to the relief of refractory symptoms, as well as other needs of patients and their families.[34,85]

Often, not even the recommended drugs – benzodiazepines – are used.[58] A systematic review performed in 2008 showed that 32 per cent of the studies mentioned midazolam as the main drug used for continuous sedation.[19] Other drugs used either alone or in combination with midazolam included haloperidol, phenobarbital and opioids. A study by Anquinet et al.[96], conducted in Flanders, The Netherlands and the UK, showed that benzodiazepines (sometimes combined with opioids and/or other drugs) were more frequently used than opioids alone to induce continuous deep sedation, especially in the home setting.[88,96] In The Netherlands, the proportion of cases in which continuous deep sedation was induced with benzodiazepines (sometimes combined with opioids and/or other drugs) was higher than in Flanders and in the UK.[96] However, the study of Chambaere found that in 2007 opioids were used in 30.7% of all sedation cases as sole drug, this was especially the case in care homes.[58]

Finally, patients and relatives are not always involved in the medical decision-making and are often ill-informed about what to expect in the course of sedation, leading to poor perceived quality of dying and issues with coping.[51] A recent study of Anquinet et al. showed that the minority of the GPs had not consulted a competent patient but had consulted a relative of the

patient and GPs provided various explanations for this.[88,97] For instance, some thought that it was better for the patient, while others indicated that they thought that the patient preferred to leave the decisions up to the physician.[97] We will further discuss this in section 1.1.5.

1.1.5. The role of the dying person in the decision-making process

The indications for continuous sedation are considered to be medical in nature where the doctor have to decide whether or not a symptom is treatable on the basis of accepted good medical practice.[71] Nevertheless, the perspectives of the patient and the relative are very important and even crucial, especially as regards the discomfort and side-effects of any possible mode of treatment.[85] Wherever possible, sedation should only be initiated with the consent of the patient or the physician must consult the patient's representative in case the patient is no longer considered to be competent to take an informed decision. [51,68] Informed consent may not be possible, for example, in case where a carotid artery has ruptured requiring rapid action by the physician, and the use of sedation without consent is not excluded in such cases.[23,42]

Patient participation in decision-making is considered to be particularly appropriate towards the end of life because end-of-life decisions are often preference-sensitive.[98–101] A Belgian population-based death certificate study of Chambaere[58] showed that there was a request or a consent to continuous deep sedation in only 30% of all sedation cases.[58,59] Similar research from the Netherlands shows that although continuous sedation is more often discussed with the patient, it is far from always discussed.[102] Moreover, although clinical guidelines strongly encourage physicians to address end-of-life care preferences with all patients at risk of dying prior to sedation and to obtain their consent, they rarely state the extent to which patient preferences should be taken into account, and how to deal with a patient's request for sedation.[23,101,103,104] Studies have suggested that although a majority of people with limited life expectancy prefer a shared or active role in decision-making, their physicians and those close to them are frequently unaware of their preferences.[101,105,106] Additionally, previous research has suggested that the practice of continuous sedation, the decision-making leading up to continuous sedation, and the

extent to which the choices and preferences of patients are taken into account, may differ between and even within countries.[42,101,107–109]

1.2. Continuous sedation until death in nursing homes

In the previous sections we have discussed in detail the complexity associated with the practice of continuous sedation until death in end-of-life care on a conceptual, ethical and clinical level. Within this dissertation, we will focus on supporting and improving the practice of continuous sedation in the specific setting of nursing homes. In the following sections we will show that these challenges appear to be particularly pervasive in nursing homes. Before moving on to these specific challenges within nursing homes, we will discuss the possible consequences of an aging population for care within nursing homes and what the long-term prospects are as it is assumed that nursing homes will be the most common place of death by 2040.

1.2.1. Growth of the ageing population

The world's population is ageing and will continue to do so in rapid numbers in the upcoming years. Current population projections at international level generally assume that gains in life expectancy will continue in the future and births will continue to decline.[110] Under these assumptions, the number and share of the population reaching 65 and older in many countries in the Organisation for Economic Co-operation and Development (OECD), will increase rapidly when the baby boomers (individuals bron between 1946 and 1964 during the post-World War II baby boom) start reaching this age group. By 2050, the share of people that are on average 65 years and older will be more than one out of four people, or 26.5% of the total population in Belgium.[111,112] This is especially true for the people aged 85 and over (the 'oldest old') who will tend to grow the fastest. For Belgium specifically, it is projected that by 2030 this share of people will double and will increase further to more than 5% in 2050, the year when the last of the baby boomers will reach the age of 85.[113]

There is of course great variation in the functional status and ability of older people, with many able to maintain a good degree of independence, social engagement and continued physical health

until a great age.[114,115] This is the ideal of 'successful ageing'. Unfortunately, this ideal is not feasible for all and not all of these years will be spent in good health. As people grow older, old age becomes the single most important common risk factor for developing serious chronic disease and dying from it. Old age is strongly associated with an increased risk for multimorbidity, with prevalence ranging from 55 to 98%.[116,117] Others argue that older people suffer from what is commonly known as 'geriatric' syndromes, which is a term that describes the unique features of the health condition of elderly such as delirium, falls, incontinence and frailty. These are highly prevalent, multifactorial, and associated with substantial morbidity and poor health outcomes.[116,118,119] These multifaceted dynamics between underlying physiological change, chronic disease, and multimorbidity in the older population may result in what is called 'a trajectory of old age' that cannot be clearly categorized into one of the most common trajectories such as cancer or organ failure.[120–122] The large, vulnerable group of older people whose health declines and whose independence decreases with age, and those who will suffer cognitive decline and dementia, will require more and more care as time goes on.

1.2.2. Nursing homes are increasingly becoming the place of care and death

Older people themselves prefer to have the choice of where they will live and receive care, with many preferring to live at home for as long as possible.[122–124] Indeed, a sizeable proportion of older people will remain at home until death.[125,125–127] However, circumstances sometimes require them to move to a long-term care facility.[124,126–128] These circumstances include the need for more skilled care, behavioural and cognitive problems and the burden on family carers.[129] In 2017, 1 out of 3 people aged 80 or older lived in a nursing home in Flanders and Brussels.[112] And while up until the first quarter of the twentieth century, people tended to die in their own homes, the process of dying has become more institutionalized in industrialised countries with increasing numbers of people dying in hospitals and nursing homes.[127] Based on numbers from the Flemish Agency of Care and Health, in 2016, 20% of men and 39% of women in Flanders died

in a nursing home. Current projections assume that nursing homes will be the most common place of death by 2040.[127,130]

1.2.3. A lack of training and knowledge of palliative care and symptom management in nursing homes

The provision of high-quality palliative care to the growing number of older people living and dying in nursing homes is a challenge in European countries.[80,131] A growing number of older people will experience multiple chronic life-limiting conditions and complex needs and will, at some point, require long-term care in a nursing home.[80,131–133] Additionally, the median length of stay in a nursing home before death is decreasing and thus nursing home residents can be increasingly considered to be at the end of life.[134–136] Research has, however, indicated that nursing homes are still struggling to meet the palliative care needs of their residents, although palliative care is considered to be the most appropriate care approach for this population[80,117,131,137,138] Many of their residents suffer from distressing symptoms such as pain, dyspnoea and depression and have unmet needs regarding physician communication, emotional support and respectful care.[139–141] Although nursing home staff have a lot of experience in caring for dying residents, they often lack – according to Smets et al.[80] - formal training and knowledge in palliative care[142–144] and knowledge of important palliative care issues such as management of pain including the use of continuous sedation is generally poor in nursing homes.[145,146]

1.2.4. Challenges with continuous sedation particularly pervasive in nursing homes

Of all patients who died in a nursing home in 2007, 9.4 % were continuously and deeply sedated until death.[58] While deciding on and performance of continuous sedation is replete with challenges, research suggests that the challenges are particularly pervasive in nursing homes, as various specific individual and institutional factors may further complicate good practice.[13,147–149]

On an individual level, most residents are dying from conditions that are more complex and unpredictable in terms of diagnosis and prognosis, complicating judgments about imminent

death and the suitability of continuous sedation until death.[13,128] This population is also characterized by high rates of medication use which further complicates determining and finding the correct dose.[150] A Dutch study performed in nursing home residents with cancer or dementia reported that according to involved relatives several residents experienced a broad range of symptoms during dying, despite the use of sedation.[151] This may indicate that sedation did not always sufficiently relieve suffering. Also, communication preceding sedation with patients may be difficult or even impossible, particularly in the case of dementia patients.[13,145,148] Guidelines recommend that the competent individuals should be actively involved in the decision making.[13,71,76] When individuals are no longer competent, the decision must be discussed with their representative.[68,72] The study of Anquinet et al,[145] however, showed that decision making regarding sedation mostly involves relatives and that competent residents are not always involved.[145] The authors suggested that 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[152–154] or the physician or the resident may have hesitated to discuss these issues.[97,155,156] On the institutional level, nursing homes are in contrast to hospital and palliative care units not specifically equipped or attended by highly specialized staff,[13] which also appeared from section 1.2.3.[147,148]

As mentioned earlier, studies show that continuous sedation until death is not always performed in accordance with the relevant guidelines or recommendation and that clinicians are not well acquainted with generally recommended indications.[15,58] The few studies available show that this may be even more the case in nursing homes. In the study of Anquinet et al.[88] sedation was used for two out of 11 residents who were not terminal, which conflicts with guideline recommendations.[145] For three residents, the general practitioner had indicated that there was a strong increase of morphine in the last day. Epidemiological studies show that 35% of sedated patients in nursing homes received opioids as sole drug.[58] This could be perceived as an indication of both ineffective and problematic sedation and some research has even suggested that continuous sedation until death is occasionally used as a substitute for euthanasia.[58,62,157] Some

clinicians in the study of Rys (implicitly) declared that co-intentions to hasten death may be involved, or that continuous sedation until death, properly initiated, may eventually slip into 'slow euthanasia'.[62] A certain degree of conceptual ambiguity still exists, resulting in misinterpretation and misuse of the practice. Several clinicians considered continuous sedation until death a form of euthanasia or situated the practice between pain relief and actively ending life. A Belgian study showed that nursing home clinicians frequently feel pressured by the patient's family to hasten death, especially when the course of sedation has taken longer than anticipated.[147,158] Research from the Netherlands reported that about one in six general practitioners experience pressure (by patients, relatives, or other persons) during the decision-making process preceding the administration of continuous deep sedation and, moreover, that this pressure had influenced decision-making in 41% of the cases.[63,159]

As a result, the current practice of continuous sedation for residents in nursing homes may not always guarantee a dying process free of severe symptoms and is therefore amenable to improvement.[97] Knowledge about the practice of continuous sedation is predominantly based on research with people with cancer, carried out in hospice or hospital environments.[13,97,148,160,161] Obviously, the findings of such studies may not, or only be partially comparable to relatively low-care settings such as nursing homes with limited relevant infrastructure and as shown in the previous section with limited palliative expertise and knowledge available.[13] The question is whether current guidelines – aimed at the widest possible patient groups – are sufficiently attuned to the specific needs and context within nursing homes, particularly when we consider the many differences between nursing home patients and the typical cancer related palliative care patients: older age groups often confronted with frailty and dementia, different metabolism, etc.[145,148] The development and refinement of guidelines and clinical practice protocols on continuous sedation may benefit from closer involvement of practicing nursing home clinicians in order to more concretely address complex issues such as estimating the remaining life expectancy of very old patients (with or without dementia), determining the refractory nature of their suffering, or the dosing of sedative drugs.[13,66,148,162]

1.3. Research aims

As this introduction has highlighted, continuous sedation until death is still a highly debated medical practice at the end of life as controversial issues persist about many aspects of the practice.[41,163] Therefore, the incidence of continuous sedation, the socio-demographic patterns in its application, the characteristics of the decision-making process and the performance all need to be monitored. Trends and developments in end-of-life practices, including continuous sedation until death, provide insight into evolutions in the quality of end-of-life practices. Additionally, studying trends allows identification of priorities for medical practice at the end of life. There are still important gaps in our knowledge about the practice of continuous sedation including the role of patients in the decision making that is considered to be medical in nature. Challenges with the practice above all turn out to be particularly pervasive in nursing homes, although it is still unknown what the specific barriers are to the decision making preceding and performance of continuous sedation in Flemish nursing homes nor ways to overcome these barriers. The results of this dissertation are being used for the development of a practice protocol adapted to the specific needs for the use of continuous sedation until death in nursing homes to enhance its quality and will lead to specific recommendations for practice, policy as well as for future research aimed at further improving the practice.

The research aims of this dissertation are two-fold:

Research aim 1: To describe the practice of continuous sedation until death in Flanders, Belgium.

Specific objectives are:

a. To describe the characteristics of the decision-making about and performance of continuous sedation until death in Flanders, Belgium and to examine changes over time;
b. To explore which factors play a part in the decision to start continuous sedation until death according to physicians and nurses;

c. To explore the role of patients in the decision-making preceding continuous sedation until death in Belgium, and compare Belgium with the Netherlands and the United Kingdom.

Research aim 2: To develop an evidence-based clinical practice tool to support the practice of continuous sedation until death in nursing homes.

Specific objectives are:

a. To give a systematic overview of existing initiatives that aim to support, facilitate and/or improve the practice of continuous sedation until death within end-of-life care;
b. To examine experienced barriers to the decision making and performance of continuous sedation until death in Flemish nursing homes according to physicians, nurses and other nursing home staff;
c. To use these results to develop a potentially feasible, acceptable and effective evidence-based practice protocol for the use of continuous sedation until death in nursing homes.

1.4. Methods

Five different studies were used for this dissertation. In all studies, we studied data from Flanders, the Dutch-speaking part of 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.

1.4.1. End-of-Life Decisions Study, a mortality follow-back survey based on death certificates (Chapter 2)

A post-mortem survey on end-of-life decisions using a representative sample of death certificates was undertaken in Flanders, Belgium in in 2007 (n=6.927 deaths) and 2013 (n=6.871 deaths) (research objective 1a).[164] This study design has been repeatedly applied and validated to evaluate end-of-life care and decision-making.[15,164–166] The survey is a replica of 3 previous large-scale nationwide studies held in Flanders in 1998, 2001 and 2007.[164,166,167]

Within two months of the death, the certifying physician received a four-page questionnaire with an introductory letter containing patient identifiers. The physician was requested to complete the questionnaire by consulting the patient's medical file. If the certifying physician was not the treating physician, the questionnaire was passed on to the treating physician. One physician could receive participation requests for up to five decedents, with at most three reminders per death.[168] Returning the questionnaire was regarded as implicit consent of the physician to participate in this study. After data collection a one-page questionnaire was mailed to all non-responding physicians inquiring about reasons for not participating. The response rate was 60.6% in 2013 compared to 58.4% in 2007. To guarantee absolute anonymity for participating physicians, a lawyer served as an intermediary between responding physicians, researchers and the Flemish Agency for Care and Health, ensuring that completed questionnaires could never be linked to a particular patient or physician.[167]

The repeatedly validated questionnaire on end-of-life decision-making first asked whether death had been sudden and unexpected.[167,168] The rest of the questionnaire was to be completed only if death had not been sudden and unexpected. The following question was posed regarding continuous deep sedation: *'Was the patient continuously and deeply sedated or kept in a coma until death by the use of one or more drugs?'*.[168] We used a descriptive definition of the practice (continuous deep sedation until death) rather than a term (palliative or terminal sedation) to avoid interpretation differences among respondents.[168] Details about the decision-making process, the types of drugs used and the estimated degree of life-shortening according to the physician, and the physicians' degree of palliative care training were also asked. Demographic and clinical patient data were obtained from the death certificate data and linked anonymously after data collection.[168]

1.4.2. The UK-Netherlands-Belgium International Sedation Study (UNBIASED), qualitative interviews with physicians, nurses and relatives (Chapter 3 and 4)

The UNBIASED study (UK Netherlands Belgium International Sedation Study) was conducted in Belgium, the Netherlands, and the United Kingdom (UK) to explore medical practitioners' and relatives' experiences with and perceptions of continuous sedation until death.[101,107,108] In all countries, senior clinical staff members identified eligible decedents: patients aged over 18 who had died of cancer and to whom sedating medications were administered continuously with the intention of decreasing awareness to alleviate otherwise uncontrollable symptoms (either physical or psychological/existential), and for whom the sedation was in place at the time of death.[101,107] In all three countries, cases were included from three settings to enable maximum variation: home, hospital and specialized palliative care settings (palliative care units in Belgium; hospices in the Netherlands and the United Kingdom).[108] 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. Nurses and physicians were invited to take part if they had been closely involved in the care of these patients and were interviewed about not more than three cases.[101,107,108] If more than one physician or nurse was involved, all were interviewed where possible.[101,169] Relatives were invited to participate via a letter and information sheet sent on behalf of the research team by the patient's physician. Interviews took place as soon as possible after death, that is, within 12weeks, to maximize recall.[88,101]

The interviews were semi-structured and supported by the use of a topic guide. Interviews focused on recollections of the patient's care and the use of continuous sedation until death in particular. Physicians and nurses could use the patient records if necessary to support them in their recollections but were asked to provide relevant information about the case in an anonymous manner.[101] All data that could identify the physician, nurses, patient or relatives were removed to preserve anonymity. In this dissertation, we studied physician and nurse interviews from Belgium (Chapter 3)[169] and all complete cases from all countries in Chapter 4.[101]

1.4.3. A systematic literature review of existing quality improvement initiatives for continuous sedation until death (Chapter 5)

A systematic review about existing initiatives to support the practice of continuous sedation until death was performed to address research objective 2a. Records were searched through MEDLINE, EMBASE, CENTRAL, CINAHL and Web of Science from inception to April 16 2020.[170] The search key was initially developed in MEDLINE and later adapted for other databases. A combination of controlled vocabulary and free text words was used to search in titles and abstracts. Studies were screened and included in the review on the basis of predefined inclusion- and exclusion criteria. Subsequently, the characteristics of the studies included were extracted to a standardized data-extraction form under the headings of general information, country, research question, design, method, setting, participants and scope of the study. The quality of the studies was appraised and evaluated using the QualSyst tools for the assessment of the quality of both qualitative and quantitative studies.[171] The studies were screened, analysed and graded for quality independently by two authors.

1.4.4. Focus groups among professional stakeholders in nursing homes (Chapter 6)

Focus groups were held with 71 health care professionals including 16 palliative care physicians, 42 general practitioners, and 13 nursing home staff members (nurses and care assistants) to address research objective 2b.[13] In order to obtain a broad range of views and experiences, participants were sampled in three ways:

(a) Three focus groups were organized during a biannual gathering of GPs working in multidisciplinary palliative home care teams who can be considered experts in palliative care who, in addition to their own practice, advise, and support GPs and other primary health care professionals in providing optimal care for palliative patients;

(b) Five focus groups were organized within local peer review GP groups that meet four times a year to discuss their practice. Every accredited GP in Belgium must be affiliated to a geographically determined peer-review group and attend at least two of four meetings per year;

(c) A third group were nursing home staff (nurses, care assistants, and coordinating and advisory physicians in nursing homes). The coordinator (or equivalent) of each nursing home selected was contacted by telephone to ask if they would agree to facilitate our study.

A semi structured topic guide was developed to ensure consistency in questions across groups covering their experiences of three main areas of continuous sedation until death in nursing homes: decision making, performance, and attitudes to quality improvements.[13] All participants filled in a short questionnaire on sociodemographic data and signed an informed consent form before the start and consented to the discussion being audiotaped. The audiotaped discussions were transcribed verbatim and analyzed by constant comparative analysis with qualitative analysis software (NVivo 12). All data that could identify the physician, nurses, patient or relatives were removed to preserve anonymity. A general conceptual coding framework was then developed by two researchers and agreed upon with all coauthors. All transcripts were then coded by the lead author and quotes were selected on the basis of their being representative of the wider data, translated and approved by all researchers.[13]

1.4.5. Expert panels to validate a practice protocol for continuous sedation until death in nursing homes (Chapter 7)

Based on the findings of our systematic review on existing quality improvement initiatives and focus groups with 71 health care professionals identifying perceived barriers for the decision-making, communication and performance of continuous sedation until death in nursing homes, we developed a preliminary practice protocol adapted to the specific context of nursing homes and based on existing guidelines (research objective 2c). The model was further refined at monthly meetings with the multidisciplinary research team consisting of medical sociologists, a health scientist, a geriatrician and a general practitioner. We also held ten expert panels with 70 stakeholders representing palliative care physicians, geriatricians, general practitioners and nursing home staff following a participatory approach to explore how the model meets their own

experiences and expectations, and to brainstorm about how to further improve the intervention model.

Professional stakeholders were eligible when they were involved in the care of nursing home residents and were sampled by launching a call at a symposium on continuous sedation until death by the Federation for Palliative Care Flanders, followed by a letter of invitation by e-mail to all symposium participants. We also organized an expert panel within local peer review GP groups, we randomly selected palliative care physicians and geriatricians and we further used the snowball method to identify other potential participants with relevant experience. Interested stakeholders were asked to identify other potential participants that were contacted by e-mail. We used pre-existing groups of physicians and nursing home staff as group discussions are expected to naturally occur during these meetings.

1.5. Outline of this dissertation

Chapters 2-7 are based on articles which have been published, accepted or submitted for publication in academic peer-reviewed journals. All of the Chapters can be read independently.

The two main aims of this PhD project are addressed in two separate parts of the dissertation. Each part consists of different Chapters that answer the specific underlying objectives and research question. **PART I** describes the rationale for this PhD project as well as its aims and objectives. **PART II** focuses on the description and monitoring of the practice of continuous sedation until death in daily clinical practice. **Chapter 2** describes the results of a population-based mortality follow-back study where we compared the prevalence and characteristics of continuous deep sedation until death in Flanders, Belgium between 2007 and 2013. **Chapter 3** explores how physicians and nurses justify their use of continuous sedation until death and further explores which factors play a part in the decision to start continuous sedation until death. **Chapter 4** describes the decision-making process preceding continuous sedation until death with particular attention to the involvement of the dying person and compared practices in Belgium, the Netherlands and the United Kingdom. **PART III** reports the development process of a practice

protocol to support the use of continuous sedation until death adapted to the context-specific needs of nursing homes. **Chapter 5** offers an overview of existing scientific initiatives to support, facilitate or improve the practice of continuous sedation until death in end-of-life care. **Chapter 6** identifies perceived barriers in the decision making about and performance of continuous sedation until death in Flemish nursing homes. **Chapter 7** describes the development process and the contents of an evidence-based practice protocol to support healthcare professionals in the decision-making, communication and performance of continuous sedation until death in nursing homes. The final section of the dissertation, **PART IV**, concludes the dissertation with a summary and discussion of the main findings, describes methodological reflections, strengths and limitations of the research methods used, and aims to suggest some useful practical implications, recommendations that might help policymakers, and what future research should focus on.

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PART II

The practice of continuous sedation at the end of life

CHAPTER 2

Trends in continuous deep sedation until death between 2007 and 2013: a repeated nationwide survey

Lenzo Robijn, Joachim Cohen, Judith Rietjens, Luc Deliens, Kenneth Chambaere.

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Abstract

Background: Continuous deep sedation until death is a highly debated medical practice, particularly regarding its potential to hasten death and its proper use in end-of-life care. A thorough analysis of important trends in this practice is needed to identify potentially problematic developments. This study aims to examine trends in the prevalence and practice characteristics of continuous deep sedation until death in Flanders, Belgium between 2007 and 2013, and to study variation on physicians' degree of palliative training.

Methods: Population-based death certificate study in 2007 and 2013 in Flanders, Belgium. Reporting physicians received questionnaires about medical practices preceding the patient's death. Patient characteristics, clinical characteristics (drugs used, duration, artificial nutrition/hydration, intention and consent), and palliative care training of attending physician were recorded. We posed the following question regarding continuous deep sedation: 'Was the patient continuously and deeply sedated or kept in a coma until death by the use of one or more drugs'.

Results: After the initial rise of continuous deep sedation to 14.5% in 2007 (95%CI 13.1%-15.9%), its use decreased to 12.0% in 2013 (95%CI 10.9%-13.2%). Compared with 2007, in 2013 opioids were less often used as sole drug and the decision to use continuous deep sedation was more often preceded by patient request. Compared to non-experts, palliative care experts more often used benzodiazepines and less often opioids, withheld artificial nutrition/hydration more often and performed sedation more often after a request from or with the consent of the patient or family.

Conclusion: Worldwide, this study is the first to show a decrease in the prevalence of continuous deep sedation. Despite positive changes in performance and decision-making towards more compliance with due care requirements, there is still room for improvement in the use of recommended drugs and in the involvement of patients and relatives in the DM process.

Introduction

Physicians caring for patients with an advanced disease are often confronted with important but complex end-of-life decisions that affect the patient's manner of dying.[1] When terminally ill patients experience unbearable symptoms that cannot be alleviated by conventional treatments, administering drugs to induce unconsciousness can be an option of last resort to relieve suffering.[2,3] Large-scale population-based surveys monitoring end-of-life practices on a nationwide scale have so far consistently shown an increased use of continuous deep sedation until death. In Flanders, the overall prevalence of this practice increased considerably between 2001 and 2007, rising from 8.2% to 14.5% of all deaths.[4,5] In the Netherlands, studies found that the prevalence of continuous deep sedation increased from 8.2% in 2005 to 12.3% of all deaths in 2010.[1,6,7]

Continuous deep sedation until death remains a highly debated medical practice, particularly regarding its potential to hasten death and its proper use in end-of-life care.[8–10] In light of the clinical and ethical challenges associated with the practice, several guidelines and recommendations have been developed around the world. In Flanders the Federation for Palliative Care implemented a guideline in 2010,[11] describing conditions under which sedation at the end of life should be performed.[12–14] Like guidelines in many other countries, it recommends that continuous deep sedation until death should only be performed close to death for unbearable and refractory symptoms without intent to hasten death [15,16]. Benzodiazepines, titrated proportionally to alleviate the symptoms, are the drug of first choice and the administration of artificial nutrition or hydration is not encouraged unless the benefits outweigh the harm.[4,12]

Empirical studies indicate that there is considerable variation regarding this medical practice and that physicians are not always well acquainted with the conditions under which continuous deep sedation until death should be performed.[17] The effectiveness of guidelines, being non-committal and non-mandatory, in changing physicians' attitudes, knowledge and practices have

been called into question.[18] In the Netherlands, where the Royal Dutch Medical Association issued a clinical guideline in 2005 and a revised guideline in 2009 [19], studies have suggested that guidelines can certainly lead to considerable practice improvements in accordance with guideline requirements [20]. Some of the results even suggest better compliance with the guidelines when physicians had more palliative care expertise.[21] This might also be the case in Belgium after the introduction of the Flemish guideline by the Federation for Palliative Care in 2010. This study describes recent developments in the prevalence and characteristics of continuous deep sedation until death in Belgium between 2007 and 2013 and studies variation in performance and decision-making depending on the degree of palliative care training of the physician.

Methods

Study design

We conducted a population-based death certificate survey identical to surveys in 1998, 2001 and 2007, based on a representative sample of deaths in Flanders, Belgium. This region has approximately six million inhabitants and 60.000 deaths annually.[4,22] To limit the time between the certification of death and the inclusion in the study, a stratified random sample of deaths in 2013 was drawn weekly from the Flemish Agency for Care and Health, the central administration authority for processing death certificates. From our previous studies[5,23,24] we know that end-of-life decisions occur more frequently among patients with a certain cause of death. We therefore adopted disproportionate sampling of deaths to include more patients with a cause of death known to have a higher likelihood of one or more end-of-life decisions. All deaths from January 1st until June 30th 2013 of Belgian residents aged one year or older were assigned to one of three strata, based on underlying cause of death as indicated on the death certificate and the estimated corresponding likelihood of an end-of-life decision. Sampling fractions for each stratum increased with this likelihood [23]. In the first stratum, all deaths for which euthanasia was mentioned on the death certificate were sampled. In the second stratum,

one third of all cancer deaths were sampled. In the third stratum, one in six deaths resulting from any other cause was sampled. This resulted in a sample of 6.871 deaths, about 21% of all deaths in the studied period.

Within two months of the death, the certifying physician received a four-page questionnaire with an introductory letter containing patient identifiers. The physician was requested to complete the questionnaire by consulting the patient's medical file. If the certifying physician was not the treating physician, the questionnaire was passed on to the treating physician. One physician could receive participation requests for up to five decedents, with at most three reminders per death; every sixth case was excluded and another death was sampled from the same stratum and the same place of death. To guarantee absolute anonymity for participating physicians, a lawyer served as an intermediary between responding physicians, researchers and the Flemish Agency for Care and Health, ensuring that completed questionnaires could never be linked to a particular patient or physician. Patients were deceased, and consent was not required. Physicians' participation was regarded as implicit consent, which was noted in the accompanying letter introducing the study. After data collection a one-page questionnaire was mailed to all non-responding physicians inquiring about reasons for not participating. The mailing and anonymity procedures were approved by the Ethical Review Board of the University Hospital of the Vrije Universiteit Brussel, the Belgian National Disciplinary Board of Physicians and the Belgian Privacy Commission.

Questionnaire

The repeatedly validated questionnaire on end-of-life decision-making first asked whether death had been sudden and unexpected. The rest of the questionnaire was to be completed only if death had not been sudden and unexpected. The following question, identical to that used in 2001[22,25] and 2007[23], was posed regarding continuous deep sedation: *Was the patient continuously and deeply sedated or kept in a coma until death by the use of one or more drugs?.* We used a descriptive definition of the practice (continuous deep sedation until death) rather than a

term (palliative or terminal sedation) to avoid interpretation differences among respondents. The physician's degree of palliative training is coded if he/she reported that they (1) had not had palliative care training; (2) had only had some palliative care training in the basic curriculum; (3) had followed continued palliative care training or (4) worked as part of a palliative care team (palliative care experts). Demographic and clinical patient data were obtained from the death certificate data and linked anonymously after data collection.

Statistical analysis

The response sample was corrected for disproportionate stratification by weighting each stratum to make the proportion in the response sample identical to the proportion in all deaths and adjusted to be representative of all deaths in the first half of 2013 in terms of age, sex, marital status, province of death, cause of death and place of death (adjustments needed for province and place of death). After this weighting procedure there were no significant differences between response sample and all deaths in any of these variables. Final weights varied between 0.11 and 1.90. This procedure was also used in previous survey years. Bivariate cross-tabulations and multivariable logistic regression models were calculated to compare prevalence and characteristics of continuous deep sedation between 2007 and 2013. Multivariable models incorporated the most important confounders: sex, age, cause of death and place of death. All statistical analyses were calculated with complex samples functions in SPSS version 22.0.

Results

Of the 6.871 deaths sampled, questionnaires were returned for 3.751 cases. From the non-response analysis we found that response was impossible for 683 deaths (e.g. because the physician did not have access to the patient's medical file or the patient could not be identified). These cases were removed from the sample. Response rate was therefore 60.6% (3.751/6.188 eligible cases) compared with 58.4% in 2007. Analysis of non-response questionnaires revealed lack of time as the most quoted reason for non-participation. Between 2007 and 2013 there was

an increased proportion of decedents aged 80+ from 50.0% to 57.1% and deaths in nursing homes rose from 22.6% in 2007 to 26.9% in 2013 (data not shown). Cancer consistently accounted for around one in four deaths.

The overall prevalence of continuous deep sedation decreased significantly from 14.5% (95%Cl 13.1-15.9) to 12.0% (95%Cl 10.9-13.2, p=0.007) (Table 1). The decreasing trend is visible in nearly all patient groups, but is statistically significant only in women (from 15.4% [95%Cl 13.5-17.6] in 2007 to 11.8% [95%Cl 10.3-13.6] in 2013), in decedents of 80 years or older (from 11.1% [95%Cl 9.4-13.0] to 8.9% [95%Cl 7.6-10.3]), in persons with primary diagnoses other than cancer (12.9%[95%Cl 11.2-14.8] to 10.4% [95%Cl 7.6-10.3]), in decedents with a high school or college/university degree (from 18.5% [95%Cl 15.3-22.2] to 13.0% [95%Cl 10.6-15.8]), among widowed decedents (11.8% [95%Cl 9.9-14.0] to 8.4% [7.0-10.1]) and among those living in care homes (9.4% [95%Cl 7.4-11.8] to 6.6% [95%Cl 5.2-8.4]). The decrease remained significant after simultaneously controlling for relevant confounding factors for the total prevalence of continuous sedation (p=0.037), among women (p=0.017), in patients with a high school or college/university degree (p=0.019), among widow(er)s (p=0.022) and those dying in care homes (p=0.035).

Table 1. Prevalence of continuous deep sedation until death (CDS) and baseline characteristics of patients receiving CDS between 2007 and 2013.[a,b]

	Number of cases		*Weighted percentages*		*Biv. P-value*
	2007	2013	2007	2013	
	N= 3623	N= 3751	% (95%Cl)	% (95%Cl)	
Total CDS	561	438	**14.5 (13.1-15.9)**	**12.0 (10.9-13.2)**	**0.007**
Sex					
Male	1875	1920	13.5 (11.8-15.6)	12.2 (10.6-13,9)	0.275
Female	1748	1826	**15.4 (13.5-17.6)**	**11.8 (10.3-13.6)**	**0.006**
Age (in years)					
1-64	741	632	19.3 (16.1-23.0)	16.5 (13.5-20.0)	0.245
65-79	1267	1100	17.1 (9.5-14.0)	16.0 (13.7-18.6)	0.540
80+	1615	2014	**11.1 (9.4-13.0)**	**8.9 (7.6-10.3)**	**0.050**
Cause of death					
Cancer	2018	1470	18.4 (16.6-20.3)	16.6 (14.7-18.8)	0.222
Non-cancer	1605	2258	**12.9 (11.2-14.8)**	**10.4 (9.1-11.9)**	**0.032**
Education					
Primary school	1196	923	13.3 (11,2-15,8)	10.2 (8.2-12.6)	0.054
High school (not graduated)	692	639	13.7 (10.8-17.3)	12.5 (10.0-15.7)	0.598

High school/college	726	778	**18.5 (15.3-22.2)**	**13.0 (10.6-15.8)**	**0.010**
Marital status					
Unmarried	357	372	12.0 (8.6-16.5)	8.7 (6.1-12.3)	0.192
Married	1798	1618	17.5 (15.4-19.9)	15.9 (14.0-18.0)	0.296
Widow(er)	1252	1445	**11.8 (9.9-14.0)**	**8.4 (7.0-10.1)**	**0.008**
Divorced	214	305	13.0 (8.6-19.0)	14.7 (10.8-19.6)	0.629
Setting [c]					
At home	1265	1133	9.8 (8.3-11.6)	8.7 (7.2-10.4)	0.336
Hospital [d]	1382	1447	19.5 (17.2-22.0)	17.0 (15.0-19.1)	0.120
Care Home	850	1038	**9.4 (7.4-11.8)**	**6.6 (5.2-8.4)**	**0.037**

[a] Figures are weighted percentages of all deaths and 95% confidence intervals. Figures in bold denote statistically significant differences between 2007 and 2013.

[b] After controlling for the most important confounders (age, sex, cause of death and place of death) differences in the following groups between 2007 and 2013 remained significant: total CDS, female, high school/college, Widow(er) and care home. The direction of bivariate associations did not change in multivariate analysis.

[c] Other place of death not included in table: 13 cases in 2007 and 12 cases in 2013.

[d] In 2013, we could distinguish different departments within the hospitals. In 2013, continuous sedation until death within the hospital was more often used in an intensive care unit (50.5%, 95%CI 43.8-57.6) than in a palliative care unit (23.9%, 95%CI 16.7-32.9) ($p<0.001$).

Benzodiazepines and opioids were the most frequently used drug combination in 2007 and 2013, and opioids were less often used in 2013 as sole drug (Table 2). Compared to 2007, sedation in 2013 was more often performed with propofol (23.1% vs 11%). The duration of sedation was relatively shorter in 2013 compared with 2007, with a higher proportion of continuous deep sedations lasting less than 24 hours (35.8% vs 24.4%). Though artificial nutrition or hydration was less often administered until death in 2013 (38.3% vs 42.5% in 2007), multivariable analysis showed this was due the increased proportion of decedents aged 80 and over, for whom artificial nutrition or hydration is less likely (not in table). Sedation was more often performed after a request from the patient in 2013 (15.3%) than in 2007 (9.7%). The lacking of patient or family consent mainly occurred in the hospital setting (89.4% vs 93.4% in 2007) and in persons with primary diagnoses other than cancer (78.6% vs 81.5% in 2007) such as cardiovascular diseases (35.1% vs 37.6% in 2007) (not in table). No significant differences were found regarding the intention of hastening death between 2007 and 2013. In 2013, the life-shortening effect of sedation was explicitly intended or co-intended in 17.9% of cases.

Table 2. Characteristics of performing continuous deep sedation until death in 2007 and 2013.[a] [b]

[a] Figures are weighted column percentages. Percentages may not always amount to 100% because of rounding.

	N		Total CDS		Chi² P-Value [c,d]
	2007	2013	2007	2013	
	N=561	N=438	%	%	
Drugs administered					**<0.001**
Only benzodiazepines	72	52	11.2	10.5	
Benzodiazepines and opioids (+other drugs)	239	213	42.4	46.2	
Propofol (+benzodiazepines/opioids/other drugs)	32	73	11.0	23.1	
Only opioids	167	79	30.7	16.7	
Other combinations	24	16	4.7	3.5	
Duration of sedation					**<0.001**
0-24 hours	125	153	24.4	35.8	
1-7 days	321	247	61.7	54.5	
1-2 weeks	58	21	11.2	6.0	
More than 2 weeks	12	12	2.7	3.7	
Artificial nutrition and hydration					**0.038**
Administered until death	159	129	42.5	38.3	
Withdrawn during sedation	43	49	9.4	12.5	
withheld	347	258	48.1	49.2	
Request or consent					0.095
Request by patient	71	83	9.7	15.3	
No request, but consent of patient	135	100	20.3	19.5	
No request or consent of patient, but request by family	78	60	11.8	13.8	
No request or consent of patient, but consent of family	186	131	38.4	35.2	
No request or consent of patient or family	74	54	19.8	16.2	
Intention of hastening death					0.329
No intention	124	99	32.4	29.2	
Taking into account possible hastening of death	280	236	51.2	52.9	
Co-intention	77	64	12.9	15.2	
Explicit intention	18	14	1.1	2.7	

Figures in bold denote statistically significant differences between 2007 and 2013.

[b] Missing cases: drugs administered (26 in 2007 and 5 in 2013), duration of sedation (45 in 2007 and 5 in 2013), artificial nutrition and hydration (12 in 2007 and 2 in 2013), request or consent (17 in 2007 and 10 in 2013) and intention of hastening death (62 in 2007 and 25 in 2013).

c After controlling for the most important confounders (age and place of death), differences in 'artificial nutrition and hydration' can be attributed to the increased proportion of decedents aged 80 and over.

[d] P-values were calculated with Fisher's exact test (in StatXact version 6).

The performance and decision-making characteristics of continuous deep sedation until death in 2013 differed according to the degree of the physician's palliative care expertise (Table 3). The use of benzodiazepines increased with palliative care expertise, whereas the use of opioids and propofol decreased ($p<0.001$). Those with training or expertise also withheld artificial nutrition or hydration more often ($p<0.001$) and sedation by palliative care experts was more often preceded by a request of the patient ($p=0.025$) and less often without any request or consent of

the patient or his or her family (p=0.001). All significant bivariate results were also found significant after controlling for the most important confounders: sex, age, cause of death and place of death. The direction of bivariate associations did not change in multivariate analysis.

Table 3. Performance and decision-making characteristics of continuous deep sedation until death in 2013 according to the degree of physicians' palliative care (PC) expertise.[a,b,c]

	No PC training	PC training in the basic curriculum	Continuing PC training courses	Specialist	Biv. P-Value [d]
	N=126	N=109	N=138	N=63	
Drugs administered					**<0.001**
Only benzodiazepines	7.8	4.2	14	22.0	
Benzodiazepines and opioids (+other drugs)	32.9	52.5	52.1	55.0	
Propofol (+benzodiazepines/opioids/other drugs)	36.2	30.1	11.7	0	
Only opioids	19.0	12.8	19.4	13.2	
Other combinations	4.1	0.4	2.8	9.8	
Duration of sedation					0.524
0-24 hours	33.3	38.4	36.5	35.9	
1-7 days	51.6	55.5	54.4	61.4	
1-2 weeks	9.6	3.4	6.1	2.8	
More than 2 weeks	5.6	2.7	2.9	0	
Artificial nutrition and hydration					**<0.001**
Administered until death	48.6	49.6	25.7	17.1	
Withdrawn during sedation	8.8	21.0	12.4	5.0	
withheld	42.6	29.4	61.9	77.9	
Request or consent					**0.009**
Request by patient	8.2	17.5	17.2	23.7	
No request, but consent of patient	21.1	15.2	21.1	21.7	
No request or consent of patient, but request by family	11.5	12.4	16.9	16.1	
No request or consent of patient, but consent of family	34.8	34.7	38.8	31.1	
No request or consent of patient or family	24.5	20.1	6.1	7.3	
Intention of hastening death					0.107
No intention	36.5	33.3	24.0	13.3	
Taking into account possible hastening of death	43.0	51.0	59.9	65.9	
Co-intention	17.2	13.2	13.7	18.4	
Explicit intention	3.3	2.4	2.4	2.4	

[a] Figures are weighted column percentages. Percentages may not always amount to 100% because of rounding. Figures in bold denote statistically significant differences according to the degree of physicians' palliative care expertise.

[b] Missing cases: drugs administered (5), duration of sedation (5), artificial nutrition and hydration (2), request or consent (10) and intention of hastening death (25).

[c] All significant bivariate results were also found significant after controlling for the most important confounders: sex, age, cause of death and place of death. The direction of bivariate associations did not change in multivariate analysis.

[d] P-values were calculated with Fisher's exact test (in StatXact version 6).

Discussion

Our robust population-based study found that after the initial rise of continuous deep sedation until death between 2001 and 2007 from 8.2% to 14.5%, its use decreased to 12.0% in 2013. The decrease particularly occurred in women, widowed people, those dying in nursing homes and the more highly educated. In 2013, compared with 2007 opioids were less often used as sole drug and the decision to use continuous deep sedation was more often preceded by an explicit patient request. Compared to non-experts, palliative care experts more often used benzodiazepines and less often opioids, withheld artificial nutrition or hydration more often and more often performed sedation after a request or with the consent of the patient or family.

So far, large-scale population-based surveys estimating the prevalence or development of continuous deep sedation until death have consistently found an increase in its use.[1,4,5,22,26,27] This study is the first to show a decrease in the use of continuous deep sedation, with the prevalence dropping from 14.5% in 2007 to 12.0% in 2013. This decrease could be attributable to Flemish physicians' and other health care workers' increased training and experience in palliative care and in controlling distressing symptoms without the need to use continuous deep sedation as an option of last resort. The decrease of continuous sedation may also be related to the specific Belgian context of end-of-life decision-making where euthanasia - defined as medical administration of life-ending drugs at the patient's explicit request – is legal under a number of conditions.[28] A recent Belgian study found increasing numbers of euthanasia requests and granting rates between 2007 and 2013.[5] This increase mainly took place in the same subgroups in which the present study found the use of continuous deep sedation to have substantially decreased during the same period.[29] There is evidence that in Flemish clinical practice euthanasia and continuous deep sedation are often discussed as alternative options, the choice between them depending on the preferences of patients and others involved.[16,30,31] It thus seems that the option of euthanasia is now chosen more often, due possibly to an increasing acceptance of euthanasia by patients, as well as by physicians and care institutions who in the past may

more often have converted euthanasia requests into continuous deep sedation.[32,33] Other possible explanations for the decrease in continuous deep sedation are that ongoing ethical and clinical insights may have led to the view that the practice of continuous sedation is not 'normal' end-of-life treatment holding back some physicians from using it,[13,16,34] or that increased attention to advance care planning, when patients are still capable of participating in end-of-life decisions, has reduced instances in which continuous sedation is performed as a crisis intervention in the absence of clear preferences or directives.[35,36]

Our study found a number of striking changes in the performance of and decision-making preceding continuous deep sedation: in 2013, more sedations were carried out using a combination of benzodiazepines and opioids, with opioids less frequently used as sole drug than in 2007 and sedation was more often performed after a patient's request, even though patient or family consent was still often lacking. In general, our study observed a number of developments in the practice of continuous deep sedation between 2007 and 2013 which are favourable in light of the recommendations described in the existing guidelines, including the 2010 Flemish guideline. This would corroborate research from the Netherlands showing that the practices of care providers had been positively influenced by the introduction of the Dutch guideline, first published in 2005, though the Dutch practice seems to fit more closely with the recommendations of the Dutch guideline than does the Flemish practice with the Flemish guideline [19,20,37]. There is still no insight into whether and to what extent guidelines, being non-mandatory, are applied in Flanders, Belgium. The fact that the Flemish guideline is issued by the Federation responsible for palliative care, rather than by a medical or health care association, can be expected to limit their spread. Our study suggests that there still is room for further improvement, particularly in the use of recommended drugs, seeking consent and not intending to hasten death. This raises the question whether guidelines alone can ensure sound practice. Too much emphasis on guidelines may encourage routinisation and could obscure the vital importance of case-by-case-based decision-making.[38] Following the proposed safeguards of Quill et al [39] for ethically complex practices such as continuous deep sedation (i.e. obtaining informed

consent, ensuring diagnostic and prognostic clarity, obtaining an independent second opinion and documenting and reviewing the processes to ensure accountability) some are therefore calling for the mandatory consultation of palliative care experts or even mandatory reporting of continuous deep sedation as is the case for regulated euthanasia in Belgium.[34,40,41] However, in this study, palliative care training was associated with end-of-life sedation practices more congruent with recommendations. Therefore, a feasible alternative to mandatory consultation or reporting could be to encourage and enhance physician training in palliative care. Dutch research has found that the choice of recommended drugs for continuous deep sedation until death was associated with the use of guidelines and with the care team including, or consulting with a palliative care expert.[1,21] This suggests that palliative care training may thus improve a physician's skills in performing end-of-life sedation as well as encourage them to adopt a multidisciplinary approach and consult end-of-life experts for this practice.

Although our study uses a robust population-based sampling method, a number of study limitations have to be taken into account. While high response rates were achieved, we cannot exclude some degree of non-response bias. However, analysis of non-response questionnaires revealed lack of time as the most quoted reason for non-participation. Our study only provides information from the physician's perspective, and does not permit in-depth case analysis. Recall bias may also have influenced results, although attempts were made to limit this by ensuring that the physician received the questionnaire no later than eight weeks after their patient's death. Sensitivity of survey topics may introduce untruthful or socially desirable reporting, but this is unlikely in our study given the explicit guarantee of anonymity and the fact that physicians were well acquainted with the survey. To minimize possible differences in the perception of sedation among the respondents we provided them with a descriptive definition of the practice (continuous deep sedation until death). Most other studies use terms such as palliative or terminal sedation, which can have various connotations. Furthermore, it is not known when the palliative care training reported by the respondents took place, nor the extent and content of the training.

Conclusions

The decreased use of continuous deep sedation until death in almost all patient groups may suggest the development of a more critical approach and a more cautious attitude towards the practice among Flemish physicians. The specific context of legal euthanasia in Belgium may also play a role, and more research into the influence of different legal and cultural contexts on performance of continuous deep sedation until death is recommended. Despite positive changes in performance and decision-making towards more compliance with due care requirements, there is still room for improvement. Future studies should focus on whether quality improvement initiatives like mandatory consultation and basic palliative care training would improve the practice.

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CHAPTER 3

Reasons for Continuous Sedation Until Death in Cancer Patients: A Qualitative Interview Study

Lenzo Robijn, Kenneth Chambaere, Kasper Raus, Judith Rietjens, Luc Deliens.

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Abstract

End-of-life sedation, though increasingly prevalent and widespread, remains a highly debated medical practice in the context of palliative medicine. This qualitative study aims to look more specifically at how health care workers justify their use of continuous sedation until death and which factors they report as playing a part in the decision-making process. In-depth interviews were held with 28 physicians and 22 nurses of 27 cancer patients in Belgium who had received continuous sedation until death in hospitals, palliative care units or at home. Our findings indicate that medical decision-making for continuous sedation is not only based on clinical indications but also related to morally complex issues such as the social context and the personal characteristics and preferences of individual patient and their relatives. The complex role of non-clinical factors in palliative sedation decision-making needs to be further studied to assess which medically or ethically relevant arguments are underlying daily clinical practice. Finally, our findings suggest that in some cases continuous sedation was resorted to as an alternative option at the end of life when euthanasia, a legally regulated option in Belgium, was no longer practically possible.

Introduction

Although conventional palliative care often contributes to a good death, some people receiving palliative care nevertheless experience severe intractable and uncontrollable symptoms.[1,2] In these circumstances palliative sedation, i.e. intentionally reducing the patient's consciousness and thus their awareness of suffering, can be an option of last resort [3,4]. Palliative sedation can be performed for short periods of time, intermittently or continuously until death, and the depth of sedation can vary from a lower level of consciousness to complete unconsciousness.[4,5] It is a quite frequently occurring practice[6,7] though its prevalence varies considerably between countries[3,8] and between settings.[9,10] Studies in various European countries have found an incidence between 2.5% and 16.5% of all deaths.[7,9,11,12]

In recent years much debate has focused on the most far-reaching type of palliative sedation, continuous sedation until death, and its ethical acceptability.[13,14] While many view it as part of normal medical practice, it is also sometimes considered to be morally equivalent to euthanasia since lowering a patient's consciousness may result in 'social death', as it not only reduces the experience of suffering, but apparently removes a patient's ability to have any experiences at all.[13,15,16] It is therefore often argued that only grave, proportionate reasons can justify such a far-reaching intervention and continuous sedation should thus only be used as a last resort.[17,18]

In order to deal with both the clinical and ethical challenges associated with continuous sedation and its existing variations in practice, a number of guidelines and recommendations have been formulated in different countries.[19,20] These guidelines recommend the circumstances under which continuous sedation may be considered and focus essentially on clinical indications [2,14,21]. Though the current guidelines differ in some respects, there are many common elements. For example, continuous sedation should, all guidelines agree, generally be applied when the disease is advanced, without prospect of improvement, when suffering becomes refractory and with death expected within hours or days.[22–24]

Some studies have explored the extent to which health care providers apply guideline conditions and have found a number of non-clinical factors influencing decision-making,[25–29] i.e. *"influences that are not within the traditional medical scientific model of disease and its therapy and are not considered to be directly related to the pathogenesis of the disease, the disease itself and the pharmacological therapeutic influences on that disease*".[27] The indications for continuous sedation may be influenced by the patient's and relatives' preferences and their values concerning notions of how sedation can contribute to a dignified and good death. However, it is also known that some patients or relatives pressure physicians or nurses to use continuous sedation and this may complicate decision-making.[30,31] Additionally, existing evidence also suggests that continuous sedation at the end of life is practiced and perceived differently between countries.[32] A qualitative study conducted in the US and the Netherlands showed that the justification for sedation differed markedly between them, where with respondents from each country attributing the life-shortening effect quite differently while reporting on similar situations.[33]

The Belgian context of end-of-life decision-making may be rather different from that of most other countries because of the federal laws in 2002 on guaranteeing a right to palliative care [34], on patient rights [35] and on regulation of euthanasia [36], defined as the administration of drugs to intentionally end a patient's life at his or her explicit request [37]. Although guidelines strictly distinguish the use of continuous sedation from euthanasia, this may not always be the case in Belgian clinical practice.[38] Therefore, we conducted a qualitative interview study of 27 cases regarding continuous sedation from the perspectives of physicians and nurses in several care settings in Belgium. The present study was undertaken to look more specifically at how health care workers justify their use of continuous sedation and which factors play a part in the decision to start continuous sedation until death.

Methods

This qualitative interview study is part of the larger UK-Netherlands-Belgium InternAtional SEDation (UNBIASED) study in which in-depth interviews were held with physicians, nurses and decedents' relatives. For a full description of the methods used we refer to the published UNBIASED study protocol.[39]

Study design, setting and participants

This paper concerns in-depth interviews with 28 physicians and 22 nurses of 27 adults who suffered from cancer and who had been continuously sedated until death. A qualitative case study design has been described in the literature as highly suitable for exploring and investigating practically and ethically complex phenomena such as continuous sedation in their real-life context involving multiple perspectives.[40]During a designated 12 weeks period in 2011-2012, potential cases of deceased patients were identified by senior clinical staff members: the patient (i) aged over 18 years; (ii) died of cancer in a palliative care unit, hospital or at home; and (iii) had been continuously sedated until death and for whom the sedation was in place at the time of death. Nurses and physicians were invited to take part if they had been closely involved in the care of these patients as soon as possible, i.e. within six weeks to maximize recall. Semi-structured interviews were held until a point of data saturation was reached. We included eleven cases from a home setting, ten cases of patients who died in a hospital and six cases where the patient died in palliative care unit. In 19 of the 27 cases we were able to interview both the physician and the nurse. Participants were not interviewed about more than three patients and if more than one physician or nurse was involved all were interviewed where possible. Ethics approval for the study was given by the Ghent University Hospital Ethics Committee, reference number: B670201010174.

Procedures

All respondents 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. Patient anonymity was preserved. Participants could use the patient records if necessary to aid recall and were interviewed as soon as possible after the death to reduce recall bias. The interviews were semi-structured and supported with the use of aide-mémoires which focused on physicians' recollections of the decedent's care and the use of sedation in particular, as well as their general ideas and attitudes regarding the use of sedation.

Data analysis

An inductive approach was used to analyze the data, making use of a 'constant comparison' method and its related open and axial coding techniques in which the emerging concepts are firmly grounded in the collected data. The interviews were transcribed verbatim and all data that could identify the physicians or nurses were removed to preserve anonymity. Transcripts were analyzed with the qualitative data analysis package NVIVO 10. Two researchers (LR and KC) independently analyzed a first transcript. Afterwards, the codes were compared and discussed until a consensus was reached. After this, the next transcript was analyzed and discussed in the same way. Using the resulting coding scheme, the first transcript was then reviewed again to check the validity of the codes. In this iterative way, all transcripts were analyzed and discussed until a final set of themes was obtained. The final coding framework comprising two main themes (clinical and 'social and practical' factors) was submitted and approved by all the authors. Finally, quotes have been provided on the basis of their being representative of the wider data and are labelled using the case number, setting and profession of the interviewee.

Results

Characteristics of the deceased patients, physicians and nurses can be found in Table 1. We studied 27 patient cases involving 28 physicians and 22 nurses. Of the 27 sedated patients, seventeen were female and about half were older than 70 years. The factors that, according to the participants, affected the decision to start continuous sedation until death in each discrete case can be primarily divided into clinical indications and other non-clinical factors.

Table 1. Characteristics of patients, physicians and nurses

	Patient n= 27	Interviewed Physicians* n=28	Interviewed Nurses* n=22	Cases with both perspectives* n=19
Setting				
At home	11	11	11	9
Hospital	10	11	7	7
Palliative care unit	6	6	4	3
Age	(30-92; 68,185)	(32-65; 45,92857)	(26-59;35,1428)	
<40	2	9	9	n/a
41-50	1	9	7	
51-60	4	9	5	
61-70	6	1	0	
71-80	8	0	0	
>80	6	0	0	
Missing	0	0	1	
Sex				
Male	10	13	3	n/a
Female	17	15	19	
Primary cancer				
Brain/glioblastoma	3	n/a	n/a	n/a
Breast	3			

Colon	3			
Sarcoma	1			
Skin	1			
Hypernephroma	1			
Pancreas	2			
Stomach	1			
Ovary	1			
Prostate	1			
Retroperitoneal metastases	1			
Lung	4			
Leukemia	2			
Multiple myeloma	1			
Uterus	1			
Not stated	1			

*More than one could have been interviewed.

Clinical factors

Intolerable suffering

In all cases, the decision to start continuous sedation was guided mainly by the clinical condition of the patient. Physicians and nurses refer to the presence of a broad range of clinical indications. Although the most commonly reported symptoms were mainly physical in nature, some respondents suggested that a patient's non-physical suffering can also be a contributing factor for the use of continuous sedation until death. In a number of cases the physical symptoms 'actually were well controlled', but despite that, patients signaled that they 'were done with their life' and that they 'didn't want to go on anymore'. When they were talking about their experienced suffering, physicians and nurses noted that patients also used terms as 'despondency', 'undignified' and 'humiliating'. Nevertheless, psychological and existential

suffering always coincided with the patient's poor physical condition and it was the interaction between the two that made the suffering unbearable.

> *'He was gasping like a fish out of water with maximum oxygen, soaked with sweat, from the stress… Terrified, unable to be at ease, up, down, with a great effort still able to chat. So pitiful that I actually decided: now I need to sedate him because it was really no longer bearable'. (Physician, Hospital, patient 12)*

In particular, physicians and nurses reported that psychological and existential suffering alone were insufficient as an indication of continuous sedation and that 'the physical deterioration must most certainly be there as well'. Most respondents said that they would wait until a combination of symptoms arose. As suggested in the above excerpt, physicians and nurses found it often difficult to determine when symptoms can be considered as intolerable, because it is ultimately the patient who determines whether his or her suffering is experienced as intolerable. Two respondents stressed the importance of knowing the patient for quite some time to better assess the situation.

'The doctor who was on the ward, also knew him from the past because he used to be in the hospital. He wasn't a stranger to him so he knew that it was a legitimate question that it did not stem from depression or was asked in that way. Someone you do not know, is always more difficult than someone you know.' (Nurse, Hospital, patient 18).

Refractoriness

Continuous sedation at the end of life was usually thought of as a last resort measure, when there were simply no alternative treatments left or when the symptoms could no longer be kept under control. Physicians and nurses indicated that they were 'with their back against the wall' and they 'couldn't do anything more'. In most cases, it was a lengthy process in which the patient had been terminally ill for quite some time, where health care workers had accompanied the patient for quite some time and where the symptoms intensified greatly. However, the decision to start continuous sedation until death was not always based on the actual suffering but often

on the need to prevent expected severe suffering or a prolonged dying phase, based on input from a multidisciplinary care team.

> *'We saw that the death process was inevitable and that the complaints would increase and so we relied on our experience while taking the decision that the process of sedation should be started'. (Physician, Home, patient 8).*

Imminent death

In general, continuous sedation was considered appropriate only when the patient was close to death. Although an exact survival prediction was never explicitly stated, physicians and nurses used terms like 'advanced stage', 'few prospects', 'death process', 'imminent death' or 'being at the end of life'. Estimating an exact prognosis was often considered difficult as it is dependent on several characteristics of the dying phase. For some patients who died while receiving continuous sedation, physicians thought they had started sedation too late.

> *'Yes, look; I could have given it earlier and the patient would have suffered much less. And often, I still notice that, indeed because you can't estimate the rate of deterioration very well, that you are euhm, there too late. That actually you're a bit like: ah, I didn't really see this'. (Physician, Home, patient 7).*

Others simply emphasized that they focus mainly on adequate symptom relief regardless of the patient's life expectancy and that sedation is started when symptoms become uncontrollable.

Social and practical factors

Personal characteristics of patients

Physicians and nurses were sensitive to a patient's personality and 'how they had lived their lives'. They reported being often confronted with patients who 'really cannot handle the dependency'. According to some respondents, many people find it sometimes more difficult to be cared for than to care for someone else and they think that people like this are perhaps more open to discussing the different possibilities at the end of life.

'Those who are quite independent, those who have gone through life making their own decisions about everything, they would consider and want to discuss euthanasia and palliative sedation and all other possibilities much sooner and be open to it'. (Nurse, Hospital, patient 3).

Involvement of the relatives

Almost all physicians and nurses mentioned that they had discussed end-of-life issues with the relatives and for many physicians it appears to be essential that the family agrees with the decision about palliative sedation, in particular when consent could not be obtained directly from the patient.

'The professor immediately said: I would opt for palliative sedation, but first discuss it with the family. If they do not agree, then we will not begin the procedure'. (Physician, Hospital, patient 14).

In a number of cases, it was actually the family who had mooted the practice of continuous sedation.

'The request mainly came from the family who could no longer stand to see him suffer so much and then the doctor talked to the patient about it'. (Nurse, Hospital, patient 12).

However, many respondents expressed concerns about the involvement of the family. Taking the varying perspectives and emotions of relatives into consideration often complicates the decision to use continuous sedation even more. According to respondents, the family is often not sufficiently informed about continuous sedation, which can then lead to 'wrong expectations'. Some respondents related that some relatives thought that the use of sedation would hasten death, just as euthanasia does. In other cases, the family cannot accept the inevitable and just want 'to give further treatment a go'. A few physicians reported sometimes feeling subjected to pressure. This is illustrated in one case where the physician indicated that palliative sedation was not yet medically justified and that he would normally not have started palliative sedation. Some respondents suggested that feeling subjected to pressure was especially true for general

practitioners because they normally 'have a good relationship with the family and they really don't want to disappoint them'.

> *'You have situations where the family asks you sooner than you would actually choose to start it, that you think like: yes, actually it's not that necessary yet, but yeah if they ask thirteen thousand times you just say: okay, yes, we can consider that, we try and postpone it a little bit, but despite that you might still start about half a day before you would have'. (Physician, Home, patient 7).*

When euthanasia was not possible

Although the issue of euthanasia was not explicitly addressed in the interviews, it often came up. In 20 of 27 patients, interviewees positioned continuous sedation until death as an alternative choice to euthanasia. Three situations could be identified. Firstly, one of the considerations mentioned was that there was a lack of time to complete the euthanasia process, given that the patient had lost capacity during the formal euthanasia process, that the situation was acute or that the formal euthanasia request had been postponed until it was too late. Secondly, in some other cases there were several options discussed including euthanasia and continuous sedation but continuous sedation was preferred, either by the physician or by the patient and his/her family, for personal, family or religious reasons. Some physicians indicated that they 'do not practice euthanasia' and that they 'could not assist' the patient in that. Finally, our respondents pointed out that they proceeded to sedation due to a number of practical considerations such as the fact that the necessary drugs for performing euthanasia were not available or that in this way they could leave the administration of sedatives to someone else. Above mentioned non-clinical considerations were never quoted or reported as stand-alone justifications, but always in combination with justifications of intolerable suffering, refractoriness and/or imminent death.

> *'And then he suddenly said like, look, I don't want this anymore, I have too many troubles; I feel that eating isn't possible anymore, I request euthanasia. Now, that nursing home where he resides, it's uh, a Catholic board of directors and they, in their admission procedure they mention that that does not fit into their vision. I*

proposed sedation to him, and both the family and the patient agreed with that'. (Physician, Home, patient 21).

'The moment that the situation physically deteriorated, so that she felt like, this is too much for me to bear, they came back to it, but it was right before Easter weekend, and for practical reasons euthanasia is not performed in the weekend. And she did not want to wait until after the weekend for physical and psychological reasons and then, after a conversation with the family too, we decided with the doctor to move to sedation'. (Nurse, Palliative care unit, patient 23).

Discussion

This exploratory study included retrospectively 27 cancer patients who were continuously sedated until death in a mix of settings, and we explored the insights and experiences of 50 medical professionals involved. Our findings indicate that both clinical and non-clinical factors are involved in the decision to use continuous sedation.

Clinical factors

Physicians and nurses in our study justified the use of continuous sedation until death by referring to the presence of a broad range of clinical indications, mentioned also in various international guidelines. However, we identified a number of issues they experienced in applying the conditions in practice. First, although guidelines on palliative sedation generally stress the importance of the presence of intolerable suffering that becomes refractory,[22–24] respondents found it rather difficult to assess the 'intolerability' of the patient's suffering, which is ultimately down to the patient and which nearly always seems to have a psychological or existential component interwoven with the physical suffering. A Dutch study[29] similarly showed that continuous sedation is used to address situations in which physical and non-physical symptoms cumulate into a 'refractory state' in which a patient suffers unbearably. The Dutch national palliative sedation guideline explicitly refers to this situation, stating that *'it is frequently a nonlinear combination of symptoms that leads to a situation that constitutes*

unbearable, intolerable suffering for the patient'.[23] Furthermore, this study suggests that the decision to start continuous sedation until death is not always based solely on the actual suffering but often also on the need to prevent future suffering.

Secondly, continuous sedation until death was considered appropriate only if a patient had a short life expectancy, yet estimating an exact prognosis was often considered difficult as it depends on several characteristics of the dying phase. Several studies have suggested that predicting survival at the end of life tends to be inaccurate and a challenging task for physicians [29,41]. The results also suggest that the guidelines and recommendations on palliative sedation may lead to uncertainty among physicians and nurses about whether and when to start continuous sedation until death. If approached too strictly, applying the conditions could lead to sedation being started too late and patients suffering needlessly at the end of life. However, if they are not strict enough in applying these conditions, health care workers risk hastening death which, even if unforeseen, is not only ethically problematic but also exactly what guidelines aim to avoid. However, it has been argued that according to the doctrine of double effect, palliative sedation with life-shortening side effects is morally justified, as long as proportionately grave reasons are present[42,43] or physicians are certain that symptoms will only increase in severity.[29]

Non-clinical factors

Although physicians should always try to act in a rational and clinically justified manner, the results suggest that the social context and the personal characteristics of individual patients also determine the outcome of a decision-making process [27]. Some guidelines and existing research on palliative sedation acknowledge that the decision-making about continuous sedation can also be influenced by the views of the patient concerning a good death, the family's sentiments or the physician's ethical and personal views.[25,26,29,44] This study corroborates previous research [25] that the patient's personality, views, values and beliefs play an important role in decision-making about continuous sedation until death, as does the family's involvement, either in assessing the intolerability and refractoriness of their symptoms – taking into account suffering resulting from

e.g. dependency – or in seeking consent or agreement. While inclusive and shared decision-making with patient and family is worthwhile and in accordance with present standards of respecting patient rights and autonomy, family involvement was, in certain instances, also found to put pressure on physicians to start sedation earlier than they would or with different expectations. This poses an added difficulty for physicians who as final decision makers are responsible for ensuring good end-of-life practice. Clear and thorough discussion involving all members of the care team as well as patient and family will increase the chances of finding the right balance in a clinical approach. More research into the content and dynamics of decision-making with patients and their families is needed.

A final notable result emerging from our study relates to the finding that continuous sedation until death was in some cases resorted to when euthanasia was not an option, either due to the patient losing capacity after euthanasia had been requested or because of practical convenience. As respondents noted, sedation is not performed with the same life shortening intention as euthanasia, but this finding illustrates the precarious ethical position of sedation until death and underlines the importance of adherence to clinical criteria set out in guidelines.[33,45,46] It would be interesting to know to what degree continuous sedation until death is 'resorted to' in countries where euthanasia is not a legal option.

Strengths and limitations

This study provides valuable insights into the clinical practices and underlying rationales associated with continuous sedation in dying cancer patients. Sedation in end-of-life care is a complex phenomenon and qualitative research is the most suitable method for investigating its nuances. The validity of this study was increased by purposively sampling physicians and nurses from different care settings who had been closely involved in the end of life care of decedents identified using standardized criteria. Although our results cannot be generalized, our findings may provide new insights that may be extrapolated to similar clinical situations. The qualitative nature of the study also implies that our findings need replication in other samples

within as well as outside the studied region. The study was limited in that it focused only on the experiences of physicians and nurses and not of the patients or their families. In addition, since the respondents were recalling past experiences, the data are potentially subject to recall bias. Finally, although most clinical decisions are based on 'traditional' clinical criteria, they are also influenced by a range of non-clinical factors. However, some influences fall into a grey area between clinical and non-clinical, making it impossible to categorize all influences on clinical decisions into one or the other as overlap exists.

Conclusion and recommendation

Our study shows that the decision to use continuous sedation until death is not limited to clinical indications alone but is also influenced by a broad range of non-clinical factors such as the social context and the personal characteristics and views of individual patients and their relatives. The complex role of non-clinical factors in palliative sedation decision-making needs to be further studied to assess which medically or ethically relevant arguments are underlying daily clinical practice. In this sense, observational studies of medical practices can be very important in understanding the reality of medicine and health care, which will always be a mix of evidence-based and otherwise-based practice.

References chapter 3

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CHAPTER 4

The involvement of cancer patients in the four stages of decision-making preceding continuous sedation until death. A Qualitative study.

Lenzo Robijn, Jane Seymour, Luc Deliens, Ida Korfage, Jayne Brown, Peter Pype, Agnes Van Der Heide, Kenneth Chambaere, Judith Rietjens, UNBIASED consortium.

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Abstract

Background: Involving patients in decision-making is considered to be particularly appropriate towards the end of life. Professional guidelines emphasize that the decision to initiate continuous sedation should be made in accordance with the wishes of the dying person and be preceded by their consent.

Aim: To describe the decision-making process preceding continuous sedation until death with particular attention to the involvement of the person who is dying.

Design: Qualitative case studies using interviews.

Setting/participants: Interviews with 26 physicians, 30 nurses and 24 relatives caring for 24 patients with cancer who received continuous sedation until death in Belgium, UK, and the Netherlands.

Results: We distinguished four stages of decision-making: initiation, information exchange, deliberation and the decision to start continuous sedation until death. There was wide variation in the role the patient had in the decision-making process. At one end of the spectrum (mostly in UK), the physician discussed the possible use of sedation with the patient, but took the decision themselves. At the other end (mostly in BE and NL), the patient initiated the conversation and the physician's role was largely limited to evaluating if and when the medical criteria were met.

Conclusions: Decision-making about continuous sedation until death goes through four stages and the involvement of the patient in the decision-making varies. Acknowledging the potential sensitivity of raising the issue of end-of-life sedation, we recommend building into clinical practice regular opportunities to discuss the goals and preferences of the person who is dying for their future medical treatment and care.

Introduction

Patient participation in decision-making is considered to be particularly appropriate towards the end of life because end-of-life decisions are often preference-sensitive,[1–4] Studies have suggested that although a majority of people with limited life expectancy prefer a shared or active role in decision-making, their physicians and those close them are frequently unaware of their preferences.[5–7] One of the most debated end-of-life practices is palliative sedation, particularly when it is used continuously until death.[8–11] It entails the use of medication intended to induce a state of decreased consciousness until death to relieve the burden of symptoms that cannot be controlled adequately by conventional palliative treatment.[12,13] Guidelines emphasize that the decision to initiate sedation should be made in accordance with the wishes of the patient and be preceded by their consent or the consent of a surrogate decision-maker if they lack decision-making capacity.[12,14,15] Empirical studies have shown, however, that patient consent is not always obtained or sought.[16,17]

Previous research has shown that continuous sedation until death is practiced differently in different countries. The international UNBIASED study[18,19] showed that in the UK the use of sedation is typically described as a gradual process involving increasing the dose in the context of symptom management, rather than as a deliberate planned event. In contrast, Belgian clinicians predominantly described it as an act of deep sedation from the start, emphasizing the importance of it being in response to a patient's request. Dutch clinicians emphasized that its use was a medical decision informed by the patient's wishes after establishing the presence of a refractory symptom. This suggests that both the practice of and the decision-making leading up to continuous sedation, and the extent to which the choices and preferences of patients are taken into account, may differ between countries. This study describes the decision-making process surrounding continuous sedation at the end of life in Belgium, the Netherlands and the United Kingdom, with particular attention to the role of patients.

Methods

This study is part of the UNBIASED project undertaken in the United Kingdom (UK), the Netherlands (NL) and Belgium (BE) and involved in-depth interviews with physicians, nurses and decedents' relatives.[18,20–23] The study was approved by research ethics committees as follows:

- United Kingdom: Leicestershire, Northampton and Rutland Research Ethics Committee 1, 10/H0406/57
- Belgium: Ghent University Hospital Ethics Committee, B670201010174
- The Netherlands: Erasmus MC Medical Ethical Research Committee, NL33327.078.10, v03.

Settings

To enable maximum variation in the cases studied, we explored the care of cancer patients who died in hospitals (oncology wards), palliative care units (PCU) (in Belgium) or hospices (in the UK and the Netherlands), and in the community (at home).

Participants and inclusion criteria for decedents

In all countries, senior clinical staff members identified eligible decedents: patients aged over 18 who had died of cancer and to whom sedating medications were administered continuously with the intention of decreasing awareness to alleviate otherwise uncontrollable symptoms (either physical or psychological/existential), and for whom the sedation was in place at the time of death. Nurses and physicians were invited to take part if they had been closely involved in the care of these patients and were interviewed about no more than three cases. If more than one physician or nurse was involved, all were interviewed where possible. Relatives were invited to participate via a letter and information sheet sent on behalf of the research team by the patient's physician. Interviews took place as soon as possible after death, i.e. within 12 weeks, to

maximize recall. This paper involves all complete cases (with at least one physician, one nurse and one relative interviewed) in order to obtain a comprehensive insight into the decision-making process.

Procedures

Interviews were semi-structured using an *aide mémoire*. Interviews focused on recollections of the care of the decedent, reasons for the use of sedation, its implementation and decision-making. Each participant gave written informed consent before taken part. The interviews were undertaken by trained interviewers and lasted approximately 60 minutes. Physicians and nurses could use the patient records if necessary to support them in their recollections but were asked to provide relevant information about the case in an anonymous manner. Interviews were audio recorded, transcribed and translated as required. Data collection was completed by the end of 2012.

Table 1. Charles et al [24] model of treatment decision-making.

	Paternalistic	Shared decision-making	Informed
Information exchange	One-way: from doctor to patient, minimum necessary for informed consent.	Two-way: doctor provides all medical information needed for decision-making, patient provides information about his/her preferences.	One-way (largely): from doctor to patient, all medical information needed for decision-making.
Deliberation	Physician alone, or with other physicians.	Physician and patient (plus potential others).	Patient (plus potential others).
Decision	Physician.	Physician and patient.	Patient.

Analysis

Qualitative analysis software (NVIVO 11) was used to organize the data. The coding procedure of the interviews strictly followed the methods of qualitative content analysis. A combined model

of inductive and deductive coding was used, where deductive coding was based on the Charles et al [24] key model of treatment decision-making (TABLE 1). Qualitative analysis software (NVIVO 11) was used to organize the data. Three researchers (LR, KC and JR) independently analysed a first set of transcripts for concepts that were directly linked to the patient's preferences for sedation and their role in decision-making. The codes were compared and discrepancies were discussed until agreement was reached. A coding tree was developed by LR, KC, LD and JR, and agreed upon with all co-authors. All interviews were coded and quotes were selected on the basis of their being representative of the wider data and approved by all researchers. We followed the COREQ guidelines in reporting this study to ensure rigour in our research [25].

Results

Table 2. Characteristics of patients.

Characteristics	United Kingdom	Belgium	The Netherlands	Total
Number of cases	7	7	10	24
Age (years)				
<50	-	1	-	1
51-60	2	2	2	6
61-70	3	-	2	5
71-80	2	3	5	10
80+	-	1	1	2
Gender				
Male	5	4	6	15
Female	2	3	4	9
Diagnosis				
adenocarcinoma	-	-	1	1
abdominal / stomach	-	-	1	1
bladder	1	-	-	1
Colon	-	1	-	1
facial maxillary	1	-	-	1
gall bladder	1	-	-	1
oesophageal	-	-	1	1
leukaemia/ myelofibrosis/ myeloma	-	2	-	2
lung /	-	1	3	4

mesothelioma				
melanoma	-	1	1	2
pancreatic	1	-	1	2
peritoneal	1	1	-	2
prostate	1	-	1	2
renal /hypernephroma	1	1	-	2
Unknown	-	-	1	1
Care setting				
Home	3	3	4	10
Hospital	-	2	3	5
Palliative Care Unit (BE)/hospice (UK/NL)	4	2	3	9

We studied all 24 complete patient cases (7 UK; 7 BE; 10 NL), involving interviews with 26 physicians (9 UK; 7 BE; 10 NL), 30 nurses (10 UK; 10 BE; 10 NL), and 24 relatives (7 UK; 7 BE; 10 NL). Table 2 provides an overview of the characteristics of the patients. Table 3 gives characteristics of the interviewees, showing that the majority of the clinicians (36 out of 56) were palliative care or hospice practitioners. Besides the three stages of decision-making as described in the model of Charles [24] (TABLE 1), the initiation phase was added as it was important to understand who initiated or raised the possibility of sedation. We were therefore able to distinguish four stages of decision-making: (1) the initiation phase to understand who initiated or raised the possibility of sedation; (2) the exchange of all necessary information; (3) the deliberation phase in which it was decided to use continuous sedation when necessary and (4) the decision to actually begin it. Table 4 gives an overview of the characteristics of the decision-making process in all three countries.

Initiating the conversation

The initiation phase appeared to be an interplay between the medical team and the patient and could best be understood as a continuum with, at the extremities, the initiative driven predominantly either by the patient or by the physician. When patients initiated it, they did so

by indicating that their suffering had become unbearable and they no longer wanted to, or could, continue their treatment or even their life. Patients expressed this by using such phrases as 'I am ready to die', 'I have had enough', 'I can no longer bear it' or 'I am done'. Others expressed more explicit requests to 'go to sleep' or to 'no longer wake up'. When a patient was no longer able to communicate, in all countries it was often the family who expressed what they believed to be the patient's preferences.

In Belgium and the Netherlands, some patients requested euthanasia. This was often the starting point of a conversation about end-of-life preferences and the possible use of sedation.

> *"We never spoke about the final stage of life and I found it difficult to start talking about it. And then two weeks before the end, he was so tired, he said, I don't want this, I cannot go on, I want euthanasia. Well a week passed and then Dr X came here, and then he discussed palliative sedation, you go to sleep and you aren't aware of anything. Well only his thumb went up..." (the Netherlands, Case 12, Home, Relative).*

In other situations, physicians initiated the conversation about the possible use of sedation, for instance when an acute exacerbation of symptoms that could not be managed in any other way was expected. During the course of the disease, physicians repeatedly discussed with the patient whether they were 'still okay' or if they could 'still bear the pain'. Nurses also had an important role in initiating discussion about the possible use of sedation.

> *"So then the option, palliative sedation actually became real, for me because it was obvious this is a major medical problem which can't be solved in another way anymore and […] the life expectancy suddenly becomes very short. He was in pain and he constantly sick, so he met the criteria of palliative sedation. And that possibility was therefore discussed at that moment. […] They always were very difficult conversations because he did not really want to address those really big issues" (the Netherlands, Case 36, Community, Physician).*

Table 3. Characteristics of physicians, nurses and relatives.

Characteristics	**Physicians (n= 26)**			**Nurses (n=30)**			**Relatives (n=24)**		
Country	UK (n= 9)	BE (n= 7)	NL (n= 10)	UK (n= 10)	BE (n= 10)	NL(n= 10)	UK (n= 7)	BE (n= 7)	NL (n= 10)
Age (years)							N/A	N/A	N/A
<40	5	2	3	1	4	6			
40-50	-	3	1	3	2	2			
51-60	-	2	5	1	4	2			
60+	-	-	1	1	-	-			
Not stated	4	-	-	4	-	-			
Gender									
Male	6	4	9	-	1	1	1	4	2
Female	3	3	1	10	9	9	6	3	8
Specialism									
Primary care	4	2	4	1	2	1	N/A	N/A	N/A
Palliative home care team	-	1	-	2	3	3			
Hospital oncology ward	-	-	2	-	2	2			
Palliative care unit/hospice care	5	4	4	7	3	4			
Nature of relationship with patient	N/A	N/A	N/A	N/A	N/A	N/A			
Partner							4	4	6
Child							3	2	2
Sibling							-	1	1
Parent							-	-	1

1 UK: United Kingdom; BE: Belgium; NL: The Netherlands 2 N/A: Not applicable 3 More than one could have been interviewed 4 Results from the relatives were identified by the relative that was identified by the physician as being the most involved.

Information exchange

Once the conversation was initiated, it was usually the physician who summarized the situation and provided information to the patient and family. We distinguished two types of decision-making. In the first, mainly in the Netherlands and Belgium, the physician had a predominantly informative role, informing the patient about their disease progression and the possibility of using sedation and the circumstances under which it could be used. They then either hoped to come to a shared decision by further exploring the preferences of the patient or they left it to the patient to make an informed decision themselves. Where desired, these physicians gave advice but during the interviews they mainly stressed the importance of responding to patient's specific requests and wishes or the fact that the final choice should lie with the patient, provided that the clinical conditions were fulfilled.

> *"He pretended for a long time that everything was alright. But certainly the sedation was discussed towards the end, because what I can remember is that we did make the offer to him, like, to go to sleep, at a time when it would be really untenable" (the Netherlands, Case 21, Hospice, Physician).*

In the second type of situation, mainly in the UK, the physician took the lead by proposing the possible use of palliative sedation to control symptoms and to relieve terminal suffering. In these cases they aimed mainly to provide all the necessary information and then eventually to obtain the informed consent of the patient and/or the family.

> *"Things were progressing…and at that time, he had got his pump in and they suggested, 'Well, we'll give him this drug that will help to calm him down, that he's not afraid… that he can rest easy and he doesn't get bad dreams and that sort of things'" (UK, Case 1, Community, Relative).*

Deliberation and the decision to use continuous sedation until death

In all three countries, the possible use of sedation was usually discussed between the person who was dying, those close to them and the professional caregivers, which ultimately led to the consent and/or decision to use sedation. In some cases there were difficulties in coming to a decision. This happened particularly in situations where patients or their relatives 'still had to

get used to the idea' or 'were not yet ready to say goodbye' or 'there was basically no time at all to cope with any of it'. For example, although one patient (UK, case 2, Hospice) was according to the physician clearly in the dying phase, his wife was 'really struggling' and worried about him being 'knocked out'.

> *"The day that he got transferred to (Hospice), so while he was still on the oncology ward, erm, his wife was not coping, she was devastated at the idea that we were gonna knock him out, or put him to sleep, and that she won't be able to speak to him again. […] And I can understand that question coming through. However, it became obvious once we'd assessed him later on that actually he was needing that. And her distress was understandable and was difficult, but I think, by the time I saw him, I think she'd probably changed to, you know, wanting us to do more for him…' (UK, Case 2, Hospice, Physician).*

In Belgium and the Netherlands the discussion sometimes specifically focussed on the 'choice' between palliative sedation and euthanasia.

> *"It was actually a completely chosen path and we knew where we were going. It depended only from how the patient then decided that they would evolve from 'here I go to the euthanasia, or there I will go to palliative sedation.' And I had well informed her about it and she has consciously made that choice" (Belgium, Case 11, Community, Physician).*

In cases of disagreement between patients and their relatives, physicians and nurses attempted to reconcile the two views. If this eventually proved impossible, physicians emphasized the importance of following the patient's wishes since 'they are the ones with pain'.

Decision phase – the moment to start continuous sedation until death

The involvement of patients in this phase was dependent whether the person who was dying was considered to have the capacity to take part in the final stages of the decision-making process or not. When competent, it was either they or the medical staff who took the final decision to begin palliative sedation. Patients in Belgium and the Netherlands indicated their

readiness for the use of sedation in the later phases by using phrases such as 'it should happen today' or 'it is enough for me now'.

> *"And the physician said 'but we cannot decide it, that is up to you to decide when you want it. And my dad said 'ah I may decide that?' 'Yes, of course' said *** 'you must decide for yourself'. And the world opened up for my dad and he said 'if that's how it is then I would like to be put to sleep as soon as possible'" (Belgium, Case 5, Palliative care unit, Relative).*

Patients were often unable to contribute to the decision to commence continuous sedation either because of an acute exacerbation of symptoms, which is what had necessitated the use of sedation, or because they were very close to death and had already lost the capacity to participate in the decision-making. Where the physician initiated the use of sedation, the decision had generally been taken at an earlier phase in anticipation of the moment when suffering would become unbearable. Some health care staff, mostly in the Netherlands, pointed out that the decision to commence continuous sedation is in the end a medical decision that physicians could take only if they 'felt that it was inevitable'.

> *"In some cases […] you see the patient is deteriorating and more and more medication is needed. Then a stage comes where you do talk with each other about gosh what are we going to do next? Patients do generally put that forward themselves, but it remains a medical decision that always lies with the doctor. And it may very well be that the doctor does not agree with the request of the patient, for the simple reason that there are no refractory symptoms or other cases […]" (the Netherlands, Case 12, Community, Nurse).*

In contrast, most health care staff in the UK pointed to a gradual progression without a particular moment of decision-making.

> *"We always start in a cautious way and build up rather than starting with a high dose and completely flattening somebody at the outset, and that can sometimes be difficult. […] The family need to know that the intention is to review regularly and to be able to give an extra dose if necessary" (UK, Case 4, Hospice, Physician).*

In other situations, family members had requested the use of sedation. For example, this was the case for a 30-year old man with a melanoma who died in a Belgian hospital (Case 12). The patient had earlier told his wife that he wanted to die 'in his sleep' and that when he lost capacity and was suffering too much she was to instruct the doctor to start the sedation. That is what eventually happened.

> *"He actually said to me as well like: when you see that I am suffering too much, then you have to tell them that they should administer that. If I have to die, I rather die in my sleep he said because I do not... That he must not feel it."*
> *(Belgium, Case 12, Hospital, Relative).*

Table 4. Characteristics of the decision-making process in the studied countries

Stages	United Kingdom (UK)	The Netherlands	Belgium
1. Initiating the conversation	A **continuum** with the initiative driven either by the patient or the physician.	A **continuum** with the initiative driven either by the patient or the physician. Euthanasia was often the starting point of a conversation about end-of-life preferences and the possible use of sedation.	A **continuum** with the initiative driven either by the patient or the physician. Euthanasia was often the starting point of a conversation about end-of-life preferences and the possible use of sedation.
2. Information exchange	The **physician** usually **took the lead** providing all the necessary information to obtain informed consent of the patient and/or relatives	The **physician had** rather **an informative role**, providing all medical information needed for decision-making, hoping to come to a shared decision by further exploring patient preferences.	The **physician** mainly **had an informative role**, providing all medical information needed for decision-making, hoping to come to a shared decision by further exploring patient preferences.
3. Deliberation and the decision to use continuous sedation until death	Usually discussed between **the patient and those close to them.** In case of disagreement, physician followed the patient's wishes.	Usually discussed between **the patient and those close to them.** In case of disagreement, physician followed the patient's wishes.	Usually discussed between **the patient and those close to them.** In case of disagreement, physician followed the patient's wishes.

4. Decision phase – the moment to start continuous sedation until death	A **gradual progression** without a particular moment of decision-making.	Generally, a **medical decision** that physicians could take only if they felt that it was inevitable.	When **competent**, in most cases either patient or the medical staff who took the final decision to start. When **no longer competent**, either family or the medical staff.

Discussion and conclusion

Main findings

This study distinguishes four stages of decision-making: the initiation phase where the issue is raised, the exchange of all necessary information, the deliberation phase in which it is decided to use continuous sedation when it becomes appropriate, and the decision to begin continuous sedation. Although the overarching goal of continuous sedation at the end of life was similar in all cases, there was considerable variation in the timing and the role played by the patient in the decision making. At one end of the spectrum, decision-making was primarily clinical and physician-driven; the physician discussed the possible use of sedation with the patient but took the final decision him/herself. These cases were especially prevalent in the UK, where respondents reported a gradual process of sedation, from the provision of low doses of sedatives to the more rarely used continuous deep sedation. At the other end of the spectrum, the patient initiated the conversation about the use of sedation while the physician's role was predominantly limited to evaluating whether, and when, the patient's condition fulfilled the medical criteria. These cases were mostly from Belgium and the Netherlands, where patients were sometimes offered the 'choice' of sedation.

Strengths and limitations

The validity of this study was increased by deliberately sampling cases from three different care settings and three different countries using standardised criteria including a descriptive definition of the practice that was studied. In order to get a broad and detailed overview of each case, we included the recollections of physicians, nurses and relatives involved in the care of a particular person. Since preferences can change during the decision-making process, a retrospective assessment takes this possibility into account. Another strength is that we used the model of Charles et al [24] which allowed us to scrutinize the different phases of decision-making and apply them to the process of continuous sedation, which is unprecedented. Limitations to this study should also be acknowledged. Our interview data was dependent on the subjective experiences and interpretations of the respondents. There is a small risk of recall bias, though this was limited in most of the cases by limiting the time between death and the interview to three months.

Discussion

A theoretical framework such as that of Charles et al [24] seems useful in exploring end-of-life decision-making, showing there are several approaches to the initial decision to start continuous sedation. Decision-making in all phases could be described as being paternalistic, shared or informed, but it sometimes changed between the different phases. For example, in some cases the physician began the process with an informative approach but eventually took charge of the final decision to begin continuous sedation. Other studies have not described the decision-making process in such detail. In our study, the possible use of continuous sedation was usually discussed with all parties and ultimately led to the consent and/or decision to use sedation if necessary. The information exchange and deliberation phases in our study closely match the three-step model for shared decision-making for clinical practice developed by Elwyn and colleagues [26], in which they made a distinction between 'choice talk' (making sure that patients know that different reasonable options are available), 'option talk' (providing more detailed

information about the options) and 'decision talk' (considering preferences and deciding what is best). From the results of this study, it is possible to distinguish two types of decision, the decision about whether to use sedation and the decision about when to start sedation. In both types, respondents placed high value on the patient's perspective, respecting their wishes, giving them explicit information about the implications and obtaining their consent.[27] However, this is far from always the case. A recent Belgian population-based death certificate study showed that the decision to use continuous sedation was in 16.2% of all cases made without a request from or the consent of the person who was dying or their family.[17]

Though clinical guidelines aim to support physicians in their decision-making and to promote best practice (e.g. the EAPC guideline for palliative sedation strongly encourages physicians to *'address end-of-life care preferences with all patients at risk of dying'* prior to sedation and to obtain their consent [12,14,15] they rarely state the extent to which patient preferences should be taken into account, and how to deal with a patient's request for sedation. They do stress, however, the need for clinical indications for the use of sedation; in cases where this is the refractoriness of symptoms, a medical assessment by a clinical expert is required.[12] Some guidelines and frameworks, like the Dutch and Belgian ones, add to this that continuous sedation can only be used in the context of unbearable suffering, judged primarily by the patient him or herself, something that was often reflected in the Belgian and Dutch cases in our study. Belgian and Dutch respondents placed emphasis on the importance of responding to the patient's request for relief of suffering, provided that the clinical conditions were fulfilled. In both countries, patients were sometimes provided with the choice between sedation and euthanasia (which is legal, provided due care criteria are met). Thus, although respondents frequently used terms related to key indications for continuous sedation, and the decision to begin it was guided mainly by the clinical condition of the patient, it can be hypothesized that interviewees in all three countries expressed views that may corresponded to medico-cultural and societal perspectives on the practice of sedation. Different concepts of what sedation should be used for and how it should be practiced may have framed the ways in which a patient's preferences were

elicited and the roles they were given in the decision-making process. Thus the focus of decision-making seems to shift from the physician-centred medical criterion (refractoriness) in the UK to a more patient-centred perspective in Belgium and the Netherlands, where more emphasis is on the unbearableness of symptoms experienced by patients.[28] It could be argued that in countries where euthanasia or physician-assisted suicide (PAS) are legal, open discussion of these and other ethically difficult end-of-life issues [28,29] allows patients, their relatives and their physicians to be more open about discussing palliative sedation.[30] Future research should further develop the evidence base for the role of legal and cultural context on end-of-life decision-making and should further focus on the effectiveness of sedation to ease refractory symptoms at the end of life.

Conclusion

Decision-making about continuous sedation goes through four stages and the involvement of the patient varies. Different conceptions of what sedation should be used for and how it should be practiced may have affected the role patients were given in the decision-making process. In order to be sensitive to a patient's individual preferences while at the same time acknowledging the potential sensitivity of raising the issue of continuous sedation until death with people who are dying, we recommend building into clinical practice opportunities to regularly discuss with them their goals and preferences regarding future medical care and treatment.

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PART III

Enhancing the practice of continuous sedation at the end of life in nursing homes

CHAPTER 5

A systematic review of quality improvement initiatives for continuous sedation until death

Lenzo Robijn, Luc Deliens, Anne-Lore Scherrens, Nele Pauwels, Peter Pype, Judith Rietjens*, Kenneth Chambaere*.

Submitted

Abstract

Background. Extensive debate surrounds the practice of continuous sedation until death (CSuD) within end-of-life care. This systematic review provides insight into existing initiatives to support the practice of CSuD and assesses feasibility and effectiveness of these initiatives.

Design. Systematic review, registered on PROSPERO (CRD42016036009)

Data sources. Records were searched through MEDLINE, EMBASE, CENTRAL, CINAHL and Web of Science from inception to April 16 2020. Peer-reviewed studies reporting original data on initiatives to support the practice of CSuD were included for review.

Results. Twenty-one studies met the criteria and were included. Initiatives were focused on assessment tools of consciousness and discomfort (9), the use of guidelines and protocols (8), and expert consultation (3). All initiatives were reported as useful, acceptable and feasible. Studies on the use of monitoring devices showed that a small proportion of patients were found to be awake, despite the patient being unresponsive according to the observer-based sedation scales. However, the wide range of values of these monitoring devices for comfortable and adequately sedated patients seems to hamper its overall implementation in daily clinical practice. Physicians reported changes in CSuD practice conform to guideline recommendations but the shift was modest at best. Expert consultation was regarded as supportive when sufficient expertise is lacking and helpful in avoiding possibly unnecessary sedations.

Conclusions. The reviewed initiatives may contribute to improvement of CSuD practice, though their evidence base is rather limited. More insight is needed into their feasibility, preconditions for effective implementation and impact in actual practice.

Background

Extensive debate within end-of-life care surrounds the practice of continuous sedation until death, which entails the deliberate lowering of consciousness in patients nearing death to alleviate unbearable suffering unresponsive to conventional therapies.[1,2] Continuous sedation until death is a frequently used end-of-life practice across all care settings where patients die, but most often in hospitals and for those with cancer.[3–5] It is usually recommended that continuous sedation should only be performed close to death for unbearable and refractory symptoms without intent to hasten death.[6–8] Benzodiazepines, titrated proportionally to alleviate the symptoms, are the first drug of choice and the administration of artificial nutrition or hydration is not encouraged unless the benefits outweigh the harm.[5,9]

Though increasingly prevalent and widespread internationally,[5,10–12] controversial issues still persist about almost every aspect of the practice.[1,13,14] Beyond the conceptual and ethical dilemmas, controversy also seems to have reached clinical practice, with discussions being raised about the conditions under which continuous sedation should be performed and how it should be performed.[15–19] Continuous sedation is sometimes performed suboptimally and clinicians are not well acquainted with generally recommended indications,[5] leading to uncertainty about whether and when to start.[20] Also, some indications such as intolerable suffering and life expectancy are difficult to assess.[21] Monitoring of the depth and dosages is often not done[22] and often the recommended drugs – benzodiazepines – are not used.[5] Patients and relatives are not always involved in the medical decision-making and are often ill-informed about what to expect in the course of sedation, leading to a perceived poor quality of dying and issues with coping.[23]

Despite the growing call for quality improvement initiatives in end-of-life care aiming to improve the quality of dying for terminally ill patients,[24] initiatives to improve the practice of continuous sedation at the end of life have never been systematically investigated. This study will improve our understanding of initiatives to support, facilitate or improve the practice of continuous sedation until death and will provide insight into the effect of these initiatives on the quality of care and death. The research questions were as follows:

1. What initiatives are there that aim to support, facilitate or improve the communication, decision-making and performance of continuous sedation until death within end-of-life care?
2. What is the feasibility and effectiveness of these initiatives?

Methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standardized guidelines to ensure quality and clarity.[25] The review protocol was registered on PROSPERO (CRD42016036009).

Eligibility criteria

When screening for relevance, studies were included if they met the following criteria:

- **Type of studies:** peer-reviewed studies reporting original data and an abstract in English;
- **Topic**: the study was about continuous sedation until death;
- **Scope of the study**: the study described one or more initiatives that aim to support, facilitate or improve the practice of continuous sedation until death and where the feasibility, acceptability or effectiveness of the initiative was evaluated. A quality improvement initiative was defined as a systematic activity that aims to improve one or more aspects of communication, decision-making or performance of continuous sedation until death.[26]

Studies were thus excluded if they were not primarily focused on the improvement of continuous sedation until death or where the original data only consist of describing how the initiative had been developed without data collection on the initiative itself. Studies for which full text was unavailable or non-existent (e.g. in the case of conference participation) were also excluded.

Search methods

We searched the databases MEDLINE (PubMed), EMBASE (Embase.com), Cochrane Central Register of Controlled Trials (CENRAL), CINAHL and the Web of Science Core Collection to ensure inclusion of medical, social science and bioethics literature from inception till April 16 2020. In addition, the cited

and citing references of the studies eventually selected were screened for eligibility. The search key was initially developed in MEDLINE and later adapted for other databases with support from an Information Specialist (see **Table 1** for search terms).

Table 1. Database search strategy.

Database	Keywords
MEDLINE (PubMed)	(“deep sedation” [Mesh] OR "deep sedation"[TW] OR “palliative sedation”[TW] OR “terminal sedation”[TW] OR “continuous sedation”[TW] OR "sedated"[TW]) AND ("Terminal care"[MESH] OR "terminal care"[TW] OR "palliative care"[MESH] OR "palliative care"[TW] OR "Terminally ill"[MESH] OR "Terminally ill"[TW] OR "End-of-life"[TW] OR "incurable"[TW] OR “palliative”[TW] OR “terminal”[TW] OR “terminally”[TW] OR “life-threatening”[TW]) NOT ("Animals"[MESH] NOT "Humans"[MESH])
EMBASE (embase.com)	('deep sedation'/exp OR ‘deep sedation’:ti,ab,kw OR ‘palliative sedation’:ti,ab,kw OR ‘terminal sedation’:ti,ab,kw OR ‘continuous sedation’:ti,ab,kw OR ‘sedated’:ti,ab,kw) AND (‘terminal care’/exp OR ‘terminal care’:ti,ab,kw OR ‘palliative therapy’/exp OR ‘palliative therapy’:ti,ab,kw OR ‘terminally ill patient’/exp OR ‘terminally ill patient’:ti,ab,kw OR ‘end of life’:ti,ab,kw OR ‘incurable’:ti,ab,kw OR ‘palliative’:ti,ab,kw OR ‘terminal*’:ti,ab,kw OR ‘life-threatening’:ti,ab,kw)
CENTRAL	([mh “deep sedation”] OR (deep sedation):ti,ab,kw OR (palliative sedation):ti,ab,kw OR (terminal sedation):ti,ab,kw OR (continuous sedation):ti,ab,kw OR (sedated):ti,ab,kw) AND ([mh “Terminal Care”] OR (terminal care):ti,ab,kw OR [mh “Palliative Care”] OR (Palliative Care):ti,ab,kw OR [mh “Terminally ill”] OR (terminally ill):ti,ab,kw OR (end of life):ti,ab,kw OR (incurable):ti,ab,kw OR (life-threatening):ti,ab,kw)

CINAHL (EBSCOhost)	("deep sedation" OR (MM "Sedation") OR "palliative sedation" OR "terminal sedation" OR "continuous sedation" OR "sedated") AND ((MM "Terminal Care") OR "Terminal Care" OR (MM "Palliative Care") OR "Palliative Care" OR (MM "Terminally Ill Patients") OR "terminally ill" OR "end of life" OR "incurable" OR "palliative" OR "Terminal" OR "terminally" OR (MM "Critical Illness") OR "life-threatening"))
Web of Science Core Collection	(TS=("deep sedation" OR "palliative sedation" OR "terminal sedation" "continuous sedation" OR "sedated")) AND (TS= ("terminal care" OR "palliative care" OR "terminally ill" OR "end-of-life" OR "incurable" OR "palliative" OR "terminal*" OR "life-threatening"))

Data collection and analysis

Selection of studies. In a first phase, study selection was based on screening of the titles and abstracts and, in a second phase, on full text evaluation. In both phases, selection was performed by two independent reviewers (L.R. and A.S.), using the Covidence tool.[27] Disagreement about the relevance of a study was resolved by discussion, and where necessary a third reviewer (J.R.) was consulted for arbitration. To ensure reliability, we undertook a testing exercise before the screening process with a random 5% sample of search results. Endnote X8 citation management software was used for deduplication of references. Multiple reports of the same study were collated.

Data extraction and management. Characteristics of the included studies were extracted using a self-developed data extraction form. The data extraction tool was piloted by two reviewers and minor adjustments were made. One researcher (L.R.) extracted data on country, type of research, method, research question (aim), setting, participants and scope of the study. These data were checked by the second reviewer (A.S.). Quality improvement initiatives were reported as mentioned in the article. Where information was missing or clarification was needed, authors of primary studies were contacted, using email addresses in the published study. Two reviewers (L.R. and A.S.) independently extracted

data on quality improvement initiatives: discrepancies were discussed and, where consensus could not be reached, a third reviewer (K.C.) was consulted for arbitration.

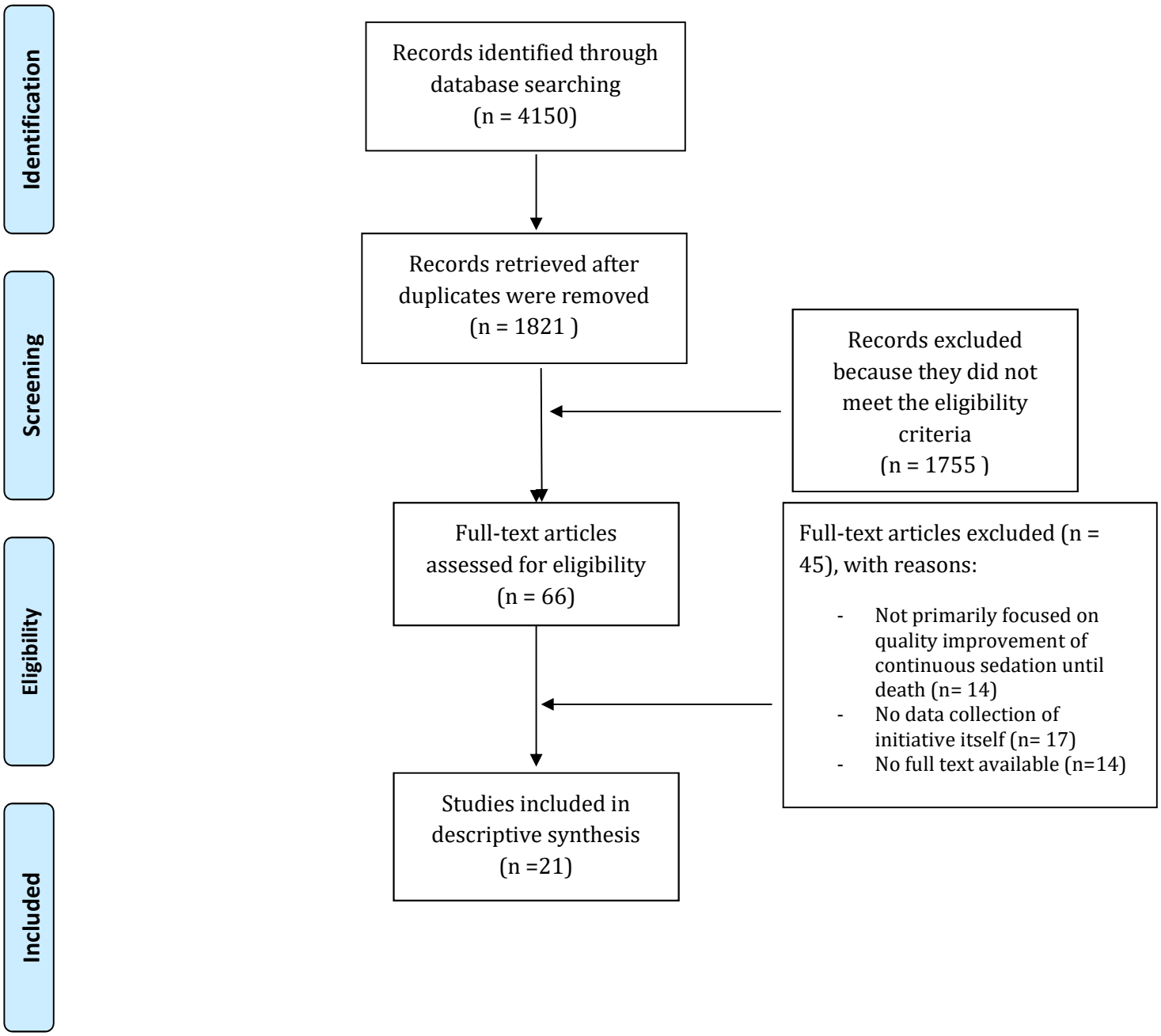
Quality assessment. We performed quality assessments of both quantitative and qualitative studies by using the QualSyst tools, constructed by researchers from the Alberta Heritage Foundation, for assessment of the quality of both qualitative and quantitative studies.[28] For assessing the quality of qualitative studies, ten standard criteria had to be scored. For quantitative studies, there were 14 criteria. The criteria for qualitative studies relate to the research question, study design, context, theoretical framework, sampling strategy, data collection method, data analysis, verification procedure, conclusion and reflexivity of the account. The criteria for quantitative studies relate to the research question, study design, method of subject selection, subject characteristics, outcome measures, sample size, analytical methods, estimate of variance, confounding, results, conclusions and, in cases of intervention studies, to the allocation and blinding. The scores could range from 0.0 to 1.0. We have not defined a minimum quality threshold for study inclusion. These quality scores do not reflect the quality of the initiatives described in these studies, but only indicate the extent to which the design, conduct and analyses minimise errors and biases.

Results

Study selection

Figure 1 presents a PRISMA Flow Diagram that summarises the study selection process and result. The initial literature search yielded 4150 hits from the five databases. After checking for duplicates, 1,821 records were assessed for eligibility based on title and abstract. Full texts of the 66 articles that appeared to potentially meet the inclusion criteria were sought. Full-text evaluation of those 66 records resulted in the exclusion of 45 articles because they did not meet the inclusion criteria. Checking the cited and citing references of the 21 included studies did not lead to any additional studies.

Figure 1. Flow diagram illustrating the inclusion of articles for this review.



Characteristics and quality assessment of relevant studies

An overview of the included studies is presented in **Appendix 1:** 21 studies were included in the review, of which two were qualitative studies (one interview study and a combination of a case study with in-depth interviews), 17 had a quantitative study design (seven prospective observational studies, six retrospective medical report studies and four cross-sectional survey studies) and one was a mixed-methods study where prospective observations, questionnaires and individual interviews were combined. Studies had been published between 2007 and 2020 originating from nine countries (eight from the Netherlands, four from Spain, two from Japan and one each from Belgium, Australia, USA, Canada, Mexico and Portugal) and from different settings (nine from a palliative care unit, six from a mixed setting, four from a hospital setting and one from the ICU). Primary outcomes of the studies were focussed mostly on measuring consciousness and discomfort (nine out of 20 studies). Regarding the quality assessment (quality score range 0.0–1.0), the studies scored between 0.40 and 0.86.

Initiatives to improve palliative sedation practice

Different types of initiatives were found and these initiatives could be grouped into three main categories: nine were focused on assessment tools of consciousness and discomfort, eight on the use of a general guideline or setting-specific protocol and three on clinical decision making consultation. In **Table 2** we summarize the features of the initiatives classified into three categories of those aimed to support, facilitate or improve the practice of continuous sedation until death. Below, we describe the categories in more detail.

Assessment tools of consciousness and discomfort (n=9)

The nine studies that focused on the use of assessment tools and scales to objectify level of consciousness and assessment of discomfort could be divided into two groups.

1. *Use of observer based sedation scales (n=5)*

The first group focused on the use of observer-based sedation scales and testing their reliability and validity in a palliative care setting and covered the 'Minnesota Sedation Assessment Tool' (MSAT)[29],

'Richmond Agitation-Sedation Scale' (RASS)[29–31], 'Vancouver Interaction and Calmness Scale' (VICS)[29], a sedation score proposed in the Guideline for Palliative Sedation of the Royal Dutch Medical Association (KNMG)[29], the 'Consciousness Scale for Palliative Care' (CSPC)[32] and the Ramsay Sedation Scale (RSS)[33]. The usefulness of the scales was assessed in four of the five studies and this shows that the RASS[29–31] and CSPC[32] are considered to be very useful, easy to use, not time consuming and can be used with minimal training.[29] One study measured the internal consistency of the CSPC, which was very high. Moderate to (very) high inter-rater reliability for the VICS, RASS, KNMG scale and CSPC. However, the study of Deol[33] indicated a disagreement amongst healthcare professionals of various disciplines when using the RSS to assess sedation in critically ill patients in intensive care units, with equal RSS ratings by nurses and non-nursing personnel in only 29% of cases. The study of Arevalo found discriminative and evaluative validity for RASS and the KNMG scale (rho=0.836), the study of Benitez-Rosario found a strong correlation of the RASS and the RSS (Spearman's p, -0.89; p< 0.001) and GCS (Spearman's p, 0.85; p< 0.001) and the study of Conçalves found a very high correlation of the CSPC to the VAS (Spearman's p 0.94, P<0.001) and GCS (Spearman's p -0.82, P<0.001).

2. *Use of monitoring devices (n=4)*

The second group focused on the use and validity of monitoring devices. The Bispectral Index monitor (BIS) was applied in three out of four studies[34–36] and another included the NeuroSense monitor and Analgesia Nociception Index monitor[37]. The BIS and Neurosense monitoring were found acceptable and feasible by patients, relatives and medical staff in the palliative care setting. However, the study of Masman[35] suggests that the wide range of BIS values in deeply sedated and comfortable patients seems to hamper its use in daily clinical practice. A strong correlation was found between BIS and the Richmond Agitation-Sedation Scale (RASS) (P< 0.0004)[34] and BIS and Patient Comfort Score (PCS) (P= 0.003), and a moderate correlation was found between BIS and Ramsay Sedation Scale (rho= -0.58 to -0.65)[35,36]. However, a small proportion of patients were found to be 'awake' by using monitoring devices, while in fact the observer-based sedation scales (RASS, PCS and RSS) indicated otherwise.[36,37]

Use of practice guidelines or a setting specific protocol (n=8)

3. Use of general guidelines (n=3)

The study of Hasselaar (2007)[38] focused on the first set of guidelines from the Comprehensive Cancer Center Middle Netherlands in 2002, followed by a more detailed set of guidelines from the Comprehensive Cancer Center East Netherlands in 2003. Two other studies[15,39] report on the use of the Dutch national guideline for palliative sedation established by the Royal Dutch Medical Association (RDMA) which is mandatory for all physicians within the Netherlands. The study of Hasselaar (2007)[38] showed that 43% of the physicians in their sample did not comply with the deep sedation prescription guidelines. The results show better compliance when the physicians themselves were palliative care experts, explicitly reported the use of a set of guidelines or protocol for deep sedation, or consulted with palliative care experts. Swart and colleagues[15] described the practice after the introduction of the Dutch guideline and found that 82% of respondents were aware of the existence of the national guideline and the practice itself largely reflected these recommendations, although some adjustments need to be made to the guideline related to the evaluation of refractory symptoms, the life expectancy of the patient, the skills of the physician, the limited information on acute and intermittent sedation, the medication schedule, and the monitoring of sedation. The study of Hasselaar (2009)[39] compared the practice of continuous sedation before and after the introduction of the guideline in 2005. After introduction, physicians reported changes in palliative sedation practice that conform the recommendations of the KNMG guideline including a significant increase in patient involvement in decision making (72.3% to 82.2%), use of benzodiazepines (69.9% to 90.4%), symptom-directed treatment during sedation (56% to 58%) and there was more often an explicit decision not to give artificial hydration during sedation (78.8% vs 56.3%).

4. Use of setting-specific protocols (n=5)

Hesselink[40] described awareness, use and supportiveness of palliative sedation practice guidelines in hospitals and found that 35% of physicians were aware of their existence and those that has used it felt supported by it. The study of Mateos-Nozal[41] measured changes in the practice of palliative sedation in hospitalised elderly patients before and after the implementation of a palliative sedation protocol. A

checklist was attached to the protocol including the medical history of the patient and a summary of the necessary steps required to carry out palliative sedation adequately. Although the use of midazolam slightly improved after the implementation of the protocol (from 1.3% to 10.4%, P=.02), the percentage of adequate sedations and the general process of sedation were mostly unchanged, which according to the authors was mainly due to the greater heterogeneity of patients. The study of Jiménez Rojas[42] examined whether the clinical protocol published by the Spanish Society of Geriatrics and Gerontology in 2005 and applied in their hospital's Acute Geriatric Unit was appropriately used. This included both requirements for clinical correctness (e.g. indications, drugs) and for ethical correctness (e.g. diagnostic accuracy, existence of refractory symptoms, explicit record of intent of sedation). Benitez-Rosario[43] developed and implemented a protocol for palliative sedation describing reasons for palliative sedation, sedation level for every clinical scenario using the Richmond Agitation-Sedation scale (RASS) and drugs and then audited the adherence to the protocol by reviewing the sedation checklist, medical information justifying palliative sedation, and the appropriateness of treatment, drugs, and doses in concordance with the clinical protocol. The results of both studies showed that the decisions and procedures for establishing palliative sedation were made with high adherence to the clinical protocol. Finally, in the study of Imai[44] the attending physician has to choose one of two developed sedation protocols (proportional sedation and deep sedation) based on their treatment intention (achieving symptom relief versus lowering consciousness) including instructions on medication and dosages. The actual outcomes of each protocol well reflected the treatment intention and expected outcomes.

Clinical decision-making consultation (n=3)

5. Consultation of specialist palliative care services (n=2)

Two Dutch studies were aimed at the consultation of specialist palliative care services before using palliative sedation. Consultation about palliative sedation with palliative care experts was according to the study of Koper[45] regarded as supportive and helpful especially when physicians lack experience. However, physicians had both practical ('patients may be suffering unnecessarily while waiting for consultation') and theoretical ('palliative sedation is perceived as normal medical practice') objections against mandatory expert consultation. The study of de Graeff[46] reported on the number and nature of

telephone expert consultations regarding palliative sedation that were recorded in a one-year period. Advice not to use palliative sedation was given in 42% of the cases mainly due to a lack of a refractory symptom or life expectancy of more than two weeks.

6. *Multidisciplinary team decision-making (n=1)*

In the study of Koike[47] a multidisciplinary team conference (MDTC) was performed for all patients considered for continuous deep sedation, prior to its administration. Six out of 1581 patients (0.38%) were considered for CDS by the attending physicians before MDTC but they did not receive it because not all pharmacological and nonpharmacological approaches had been exhausted.

Discussion

Main findings

This systematic review included 21 studies and identified three types of existing initiatives to support the practice of continuous sedation until death within end-of-life care: assessment tools of consciousness and discomfort, use of a general guideline or a setting-specific protocol, and initiatives that were focused on clinical decision-making consultation. Both observer-based sedation scales and the use of monitoring devices assessing consciousness and discomfort are considered to be very useful, acceptable and feasible by patients, relatives and medical staff. Studies on the use of monitoring devices showed that a small proportion of patients were found to be awake, despite being unresponsive according to the observer-based sedation scales. However, norm values for continuous sedation are not yet available and the wide range of values of these monitoring devices for comfortable and adequately sedated patients seems to hamper its overall implementation in daily practice. Guidelines and setting-specific protocols are regarded as supportive; however, not all physicians are aware of their existence. In general, a high level of compliance with different protocols and general guidelines was found. Physicians reported changes in palliative sedation practice conforming to the guideline recommendations but the shift was modest at best. Expert consultation is regarded as supportive and helpful especially when sufficient experience is lacking. These studies suggest that expert consultation

can ensure that all options are exhausted and that conditions for sedation are fully clarified and clear, avoiding possible unnecessary sedations.

Interpretation of the findings

The review identified nine out of 21 initiatives focused on assessment tools of consciousness and discomfort that have mainly been used in intensive care units concerning both the use of observer-based scales validated for a palliative care setting and the use of monitoring devices and their feasibility and acceptability in a palliative care setting. Monitoring of continuous sedation is generally regarded as essential to ensure that the patient is comfortable and does not receive too much or too little sedation, and that adverse effects can be recognized and acted on.[22] However, there is currently no consensus on the optimal level of sedation necessary for the relief of suffering, nor on the ideal method to assess the level of consciousness.[35] We know from previous research that, in practice, palliative care clinicians often rely on a number of observational scales based on the patient's ability to react to different stimuli.[48] Our findings, however, raise the question of whether the current assessments based on these observational scales are accurate as subjective experiences have been reported using monitoring devices despite the patient being unresponsive according to observer-based scales. It therefore cannot be excluded that patients, even though they appear unconscious, are still aware of their situation and still experiencing discomfort.[48] Using devices such as the Bispectral Index (BIS) monitor would therefore allow clinicians to more accurately determine the appropriate doses of medication and would encourage more vigorous symptom management.[34,48] The studies in our review suggest that the use of monitoring devices is acceptable and feasible to patients, relatives and medical staff in a palliative care setting. Their overall implementation in daily clinical practice is not yet a fact since norm values for continuous sedation (with midazolam) are not yet available and BIS values for comfortable and adequate sedation are variable.[35]

Table 2. Components and outcomes of initiatives to support and improve the practice of continuous sedation until death in research.		
Assessment tools of consciousness and discomfort (n=9) Problem definition: Monitoring palliative sedation is still based on observational scales only. A main problem with these scales is that they consider unresponsiveness equal to unawareness, the correctness of which has been questioned. In general, there is no consensus on the optimal level of sedation necessary to relief suffering, nor the ideal method to assess a patient's level of consciousness. Main focus: To objectify level of consciousness and assessments of discomfort (including pain).		
Components	**Component description**	**Main outcomes**
1. Use of observer-based sedation scales (n=5) Arevalo JJ et al.[29] Benitez-Rosario MA et al.[30] Bush SH et al.[31] Deol H et al.[33] Gonçalves F et al.[32]	Physicians and nurses performed physical or auditory stimulation in the patient during the assessments when required. It concerns the following scales: - Richmond Agitation Sedation Scale (RASS); - Minnesota Sedation Assessment Tool (MSAT) with arousal (MSATa), motor (MSATm) and quality of sedation (MSATq) subscales; - Vancouver Interaction and Calmness Scale (VICS) with the interaction (VICSi) and calmness (VICSc) subscales, - Glasgow Coma Scale (GCS) - Consciousness Scale for Palliative Care (CSPC) - Visual Analogue Scale (VAS) - Ramsay Sedation Scale (RSS) - KNMG scale - Patient Comfort Score (PCS)	Feasibility and acceptability The RASS and CSPC are considered to be very useful tools for assessing consciousness in palliative care patients, are very easy to use, not time consuming and can be used with minimal training. Effectiveness Very high consistency for the CSPC. Moderate to (very) high inter-rater reliability for the VICS, RASS, KNMG scale and CSPC. In one study, only in 29% of cases equal RSS ratings for non-nursing healthcare personnel and nurses' evaluations. Discriminative and evaluative validity for RASS and KNMG scale, strong correlation of the RASS and the RSS and GCS and very high correlation of the CSPC to the VAS and GCS.
2. Use of monitoring devices (n=4) Barbato M et al.[34] Masman A et al.[35] Monreal-Carrillo E et al.[36] Six S et al. [37,48,49]	Each patient is connected to the monitor via an adult Quatro Sensor applied to the forehead. The monitor analyses electroencephalogram input from the frontal cortices and converts this by means of a validated algorithm into a dimensionless score. The score is calculated every 15 to 30 seconds and a continuous one-hour record appears on a rolling display together with measures of electro-myographic (EMG) activity from the frontalis muscle and signal quality (SQ). - BISs range from 100 (fully awake and aware) to 0 (brain death).	Feasibility and acceptability BIS and NeuroSense monitoring were acceptable and feasible to patients, relatives, and medical staff. One study suggests that the wide range of BIS values in deeply sedated and comfortable patients seems to hamper its use in daily clinical practice. Effectiveness A strong correlation between BIS and PCS and RASS, and BIS moderately correlated with RSS,

	- The NeuroSense monitor displays two frontal electroencephalogram (EEG) signals and calculates a number of parameters including the bilateral WAVcns (Wavelet Anesthetic Value for the Central Nervous System) index ranging from 100 (awake) to 0 (flat EEG). The lower the index, the lower the likelihood of consciousness. - The Analgesia Nociception Index monitor continuously monitors heart rate variability (HRV) and transforms this into an ANI (0–100), which assesses parasympathetic activity as a possible measure of nociception.	A small proportion of patients were found to be 'awake' by using monitoring devices, while in fact the observer-based sedation scales (RASS, PCS and RSS) indicated otherwise.
Use of practice guidelines or setting-specific protocols (n=8) Problem definition: The clinical decision-making about continuous sedation until death is very precarious and physicians do not always have very much experience. There are marked variations among physicians and nurses in the decision-making and use of palliative sedation. Main focus: Guidelines on medical end-of-life decisions can help health care professionals to improve the quality of their clinical decision-making by offering authoritative recommendations that reassure them about the appropriateness of their treatment policies and could improve efficiency and consistency of care by standardizing it. Clinical guides and performance protocols for sedation will help clinics to make more rigorous decisions.		
Components	**Component description**	**Main outcomes**
3. Use of general guidelines (n=3) Hasselaar J et al.[38,39] (2007 & 2009) Swart S et al.[15]	Guideline of the Royal Dutch Medical Association sought to define palliative sedation (including continuous sedation), to set the rules for indications and contra indications, and to give recommendations for medication and practical procedures.	Feasibility and acceptability NA Effectiveness After the introduction of general guidelines, physicians reported that changes in palliative sedation practice conform to the recommendations of this guideline. For example, benzodiazepines were used for sedation more frequently than before and patient involvement in the decision-making improved.
4. Use of setting-specific protocols (n=5) Benitez-Rosario MA et al.[43] Hesselink BA et al.[40] Imai K et al.[44] Jiménez Rojas C et al.[42] Mateos-Nozal et al.[41]	Guideline for palliative sedation in the specific institution, to set the rules for indications and contra indications, and to give recommendations for medication and practical procedures.	Feasibility and acceptability Not all physicians were aware of the existence of the practice guideline in their institution (35%). 94% of physicians who used the guideline felt supported by it. Effectiveness In general, a high level of compliance by the physicians to different protocols. In one study, the use of midazolam slightly improved after the implementation

		of a hospital protocol on palliative sedation. However, the percentage of adequate sedations and the general process of sedation were mostly unchanged by the protocol.
Clinical decision-making consultation (n=3) Problem definition: Palliative sedation is an unusual and extraordinary intervention that requires specific knowledge and experience. Therefore, consultation with palliative care experts is advisable if not mandatory as physicians generally lack sufficient knowledge and experience. The skills needed to appropriately perform palliative sedation cannot be assumed to be present in every physician, despite the availability of guidelines. Main focus: Decision-making process as well as the medical rationale for palliative sedation should be based on the input of a multi-professional palliative care team rather than from a single treating physician. Involving specialist palliative care services will help physicians develop expertise in palliative care and will lead to palliative sedation administered more safely and appropriately.		
Components	**Component description**	**Main outcomes**
5. Consultation of specialist palliative care services (n=2) Koper I et al.[45] De Graef A et al.[46]	These consultation teams consist of experienced physicians and nurses who are trained in palliative care that can be consulted by all healthcare professionals by telephone. If caregivers or family or families feel the need for consultation at the home of the patient, consultation teams are prepared to do home visits.	Feasibility and acceptability Consultation about palliative sedation with specialist palliative care services is regarded as supportive and helpful when physicians lack expertise. There is little support for obligatory consultation. Effectiveness Negative advice was given in 42% of the cases where advice was requested from the expert.
6. Multidisciplinary team conference (MDTC) (n=1) Koike K et al.[47]	Prior to administration of CDS, an MDTC should be performed for all patients considered for receiving CDS by the responsible physician. The MDTC included attending physicians, palliative care physicians, registered general nurses, clinical pharmacists, medical social workers, a music therapist, a chaplain, and nutritionists.	Feasibility and acceptability This has not been investigated, the questionnaire only focused on family satisfaction with CDS. Effectiveness Six patients (0.38%) of 1581 were considered for CDS by the responsible physician before the MDTC, but these six patients did not meet the appropriate criteria for CDS according to the MDTC and so did not receive it.

Worldwide, guidelines and protocols are used for standardising and improving practice, encouraging prudence and closing the gap between research and practice.[5] As shown in our review, physicians reported that changes in palliative sedation practice conform to guideline recommendations after the introduction of general guidelines;[15,38,39] the question is whether this can be attributed solely to the use of guidelines. We know from the study of Hesselink[40] that many clinicians are not even aware of their existence. Rather than the impact of the guidelines, it could also – as was suggested by Orentlicher – reflect growing experience with palliative sedation since the same improvements could be seen in Italy.[50] The study of Robijn et al.[5] observed a number of developments in Flemish practice which are positive in the light of guideline recommendations. However, according to Dutch studies, Dutch practice seems to fit more closely with the recommendations of the Dutch guideline than does the Flemish practice with the Flemish guideline. The fact that the Flemish guideline is issued by the federation responsible for palliative care, rather than by a medical or health care association, may be expected to limit its spread and use.[5]

When a physician has doubts regarding his/her own expertise, or has difficulty balancing the different considerations involved in starting continuous sedation (e.g. indications, life expectancy and the importance of exercising due care), guidelines strongly recommend consulting an appropriate expert in good time.[51] According to the European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care, injudicious use of sedation occurs in 'situations in which before resorting to sedation, there is a failure to engage with clinicians who are experts in the relief of symptoms despite their availability'.[52,53] However, research reveals that consultation with experts prior to continuous sedation is rather rare: Rietjens and colleagues have reported that specialist palliative care services were consulted in only one fifth of all palliative sedation cases.[15,54] Two studies from our review indicate the importance of expert consultation. A report from the Netherlands showed that when a palliative care team was consulted by phone, it was deemed unnecessary to proceed with palliative sedation in 47 out of 113 (41%) cases[46]. In the study of Koike[47] a multidisciplinary team conference (MDTC)

was performed for all patients considered for continuous deep sedation prior to its commencement. This eventually led to six cases where not all treatment options had been exhausted. According to Twycross there seems to be a strong case for mandating referral to a specialist palliative care service before proceeding to continuous sedation until death.[55] Although consultation with specialist palliative care services can be regarded as supportive and helpful when physicians lack expertise, Koper et al.[45] found that Dutch physicians had principled objections to obligatory consultation. This is of course not a legitimate reason not to make expert consultation mandatory; however it does point to the existence of potential barriers to any implementation. In any case, there is a further need for empirical/ethical analysis to provide insights into whether consultation effectively improves the decision making and practice of continuous sedation and which physicians and patients stand to benefit the most.[56]

Strengths and limitations

To our knowledge, this is the first study to conduct a thorough systematic search of the available literature concerning initiatives to support the practice of continuous sedation until death within end-of-life care. We believe it represents a comprehensive picture of types of initiatives that have been undertaken and that have been scientifically evaluated. We used a strong methodology based on the PRISMA[25] and consolidated criteria for reporting qualitative research (COREQ) guidelines[57] for the study design and the reporting of results. The search was comprehensive and broad in terms of databases, year range and study design to ensure it captured all relevant research evidence. Nevertheless, there are also some limitations. Given that only 21 papers met the inclusion criteria, none were excluded on the basis of quality scores. As a result, our findings were derived from research papers of potentially variable quality. Another noteworthy limitation is that this review did not always have insight into the detailed content of all initiatives. However, this has no significant impact on the results as the research questions were mainly aimed at giving an overview of existing initiatives and what we know about them in terms of acceptability and effectiveness.

Implications for practice, policy and future research

As was shown in our review, some initiatives do indeed seem to improve practice or at least a part of it. However, the relevant evidence base of the initiatives is rather limited. More evidence is urgently required not only to develop initiatives that really make a difference but also to inform policy makers and practice about the available initiatives, their preconditions and their expected impact on daily practice. Against this background, our systematic overview may serve as a starting point for identifying gaps in the evidence that should be addressed to further improve the practice of continuous sedation until death in a robust evidence-based manner. In order to further monitor and improve the practice of continuous sedation, developing a gold-standard core outcome set reflecting its overall quality will be fundamental to facilitating meaningful evaluations and comparisons between different clinical improvement studies and will be crucial for clinical practice to make more informed health decisions. All included studies in our review focused on a limited number of domains such as the level of consciousness. However, merely focusing on one aspect of the practice may neglect important information on other domains, leading to an incomplete evaluation of the overall quality of continuous sedation until death. Moreover, developing such initiatives e.g. guidelines is only the first step in improving the practice. Additional efforts are needed to promote awareness, acceptance, adoption, and adherence to these initiatives, including wide dissemination and the use of thorough implementation strategies.[58] For example, guidelines and protocols could also be a common point of reference for prospective and retrospective audits of clinicians' practices with the recommendations providing readily available process measures or review criteria for rating compliance with best care practices or for the formulation of useful educational approaches.[23,59]

Conclusion

This systematic review found a limited number of initiatives to support, facilitate or improve the practice of continuous sedation until death within end-of-life care. We identified three types of initiatives: assessment tools of consciousness and discomfort, use of a practice guideline or a

setting specific protocol, and clinical decision-making consultation. The included studies may improve the practice in some ways although the evidence base of the initiatives discussed is rather limited. More insight is needed into their feasibility, preconditions for effective implementation and their impact in daily practice. Additional efforts are needed to promote awareness, acceptance, adoption, and adherence to these initiatives, including wide dissemination and the use of thorough implementation strategies.

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Appendix 1

Appendix 1. Table of included studies							
Author (Year) - Country	**Aims**	**Methods**	**Outcomes**	**Setting and participants**	**Most important findings**	**Recommendations regarding the initiative**	**Quality assess-ment**
Hasselaar et al.[38] (2007) – The Netherlands	To determine adherence to the guidelines for palliative sedation with regard to prescription.	Quantitative: questionnaire (cross-sectional study)	**Primary:** (non)compliance with Dutch guidelines with regard to prescription. **Secondary:** type of physician, palliative care consultant or not, consultation of palliative expertise, indications for deep sedation, use of specific guidelines or protocol.	Mixed: 297 cases General practice: 128 GPs Hospital: 123 medical specialists Nursing home: 46 nursing home physicians.	▪ 57% of the physicians complied with the prescription guidelines. ▪ Better compliance when (1) physicians were palliative care experts; (2) explicitly reported the use of guidelines or protocol; (3) consulted with palliative care experts. ▪ 43% noncompliance was mostly owing to the omission of continued antipsychotic	To increase adherence: (1) Better use and knowledge of the guidelines; (2) larger involvement of consultation teams.	0.70

					treatment for delirium and the use of morphine as the single therapy for the purpose of deep sedation.		
Gonçalves et al.[32] (2008) - Portugal	To validate a Consciousness Scale for sedation in palliative care.	Quantitative: Prospective Observational study	**Primary:** level of consciousness assessed with the Consciousness Scale for Palliative Care (CSPC) **Secondary:** Visual Analogue Scale (VAS) of 100mm, anchored in the terms 'awake' and 'unarousable', and Glasgow Coma Scale (GCS).	Hospital: 38 cases and 176 observations by 4 observers (2 nurses and 2 doctors).	▪ Very high internal consistency (0.99) ▪ Good inter-rater reliability of the scale for all patients (coincident scores in 90% of cases) ▪ The correlation of the CSPC to the VAS and the GCS was very high (criterion validity)	Useful tool in palliative care patients, easy to use, not time consuming and can be used with minimal training. The CSPC scale should be evaluated in other locations.	0.70
De Graeff et al.[46] (2008) – the	To gain insight into the role of consultation in	Quantitative: Retrospective analysis of	**Primary:** nature of the consultation, data from the person asking for the consultation,	Mixed: 206 consultations by a GP (147), by a nursing	▪ Negative advice given in 41% of the consultations on starting PS, mainly	NA	0.45

Netherlands	palliative sedation.	consultation reports	patient data, consultation request, indication for palliative sedation and nature of the advice given.	home physician (7), by a nurse (4), by a pharmacist (4) and 1 unknown.	because there was no question of an untreatable physical symptom. ▪ In 22% of cases: explicit trade-off was made between euthanasia and palliative sedation, where there was almost no indication for PS. ▪ The high percentage of negative advice indicates that expert consultation has added value to check whether all treatment options have actually been exhausted.		
Hasselaar et al.[39] (2009) – The Netherlands	To investigate whether the practice of continuous sedation has changed after the introduction of the Dutch	Quantitative: questionnaire (pre-post cross-sectional study)	**Primary**: (non)compliance with Dutch guideline	Mixed: 160 physicians who reported a last case in both study periods: Hospital (62)	▪ Changes in palliative sedation practice conform to the recommendations. ▪ Significant increase in patient involvement in	NA	0.75

	national guideline for continuous palliative sedation.			General practice (67) Nursing home (31)	decision making (72.3% to 82.2%), use of benzodiazepines (69.9% to 90.4%), symptom-directed treatment during sedation (56% to 58%), not giving artificial hydration during sedation (78.8% vs 56.3%).		
Hesselink et al.[40] (2010) – The Netherlands	To describe awareness, use and supportiveness for physicians of three practice guidelines on medical end-of-life decisions (do-not-resuscitate, euthanasia and palliative sedation), and to identify factors associated with increased awareness of these guidelines.	Quantitative: questionnaire (cross-sectional study)	**Primary:** Physicians awareness, use and supportiveness of the practice guidelines on palliative sedation (if they had been in a situation to make a decision). **Secondary:** Physicians' attitudes towards practice guidelines on medical end-of-life decisions and respondent's demographic characteristics (department type, clinical experience and involvement in the development of the three guidelines).	Hospital: 184 physicians from 12 hospitals.	▪ 35% of the physicians were aware of the existence of a practice guideline on PS. ▪ In situations in which the practice guideline was applicable they had all used the guideline when handling a request for PS. ▪ More positive attitudes towards guidelines and	NA	0.64

					involvement in guideline development associated with increased awareness of the presence of guidelines.		
Arevalo JJ et al.[29] (2012) – The Netherlands	To study the reliability and validity of observer-based sedation scales in palliative sedation.	Quantitative: Prospective Observational study	**Primary:** level of consciousness: The Minnesota Sedation Assessment Tool (MSAT), Richmond Agitation-Sedation Scale (RASS), Vancouver Interaction and Calmness Scale (VICS), and a sedation score proposed in the Guideline for Palliative sedation of the Royal Dutch Medical Association (KNMG).	Palliative care institutions (3): 54 patient cases performed by 52 nurses.	▪ Moderate to high inter-rater reliability for the VICS interaction subscale (ICC¼0.85), RASS (ICC¼0.73), and KNMG(ICC¼0.71). ▪ The largest correlation between scales was found for the RASS and KNMG (rho¼0.836). ▪ All scales showed discriminative and evaluative validity, except for the MSAT motor subscale and VICS calmness subscale. ▪ RASS was less time consuming, clearer,	We suggest the use of the RASS and/or KNMG scales.	0.75

					and easier to use than the MSAT and VICS.		
Benitez-Rosario et al.[43] (2012) - Spain	To assess the feasibility of a quality care project (a clinical protocol) in palliative sedation therapy included in a quality assurance project for care of the dying.	Quantitative: retrospective analysis of reports	**Primary:** Adherence to the guideline. **Secondary:** patient and cancer characteristics, length of stay in the PC-IU, and time from sedation to death.	PCU in hospital: 123 medical patient charts: 60 in 2007 and 63 in 2008.	▪ Decisions and procedures for establishing PS were made with high adherence to the clinical protocol.	Our strategy could be useful to other PCU by considering that which includes the presence of both a guide for carrying out palliative sedation and an audit plan.	0.45
Swart et al.[15] (2012) – The Netherlands	To describe the practice of continuous palliative sedation until death (CPS) after the introduction of a national palliative sedation	Quantitative: questionnaire (cross-sectional study)	**Primary:** Adherence to the Dutch national guideline. **Secondary:** respondent's experiences with the national guideline.	Mixed: 370 physicians about their most recent case. Hospital (64)	▪ 82% were aware of the national guideline ▪ Practice largely reflecting guideline recommendations: Palliative care expertise more	Problem areas identified that were not sufficient mentioned in the guideline:	0.64

	guideline in the Netherlands			General practice (250) Nursing home (64)	often consulted, more use of the recommended drug, opioids as a stand-alone drug were used less frequently, nearly all physicians had indicated that they had kept a written document regarding the course of events on CPS. ▪ Practice not reflecting guideline: in 1/5 cases there was no physician present at the start of continuous sedation, in a minority of cases artificial fluids were administered. ▪ 14% of physicians felt pressured to start sedation.	evaluation of refractory symptoms, life expectancy of the patient, the skills of the physician, limited information on acute and intermittent sedation, medication schedule, and monitoring.	
Benitez-Rosario et al.[30]	To test the appropriateness and reliability of the Richmond	Quantitative: Prospective	**Primary:** level of consciousness: Richmond Agitation-Sedation	PCU in a hospital: 156 patients with advanced	▪ The team considered the RASS to be a very useful	Following modifications necessary:	0.70

(2013) – Spain	Agitation-Sedation Scale (RASS) in Spanish patients with advanced cancer	Observational study	scale (RASS) translated into Spanish **Secondary:** level of consciousness: the Ramsey Sedation scale and the Glasgow Coma Scale.	cancer (322 observations)	tool (very good face validity) ▪ The weighted kappa values were practically ≥ 0.90 between nurses and nurses and physicians. The agreement level between observers for each RASS score was roughly 90% (inter-rater reliability) ▪ Criterion validity: The RASS had a strong correlation with both the Ramsay (Spearman's p,-0.89;P<0.001) and the Glasgow Coma Scales (Spearman's p, 0.85;P<0.001).	1) removal of the reference to assisted ventilation from the definition of agitation level; 2) RASS score +1, or restless, can be present in patients who are not fully alert.	
Bush et al.[31] (2014) - Canada	To investigate the validity and feasibility of the RASS-PAL, a version of the RASS slightly	Mixed methods: Prospective Observational study, questionnaire	**Primary:** Level of consciousness: The Richmond Agitation-Sedation Scale modified for palliative care inpatients (RASS-PAL).	Palliative care unit: 13 health care professionals (physicians and nurses)	▪ This study provides preliminary validity evidence for the use of the RASS-PAL by physicians and	The need for formal education on why and how to use the	0.85

	modified for palliative care populations, in patients experiencing agitated delirium or receiving PS.	, and 13 in-depth interviews.	**Secondary:** the ease of using the scale, how well the scale measured sedation and agitation, whether the scale assisted in the monitoring of patients for sedation purposes and patients with an agitated delirium, and whether the scale improved patient care and aided health care professional communication.	assessed 10 consecutive patients with an agitated delirium or receiving palliative sedation.	nurses working in a PCU. ▪ The inter-rater intraclass correlation coefficient range of the RASS-PAL was 0.84 to 0.98 for the five timepoints. ▪ Professionals agreed that the tool was useful for assessing sedation and was easy to use and they felt as it may assist interprofessional communication. However, its role in monitoring delirium was deemed problematic.	instrument was highlighted.	
Koper et al.[45] (2014) – The Netherlands	To investigate the considerations of Dutch physicians concerning consultation about palliative sedation with specialist	Qualitative: in-depth interviews	NA	Mixed: 54 physicians were interviewed on their most recent case of palliative sedation:	▪ Consultation about PS with specialists is regarded as supportive and helpful when physicians lack expertise.	NA	0.70

	palliative care services.			Hospital (8) General practice (23) Nursing home (23)	▪ Reasons not to consult: practical problems, such as time, and the fact that several physicians considered palliative sedation to be part of the normal medical practice. ▪ Although there was support for low-threshold facultative consultation, Dutch physicians have both practical and theoretical objections against mandatory consultation.		
Jiménez Rojas et al.[42] (2015) - Spain	To examine whether the protocol established in our hospital for terminal sedation was appropriately applied for those patients who passed away over	Quantitative: Retrospective analysis of reports	**Primary:** Adherence to the protocol: the irreversible clinical process which necessitated end of life care and the written record of the quality parameters in the patient's clinical history which were used in the application of the protocol, and measured against a record of	Acute Geriatric Hospital: Clinical records of 146 patients who died in the hospital's AGU over the	▪ In our study, a second opinion of another professional was turned to in only 51.4% of cases, although once the decision was made, the plan of action was shared in all	The systematic analysis of quality criteria was extremely enriching and useful as a professional	0.40

	the course of one year in our unit, and who received sedation in their final days.		ethical safeguards in the terminal sedation process written by the authors of the protocol and approved by the hospital's mortality commission	course of one year.	cases with the rest of the medical team. ▪ The percentage of explicit consent was very low, which may have been influenced by the high prevalence of cognitive deterioration in the sample group and by the frequency of delirium as a refractory symptom.	development tool and as a teaching tool.	
Koike et al.[47] (2015) - Japan	To explore the efficacy of a multidisciplinary team conference (MDTC) concerning decision-making surrounding application for continuous deep sedation until death.	Quantitative: Retrospective analysis of reports and questionnaire to bereaved family members	**Primary:** The frequency and characteristics of CDS (patient background, all target symptoms, medications used for sedation, duration, family's satisfaction, and distress).	Palliative care unit: records of 1581 cancer patients who had died at the PCU. Of these 1581 22 patients had received CDS. Patient and family satisfaction surveys were sent to 20 families	▪ Six patients (0.38%) of 1581 did not meet the appropriate criteria for CDS according to the MDTC and so did not receive it, although they were considered for CDS by the attending physicians before the MDTC. ▪ Although bereaved families were generally	Despite the availability of guidelines, the skills needed to appropriately perform palliative sedation cannot be assumed to be present in every physician. The use of a	0.60

				(90.9%), responses from 13/20 (65.0%)	comfortable with the practice, some expressed a high level of emotional distress.	MDTC ensures that it is solely carried out for appropriate indications.	
Masman et al.[35] (2016) – the Netherlands	To determine the feasibility and validity of BIS monitoring in terminally ill patients.	Quantitative: Prospective Observational study	**Primary:** Level of sedation assessed with Bispectral index (BIS) monitoring. **Secondary:** Level of sedation assessed with the Ramsay score, Pain assessed with self-reported Numeric Rating Scale (for communicative patients) and with the Rotterdam Elderly Pain Observations Scale (for noncommunicative patients). Delirum was assessed with the Delirium Observation Screening Score, and the degree of comfort was measured with an Numeric Rating Scale from 0 (no comfort at all) to 10 (optimal comfort).	Palliative care center: 516 patients during the study period were eligible to participate. 58 patients were included in the final analysis.	BIS monitoring was acceptable to patients, relatives, and medical staff. Even the medical appearance of the sensor on the patients' forehead did not bother relatives. ▪ BIS values were moderately correlated with Ramsay scores (0.46) but were highly variable for deeply sedated patients. ▪ BIS values changed significantly before and after a midazolam dose (P<0.001). Midazolam treatment resulted on average in a	Based on our results, the wide range of BIS values in deeply sedated and comfortable patients seems to hamper its use in daily clinical practice.	0.86

					statistically significant reduction of the BIS values (-4.5, 95% CI -7.0 to -2.0), whereas morphine and haloperidol did not.		
Mateos-Nozal et al.[41] (2016) - Spain	To measure changes in the practice of palliative sedation during agony in hospitalised elderly patients before and after the implementation of a palliative sedation protocol.	Quantitative: Retrospective analysis of reports before and after the implementation of a palliative sedation protocol.	**Primary:** Adherence to the palliative sedation protocol: refractory symptom treated, drug doses, assessment and use of other drugs. **Secondary:** patient and admission characteristics, the consent process, withdrawal of life-sustaining treatments	Hospital: 143 hospitalised patients over 65 years old who received midazolam during hospital admission in two 3-month periods, before and after the implementation of the protocol: 76 in 2011 (before) and 67 in 2012 (after).	▪ The percentage of adequate sedations and the general process of sedation were mostly unchanged by the protocol. ▪ Practice reflecting protocol recommendations: more informed consent (91% vs 84%), induction and maintenance doses of midazolam followed protocol recommendations (10.4% vs 1.3%), midazolam doses were significantly lower (9.86 mg vs 18.67 mg), Ramsay sedation score was	Implementing a protocol in a single disease (cancer) is already complex, implementing a cultural change that affects many patients can be even more complex. The protocol	0.64

					more often used (12% vs 8%). ▪ The Palliative Care Team was involved in 35.5% and 16.4% of the cases (P=.008) before and after the protocol, respectively.	can reduce the perception of need for specialized expert support. More education and further assessment is needed to gauge the effect of these measures in the future.	
Barbato et al.[34] (2017) - Australia	To determine the validity and reliability of both the Bispectral Index monitor (BIS) and two observational scales (the Richmond Agitation and	Quantitative: Prospective Observational study	**Primary:** Level of consciousness with an objective measure Bispectral Index (BIS) monitor, and two observational scales: Richmond Agitation-Scale (RASS) and the Patient Comfort Score (PCS)	Palliative care unit in a hospital: 40 patients were monitored from the onset of unconsciousness until death.	▪ A strong correlation was found to exist between BIS and RASS (P<0.0004) and BIS and PCS (P=0.003). ▪ The scatter plots for RASS and PCS show most scores are concentrated at the	The BIS may be useful addition to observational scales in assessing sedation, comfort, and the patient's	0.75

	Sedation Scale, RASS, and the Patient Comfort Score, PCS) used to assess sedation and comfort in unconscious palliative care patients.				lower end of each scale. Corresponding BISs, however, are widely scattered ranging from a high of 95 to a low that approaches zero. ▪ The concentration of RASS and PCS at the lower end of their respective scales has led us to conclude that both scales (and by extension other observational scales) are relatively blunt instruments particularly at their lower reaches, just where greater acumen is needed.	own experience.	
Monreal-Carrillo et al.[36] (2017) - Mexico	To characterize the level of consciousness in patients undergoing palliative sedation using Bispectral	Quantitative: Prospective Observational study	**Primary:** level of consciousness assessed with BIS monitoring **Secondary:** level of sedation assessed with Ramsay Sedation Scale (RSS)	Palliative care unit: 20 patients with a diagnosis of advanced cancer with no further disease-modifying	▪ BIS was feasible in the palliative care setting. It was easy to apply for continuous monitoring, and family caregivers	Our study supports that BIS may be a promising tool to augment clinical assessment	0.60

	Index (BIS) monitoring.			treatment options	found its use to be acceptable. ▪ Using BIS to augment clinical observation to adjust medications during PS, has resulted in a greater proportion of patients achieving sedation within the first 24 h. ▪ Moderate correlation between BIS and RSS. ▪ A sizable proportion of patients with low RSS of 4–6 still had BIS readings, suggesting that they may be conscious.	for patients undergoing palliative sedation.	
Imai et al.[44] (2018) - Japan	To investigate the effects of two intervention protocols, i.e., proportional sedation and deep sedation.	Quantitative: Retrospective analysis of prospectively recorded reports	**Primary:** Treatment goal achievement at 4h: 1) In proportional sedation: achievement of symptom relief (Support Team	Palliative care unit of a cancer hospital: 50 terminally ill cancer patients of	▪ The actual outcomes of each protocol well reflected the treatment intention and expected outcomes, i.e., proportional	A protocol-based definition of palliative sedation therapy would	0.73

			Assessment Schedule, STAS ≤1) and absence of agitation (modified Richmond Agitation-Sedation Scale, RASS ≤ 0) 2) In deep sedation: achievement of deep sedation (RASS ≤ -4). **<u>Secondary:</u>** mean scores of STASS and RASS, deep sedation as a result, and adverse events.	which 32 received proportional and 18 received deep sedation.	sedation to achieve acceptable symptom relief with maintained consciousness and deep sedation to induce unconsciousness. ▪ The treatment goal achievement rate was 68.8% (22/32, 95% confidence interval 52.7–84.9) in the proportional sedation group vs. 83.3% (15/18, 66.1–100) in the deep sedation group. STAS decreased from 3.8 to 0.8 with proportional sedation at 4 h vs. 3.7 to 0.3 with deep sedation; RASS decreased from + 1.2 to−1.7 vs. + 1.4 to−3.7, respectively.	enable comparisons and interpretations of empirical research uniformly all over the world, and further, large-scale cohort studies are promising.	

Deol H et al.[33] (2019) - USA	We evaluated inter-rater reliability (IRR) using RSS and its relationship to variations in dosing to determine whether additional training in sedation scale assessment is necessary at our community institution.	Quantitative: prospective observational study	**Primary:** level of consciousness assessed with Ramsay sedation scale	ICU: 83 random RSS assessments conducted in 44 patients. Non-nursing healthcare personnel (physician or pharmacist) conducted independent sedation assessments using the RSS and compared their evaluations to those documented by the nursing staff.	▪ Non-nursing healthcare professionals' assessments were compared to nurses' and observed to be equal in 29%, higher in 59%, and lower in 12% of the case. ▪ Of the 83 assessments, the average RSS score non-nursing healthcare professionals assigned was 4.8 +/1.6 while the nurses' charted average was 3.39 +/- 0.97; a mean difference of 1.45, 95% CI (1.04 - 1.85) p< 0.0001.	Without proper education, the RSS may not be a reliable tool for sedation assessments and may result in over-sedation of critically ill patients. Recurrent nursing education is warranted to ensure proper use and optimizatio n of the RSS.	0.50
Six S et al.[37,48,49] (2020) - Belgium	To determine measures are potentially useful in the assessment of comfort and pain during	Qualitative: a case report and in-depth interviews	**Primary:** Assessment of pain and discomfort: NeuroSense monitor and Analgesia Nociception Index monitor.	Mixed: 1) A case of an 80+ patient with chronic lymphatic	▪ 13 assessments made with the RSS showed that the patient was considered to be in a deep sleep, while in fact the NeuroSense	Future research should focus on developing implementa tion	0.70

	palliative sedation.		**Secondary:** Ramsay Sedation Scale (RSS)	leukaemia, depression, and a cerebrovascular accident, with right-sided hemiplegia and aphasia. 2) 20 professional caregivers from hospitals and nursing homes and 15 family members.	monitor indicated otherwise. ▪ Using monitoring devices to objectify assessments of pain and discomfort was feasible and had potential advantages in palliatively sedated patients. ▪ Family members and professional caregivers found the use of monitors during CSD acceptable. ▪ Being aware that care can be improved, good communication, shared decision making and continuing professional education could overcome identified barriers (the tenet to avoid technology	strategies and guidelines for introducing objective monitoring devices in diverse palliative care settings.	

					and recreate a home environment)		

CHAPTER 6

Barriers in the decision making about and performance of continuous sedation until death in nursing homes

Lenzo Robijn, Luc Deliens, Judith Rietjens, Peter Pype*, Kenneth Chambaere*.

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Abstract

Objectives: While decision-making about and performance of continuous sedation involve many challenges, they appear to be particularly pervasive in nursing homes. This study aims to identify barriers to the decision-making and performance of continuous sedation until death in Flemish nursing homes as experienced by the healthcare professionals involved.

Methods: Ten focus groups were held with 71 healthcare professionals including 16 palliative care physicians, 42 general practitioners and 13 nursing home staff. Discussions were transcribed verbatim and analyzed using a constant comparative approach.

Results: Perceived barriers concerned factors prior to and during sedation and were classified according to three types: (1) personal barriers related to knowledge and skills including the lack of clarity on what continuous sedation should be used for (linguistic ambiguity) and when and how it should be used (practical ambiguity); (2) relational barriers concerning communication and collaboration both between healthcare professionals and with family; (3) organizational barriers related to the organization of care in nursing homes where e.g. there is no on-site physician, or where the recommended medication is not always available.

Discussion and implications: The findings suggest there are considerable challenges for sound decision-making about and performance of continuous sedation until death in nursing homes. There is a need for multicomponent initiatives that provide guidance in the context of the complexity of a resident's medical situation, the family and the specific organization of care, which would have the potential to facilitate and improve the decision-making process and performance of continuous sedation in nursing homes.

Introduction

Some people approaching death experience devastating symptoms that cannot be alleviated despite intensive medical and palliative treatment.[1,2] This leaves healthcare professionals, patients and relatives with a last-resort treatment, continuous sedation until death [3], which entails the use of sedating drugs to induce a state of decreased consciousness until death, with the added effect that it takes away the persons experience of symptoms.[4,5] Findings from surveys of physicians suggest that continuous sedation is a frequently used practice across all care settings estimated to involve between 2.5 and 18.2% of all deaths in Europe[6–11] and 10% in the USA.[12] Nevertheless, continuous sedation until death remains a highly debated medical practice, particularly regarding its potential to hasten death and its proper use in end-of-life care.[13,14]

To support physicians in their decision-making, to ensure best practice and to encourage prudence, generic clinical guidelines and position statements have been developed for its use.[15,16] These statements describe conditions under which sedation at the end of life should be performed, including the recommendation that it should only be used close to death and for unbearable and refractory symptoms without the intent to hasten death.[16,17] Benzodiazepines, titrated proportionally to alleviate the symptoms, are the drug of first choice and the administration of artificial nutrition or hydration is not encouraged unless the benefits outweigh the harm.[18]

Knowledge about the practice of continuous sedation is predominantly based on research with people with cancer, carried out in hospice or hospital environments.[19–23] While deciding on and performing continuous sedation is replete with challenges,[24] research suggests that these are particularly pervasive in nursing homes, as various specific individual and institutional factors may further complicate good practice.[25,26] For example, on an individual level, the large majority

Recruitment of participants

In order to obtain a broad range of views and experiences, participants were sampled in three ways:

(1) Three focus groups were organized during a biannual gathering of GPs working in multidisciplinary palliative home care teams who can be considered experts in palliative care who, in addition to their own practice, advise and support GPs and other primary healthcare professionals in providing optimal care for palliative patients;

(2) Five focus groups were organized within local peer review GP groups that meet four times a year to discuss their practice. Every accredited GP in Belgium must be affiliated to a geographically determined peer-review group and attend at least two of four meetings per year. We contacted by e-mail several groups from different regions, and five were selected according to their availability.

(3) A third group were nursing home staff (nurses, care assistants and coordinating and advisory physicians in nursing homes). The coordinator (or equivalent) of each nursing home selected was contacted by telephone to ask if they would agree to facilitate our study.

Table 1. Characteristics of the participants.

	Palliative care physician (n=16)	**General practitioners (n=42)**	**Nursing home staff (n=13)**	**Total (n=71)**
Number of focus groups	3	5	2	10
Sex				
Male	11	20	1	32
Female	5	22	12	39
Age				
≤ 30	2	7	1	10
31-40	0	12	3	15
41-50	7	7	1	15
51-60	1	7	7	15
61-70	2	6	1	9
> 70	0	2	0	2
Unknown	4	1	0	5

Palliative care expertise				
No PC training	0	19	2	21
PC training in the basic curriculum	0	12	3	15
Continuing PC training	16	11	8	35

Procedures

Focus groups were held between June 2017 and May 2018. All discussions lasted between 60 and 120 minutes and were moderated and observed by two researchers with experience in qualitative end-of-life care research and knowledge of the items to be discussed. A semi-structured topic guide was developed to ensure consistency in questions across groups (**Box 1**) covering their experiences of three main areas of continuous sedation until death in nursing homes: decision-making, performance and attitudes to quality improvements. All participants filled in a short questionnaire on socio-demographic data and signed an informed consent form before the start and consented to the discussion being audiotaped.

Box 1. Topic guide of the focus groups with professional caregivers

Introduction

Theme 1: Experiences with the decision-making process

1. How did the decision-making process go according to your experiences?
PROMPTS: What were the main indications? Who was involved in the decision-making? What was the relatives' role? How was the communication between health care professionals on the one hand and the relatives on the other? Were prior agreements made with the person who died or those close to them? Who took the final decision?
2. According to you, what went well in the decision-making process?
3. What, in your opinion, could have been done better in decision-making and how could it have been done better?

Theme 2: Experiences with the performance of continuous sedation in nursing homes

1. How did the performance of continuous sedation go according to your experiences?
PROMPTS: Was someone (for example an expert) consulted? How did the follow-up happen? Which medication and dosage was used? Was the pain treatment continued? How was the communication between healthcare professionals and between them and relatives?
2. According to you, what went well with the performance of continuous sedation until death?
3. What, in your opinion, could have been done better and how could it have been better?

Theme 3: **Reflections on quality improvement initiatives**
1. How do you think we can improve or facilitate the practice of continuous sedation until death in nursing homes? 2. When would you use it for yourself?

Data analysis

The audiotaped discussions were transcribed verbatim and analyzed by constant comparative analysis with qualitative analysis software (NVivo 12). Transcripts were anonymized. Two researchers (LR, KC) independently analysed a first set of transcripts for concepts that were directly linked to barriers for the decision-making about and performance of continuous sedation until death in nursing homes. The codes were compared and discrepancies were discussed until agreement was reached. A general conceptual coding framework was then developed by the two authors and agreed upon with all co-authors. All transcripts were coded by the lead author (LR) and quotes were selected on the basis of their being representative of the wider data, translated and approved by all researchers.

Ethical considerations

Ethical approval for this study (B.U.N 143201732331) was given by the Medical Ethics Commission of the Brussels University Hospital (2017/166) and by the Ghent University Hospital Ethics Committee (2017/0631).

Results

Seventy-one healthcare professionals (16 palliative care physician, 42 GPs and 13 nursing home staff) attended one of the ten focus groups. Their characteristics are displayed in **Table 1**. Perceived barriers were classified according to three types as shown in **Table 2**: (1) personal barriers related to knowledge and skills; (2) relational barriers concerning communication and collaboration both between professionals and with the family; and (3) organizational barriers related to the organization of care in the nursing home. We will discuss the most prominent barriers here.

Table 2. Barriers to the decision-making and performance of continuous sedation until death in nursing homes

	Decision-making	FG	PC	GP	NH	Performance	FG	PC	GP	NH
Personal barriers	Lack of conceptual clarity of what sedation is and what sedation should be used for (see 3.1.1)	1,2,3,5,6, 7,8,9,10	x	x	x	Lack of clarity, knowledge and experience about how sedation should be performed (see 3.1.3)	1,2,3,5,6, 7,8,9,10	x	x	x
	Uncertainty about indications in nursing home residents (see 3.1.2)	1,2,3,6	x	x		Uncertainty about doses and drug effects on survival/life shortening in the specific group of NH residents (see 3.1.2)	1,2,3,9, 10	x		x
	Fear among physicians that it could be associated with euthanasia	3,4,6,8	x	x						
Relational barriers	**<u>Between health care professionals</u>**					**<u>Between health care professionals</u>**				
	Unclear who should take the leading role and unclear division of roles (see 3.2.1.1)	1,2,3,4,5, 6,7,8,9, 10	x	x	x	Inadequate briefing and reflection moments during and after continuous sedation or during transfer of care (see 3.1.1.2)	2,4,5,6,8, 9,10	x	x	x
	Insufficient information flow, briefing and continuation of care (see 3.2.1.2)	1,2,3,4,5, 6,7	x	x		Uncertainty about how to handle suspicions from care team (nursing assistants) who don't understand	6,8,10		x	x
	Uncertainty about how to handle conflict situations between GP and nursing home staff	1,2,9,10	x		x					
	<u>Family and resident</u>					**<u>Family and resident</u>**				

	Uncertainty about how to involve family and what to say to the family (see 3.2.2.1)	1,2,3,4,5, 6,7,8,10	x	x	x	Uncertainty about how to handle family emotions and frustrations (see 3.2.2.1)	1,2,3,4,5, 6,8	x	x	
	Uncertainty about how to handle family emotions and conflicting views among family (see 3.2.2.1)	1,2,3,4,5, 6,8,10	x	x	x	Family pressure to increase the dose	1,2,3,4,7, 8	x	x	
	Consent of resident not always possible	1,3,4,5,7, 8,9,10	x	x	x					
Organizational barriers	Less openness about end-of-life decision-making and PS in Catholic institutions	1,4,6,7,8, 9,10	x	x	x	Unavailability of medication or material (see 3.3.1)	1,6,8	x	x	
	No protocols for decision-making	1,2	x							
	No regular general practitioner within a nursing home	9			x					

Personal barriers

Lack of conceptual clarity

A lack of conceptual clarity of what sedation is and what it should be used for was observed in all focus groups. In general, we could distinguish two types of ambiguity. The first concerned the confusion between continuous sedation and regular symptom control. All professional health care professionals in our study generally found it difficult to distinguish continuous sedation from regular symptom control, particularly because 'continuous sedation is a form of intensive symptom control'. Participants generally agreed that the goal of continuous sedation is the relief of suffering via the titration of medication until the cessation of experienced symptoms and that the outcome is a lowered level of consciousness. However, it does not always seem clear when symptom control turns into continuous sedation because the one often tacitly passes into the other, without this being explicitly communicated. When asking respondents where they thought symptom control ends and sedation begins, they all said that in theory it amounts to intention, even though the intention is not always explicitly stated and discussed in practice.

> *"Sedation means that you have a refractory symptom, that you can only treat the patient by rendering them unconscious for their own comfort. The intention is to render the patient unconscious. Sometimes the morphine dose is so high that the patient becomes calmer and consciousness is reduced, but that isn't your intended aim, of course. It's the side effect you get, but that isn't the same as sedation.". (FG8 – general practitioners)*

The second type of conceptual confusion concerned the distinction between continuous sedation, often mentioned by respondents as 'slow euthanasia', and 'real euthanasia', although theoretically these are two different practices at the end of life. Respondents indicated that sedation is often perceived by all involved as an 'alternative to euthanasia', which is hoped to have a life-shortening effect and where the decision to use sedation is rather a 'choice of the patient', and where the control of the initiation of the dying process lies with the person who is dying, as with euthanasia. In nursing homes, however, it is mainly about 'persons who are no longer considered legally competent' and who are often 'at an advanced stage of dementia'. In these

circumstances euthanasia is not a legal option, since such decisions must involve people who are have mental capacity at the time of the request. The only possibility then is to find a compromise where sedation is gradually increased, partly to prevent death from taking too long.

> *"Well, yes, patients with dementia can't give consent to euthanasia. So then there are no possibilities for administering euthanasia, is what I say. But what we can do is increase the level of sedation and, er, adjust the dose day by day, for example. Er, in fact it's necessary to do that, because you see the general state of health is deteriorating bit by bit, of course. The organs start to fail a bit, sometimes there are bed sores here and there, discolouration of the skin. In fact you really mustn't let it go on too long, because then you get so much physical deterioration that, well, it's terrible to watch, let me put it like that." (FG4 – general practitioners)*

Uncertainty about indications for continuous sedation in nursing home residents

Most professionals indicated that the large majority of residents are dying from conditions that are complex and unpredictable in terms of diagnosis and prognosis. The pathology of nursing home residents could be characterized as 'prolonged dwindling', for example in the case of the ever-increasing proportion of frail residents with dementia. This further complicates judgment about possible indications for continuous sedation and whether these symptoms are refractory and in estimating life expectancy, as the disease process is characterized by a slow decline.

> *"In the residential care centres, that population, they're not always easy to monitor. Especially if you get called in suddenly as, as a palliative care expert, to assess at that point what the prognosis is for that patient. Are they actually terminally ill? It isn't always easy, because these are trajectories of, of frailty. You know, dementia trajectories. Er, so they are wonderful people who can sometimes carry on, er, stay alive for a very long time despite their, their poor condition. That is difficult to assess, it is a really difficult decision, it isn't easy for the team. So it means you need to figure things out." (FG1 – palliative care physicians)*

Lack of clarity, knowledge and experience of how continuous sedation should be performed

Besides the complexity in decision-making, respondents also encountered a lack of clarity about how continuous sedation should be used. It is not 'a routine practice' due to its medical and technical complexity. Physicians made the comparison between the use of continuous sedation with the use of euthanasia which is much more straightforward, regardless of its potentially greater emotional impact. Participants found it difficult to sedate residents properly and to find the right dose and indicated that they do not feel adequately educated and experienced, as 'you have to acquire sufficient experience through the years' with 'trial and error'. On the one hand, the use of medication such as benzodiazepines is quite common in nursing home populations but on the other hand the resident often turned out to be weaker than expected and even the guideline starting dose was too high, risking sedation being too deep. In nursing homes, the depth of sedation is evaluated only by clinical assessment rather than by observer-based instruments that can estimate the depth of sedation more objectively, although these scales are hardly validated for use in palliative patients.

> *"As a general practitioner, how many sedations do you administer per year? You can count the cases on one hand, certainly for a young GP, a young practice, you'd have very little experience of it, because with an older practice you might have a bit more, but even then, you can't gain that experience based on two cases a year, that just doesn't work. You can't expect them to know everything."*
> *(FG2 – palliative care physicians*

In cases where there is not enough expertise available around the death bed or in cases of a conflict, external palliative care experts can be called in to check whether all conditions are met, to adjust things if necessary and as support for the doctor. Nevertheless, it is recommended that this expertise is called in in time as physicians in our study indicated that it is very difficult to assess a dying person you barely know. The majority of end-of-life care revolves around communication and if you are called in as an expert just before sedation starts, you have already missed most of the process, which can make it impossible to correct errors such as a promise already made to a resident or family.

Relational barriers: communication and collaboration between health care professionals

Lack of coordination of care: collaboration does not always go smoothly

In Belgian nursing homes there is no structural partnership between GPs and the home as no regular GP is associated with the institution and every resident is able to keep their own GP. This causes extra difficulties since it is often unclear who should take the leading role. It depends, for example, on how the GP wants to fulfill his/her own role and which role is reserved for the team, but also in the perceived expertise and experience of the team and the extent to which they can trust each other.

> *"Moderator: We are currently discussing the role of the GP. How does collaboration with the GP go?*
> *Respondent 1: Sometimes it goes well, sometimes less well.*
> *Respondent 2: Sometimes very well, sometimes very bad.*
> *Respondent 3: Sometimes very bad indeed.*
> *Respondent 2: Sometimes you have terribly therapeutic, tenacious, to cry about.*
> *Respondent 4: We do our best. In the end, it is the therapeutic liberty of the physician. But sometimes we ourselves refuse to perform tasks that the GP asks in the last phase of life.*
> *Respondent 1: Here we have a culture that we built step by step, we have a palliative collaboration as well. I think that you as head nurse could achieve a lot with GPs that themselves have insufficient knowledge, that we help them, that we provide it to those GPs". (FG10 – nursing home staff)*

It is also necessary to check whether everyone interprets the concept and practice in the same way each time. The collaboration between the GP and nursing home team has therefore been described as 'potentially difficult' by all involved, for various reasons. GPs often felt pressured by the team, for example, 'to come immediately to start sedation', especially in those teams with little or no palliative expertise and experience. Nursing home staff often had the feeling that 'GPs are not always open to their opinion and expertise' and they found it 'difficult to go against the advice of a doctor'.

> *"Respondent 1: It does take some time and energy. Because people, everyone thinks differently about it. You've got a patient, you've got a family, you've got*

the family doctor. Those three groups all have their own notion of what sedation is and that causes confusion.
Respondent 2: I find the family doctors the most difficult group, actually. Because they have talked to the family and the patient ten times already but often they have explained it wrongly. So you need to set that straight, but you can't." (FG2 – palliative care physicians)

In principle, the coordinating and advisory physician (CRA), who is responsible for the coordination and organization of care policy in nursing homes, can in the event of a conflict be consulted to mediate. However, according to our respondents, this role is insufficiently taken up and does not meet expectations.

"But that is a task for the coordinating and advisory doctor, isn't it, that they coordinate, that they encourage the communication between management, and also with family doctors and other bodies. In fact that's the point of a coordinating and advisory doctor, isn't it? They are actually the liaison between management, institutions and visiting family doctors. That was the original intention in fact. Er, but of course they didn't organise it very well, er, not very well at all, if you ask me. Right, so the, the coordinating and advisory doctors are appointed by management, aren't they. You see, but, er, you have to, you also have to get them approved by the visiting family doctors, don't you. That's how it was for a long time, er, recently something changed. (FG4 – general practitioners)

Insufficient (de)briefing and continuity of care

A major barrier in the communication between healthcare professionals lies in the fact that the GP is normally not present at the meeting to discuss each case. It is practically impossible for a GP to be present at the consultation in every institution where they have a patient. Care assistants too are often absent at such consultations, which can cause difficulties if they have not been informed that continuous sedation had been initiated or simply cannot understand that the resident - whom they have fed for years - is no longer allowed to eat and drink. Another common problem is continuation of care and information transfer at the weekend which in principle is the responsibility of the GP. In many cases described the GP could not be reached and the doctor on call had to take on a case they did not know well and where they did not know the intention of the treating physician.

Relational barriers: communication between healthcare professionals and family

Uncertainty about how to involve family

In nursing homes the family appears to play a very important role since residents are often no longer able to participate in decisions because they have dementia or are too frail. All respondents stressed the importance of talking with the family to answer as many questions as possible and to deal with their uncertainties. However, respondents do not consider themselves sufficiently prepared and trained for this and did not always know the best way to involve them. They are often uncertain about what to say and how to say it, as talking about the death is often perceived as a taboo, both by the professionals and the family. Moreover, communication appeared to be even more difficult in nursing homes because the message is often not coordinated and can be conveyed by different participants, each with their own emphasis and interpretations. According to our respondents, this often means that the information given to the family by different professionals may conflict, making them even more confused and distressed.

> *"The family doesn't always see it, people often pretend to be healthier than they are with their family than with us. We also examine people, which means we see that there is pain or problems with comfort, the family doesn't see that, do they, if someone is sitting in their armchair they don't see what happened beforehand. And residents don't always like us to say that a person is deteriorating. They don't want to upset the children, they don't want them to have to worry about it. And not all families want to hear it either, do they? Sometimes it's a bit of a taboo. They don't always want to know. That's also something we've encountered many times." (FG9 – nursing home staff)*

Another aspect is the way the family copes with grief, both their own and that of the dying person, in the run-up to and during sedation. Relatives must handle grief while addressing a multitude of practical issues. You 'have to give the family sufficient time, also to say goodbye to the resident' and you have to 'repeat the message over and over again'. Nevertheless, staff are often confronted with emotional reactions from the family which they feel uncertain about handling and find themselves mediating while time is running out.

"That reminds me of an old lady who was dying last week. She died naturally: it took twenty-four hours. And one of those daughters was there, but she was, she had learning difficulties and she put a lemonade bottle into her mother's mouth to make sure she got something to drink. Because you're going to die, Mum. The other children had to pull her away, because she didn't understand. She couldn't understand, if you can't drink, it's terrible. So it was the extreme reaction of, I'm going to do something because she's not drinking. And so you do always need to explain, eating and drinking really aren't necessary and they really don't feel it. But sometimes they can't understand." (FG5 – general practitioners)

Organizational barriers

Unavailability of medication

Within nursing homes, there is often insufficient medication available for proper performance of continuous sedation. There is always an emergency package available, but that it only enough to start sedation or to last for a few hours. This also means that GPs sometimes have to work with products and dosages they are less familiar with, which causes additional uncertainty for less experienced doctors.

"Respondent 1: "What went wrong? There was no medication available again, you see. It's a disaster, isn't it?
Respondent 2: We're a developing country in that respect, aren't we?
Respondent 3: Yes, it's absolutely terrible.
Moderator: What is the problem?
Respondent 2: It's on and off, you see. Sometimes we can, sometimes we can't, then the dose changes, then it's that...
Respondent 1: The thing that's always available is 1 milligram per millilitre, but that's no use at all, is it?
Respondent 3: It's turned into hospital medication, hasn't it? They are older products by now and the profit margin is no longer as big. So the supply chain is blocked somewhere." (FG 1 – palliative care physicians)

Discussion

Summary

The purpose of this study was to identify perceived barriers to decision-making about and performance of continuous sedation until death in nursing homes. Barriers were classified on three levels including personal barriers related to knowledge and skills, relational barriers concerning communication and collaboration both between professionals and with the family, and organizational barriers related to the organization of care in nursing homes. We found a lack of clarity and conceptual ambiguity among the healthcare professionals about what sedation is, what it should be used for and how it should be used. Physicians and nurses in our study clearly indicated that the decision-making and performance of sedation is much more complex in a nursing home population, both in terms of assessment of frail older persons and of collaboration and communication between healthcare providers.

Strengths and limitations

The qualitative design, using different recruitment strategies, allowed us to gain insight into the complex range of views and experiences regarding the use of continuous sedation until death in nursing homes from different perspectives (palliative care specialists, physicians, nurses, care assistants). We believe that this study provides several valuable insights into which factors are likely to influence physicians in decision-making and implementation. Limitations should also be acknowledged and should be taken into account when interpreting the results. The sensitivity of the topic might have led to socially desirable answers by focus group participants and they may have been reluctant to state their true opinions. Even without this type of bias, the opinions we gathered are not necessarily reflective of the actual behaviour of the participants in their clinical practice. The size and religious affiliation of nursing homes were taken into account for the sampling plan, because of the possibility that these factors result in different attitudes and

knowledge among healthcare professionals. However, despite our best attempts we were not able to find institutions with a religious affiliation willing to participate in a focus group discussion.

Discussion of the main results

Conceptual ambiguity among healthcare professionals still exists about what sedation is, what it should be used for and how it should be used, even among palliative care physicians. For example, there is a lot of confusion about how continuous sedation relates to regular symptom control on the one hand and euthanasia (which is a legal option in Belgium) on the other. The international qualitative UNBIASED study has shown that continuous sedation may refer to different practices.[30–32] This study shows that this ambiguity is even more complex in the setting of residential care centres where a huge variety of actors are involved in the care of the resident, each with their own emphasis and interpretation of the concept of sedation. If there is no agreement as to which practices do and do not fall under the term, there is a great risk that discussion becomes meaningless as different narratives become indistinguishable from each other. Even without this conceptual ambiguity, our results show that the decision-making and performance of the practice of sedation in nursing homes itself is highly complex e.g. determining whether a symptom is refractory, estimating the remaining life expectancy or finding the right dose in residents who are very old and frail and often habituated to medication. Our results therefore suggest that existing recommendations on continuous sedation are not always adapted and fully applicable to the complex reality of a nursing home. Although high-quality guidelines may be seen as necessary for reducing variations in practice, customizing a clinical practice guideline to a particular organization or context may further improve acceptance and adherence [33]. Specific attention can also be paid to the coordination of care with a clear division of roles and tasks. In Belgium, for example, there is no structural partnership between GPs and nursing homes as no regular GP is associated with the institution, while medical supervision is mostly provided by each resident's regular GP. However, the healthcare professionals in our study indicate that this role is rather unclear in practice and there is still a serious lack of coordination,

communication and continuity of care and it is often very unclear who should take the leading role.

Our study clearly shows that physicians and nurses do not consider themselves sufficiently prepared and trained in dealing with family e.g. they are uncertain how to involve them in decision-making and how to handle their emotions or conflicting views. Guidelines on the use of sedation in end-of-life care also include recommendations to protect the well-being of relatives.[15,34] According to them, relatives should be involved in decision-making and might benefit from being involved in monitoring the waking state of the resident and providing light care such as mouth moistening.[35,36] The review of Bruinsma et al[36] indicates discrepancies between the recommendations made in guidelines and the actual experiences of relatives with the practice of continuous sedation. Despite the fact that the majority were reported to be comfortable with the use of sedation, their review showed that they may express distress before and during the process. Although all guidelines stress the importance of involving relatives in the sedation process and supporting them before, during and after it,[37] they rarely state how to do this.

Implications

While it is commonly argued that the adoption of a single, clear-cut and well-defined term for the use of continuous sedation until death, and a clear definition of the practice, would greatly improve its quality,[38] simply using a common term does not guarantee a shared concept, let alone a common practice.[39] The practice would further benefit from inter-professional training and even team training in which it is made clear with common terminology what continuous sedation, as opposed to symptom control or euthanasia, entails, and what its modalities are. To ensure that relatives' concerns are addressed, their needs should be continuously monitored [36,40]. Providing full information and regular updates about e.g., the level of consciousness, clinical symptoms, and lack of potential alternatives is important. It is also important that there is a common understanding of terms and phrases used for all involved (relatives and health care professionals)

and that checks are made to ensure this understanding is maintained throughout the process [37,40]. Other perspectives such as those of residents and their families could provide additional insights that would contribute to a better understanding of the problems of continuous sedation and to the formulation of useful educational approaches.

Conclusions

Our findings suggest there are considerable challenges for sound decision-making about and performance of continuous sedation until death in nursing homes. We provide empirical support for the need for multicomponent initiatives that provide guidance in the context of the complexity of a resident's medical situation, the distress of their family the specific organization of care, the use of standardized terminology and interprofessional training which would have the potential to facilitate and improve the decision-making process and performance of continuous sedation in nursing homes.

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CHAPTER 7

Enhancing the quality of continuous sedation until death: the development of a practice tool adapted to the specific needs of nursing homes

Lenzo Robijn, Marie-José Gijsberts, Peter Pype, Judith Rietjens, Luc Deliens*, Kenneth Chambaere*.

Submitted

Abstract

Objectives. Challenges inherent in the practice of continuous sedation until death (CSuD) appear to be particularly pervasive in nursing homes. In order to address these challenges more concretely, we aimed to develop a protocol to improve the quality of the practice of CSuD in nursing homes.

Design. A mixed methods design based on the Medical Research Council (MRC) Framework, including a systematic review, qualitative focus groups and expert panels.

Methods. The development of the protocol made use of findings of a systematic review of existing improvement initiatives and focus groups with 71 health care professionals identifying perceived barriers to the use of CSuD in nursing homes. Additionally, this protocol was reviewed and refined by another 70 health care professionals through ten expert panels.

Results. The final protocol (included as Appendix to the paper) was signed off by an expert panel after two consultation rounds in which remaining issues were ironed out. The protocol encompassed seven sequential steps according to the expected chronological course of practice and is primarily focused on clarification of the medical and social situation, communication with all care providers involved and with the resident and/or relatives, the organisation and coordination of care, the actual performance of continuous sedation, and the supporting of relatives and care providers during and after the procedure. While consistent with existing guidelines, our protocol describes more comprehensively recommendations about coordination and collaboration practices in nursing homes as well as specific matters such as how to communicate with fellow residents and give them the opportunity to say goodbye in some way to the person who is dying.

Conclusions. This study succeeded in developing a practice protocol for CSuD adapted to the specific context of nursing homes. Before implementing it, future research should focus on developing profound implementation strategies and on thoroughly evaluating its effectiveness.

Introduction

Palliative care has become an important part of health care in many countries, aiming to ensure that in the last phase of life people receive high-quality, appropriate care that is in line with their wishes and values and which relieves their suffering.[1,2] However, some people approaching death still experience devastating symptoms, such as intractable pain, dyspnoea and delirium that cannot be alleviated despite intensive medical and palliative treatment.[3,4] This leaves health care professionals, people who are dying and those close to them with a last resort treatment, continuous sedation until death (CSuD), which entails the administration of sedative drugs to induce a state of unconsciousness until death ends these symptoms.[5,6]

While the deciding on and performing of continuous sedation is replete with challenges in all settings, research suggests that they are particularly pervasive in nursing homes as various specific individual and institutional factors may further complicate good practice.[7–9] For example, on an individual level, the large majority of residents are dying from conditions that are complex and unpredictable in terms of diagnosis and prognosis, complicating judgments about imminent death and the suitability of CSuD. This population is also characterized by high rates of medication use which further complicates determining the correct dose.[10] Also, communication preceding sedation may be difficult or even impossible, particularly in cases of dementia.[8,11] On the institutional level, nursing homes are, in contrast to hospitals and palliative care units, not highly medically equipped.[7,8] Thus, it is clear that the decision making and performance of CSuD may be particularly difficult and may not always guarantee a dying process free from severe symptoms and is thus in need of improvement.[12]

To support physicians in their decision making, to ensure best practice and to encourage prudence, generic clinical guidelines have been developed for its use.[13,14] The question is whether general guidelines aimed at the widest possible patient groups are sufficiently attuned to the specific needs and context of nursing homes, particularly when we consider the many differences between nursing home patients and typical cancer-related palliative care patients: older age

groups often with frailty and dementia, different metabolisms, etc.[8,11] The development and refinement of guidelines and clinical practice protocols may benefit from the closer involvement of practising nursing home clinicians in order to more specifically address complex issues such as estimating the life expectancy of very old people and those with dementia, determining the refractory nature of their suffering, or the dosage of sedative drugs.[15] In order to enhance the quality of the practice of CSuD in nursing homes, the aim of this study was to develop a practice protocol for its use adapted to the context-specific needs of nursing homes. In this paper, we report on the development process and the contents of the protocol resulting from the various research methods employed.

Methods and materials

Study design

We developed a practice protocol adapted to the specific context of nursing homes following the guidance of the Medical Research Council (MRC) for development and evaluation of complex interventions.[16] An overview of the methods used for the development of our practice protocol can be found in **TABLE 1.**

Table 1 – Overview of phases and methods used for the development of our practice protocol following the guidance of the MRC framework

Phase	Methodology
A. Phase 0: identifying the evidence base	
A1. Exploring the Flemish context of nursing homes and identifying existing barriers for continuous sedation until death in nursing homes	1. 10 Focus groups with 16 palliative care physicians (n=3), 42 general practitioners (n=5), and 13 nursing home staff (n=2)
A2. Identifying evidence on existing improvement initiatives	2. Literature search on existing initiatives to support continuous sedation until death.
B. Phase 1: modelling of the intervention	
B1. Selection of key intervention components	1. Identification of key components 2. Creation of preliminary practice protocol 3. Feedback on preliminary practice protocol by monthly meetings with multidisciplinary research team

	consisting of medical sociologists, health scientist, geriatrician, and a general practitioner
B2. Improving the practice protocol and increasing feasibility and acceptability	1. Professional stakeholders consultation including palliative care physicians, geriatricians, general practitioners and nursing home staff following a participatory approach.
B3. Finalising the practice protocol	1. Monthly meetings with multidisciplinary research team. 2. Final approval by the professional stakeholders involved.

Phase 0: identifying the evidence base

Two complementary methods were used to inform the development and content of our practice protocol and to ensure that it is adapted to the specific qualities and needs of nursing homes.

1. *Focus groups among professional stakeholders in nursing homes*

We conducted ten focus groups with 71 health care professionals including 16 palliative care physicians, 42 general practitioners and 13 nursing home staff (nurses and care assistants) to gain insight into perceived barriers to decision-making and communication about and performance of CSuD in nursing homes. We also discussed initiatives that health professionals thought could support the practice, with the aim of reflecting on them and of preliminarily gauging the acceptability of possible supporting tools. A more detailed description of the methods can be found elsewhere.[15]

2. *Systematic literature search of existing quality improvement initiatives for continuous sedation until death*

We systematically reviewed available initiatives aimed at supporting the practice of CSuD within end-of-life care and assessing its feasibility and effectiveness. Records were searched through MEDLINE, EMBASE, CENTRAL, CINAHL, BioMed Central and ISI Web of Science from inception to

May 16, 2020. Peer-reviewed primary studies reporting on initiatives to support the practice were included for review.[17]

Phase 1: modelling the intervention to nursing homes

3. *Professional stakeholders consultation to validate a practice protocol for continuous sedation in nursing homes*

Based on the insights of phase 0, we developed a preliminary practice protocol adapted to the specific context of nursing homes and based on existing guidelines. The model was further refined at monthly meetings with the multidisciplinary research team consisting of medical sociologists, a health scientist, a geriatrician and a general practitioner (GP). We also held ten expert panels with 70 stakeholders representing palliative care physicians, geriatricians, GPs and nursing home staff following a participatory approach to explore how the model meets their own experiences and expectations, and to brainstorm about how to further improve the intervention model (**TABLE 2**). Professional stakeholders were eligible when they were involved in the care of nursing home residents and were sampled by launching a call at a symposium on CSuD by the Federation for Palliative Care Flanders, followed by a letter of invitation by e-mail to all symposium participants. We also organized an expert panel within local peer review GP groups, randomly selected palliative care physicians and geriatricians and further used the snowball method to identify other potential participants with relevant experience. Interested stakeholders were asked to identify others who were then contacted by e-mail. We used pre-existing groups of physicians and nursing home staff, as group discussions are expected to naturally occur during these meetings.

Table 2. Characteristics of the professional stakeholders (n= 10)

	Round 1		**Round 2**		
	Nursing home	**Physicians**	**Nursing home**	**Physicians**	**Total**
# workshops	3	1	2	4	10
# participants	31	3	15	21	70
Discipline*					
CRA	2	2	2	5	11
GP	2	3	2	19	26

PC physician	0	3	1	5	9
Geriatrician	0		0	2	2
Head nurse	5		2		7
Nurse	14		7		21
Care assistant	9		3		12
Volunteer	1		1		2
Sex					
Male	4	0	2	9	13
Female	27	3	13	12	55
Age					
≤ 30	7	0	3	2	12
31-40	6	1	5	7	19
41-50	4	1	4	6	14
51-60	11	1	2	4	17
61-70	3	0	1	2	6
> 70	0	0			0
Unknown	0	0			0
Palliative care expertise					
No PC training	6	0	7	4	17
PC training in the basic curriculum	10	0	0	8	18
Continuing PC training	15	3	8	9	33

Note: PC= palliative care, PC physician= palliative care physician, GP= general practitioner, CRA= Coordinating and advisory physician in a nursing home.
* Stakeholders can represent multiple disciplines

Results

Phase 0: identifying the evidence base of the intervention

The focus group study identified the most prominent barriers to decision-making, communication and performance of CSuD in nursing homes and these were classified on three levels. Firstly, personal barriers relating to a lack of knowledge and skills including a lack of conceptual clarity among the health care professionals about what sedation is, what is should be used for and how it should be used; this ambiguity may even be more complex in this setting due to the involvement of a huge variety of actors in the care of the resident, each with their own emphasis and interpretation of the concept of sedation. Secondly, relational barriers concerning communication and collaboration both between health care professionals and with family. On the one hand, not all staff are involved or even aware of the decision to start sedation and it is further also unclear who should take the leading and coordinating role, what the specific tasks are of everyone involved and how to handle conflict situations between GPs and nursing home staff. On

the other hand, there was uncertainty about how to involve resident and family in the decision-making process, what to say to them and how to handle family emotions and frustrations prior to, during and after sedation. Thirdly, organizational barriers relating to the organization of care in nursing homes, where, for example, there is no on-site physician, the recommended medication is not always available or where there is simply no uniformity between different nursing homes. A more detailed report on these focus groups has been published elsewhere.[15]

The screening of the literature resulted in 21 studies and initiatives that could be grouped into three main categories: nine studies were focused on assessment tools of consciousness and discomfort, eight initiatives were focused on the use of a general guideline or a setting-specific protocol and three initiatives were focused on clinical decision-making consultation. For assessing consciousness, the 'Richmond Agitation-Sedation Scale' (RASS) was considered to be very useful, easy to use with minimal training and not time consuming. Guidelines and setting-specific protocols are regarded as supportive; however, not all physicians are aware of their existence. Physicians reported some modest changes in their practice were necessary to conform to the guideline/protocol recommendations. Expert consultation is regarded as supportive and helpful especially when sufficient experience is lacking. In general, reviewed initiatives may contribute to improvement of CSuD practice, though the evidence base of these initiatives was rather limited. This review has been reported in full elsewhere.[17]

Phase 1: modelling and development of the intervention

Table 3 indicates how we linked specific barriers and insights from the literature to the elaboration of a preliminary practice protocol. Further adjustments were made by consulting 70 relevant professional stakeholders involved in the care of nursing home residents. In the end this resulted in a final practice protocol (**Annex 1**) approved by all stakeholders involved encompassing seven sequential steps that were classified according to the expected chronological course of practice: (1) clarifying the medical and social situation; (2) communication with all health care professionals involved; (3) communication with the resident and/or next of kin; (4)

organisation and coordination of care; (5) actual performance of the sedation; (6) supporting next of kin and care workers during sedation; and (7) aftercare. In the remainder of this section we discuss and summarize the most prominent themes throughout these seven steps.

1) Conceptual clarity.

The protocol is directed to the 'administration of sedative drugs to induce a state of unconsciousness until death', also known as continuous sedation until death (CSuD). We intended to use the term 'continuous sedation until death' in the title of our protocol (STEP 0); however, our experts advised that this term could be confusing for professionals as they are most familiar with the term 'palliative sedation'. We therefore decided to use the term 'palliative sedation' in the title and stated at the outset that the protocol is primarily aimed at a form of palliative sedation, namely continuous sedation until death.

2) Coordination, collaboration and communication between healthcare professionals.

Experts agreed that GPs do not spend enough time in nursing homes to be the central coordinator of care, despite this being medically desirable; a coordinator will therefore be designated from within the nursing home staff (STEP 0), ideally a head nurse or the reference person for palliative care (who is responsible for the establishment of a supportive palliative care culture, provision of training and coordinating palliative care generally) but this can be decided separately within each nursing home. The protocol also recommends using all perspectives in the decision-making process (STEP 1), especially as nursing home staff may best assess the situation, having observed the trajectory of the patient's condition. An important point in the protocol is the organization of a short formal meeting with all health care professionals closely involved in the care as well as next of kin if possible (STEP 2). Opinions within the expert panels were divided on this, but it was generally pointed out that this is more or less what happens in practice, although our focus group study showed that the GP was not always present at these meetings and also that often some care assistants were unaware that a decision to start sedation had been made. Experts agreed that the meeting in which the division of tasks is agreed and where everyone has the final opportunity to

express their concerns should be kept short, though it provides the chance to achieve a shared understanding of the practice and its intention.

3) Involving and communicating with resident and family

We know that physicians and nurses do not consider themselves sufficiently prepared for and trained in dealing with family and sometimes even feel pressured by them, for instance in cases where they may have the wrong expectations or are dealing with conflicting information from different health care professionals; we therefore provide a list of topics and information that must be discussed with the family and the patient (STEP 3). Since experts indicate that communication often goes through the GP alone and thus varies from doctor to doctor, we recommend also involving the coordinator so that staff are aware of what has been said and to give the them the opportunity to supplement or even adjust the information where necessary. To avoid misunderstandings, both family and nursing home staff should designate a contact person through whom all communication takes place (STEP 3). Finally, we refer to specific tools that can be used to support the family during sedation (STEP 6), for instance by involving them in providing light care such as mouth moistening, and, afterwards (STEP 7), by inviting them to share their experiences of the death.

4) Performance and monitoring of continuous sedation until death

As health care professionals sometimes found difficulty in sedating someone properly and in finding the right dose, the protocol incorporated the medication scheme of the sedation guideline of the Flemish Association for Palliative Care[18], as our experts rated this scheme as being accurate and easy to use (STEP 5). In cases of doubt, we again refer to the possibility of obtaining external advice from palliative care experts. The depth of sedation is usually evaluated only by clinical assessment rather than by observer-based instruments. On the recommendations of palliative care physicians, we included the Richmond Agitation-Sedation Scale as we found in our systematic review that this is considered to be very useful, easy to use and not time-consuming

and can be used with minimal training (STEP 5). Finally, we supplemented our detailed step-by-step description with a brief checklist.

Discussion

This article describes the development and contents of an evidence-based practice protocol to support health care professionals in the decision-making, communication and performance of continuous sedation until death (CSuD) in nursing homes. The protocol is based on the results of a qualitative study on perceived barriers to the use of CSuD in nursing homes, insights from the literature on existing quality improvement initiatives, and close involvement of 70 stakeholders in the development and refinement of the protocol. The final protocol (Annex 1) encompasses seven sequential steps according to the general chronological course of practice, with particular focus on: (1) clarifying the medical and social situation; (2) communication with all health care professionals involved; (3) communication with the resident and/or their next of kin; (4) organisation and coordination of care; (5) actual performance of sedation; (6) support for the next of kin and professionals involved during sedation; and (7) aftercare.

The main strength of this study is the use of a mixed methodology based on the MRC framework,[19] combining a systematic review including all currently available evidence on existing quality improvement initiatives for continuous sedation until death, with elaborate and in-depth qualitative data from 141 different health care professionals involved in the care of people dying in nursing homes. Including a wide variety of stakeholders in the expert panels allowed us to co-develop our protocol with those who will potentially use it. It has been argued that such a participatory stakeholder approach enhances the feasibility and effectiveness of the intervention because the content of the protocol is strongly grounded in daily clinical practice.[20] However, although the expert panels were purposively sampled, not all relevant experts, such as patient representatives and relatives, were represented. This would have made it possible to identify outcomes that matter most to them. Finally, our protocol is not directly generalizable to other countries, because some elements are specific to the context of Flanders, Belgium (e.g. the use of

Table 3. Description of steps of the practice protocol, informed by evidence from phase 0 studies and phase 1 expert panels.			
	Phase 0		Phase 1
Protocol description	Results of focus groups	Results of systematic review	Results of expert panels
STEP 0. Definition and conceptual clarity			
a. **Term: palliative sedation** and at the outset it is stated that the protocol is primarily aimed at continuous sedation until death.	Lack of conceptual clarity among the health care professionals about what sedation is, what is should be used for and how it should be used.	No single term in the literature.	Professional stakeholders in the nursing home are most familiar with the term 'palliative sedation' and it would only be more confusing to speak of continuous sedation until death.
b. Palliative sedation defined according to the **definition of the 'Federation for Palliative Care Flanders'.**	Lack of conceptual clarity among the health care professionals about what sedation is, what is should be used for and how it should be used.	Palliative sedation was defined in analogous ways in all guidelines as the deliberate lowering of a patient's level of consciousness instituted solely for the purpose of refractory symptom control at the end of life.	Definition of the Flemish Federation for Palliative Care or from the Dutch national guideline best known to professional stakeholders.
STEP 0. Appointing a fixed coordinator of the protocol and care			
a. A **coordinator is designated** within the nursing home and called in in case of refractory symptoms and when palliative sedation is proposed as a possible option. Ideally a head nurse or reference person for palliative care.	In Belgian nursing homes, no regular GP is associated with the nursing home and every resident is able to keep their own GP. It is therefore often unclear who should take the leading role.	Attending physician central coordinator of care.	Although medically indicated, the attending physician is insufficiently present in nursing homes to be the central coordinator of care.
STEP 1. Clarifying the medical and social situation			
a. A **preparatory consultation** should take place with the resident (if still possible) and his/her next of kin. It is also stated that the	The large majority of residents are dying from conditions that are complex and unpredictable in terms of diagnosis and prognosis.	Guidelines also include recommendations to involve the dying person and relatives in	Advance care planning conversations are increasingly done and tracked. It is either discussed with the person who is

decision should be based on the resident's disease (clinical picture, intensity of symptoms, refractoriness, remaining life expectancy), the resident's experiences (impact on quality of life and dignity and unbearableness of symptoms) and the resident as a person (remaining expectations and goals).	This further complicates judgment about possible indications, whether these symptoms are refractory and in estimating life expectancy, as the disease process is characterized by a slow decline.	decision-making. However, they rarely state how to do this.	dying if still capable, or with the family in case of dementia for instance.
b. Emphasis on the **importance of consulting all care providers** who are closely involved in the care of the resident, with an explicit reference to the added value of nursing home staff.	Nursing home staff often had the feeling that GPs are not always open to their opinion and expertise and they found it difficult to go against the advice of a doctor.	Whenever possible, the medical rationale for sedation as well as the decision-making process should be based on input from the multi-professional palliative care team, rather than by the treating physician alone.	Attention to the added value of nursing home staff in decision making (for instance estimating the general decline of the resident).
c. Recommendation to **make the treatment intention explicit** to all involved and to explicitly include the intention in the patient file.	Respondents indicated that sedation is often perceived by all involved as an "alternative to euthanasia," which is hoped to have a life-shortening effect.	Guidelines and protocols are giving an overview of ethical aspects including treatment intention (relieve suffering and not to hasten death).	Intention not always clearly communicated causing further confusion among nursing home staff.
d. **In case of questions or doubts,** we recommend to **consult** palliative care **experts** within and beyond the nursing home and/or disease-specific experts.	Lack of sufficient knowledge and/or experience among the health care professionals about what sedation is, what is should be used for and how it should be used.	If there is uncertainty in the patient evaluation, especially with regard to whether all options to relieve distress have been considered, consultation with experts (e.g. psychiatrists, anaesthetists, pain specialists, oncologists and	In case of conflict, the coordinating and advisory physician (CRA) can play a mediating role. Additionally, in case of doubt and conflict, more 'neutral' external palliative expertise can also be called upon.

		specialist nurses) should be sought.	
STEP 2. Communication with all care providers involved			
a. It is advised to organise **a short formal meeting with all care providers** closely involved in the care of the resident, as well as, if possible, next of kin. It is important that after this briefing, all those involved who could not be present are still informed (for instance care assistants).	A major barrier is that the GP is normally not present at the meeting to discuss each case. Care assistants too are often absent at such consultations, which can cause difficulties if they have not been informed that continuous sedation had been initiated or simply cannot understand that the resident - whom they have fed for years -is no longer allowed to eat and drink.	In one study, a multidisciplinary team conference (MDTC) was performed for all patients considered for receiving continuous deep sedation, prior to its administration. Six out of 1581 patients (0.38%) were considered for CDS by the attending physicians before MDTC but they did not receive it because not all pharmacological and nonpharmacological approaches were exhausted.	A lot of discussion and disagreement. Some point to the fact that there is usually not much time, others to the fact that it takes effort but it can offer an added value and it often already happens informally.
b. This formal meeting also serves to **resolve misunderstandings** and to **have a shared understanding** of the treatment and its intention.	GPs often felt pressured by the team, especially in those teams with little or no palliative expertise and experience. Nursing home staff often had the feeling that GPs are not always open to their opinion and expertise and they found it difficult to go against the advice of a doctor.	Guidelines are intended to provide clarity in definition, indications and implementation.	It is important that there is a common understanding of terms and phrases used for all involved (relatives and health care professionals) and that checks are made to ensure this understanding is maintained throughout the process.
c. It is recommended to **make clear agreements** with all involved **regarding the role** of everyone involved, the **accessibility, availability and**	The division of tasks depends on how the GP wants to fulfill his/her own role and which role is reserved for the team, but also in the perceived expertise and	Not specifically described.	It is not always clear to anyone what is expected of them and what their specific role is.

transfer of care, as well as clear agreements with al care providers involved regarding **monitoring**.	experience of the team and the extent to which they can trust each other.		
	Another common problem is continuation of care and information transfer. The GP could not be reached and the doctor on call had to take on a case they did not know well and where they did not know the intention of the treating physician.	In principle, the responsibility of the GP.	As a GP, it is not always clear who is responsible and should be addressed in nursing homes. It is not always clear to anyone what is expected of them and what their specific role is.
STEP 3. Communication with the resident/and or next of kin			
a. A topic guide is provided with the **essential information** that must be **discussed with the family** and the patient.	Physicians and nurses do not consider themselves sufficiently prepared and trained in dealing with family, for example, they are often uncertain about what to say and how to say it, as talking about the death is often perceived as a taboo, both by the professionals and the family.	Guidelines recommend to provide sufficient information to the family, to support the family by talking with each party and finding a solution that is acceptable to both and to provide psychological support to families.	Communication does not always run smoothly and often done by the GP. As nursing home staff, you often have to adjust the communication afterwards because sometimes false promises have been made which creates extra tension and conflict during the sedation.
b. The **GP involves the coordinator** of the protocol in the conversation with the patient and the family.	Communication appeared to be even more difficult in nursing homes because the message is often not coordinated and can be conveyed by different participants, each with their own emphasis and interpretations. This often means that the information given to the family by different professionals	Not specifically described.	
c. One person is designated both within the nursing home staff and within the family as a **contact person.**		Not specifically described.	There is a legal representative with the dying person that you can address, but it would be good if one person also coordinates

	may conflict, making them even more confused and distressed.		communication within the team to avoid conflicting messages.
STEP 4. Organisation and coordination of care			
a. The protocol contains **contact details** of the coordinator, the 'coordinating and advisory physician' (CRA), reference person for palliative care and external palliative care experts.	No regular GP is associated with the nursing home and every resident is able to keep their own one. As a result, GPs do not always know who is responsible, who to address and how.	Not specifically described.	As a GP, it is not always clear who is responsible and should be addressed in nursing homes.
b. It is recommended to give relatives and people who have a special relationship with the resident (co-residents, care providers and volunteers) the **opportunity to say goodbye.**	Another aspect is the way the family copes with grief, both their own and that of the dying person, in the run-up to and during sedation. Relatives must handle grief while addressing a multitude of practical issues.	Families should be allowed and encouraged to be with the patient and, in many situations, an opportunity to say goodbye may be of critical importance.	Family are an important link in the patient's monitoring and are sometimes given a clear task, for example to moisten the mouth of the dying person.
STEP 5. Actual performance of the sedation			
a. **Medication scheme** of the Flemish guideline incorporated in the protocol.	Participants found it difficult to sedate residents properly and to find the right dose and indicated that they do not feel adequately educated and experienced.	Guidelines and protocols provide help with the dosage of sedative medications.	Medication scheme of the Flemish guideline is accurate and easy to use
b. The Richmond Agitation-Sedation Scale (RASS) is used to measure **the depth of sedation**.	In nursing homes, the depth of sedation is evaluated only be clinical assessment rather than by observer-based instruments that can estimate the depth of sedation more objectively.	There is no consensus on the optimal level of sedation necessary to relieve suffering, nor the ideal method to assess a patient's level of consciousness. Studies on the use of monitoring devices showed that a small proportion of patients were found to be awake, despite	The use of an observer-based instrument was not regarded as essential for nursing home staff. Palliative care experts, however, found it essential to objectify assessments certainly due to the presence of many different actors in nursing homes. According to

		the patient being unresponsive according to the observer-based sedation scales. However, the wide range of values of these monitoring devices for comfortable and adequately sedated patients seems to hamper its overall implementation in daily clinical practice. The RASS is considered to be very useful, easy to use, not time-consuming tools for assessing consciousness in palliative care patients that can be used with minimal training.	these expert, the scale could also be used to make clear the intention of the treatment to all involved (e.g. lowering awareness) instead of assessing symptoms which turned out to be refractory and therefore untreatable.
STEP 6. Supporting next of kin and care providers during sedation			
a. **Information**, explanations, cooperation and **continuous evaluation of the situation** are **essential** to ensure that continuous sedation runs smoothly and to give all those involved a meaningful farewell.	You have to give the family sufficient time, also to say goodbye to the resident and you have to repeat the message over and over again. Nevertheless, staff are often confronted with emotional reactions from the family which they feel uncertain about handling and find themselves mediating while time is running out.	The needs of the patient and his/her family are paramount in palliative care. The anxiety and fear regarding death may assume such dramatic forms for the patient and his family that the physician must attach considerable weight to them. The physician can be expected to adopt an open attitude and to raise any differences of opinion with the patient in good time.	Relatives might benefit from being involved and providing light care such as mouth moistening.
STEP 7. Aftercare (after death)			

a. After the death of their loved one, the **family will be invited to discuss the care** to find out how they experienced it in order to further improve care towards the family.	Uncertainty how to handle family emotions and conflicts.	Guidelines recommend to provide psychological support to families.	There is informal talk with the family when emptying the room of their loved one, but there is no structural conversation.
b. **Every sedation case will be discussed during team meetings** to see how it went, what feeling everyone has, what went well and especially what could be done better or differently.	Inadequate reflection moments after continuous sedation.	An audit of adherence to due care criteria can be carried out as follows: 1) a yearly assessment, for two years, of a sample of charts of patients who died in the PC-IU and 2) feedback of data to the team after each assessment.	Situations that could have been better are already discussed at a team meeting afterwards, but it may not be done systematically.
EXTRA: Check-list			
a. Use of a **brief check-list** at the end of the protocol.	Guidelines are generally too long to read quickly	Use of a checklist that can be used for audit purposes	Need for a detailed description (step-by-step) supplemented with a brief checklist at the end.

the term and the unique and specific function of 'reference person for palliative care' in the Belgian system, or the fact that GPs are not part of the regular care team in the nursing home).

Over the past decades, clinical guidelines and protocols have increasingly become part of clinical practice with the aim of improving the quality of decision-making and performance of clinical practices.[21] Guidelines on end-of-life sedation are generally intended for all clinicians involved in the care of dying people across all settings.[3] Research, however, clearly shows that such general guidelines are often not sufficiently attuned to the specific needs and context of nursing homes.[8,11,22] Therefore, by closely involving health care professionals in and around nursing homes, we have developed a practice protocol that describes more comprehensively recommendations about specific practice issues that are possibly more complex in nursing homes. For example, a coordinator is designated within the nursing home, since the GP is insufficiently present to be the central coordinator of care. Nursing homes have a multitude of actors, each with their own interpretation and understanding of what continuous sedation is and what its modalities are, which leads to confusion, misunderstandings and even tensions between professionals, and with the family, who are sometimes confronted with conflicting messages. This protocol tries to achieve a shared understanding by organizing a formal consultation. To avoid misunderstandings, both family and nursing home staff designate a contact person through whom all communication takes place. Finally, the protocol also takes into account the unique living environment of care homes with specific attention given to how to involve fellow residents and give them the opportunity to say goodbye to the dying person in some way.

Despite widespread recognition of their crucial function, guidelines and protocols are not always translated into policy or practice.[23] Research generally suggests that implementation is most beneficial when a range of strategies is used.[17,24,25] In implementing this protocol in daily clinical practice, it is important to keep in mind that there are multiple preconditions at micro, meso and macro level, related to successfully implementing the protocol in the complex nursing home setting. Gilissen[26] emphasizes the importance of engaging nursing home management in order to

achieve better implementation and sustainability. Based on our expert panels, short information sessions could be organized for all nursing home staff and GPs to alert them to the existence of the protocol and how to use it in daily clinical practice. However, before implementing it, future research should focus on the preconditions for implementing a practice protocol on continuous sedation in the nursing home setting and must take into account specific barriers to implementation such as the personal characteristics of the professionals involved (knowledge and attitude) as users have to be motivated to effectively use them, factors relating to the guidelines themselves such as poor layout or poor access and external factors such as lack of resources, heavy workload etc.[27]

While developing an evidence-based protocol and accompanying implementation strategies is complex, it may be even more complex to examine their effectiveness in daily clinical practice and especially to the extent in which they improve the use of CDuD in nursing homes. Merely checking whether certain due care criteria have been met does not necessarily say anything about the overall quality of the practice and may even lead to an incomplete evaluation of our initiative. In order to further monitor and improve the practice of CSuD, developing a gold-standard core outcome set reflecting the overall quality of continuous sedation will be fundamental to facilitate meaningful evaluations and comparisons between different clinical improvement studies, and will be crucial for clinical practice in making more informed health decisions.

Conclusions and implications

Combining all currently available evidence on existing quality improvement initiatives for continuous sedation until death with elaborate and in-depth qualitative data from 141 health care professionals involved, we have developed a practice protocol for the use of continuous sedation until death in nursing homes. The protocol contains seven sequential steps and meets the specific needs and context of care in nursing homes. Having developed and modelled this specific intervention for the nursing home setting, further steps include evaluating implementation, feasibility and effectiveness.

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Annex 1

PROTOCOL – Palliative sedation in nursing homes

OBJECTIVE OF THIS PROTOCOL

This protocol is intended as a care guideline to facilitate **palliative sedation** in **residential care homes** and to **support** you as a caregiver (doctor, nurse, carer) with **communication, decision-making and implementation**.

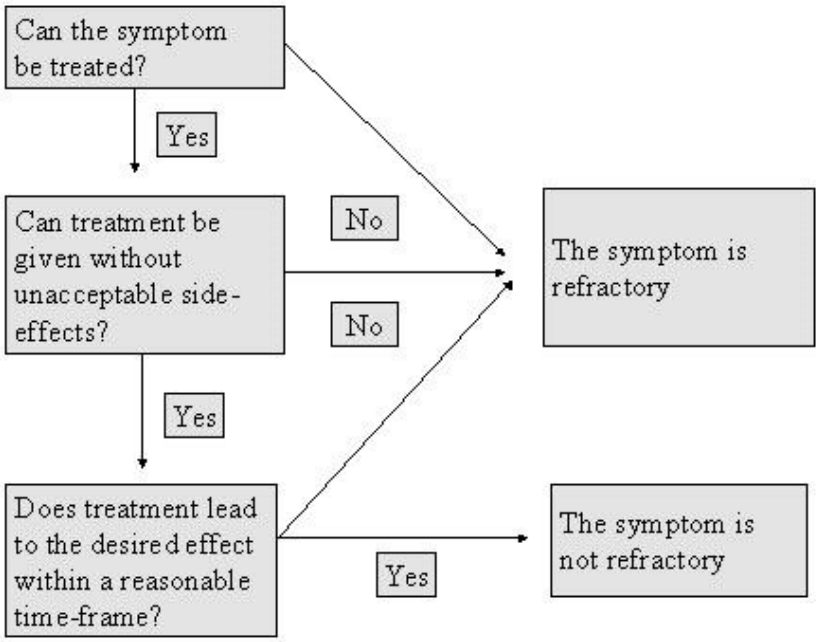
WHEN DOES THE PROTOCOL APPLY?

In this residential care home, this protocol is **coordinated by** XXXXX, who is approached as soon as possible **refractory symptoms arise** (see figure 1) and **palliative sedation is proposed** as a **possible option** to alleviate the resident's suffering in the last phase of life. The protocol is specifically aimed at optimising continuous sedation until death.

CONCEPTS AND DEFINITION

Palliative sedation is '*the administration of sedatives in doses and combinations required to reduce **a patient's** consciousness to the extent necessary to control **one or more refractory symptoms** adequately*". (More info: www.pallialine.be)

Figure 1: Refractory symptom



STEP-BY-STEP PLAN

STEP 1: CLARIFICATION OF THE MEDICAL AND SOCIAL SITUATION

From the time that sedation is raised as a current option by one of the caregivers or the patient / next of kin, a preparatory **consultation** must be held with **the resident** (if still possible) **and his/her next of kin**, in which both the resident's medical situation and their social situation are discussed. Although the decision to proceed to palliative sedation until death is mainly **a medical decision**, it is the patient him/herself who feels the complaints most clearly and can assess the value of the treatments best.

The **decision to proceed with palliative sedation** is **based on** the following points:

- ***Resident's illness:***
  - What is the resident's disease profile?;
  - Intensity of the symptoms;
  - Can the resident's complaints still be alleviated or treated in another way and can the symptoms therefore be seen as refractory?;
  - Are they close to death (one to two weeks)?
- ***Resident's experiences:***
  - The impact of the symptoms on the resident's quality of life, the resident's suffering and the resident's dignity;
  - Does the resident consider the symptoms to be unbearable?
- ***The resident as a person:***
  - What goals and expectations does the resident still have?;
  - Are the patient's wishes perhaps included in an advance care plan (if completed)?

Furthermore, it is important for **consultation** to take place with **caregivers who are closely involved in caring for the resident** in order to obtain as complete a picture as possible of the resident's medical situation. This allows the ultimate decision to proceed to palliative sedation to be optimally argued and supported. Ensure that the **intention** is discussed clearly. Palliative sedation is intended to **reduce consciousness** as far as necessary to render the resident unaware of his/her symptoms.

Palliative sedation until death is not an everyday practice and **requires a certain degree of experience and specific knowledge** from all the professional caregivers involved. For example, symptoms that are difficult to treat are not always necessarily refractory symptoms. In the event of questions or doubts, it is **advisable to consult palliative care experts** (for example the regional multidisciplinary coaching team or the palliative care reference person in the care home) **and/or disease-specific experts**.

In this residential care home, you can turn to the following persons for this:

1) Coordinating and advisory doctor (CAD) XXXX (tel.: XXX)
2) Head nurse XXX (tel.: XXX)
3) Palliative Care reference person within this residential care home: XXXX (tel.: XXX)
4) Multidisciplinary support team: XXXX (tel.: XXX)

STEP 2: COMMUNICATION WITH ALL CAREGIVERS INVOLVED

It is advisable to organise a short, **formal consultation with everyone involved who is able to attend:** both **all caregivers** closely involved in the resident's care and, if possible, **next of kin**. It is important for **everyone involved who is unable to attend to be informed** after this briefing.

The goal is to **coordinate** the following:

- the **indications** for the application of palliative sedation until death
- the extent to which the symptoms are **refractory**
- the **limited life expectancy** of the resident (one to two weeks)?
- whether palliative sedation until death is the **only possible option** that corresponds to the wishes of the resident and/or next of kin.

In complex situations or where caregivers have questions or doubts, cooperation with the **multidisciplinary palliative coaching team** in the region may be considered.

Make clear **arrangements with the next of kin and all professional caregivers**, both in terms of the role of everyone concerned (including the next of kin), their contact details, availability and transfer of care, as well as clear arrangements with all caregivers involved concerning the evaluation of the symptom-controlling effect. Also ensure that this is closely monitored throughout the entire period of palliative sedation. Given their emotional bonds with the resident, allow other carers to choose whether they want to take on a role and what role this should be. Arrange with the next of kin who they can contact if anything happens.

STEP 3: COMMUNICATION WITH THE RESIDENT AND/OR NEXT OF KIN

The decisions made in STEP 2 must always be communicated to the resident or, if communication with the resident is no longer possible, with the next of kin.

Find out about the wishes, expectations and uncertainties of the resident and/or next of kin, and explore whether the next of kin want to be involved in care, for example moistening the resident's lips.

Discuss with the resident and/or next of kin **who the contact person is** who can be approached in the event of questions or problems during sedation: both the contact person among the next of kin and the contact person at the residential care home.

Explain to the resident (if this is still possible) or, if necessary, to the next of kin:

- ... that the **aim** of palliative sedation until death is only to **alleviate unbearable, untreatable symptoms** by **reducing the resident's consciousness**.
- ... how you will administer the drugs and what effect they will have. Make it clear that **stable sedation is not always achieved immediately** and that the **time until death is highly variable.**
- ... that during palliative sedation until death, **fluids and food are not usually artificially administered** or such administration is ceased. Make it clear to the resident that stopping fluids and food will not cause any extra suffering.

Lastly, summarise what has been **agreed** with the resident and the family and **record this in the resident's file.**

Make the necessary practical arrangements for the place and time of implementation. If available, also give the next of kin a brochure or information that they can refer to again after the conversation.

STEP 4: ORGANISATION AND COORDINATION OF CARE

Check whether **all the relevant information** concerning the resident, his/her condition, the decision regarding palliative sedation until death, the medical prescription for implementation, the evaluation and any adjustments to the dosage are **recorded in the file.** Determine what drugs will be used and how they will be administered. If in doubt, contact the multidisciplinary coaching team. **Ensure that you get hold of these drugs in good time and in sufficient quantities.**

Go over all the arrangements made with the next of kin and all the professional caregivers again, in terms of everyone's role, contact details and availability during sedation, as well as specific arrangements concerning follow-up and monitoring.

Be sure to provide a **serene setting**. Give the resident and next of kin another opportunity to ask questions or express concerns. Check whether everyone directly involved is aware of the time when sedation will begin and how sedation will proceed. Ensure, in consultation with the resident and/or family, that people other than family who have a special relationship with the resident **(other residents, caregivers and volunteers)** can say goodbye. Discuss with the team how **farewells** can be organised **before sedation begins.**

STEP 5: ACTUALLY IMPLEMENTATION OF SEDATION

Cease all medical and nursing activities and all medication that is not having a clearly positive effect on the patient's comfort. Continue the specific treatment of symptoms experienced by the patient (such as pain, nausea, shortness of breath etc.) with the appropriate medication.

In palliative sedation, the aim is a proportionate, step-by-step approach (see medication scheme, figure 2). The proportionate, step-by-step approach means that the lowest level of medication is to be applied that provides optimal comfort for the patient (figure 2, level 6). If a given step and dosage does not achieve or no longer achieves the desired comfort, this dosage can be increased (bolus and maintenance dose) or, if the maximum dose in the step concerned has been reached, the next step can be taken.

In that case, **consider consulting the multidisciplinary coaching team.** In this way, palliative sedation is and always remains in proportion with optimal comfort for the patient. It is best to administer the sedatives using a separate pump.

Figure 2: Medication schedule according to the Palliative Sedation Directive (more info: www.pallialine.be)

	Drug	Induction (bolus)	Maintenance dosage (syringe driver)
Stage 1 *Light and deep palliative sedation*	Midazolam (Dormicum®)	At the start of light palliative sedation: - 2.5 mg SC - 1.25 mg IV	After starting sedation (with starting bolus), 1/2 of the total (!) starting

		At the start of deep palliative sedation: - 5 to 10 mg SC - 2.5 to 5 mg IV If the effect is insufficient after 5 min. (IV) up to 1/2 h (SC), add half the starting dose. It is not uncommon to give 2 to 3 additional boluses during the first hours of sedation (even if the maintenance dosage is not increased afterwards).	dose per hour as a maintenance dose. This total starting dose includes the dose given during the 1st two hours (SC) or the 1st half hour (IV). Maintenance dose for light sedation 60 mg/d SC or 30 mg/d IV; maintenance dose for deep sedation 60 to 240 mg/d. For example, (light sedation): at the starting dose of 2.5 mg SC where 2 x 1.25 mg was added to achieve sufficient effect, the total starting bolus is 5 mg. This includes a maintenance dosage of 2.5 mg/h or 60 mg/d.
		If the dosage is adjusted:	
		Increase induction: for each increase, one bolus should be given (1/2 of the total starting dose).	Increase or decrease maintenance dosage by half.
Stage 2 *Deep sedation. Always together with midazolam.*		In consultation with team doctor.	
	Clotiapine (Etumine®)	20 mg SC or IV	40 to 160 mg/d
	Levomepromazine (Nozinan®)	25 mg SC or IV	25 to 200 mg/d
Stage 3 *Deep sedation*	Anaesthetics	In consultation with and by anaesthetist.	

(more info: www.pallialine.be)

Close monitoring is crucial. Evaluate the **level of sedation** regularly. The **Richmond Agitation-Sedation Scale (RASS) can be used** for this evaluation, in order to standardise the assessment.

Figure 3 Richmond Agitation-Sedation Scale (RASS)

Ramsay score	Level of sedation
1	Anxious, agitated, restless
2	Oriented, tranquil
3	Responds to commands
4	Brisk response to light glabellar tap
5	Sluggish response to light glabellar tap
6 (deep sedation)	No response

(Ramsey et al. 1974)

Possible expressions of discomfort in the patient including a frowning expression, groaning, restless movements, muscular tension). Check regularly whether these expressions are under control. In doing so, monitor the patient's level of consciousness and adjust it if necessary.

Check regularly whether the **administration route and resorption of the medication** is working properly and that there are no disturbing factors (such as a full bladder, constipation etc.) **If the palliative sedation lasts for a longer period** (more than three days), take into account a **cumulative effect** and reduce the dosage if necessary.

STEP 6: SUPPORTING NEXT OF KIN AND CAREGIVERS DURING SEDATION

Besides implementation itself, palliative sedation also involves consoling and supporting the resident's family and friends during implementation. Next of kin may experience feelings of doubt, guilt, fear, sadness and grief when the decision is made to initiate sedation. However they may also feel relief that their loved one's suffering is going to end. **Information**, explanations, co-operation and **constant evaluation of the situation** are **essential** here to ensure that **palliative sedation proceeds serenely** and to give everyone involved a meaningful farewell.

Next of kin can be an **important source of information** on the patient's welfare. It is useful to call in often for periodic updates on the state of affairs or to be able to discuss new situations that arise with them. It also offers the opportunity to attend to the welfare of the next of kin as a professional caregiver and to support them in that way, for example by encouraging them to take care of themselves. **Speak to colleagues if you notice that they are experiencing difficulties.**

STEP 7: AFTERCARE (FOLLOWING DEATH)

Invite the next of kin for a conversation after death. Enquire about how the next of kin experienced the entire disease process, more specifically the sedation, and any problems they may have encountered. Surviving next of kin may develop feelings of guilt along with their grief that can exacerbate the grieving process. Where necessary, you may consider referring the next of kin to possible support from a psychologist, grief consultant or spiritual care.

The confrontation with death in general and palliative sedation in particular may also be confrontational for the various caregivers, leaving a strong impression. That makes it **useful to be able to talk about personal experiences with other people.** Organising a team meeting may offer an opportunity to talk through what has happened and look at what went well and what can perhaps be done better in the future.

CHECK-LIST

STEP 1: CLARIFICATION OF THE MEDICAL AND SOCIAL SITUATION

□	Death expected within 2 weeks.
□	1 or more refractory symptoms are present: □ physical □ dyspnoea/choking sensation □ pain □ nausea/vomiting □ bleeding □ confusion/delirium □ exhaustion □ other: □ mental/existential/social □ disquiet □ other: □ fear
□	Palliative sedation is in accordance with the wishes of the resident and next of kin.
□	In the event of questions or doubts, a consultation is requested with the multidisciplinary support team in the region.

STEP 2: CONSULTATION WITH ALL CAREGIVERS INVOLVED

□	A consultation is organised with everyone involved as indicated.
□	There is a consensus among the treating team.
□	In the event of questions or doubts, a consultation is requested with the multidisciplinary support team in the region.
□	Palliative sedation is in accordance with the wishes of the resident and/or next of kin.
□	Agreements have been made with next of kin and care providers and recorded in the file about: □ the allocation they wish to fulfil; □ contact details and availability of the treating physician during sedation; □ who can contact next of kin if anything happens; □ the transfer of care; □ the evaluation of symptoms and depth of sedation.

STEP 3: COMMUNICATION WITH RESIDENT AND NEXT OF KIN

□	There is communication with the resident and/or next of kin concerning the decision and decision-making regarding palliative sedation
□	Find out about the wishes, expectations and uncertainties of the resident and next of kin, and draw up a report of the conversation.
□	There is communication with the resident and/or next of kin concerning implementation: □ the aim is to alleviate the resident's suffering and ensure their comfort; □ it can sometimes take a while before the desired effect is achieved and the resident may wake up sometimes; □ sedation can sometimes last a few days or even longer; □ enteral of parenteral administration of fluid or food is stopped and this does not lead to feeling thirsty or hungry; □ palliative sedation does not hasten the time of death and in that sense it is not an alternative to euthanasia;

	□ the waiting can become difficult (advise the use of a rotation scheme for attending the patient).
□	One contact person is appointed among the next of kin and one among the caregivers for communication.
□	The family is given a brochure containing all the information about the sedation.

STEP 4: ORGANISATION AND COORDINATION OF CARE

□	Check whether all the relevant information concerning the patient is present in the file.
□	The necessary medication and the materials for administration and monitoring are present in sufficient quantities.
□	Repeat the arrangements made with the next of kin and caregivers in step 2.
□	The time of initiating sedation has been discussed with everyone involved.
□	Ensure a serene atmosphere and make sure that both next of kin and other people who have a special relationship with the resident have been able to say their farewells.

STEP 5: IMPLEMENTATION OF THE SEDATION

□	The current treatment of symptoms with medication (specifically opioids or haloperidol) is theoretically continued independently of the sedation. All other medication is ceased.
□	Any artificial administration of fluids or food is ceased
□	If necessary, a urinary catheter is introduced after the patient has been sedated.
□	A step-by-step approach is taken in accordance with the medication scheme in the Flemish palliative care guidelines.
□	The effect of sedation is initially evaluated every 2 hours until sufficient comfort for the resident is achieved. This is important when administering a bolus (every 2 hours) and the need to state the maintenance dose (every 4 hours).
□	The care is evaluated every day in accordance with the arrangements made and recorded in the file.
□	The symptoms, depth of sedation and level to which the resident reports comfort (or discomfort) are closely monitored. Is the symptom under control?
□	Check regularly whether the administration route and resorption of the medication is working properly.
□	If the ongoing sedation lasts for a longer period (>3 days), take into account a cumulative effect and reduce the dosage if necessary.

STEP 6: SUPPORTING NEXT OF KIN AND CAREGIVERS DURING SEDATION

□	Observe the burden / ability to bear the burden in next of kin and caregivers.
□	Make sure the next of kin and caregivers are able to talk about their concerns and fears.

STEP 7: AFTERCARE

□	The next of kin are offered the opportunity for an aftercare conversation.
□	Evaluate the decision-making, communication and implementation of the palliative sedation until the death of the resident concerned with all the care professionals involved. Discuss what went well and what can be done better in the future.

PART IV

General discussion and conclusions

CHAPTER 8

General discussion and conclusions

8.1. Introduction

The central aims of this dissertation were to study the practice of continuous sedation until death in Belgium and to develop an evidence-based clinical practice tool to support the practice in nursing homes. The specific research aims were:

1. To describe the characteristics of the decision-making about and performance of continuous sedation until death in Flanders, Belgium and to examine changes over time (Chapter 2);
2. To explore how professional stakeholders justify their use of continuous sedation until death and to explore which factors play a part in the decision to start continuous sedation (Chapter 3);
3. To explore the role of patients in the decision-making preceding continuous sedation until death in Belgium, and compare Belgium with the Netherlands and the United Kingdom (Chapter 4);
4. To give a systematic overview of existing initiatives that aim to support the practice of continuous sedation until death within end-of-life care (Chapter 5);
5. To examine experienced barriers to the decision making and performance of continuous sedation until death in Flemish nursing homes according to physicians, nurses and other nursing home staff (Chapter 6);
6. To develop a potentially feasible, acceptable and effective evidence-based practice protocol for the use of continuous sedation until death in nursing homes (Chapter 7).

In this part of the dissertation the main findings of the included studies are discussed. First, the methodological strengths and limitations of the studies presented in this dissertation are considered, followed by a summary of the main findings. Finally, the importance and relevance of the findings in the light of the current state of affairs within research on continuous sedation and their implications for practice, policy and future research are discussed.

8.2. Methodological considerations, strengths and limitations

To answer the research questions of this dissertation, several methods and different study designs were used. Chapter 2 was based on results of a mortality follow-back study using a representative sample of death certificates. Chapter 3 and 4 show the results of qualitative interviews with physicians, nurses and relatives within the UNBIASED study. Chapter 5 used a systematic literature review to provide an overview of existing quality improvement initiatives for continuous sedation. In Chapter 6 a focus group methodology was used to gain in-depth insights into perceived barriers for the use of continuous sedation within nursing homes. The protocol developed within this dissertation was validated by expert panels in Chapter 7. In the following paragraphs, key methodological considerations, strengths and limitations are discussed.

8.2.1. End-of-Life Decisions study, a mortality follow-back survey based on death certificates

8.2.2.1. Strengths of the study

In Chapter 2, we report the results of a mortality follow-back survey using a representative sample of death certificates that has repeatedly been proven to allow reliable estimates of incidences of end-of-life decisions, including continuous deep sedation until death, representative for an entire population or time period.[1–4] The questionnaire used is validated and entails same set of key questions from questionnaires, including the same descriptive definition of continuous deep sedation until death, used in previous European studies, allowing international comparison. [1–4] A major strength of this study is the use of death certificates.[5,6] Firstly, the unit of measurement in a death certificate study is evidently the death case, which provides a clear and uncomplicated denominator for epidemiological research.[5] In contrast for instance in studies based on a survey of physicians reporting on their last attended death, the unit of measurement is the physician, and there are some problems in extrapolating representative incidence estimates from the findings, as physicians can differ in the number of deaths they attend

to, whereas the death certificate method allows sampling of deaths within a fixed period in time.[5,7] 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 the end of life. Patients' and physicians' anonymity is safeguarded by a complex mailing procedure and the involvement of a lawyer bound by confidentiality. Ensuring anonymity will have encouraged physicians to participate in the study and will have reduced the chances of underreporting end-of-life practices or socially desirable answers.[5] Don A. Dillman's Total Design Method was followed in order to limit nonresponse as much as possible by using an intensive follow-up mailing procedure of three reminders per death case, further strengthening the study design and its findings.[8] A non-response survey was also performed in which it was found that physicians most frequently indicated lack of time as reasons for non-participation. Comparison of the response and non-response cases revealed no significant differences in sex, age and cause of death, and only slight differences in terms of place of death and province.[9,10]

8.2.2.2. Limitations of the study

Although this study used a robust population-based sampling method, a number of study limitations have to be taken into account. Recall bias and memory bias may have influenced our study results.[9,10] With regard to recall bias, physicians are asked questions about a death that occurred some time before filling in the questionnaire. Physicians' recollections of the specific circumstances of decision-making and end-of-life care before the patient's death may have been incomplete.[11] Certain memories may be enhanced or impaired due to errors in physicians' own perception of the medical act.[9,10] To mitigate recall bias and memory bias, physicians routinely received the questionnaire no later than eight weeks after the patient's death.[5] Also, physicians were encouraged to consult the patient's medical file when filling in the questionnaire. 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 use of death certificates entails some disadvantages. Firstly, the physician who completes the death

certificate is not always the attending physician. To overcome this problem, physicians were asked in the letter accompanying the questionnaire to pass on the questionnaire to the treating physician in case the certifying physician was insufficiently informed on the end-of-life care and the decision-making of the patient. [9,10] Secondly, using the death case as the unit of measurement implies that one physician can have certified multiple deaths in the sample. In this study, the maximum number of death cases one physician could be asked to report on was limited to five. Responder fatigue even before the physician reaches this cut-off occurred.[5,12] It was observed that mainly after three death cases response dropped considerably.[10] Thirdly, sensitivity of survey topics may introduce untruthful or socially desirable reporting, but this is unlikely in our study given the explicit guarantee of anonymity.[7]

8.2.2. The UK- Netherlands-Belgium International Sedation Study (UNBIASED), qualitative interviews with physicians, nurses and relatives

8.2.2.1. Strengths of the study

The UNBIASED study is a cross-national interview study undertaken in the United Kingdom (UK), The Netherlands and Belgium exploring decision-making surrounding the practice of continuous sedation until death in contemporary clinical practice (home, hospital and specialized palliative care setting) from different perspectives (physicians, nurses and relatives).[13,14] Chapter 3 and 4 report on the results from the case study phase of the UNBIASED study, which 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.[15,16] In all countries, senior clinical staff members identified eligible decedents: patients aged over 18 who had died of cancer and to whom sedating medications were administered continuously with the intention of decreasing awareness to alleviate otherwise uncontrollable symptoms, and for whom the sedation was in place at the time of death.[13,14,16,17] By purposively 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, we were able to compare the practice of continuous sedation until death in these settings, between but also within the studied countries. In order to get a broad and detailed overview of each case, we included the recollections of physicians, nurses and relatives involved in the care of a particular person.[16,17] Also, cases in each country were sampled 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. The semi-structured interviews were guided by a topic guide containing similar 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 the practice of continuous sedation until death. Also, it allowed us to be sensitive to the language that was used by the interviewee and to explore it in depth.

8.2.2.2. Limitations of the study

There are a number of limitations to this study, which stem partly from the sensitivity of the subject and partly from the methodological challenges of studying a phenomenon which is associated with such intense debate about its definition, indications and practice.[13] The interview data were dependent on the subjective experiences and interpretations of the respondents, which is inherent in qualitative research.[17] There is a small risk of recall bias, although this was limited in most cases by limiting the time between death and the interview to 3 months.[14,17,18] Perhaps the most challenging and yet most interesting aspect concerns matters of definition and meaning: achieving consensus and thus comparability across cases and between national studies is likely to be difficult given the range of current understandings about the meaning and appropriateness of sedation in end-of-life care and the different interpretations of refractory symptoms and distress.[13,14,19] The study therefore used a general description of the practice across all countries and settings: "*the continuous administration of sedating medications with the intention to decrease*

awareness to alleviate otherwise uncontrollable symptoms, either physical or psychological/existential, and where the sedation was in place at the time of death".[13,14,17]

8.2.3. A systematic literature review of existing quality improvement initiatives for continuous sedation until death

8.2.3.1. Strengths of the study

To identify the existing literature concerning initiatives that support, facilitate or even improve the practice of continuous sedation until death, a systematic literature review was carried out in Chapter 5. The search was comprehensive and broad in terms of databases, year range and study design to ensure the search captured all relevant research evidence. Records were searched through MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL and the Web of Science Core Collection to ensure inclusion of medical, social science and bioethics literature. The search key was initially developed in MEDLINE and later adapted for other databases with support from an Information Specialist. We used a strong methodology based on the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA)[20] for the study design and the reporting of the results. An important strength of the study is that all required methodological steps to complete a systematic review were implemented and performed separately by two reviewers (LR and AS).[21] The titles and abstracts of all identified reports were screened independently by these two reviewers using a standardized study selection form, as well as the eligibility of selected studies.[21] Disagreement was resolved by discussion and a third reviewer (KC) was available for arbitration. The characteristics of the studies included were extracted to a standardized data-extraction form under the headings of general information, country, type of research, method, research question (aim), setting, participants and scope of the study. Quality improvement initiatives were reported as mentioned in the article. We performed quality assessments by using the QualSyst tools for assessment of the quality of both qualitative and quantitative studies. We believe our review represents a

comprehensive picture of types of initiatives that have been undertaken and that have been scientifically evaluated.

8.2.3.2. Limitations of the study

Our review focused on existing initiatives that enhance or facilitate the practice of continuous sedation in nursing homes. However, a gold-standard core outcome set reflecting the overall quality of continuous sedation is currently lacking. Another noteworthy limitation is that this review did not always gain insight into the detailed content of all initiatives. However, this had no significant impact on the results of our review as the research questions were mainly aimed at giving an overview of existing initiatives and what we know about these initiatives in terms of acceptability and effectiveness. Also, in the literature, several terms are used for continuous sedation, for example, palliative sedation or terminal sedation, potentially limiting full comparison and extrapolation of the studies. Lastly, we did not define a minimum quality threshold for study inclusion. Such quality scores would not have reflected the quality of the initiatives described in these studies, but would have indicated the extent to which the design, conduct and analyses minimize errors and biases. As a result, the findings of this review were derived from research papers of potentially variable quality.

8.2.4. Focus groups among professional stakeholders in nursing homes

8.2.4.1. Strengths of the study

A key strength of this focus group study was that it included the perspectives of a diverse range of people who are important actors in the care for people near the end of life in nursing homes, including palliative care physicians, general practitioners, nurses and care assistants). Focus groups were used as a method for data collection among all targeted groups because they stimulate the exchange of views and opinions through discussion and allow mutual differences or similarities to drive the conversation and allow salient themes to emerge. Another key strength

is the number of focus groups and participants in the study. Ten focus groups were conducted, involving a total of 71 participants including 16 palliative care physicians, 42 general practitioners and 13 nursing home staff members ensuring a large number and wide variety of perspectives represented in the data. The multidisciplinary composition of the research team (consisting of medical sociologists, a GP and a health scientist, all with experience in qualitative research) guaranteed interpretation of data from a range of perspectives.

8.2.4.2. Limitations of the study

The limitations of this study include the potential for socially desirable answers by focus group participants and participants may have been reluctant to state their true opinions.[22] Even without this type of bias, the opinions we gathered are not necessarily reflective of the actual behaviour of the participants in their clinical practice.[22] Another potential limitation is that the focus groups were internally homogeneous in terms of disciplines. This was done to represent clear perspectives through each focus group that could be compared in the analysis, and to avoid letting power imbalances (for instance between the physician and nurse) influence the conversation. However, it is possible that there exists conflict in views and opinions between the various disciplines that did not emerge due to the homogeneous set-up and were therefore not captured by the researchers. Although the expert panels were purposively sampled, not all relevant experts, such as patient representatives and relatives, were represented. The size and religious affiliation of nursing homes were taken into account for the sampling plan, because of the possibility that these factors result in different attitudes and knowledge among health care professionals.[22] However, despite our best attempts, we were not able to find institutions with a religious affiliation willing to participate in a focus group discussion.[22]

8.2.5. Expert panels to validate a practice protocol for continuous sedation in nursing homes

8.2.5.1. Strengths of the study

We developed a preliminary practice protocol adapted to the specific context of nursing homes and based on existing guidelines. The model was further refined at monthly meetings with the multidisciplinary research team consisting of medical sociologists, a health scientist, a geriatrician and a general practitioner. We also held ten expert panels with a wide variety of stakeholders (n=70) representing palliative care physicians, geriatricians, general practitioners and nursing home staff following a participatory approach to explore how the model meets their own experiences and expectations, and to brainstorm about how to further improve the intervention model.[23] This allowed us to co-develop our protocol with potential end-users. It has been argued that such a participatory stakeholder approach enhances feasibility, and even the effectiveness of the intervention because the content of the protocol is strongly grounded in daily clinical practice.[24,25] The final protocol was signed off by expert panel after two consultation rounds in which remaining issues were ironed out.

8.2.5.2. Limitations of the study

Although the expert panels were purposively sampled, not all relevant experts, such as patient representatives and relatives, were represented. Recent literature, however, has shown that it is feasible to include older people, including those with dementia and their family caregivers, when co-designing an intervention regarding end-of-life care.[26] Involving patients and family caregivers in this process would have made it possible to identify outcomes that matter most to them. Finally, our protocol is not directly generalizable to other countries, because some elements are specific to the context of Flanders, Belgium (e.g. the use of the term 'reference person', the unique role of reference persons in nursing homes, or the fact that GPs are not part of the regular care team in the nursing home).

8.3. Summary of main findings

8.3.1. Trends in the prevalence and characteristics of continuous deep sedation until death in Flanders, Belgium.

In **Chapter 2** we reported on the results of a population-based mortality follow back study in 2013.[6] We compared these with the results of an identical study conducted in 2007. Response rate was 60.6% (3751/6188 eligible cases) in 2013 compared with 58.4% in 2007. We found that after the initial rise of continuous deep sedation until death between 2001 and 2007 from 8.2% to 14.5%, its use decreased to 12.0% in 2013.[6] The decrease particularly occurred in women, widowed people, those dying in nursing homes and the more highly educated. In 2013, compared with 2007 opioids were less often used as sole drug and the decision to use continuous deep sedation was more often preceded by an explicit patient request. In general, we observed a number of developments in the practice of continuous deep sedation between 2007 and 2013 which are favourable in light of the recommendations described in the existing guidelines, including the 2010 Flemish guideline. However, our study suggests that there still is room for further improvement, particularly in the use of recommended drugs, seeking consent and leanings toward hastening death. We also studied the decision-making and performance characteristics in relation to the degree of palliative care training of the treating physician. Compared to non-experts, palliative care experts more often used benzodiazepines and less often opioids, withheld artificial nutrition or hydration more often and more often performed sedation with the consent of the patient or family. Palliative care training was thus associated with end-of-life sedation practices more congruent with recommendations.[6]

8.3.2. How do health care professionals justify their use of continuous sedation until death?

In **Chapter 3** we explored the insights of 28 physicians and 22 nurses to explore how these health care professionals justify their use of continuous sedation and to study which factors play a part

in the decision to start continuous sedation until death.[16] Physicians and nurses in our study justified the use of continuous sedation until death by referring to the presence of a broad range of clinical indications, mentioned also in various international guidelines. However, we identified a number of issues they experienced in applying the conditions. First, respondents found it rather difficult to assess the 'unbearableness' of the patient's suffering since this could only be experienced by patients. Our results suggest that the decision to start continuous sedation is not always based solely on the actual suffering but often also on the need to prevent future suffering. Second, continuous sedation until death was considered appropriate only if a patient had a short life expectancy, yet estimating an exact prognosis was often considered difficult as it depends on several characteristics of the dying phase. Although physicians should always try to act in a rational and clinically justified manner, the results also suggest that the social context and the personal characteristics of individual patients also determine the outcome of a decision making process. For instance, physicians and nurses were sensitive to a patient's personality and 'how they had lived their lives' and they reported being often confronted with patients who 'really cannot handle the dependency'. A final notable result relates to the finding that continuous sedation until death was in some cases resorted to when euthanasia was not an option, either due to the patient losing capacity after euthanasia had been requested or because of practical matters. In summary, our findings in this chapter indicate that medical decision-making for continuous sedation is not only based on clinical indications but also related to morally complex factors contributing to decision making such as the social context and the personal characteristics and preferences of individual patients and their relatives.[16]

8.3.3. What is the specific role of patients in the decision-making process preceding continuous sedation until death?

In **Chapter 4** we described the decision-making process preceding continuous sedation until death with particular attention to the involvement of the person who is dying and compared practices in Belgium, the Netherlands and the United Kingdom (UK).[17] We used the Charles et al[27]

model of treatment decision-making that allowed us to scrutinize the different phases of decision-making and apply them to the process of continuous sedation. Our study distinguishes four stages of decision-making: the initiation phase where the issue is raised, the exchange of all necessary information, the deliberation phase in which it is decided to use continuous sedation when it becomes appropriate and the decision to begin continuous sedation.[17] Although the overarching goal of continuous sedation at the end of life was similar in all cases, there was considerable variation in the timing and the role played by the patient in the decision-making. At one end of the spectrum, decision-making was primarily clinical and physician-driven; the physician discussed the possible use of sedation with the patient but took the final decision him/herself. These cases were especially prevalent in the UK, where respondents reported a gradual process of sedation, from the provision of low doses of sedatives to the more rarely used continuous deep sedation. At the other end of the spectrum, the patient initiated the conversation about the use of sedation while the physician's role was predominantly limited to evaluating whether, and when, the patient's condition fulfilled the medical criteria. These cases were mostly from Belgium and the Netherlands, where patients were sometimes offered the 'choice' of sedation.[17]

8.3.4. What initiatives are there that aim to support, facilitate or improve the practice of continuous sedation until death in end-of-life care?

In **Chapter 5** we included 21 studies in our systematic review and we identified three types of existing initiatives to support the practice of continuous sedation until death within end-of-life care: nine initiatives were focused on assessment tools of consciousness and discomfort, eight initiatives were focused on the use of a general guideline or setting-specific protocol; and three initiatives were focused on clinical decision making consultation. Both observer-based sedation scales and the use of monitoring devices assessing consciousness and discomfort are considered to be very useful, acceptable and feasible to patients, relatives and medical staff. Studies on the use of monitoring devices showed that a small proportion of patients were found to be awake, despite the patient being unresponsive according to the observer-based sedation scales.

However, norm values for continuous sedation are not yet available and the wide range of values of these monitoring devices for comfortable and adequately sedated patients seems to hamper its overall implementation in daily clinical practice. Guidelines and setting-specific protocols are regarded as supportive, however, not all physicians are aware of their existence. In general, a high level of compliance to different protocols and general guidelines was found. Physicians reported changes in palliative sedation practice conform the guideline recommendations but the shift was modest at best. Expert consultation is regarded as supportive and helpful especially when sufficient experience is lacking. These studies suggest that expert consultation can ensure that all options are exhausted and the conditions for sedation to be fully clarified and clear avoiding possible unnecessary sedations. In conclusion, the reviewed initiatives may contribute to improvement of continuous sedation until death practice, though their evidence base is rather limited.

8.3.5. What are the perceived barriers to the decision making and performance of continuous sedation until death in Flemish nursing homes?

In **Chapter 6** we identified perceived barriers to decision making about and performance of continuous sedation until death in nursing homes. Barriers were classified on three levels including personal barriers related to knowledge and skills, relational barriers concerning communication and collaboration both between professionals and with the family, and organizational barriers related to the organization of care in nursing homes.[22] We found a lack of clarity and conceptual ambiguity among the health care professionals about what sedation is, what it should be used for and how it should be used. For example, there is a lot of confusion about how continuous sedation relates to regular symptom control on the one hand and euthanasia on the other. Our study shows that this ambiguity may even be more complex in the nursing home setting where a huge variety of actors are involved in the care of the resident, each with their own emphasis and interpretation of the concept of sedation. Even without this conceptual ambiguity, our results show that the decision making and performance of sedation is

much more complex in a nursing home population, both in terms of assessment of frail older persons (for example, determining whether a symptom is refractory, estimating the remaining life expectancy, or finding the right dose in residents who are very old and frail and often habituated to medication) and of collaboration and communication between health care providers. Our study clearly shows that physicians and nurses do not consider themselves sufficiently prepared and trained in dealing with family, for example, they are uncertain how to involve them in decision making and how to handle their emotions or conflicting views. Thus, our findings suggest that there are considerable challenges for sound decision making about and performance of continuous sedation until death in nursing homes.[22]

8.3.6. The development of a practice protocol adapted to the specific needs of nursing homes.

In **Chapter 7** we describe the development process and the contents of an evidence-based practice protocol to support healthcare professionals in the decision-making, communication and performance of continuous sedation until death in nursing homes. The protocol is based on insights from the literature on existing quality improvement initiatives (Chapter 5), on the results of a qualitative study on perceived barriers for the use of continuous sedation in nursing homes (Chapter 6), and close involvement of 70 stakeholders in the development and refinement of the protocol. The protocol contains seven sequential steps and meets the specific needs and context of care in nursing homes; While the essential parts of the protocol are consistent with existing guidelines and protocols, our protocol describes more comprehensively recommendations about issues in practice, coordination and cooperation particularly pervasive in nursing homes, common terminology and understanding what continuous sedation is and its modalities are, communication between health care professionals and with family as well as specific matters such as attention on how to communicate with fellow residents and giving them the opportunity to say goodbye to the dying person in some way. Having developed and modelled this specific intervention for the nursing home setting, it will be important to develop profound

implementation strategies and on evaluating the protocol's effectiveness thoroughly in a phase II trial.

8.4. Discussion of findings in the light of current challenges and state of affairs

In the following sections, some reflections on the findings of this dissertation are provided. In each section, an in-depth discussion will be presented on one of the topics studied in this dissertation.

8.4.1. Patients' involvement in decision making and patient requests for continuous sedation

Palliative care has become an important part of health care in many countries, aiming to ensure that at the end of life, people receive high-quality, appropriate care that is in line with their wishes and values and which relieves their suffering.[28] People are entitled to be the architects, as much as possible, of how they die.[29] Patient involvement is deemed particularly and increasingly important towards the end of life because these decisions involve extensive uncertainty and are heavily influenced by personal values.[30–32] Guidelines for sedation emphasize that the decision to initiate continuous sedation should be in accordance with the wishes of the patient and be preceded by their consent or the consent of a surrogate decisionmaker if they lack decision-making capacity.[17,33–35] Epidemiological findings show, however, that patient consent is not always sought and obtained by the physician. The findings from Chapter 2 have shown that patient or family consent was still lacking in 16.2% of all sedations in 2013 (versus 19.8% in 2007).[6] Continuous sedation is often used for patients who suffer from severe pain and for whom pain management has failed.[36] However, if pain is severe enough, reflective, unimpaired consent may be impossible, necessitating surrogate decision-making.[37] Last resort considerations as well as double effect considerations can survive perfectly in the absence of consent.[29,38,39] Autonomy-based considerations, which emphasize the need for consent, are independent from, and

supplementary to, the lines of reasoning implied in last resort and double effect considerations.[29,37,38,40] According to Margaret Battin, even when consent to continuous sedation at the end of life is obtained, the patient may not have been well informed, or may even have been misled with respect to what she is consenting to.[29,38]

Another main problem in these sedation guidelines is that they rarely state the extent to which patient preferences should be taken into account, how to do it and what to do, for example, with a patient's request for sedation.[17] A recent systematic review of Heijltjes[41] showed an increase of continuous sedation until death at the request of the patient or the family in various countries and subpopulations.[41] From our own findings, we known that sedation was more often performed after a request from the patient in 2013 (15.3%) than in 2007 (9.7%).[6] During the same period the percentage of continuous sedation on requests of the family slightly increased from 11.8% in 2007 to 13.8% of all deaths in 2013.[6] From 1995-1999 to 2000-2002 there was an increase in requests from patients for sedation from 19% to 34% in an inpatient palliative care unit in Germany.[41,42] What is the meaning of a patient request for a decision to initiate continuous sedation and what should we think of the increase of continuous sedation at the request of the patient and/or family? How much of a problem is this? Does it, for example, point to people being increasingly aware of their needs and preferences for the last phase of their lives or to people being increasingly aware of continuous sedation as an option to relieve suffering in the dying phase which makes them more likely to request it when they are in such a situation?[41] Or does this suggest that continuous sedation is increasingly seen as a 'choice'?[43]

Guidelines generally stress the need for clinical indications for the use of sedation referring to the 'refractoriness' of symptoms in which a medical assessment by a clinical expert is required.[17,33] In that case, a patients' request for a decision to initiate continuous sedation seems unproblematic as it is ultimately the physician who makes the final assessment of whether it meets all the clinical criteria. However, what defines refractoriness is not the nature of a symptom, but how one may fail to treat it. In fact 'refractoriness' is an outcome of the patient's disease symptoms and the

available medical resources, including the physician's abilities.[38,40] Sterckx and colleagues[40] suggest that the fewer palliative care resources available, the higher the number of refractory symptoms. This may even indicate that the practice of continuous sedation is also being used in patients with 'non-refractory symptoms', for example when a treatment may exist, yet not be known or sufficiently mastered by the patient's physician.[38,39,44] In our systematic review described in Chapter 5, we found two studies indicating that some sedations could be avoided after expert consultation, mainly because not all pharmacological and nonpharmacological approaches were exhausted and thus some of the perceived refractory symptoms were according to the experts consulted still treatable.[45–47]

Some guidelines and frameworks, like the Dutch and Belgian ones, add to this that continuous sedation can only be used in the context of unbearable suffering, judged primarily by the patient him or herself.[17,34,35] Allowing a patient to die a good death may require bringing for instance existential suffering within the reach of medical action.[38,39,48] This remains highly controversial and existing professional guidelines contradict each other in this respect, in that some include existential suffering as an indication for continuous sedation at the end of life, while others do not.[38,40,48,49] Findings from Swart[50] showed that the indication for sedation typically originates from physical symptoms and non-physical factors 'adding up' to a situation in which a patient in the last phase of life suffers unbearably.[50] The findings of this dissertation clearly showed that medical decision making seems not only to be based on clinical indications alone, but also related to morally complex factors contributing decision-making as the social context and the personal characteristics and preferences of individual patients and their relatives.[16] The key question is – where guidelines currently provide insufficient direction – how to balance the clinical indications with the overall socio-ecological context of the dying person.[51] And again, a patient request for continuous sedation seems unproblematic in the presence of clinical indications described in these guidelines such as refractory symptoms when death is imminent. Belgian and Dutch respondents in our study placed emphasis on the importance of responding to the patient's request for relief of suffering, provided that the clinical conditions were fulfilled.[17] However, this

seems not always the case. In the study of Anquinet, sedation was used for two out of 11 residents who were not terminal. For three residents, the general practitioner had indicated that there was a strong increase of morphine in the last day.[52] In one of our focus groups among professional stakeholders in nursing homes, a case was described of a person who had been asking for euthanasia every day for almost two years long, however, this person was at an advanced stage of dementia. In close consultation with the family, they decided that despite his dementia they could still consider it as a competent question and they waited until the person had pneumonia to start the sedation. The team admitted that this person would normally have survived the pneumonia, but considered it important to act humanly.[22]

Although attention is paid to the role of patients in decision making, an additional problem appears to be that in the evaluation of the practice and its quality one mainly focus on the clinical aspects of the practice, which are unlikely to reflect overall sedation quality.[47] Image, for example, a situation in which all clinical conditions are met, but in which the family had not the opportunity to say goodbye to the dying person, or the family was unable to express their concerns before, during or after the sedation. Could we then consider this case as an example of a successful sedation or not? Probably from the perspective of doctors, but does this also apply to the next of kin? Merely focusing on one aspect of the practice may neglect important information on other domains, leading to an incomplete evaluation of the overall quality of continuous sedation in end-of-life care. It should go beyond just checking whether or not patient and family consent is obtained, but for instance also looking how one was informed and whether this meets the expectations and needs of the patients and all involved relatives. Given the considerable dissonance between guidelines and practice and in order to further monitor and improve the practice of continuous sedation, the development and application of a standardized set of core outcomes, known as core outcome sets (COS), is an essential next step to evaluate the practice in all its complexity and in its entirety.

8.4.2. The practice of continuous sedation until death within end-of-life care: need for rigorous quality improvement initiatives

Despite a number of improvements in practice that are favourable in light of recommendations described in the existing guidelines, including the 2010 Flemish guideline,[35] our findings have indicated that continuous sedation is often suboptimally performed[6] and that professional caregivers are not always well acquainted with generally recommended indications for continuous sedation.[16,22,43] In our population-based death certificate study we found that the life-shortening effect of sedation was explicitly intended in 2.7% of all sedation cases.[6] This has led some policymakers, clinicians and scientists to call for some form of controlling the practice, whether organised by the legislator like it is the case with euthanasia or within the profession of physicians.[11,40,51,53]

One of the possible control measures that has already been suggested concerns, as with euthanasia, a legal framework for the practice of continuous (deep) sedation, as is already the case in France.[53] A law would make continuous sedation according to Raus et al.[53] a '*sui generis*' end-of-life practice and it would thus suggest that the practice is clearly and relevantly different from both symptom control and euthanasia or physician-assisted suicide.[53,54] It could also be seen as an expression of a lack of trust in physicians to adequately and effectively control refractory symptoms and patients' suffering at the end of life.[54] Additionally, there are also a number of practical matters that must be taken into account. Numerous attempts have been made to describe and define sedation in end-of-life care over time.[55] Our results show that a lack of conceptual clarity and even conceptual ambiguity among health care professionals still exist about what sedation is, what is should be used for and how it should be used, even among palliative care physicians.[22] And even when a common term would be used, different interpretations could still be given to the concept[56,57] One may wonder whether or not it is possible to incorporate this complexity in a law and what's the best way to do it? French legislation suggests that it is not necessarily impossible.

Another possible control measure is mandatory registration, possibly within a legal framework in accordance with the mandatory registrations for euthanasia, or organized by the care institutions themselves, which could be a way to make it clear to doctors that this practice must also meet all necessary due care requirements. This assumes that physicians could make a clear distinction between regular symptom control, continuous sedation as an extensive form of symptom control and euthanasia themselves, and thus that they know in which case they have to register it. And even if it succeeds, the question is who will check this and how this will be done knowing that in Flanders continuous sedation occurs three times as much as euthanasia.[4,6,10]

According to the European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care, injudicious use of sedation occurs in '*situations in which before resorting to sedation, there is a failure to engage with clinicians who are experts in the relief of symptoms despite their availability'*.[58] In the study of Koike,[46] a multidisciplinary team conference was performed for all patients considered for continuous deep sedation prior to its administration. Six out of 1.591 patients (0.38%) were considered for continuous deep sedation by the attending physicians before the team conference, but did not receive it because not all pharmacological and nonpharmacological approaches had been exhausted. At the very least it suggests that proper control measures could prevent patients with inappropriate indications from being sedated, although the effect is rather limited (0.38% of all cases).[45,46] However, as already mentioned in 8.4.1., this may not take sufficient account of patient autonomy and the entitlement of people to be the architects of their own life and how they die. Perhaps the most important question is whether it is feasible, for example, for existing palliative care services to cope with the influx of consultation requests. To increase the feasibility, it may be possible to look at consulting individual experts, however, who do you consider an expert? Just consulting a second physician possibly without sufficient expertise and experience does not always guarantee proper use.[59]

According to Quill et al,[60] second opinions, mandatory palliative care consultations and mandatory education about basic palliative care and management of refractory cases will ensure that more standard palliative care interventions have been fully considered and tried before turning to continuous sedation.[60,61] In Chapter 2, we found that decision-making and performance characteristics of continuous sedation were more congruent with recommendations when the treating physician followed some (additional) palliative care training.[6] Dutch research suggested that palliative care training may not only improve a physician's skills in performing end-of-life sedation but also encourage them to adopt a multidisciplinary approach and consult end-of-life experts for this practice.[6,62,63]

And finally, guidelines and protocols are generally regarded as supportive, although they are not always known.[64] Our study points to a number of improvements in practice in 2013 compared with 2007 which are favourable in light of the described recommendations[6,35]: more sedations were carried out in combinations of benzodiazepines and opioids, with opioids less frequently used as sole drug and sedation was more often performed after a patient's request, even though patient and family consent was still often lacking.[6] Our findings corroborate research from the Netherlands showing that the practices of care providers had been positively influenced by the introduction of the Dutch guideline issued by the Royal Dutch Medical Association.[6,34,63,65,66] However, the Dutch practice seems to fit more closely with the recommendations of the Dutch guideline than does the Flemish practice with the Flemish guideline.[6,17,67] The fact that the Flemish guideline is issued by the Federation responsible for palliative care, rather than by a medical or health care association, can be expected to limit their spread.[6]

So far it is still unclear how clinicians themselves perceive these possible monitoring measures as this may serve as an indication for policy makers to predict which specific measures for continuous sedation and to what extent these would be efficient and effective as they should apply those directly into practice.[51] Physicians generally claim that external control undermines professional autonomy and medical expertise.[51] In the case of expert consultation, Koper et al.[68]

found that Dutch physicians regarded consultation as supportive and helpful especially when physicians lack experience, however, they had principled objections to obligatory consultation. This is of course not a legitimate reason not to make expert consultation mandatory, however, it does point to the existence of potential barriers to any implementation.[59] The question now is which measure should be taken to improve the practice. In answering this question, it is important to keep in mind what problem these control measures are specifically focusing on, whether this is for instance the inadequate use or its life-shortening effect, and whether you assume that doctors are always fully aware on the fact that they are not acting in accordance with the recommendations. For example, some suggest mandatory registration of continuous sedation, with information on procedures used and the decision-making process, could make doctors aware of their own (in)adequate actions, assuming that they were not aware of them until then, but it is uncertain whether this will also influence those doctors who may use it with an explicit life-shortening intention. To take the most appropriate measure, more in-depth insight is needed in the specific measures and their effect in daily clinical practice and in monitoring possible side-effects that accompany it. The results from this dissertation could be used as a starting point for identifying gaps in the evidence that should be addressed in a robust evidence-based manner.

8.4.3. Enhancing the quality of continuous sedation until death in nursing homes

An important part of this dissertation was focused on the practice of continuous sedation until death in nursing homes. There is consistent evidence of significant variation in the quality of end-of-life care among nursing homes, with many nursing homes ill-prepared to provide optimal end-of-life care that is sensitive and respectful to the needs and preferences of its residents and their families.[69–71] The current practice of sedation for nursing home residents does not always guarantee a dying process free of symptoms and might therefore amenable for improvement.[52] While deciding on and performance of continuous sedation is replete with challenges, the results of this dissertation have clearly indicated that there are considerable challenges for sound decision making about and performance of continuous sedation until death in nursing homes.[22]

For example, in determining whether a symptom is refractory, estimating the remaining life expectancy, or finding the right dose in residents who are very old and frail and often habituated to medication.[22,72,73] Moreover, Epidemiological studies, like the one in Chapter 2, showed that 35% of sedated patients in nursing homes received opioids as sole drug and that in 38% of the nursing home residents who received continuous sedation, the physician partially (33%) or explicitly (5%) intended to hasten death.[6,74]

In Chapter 6, we identified the most prominent barriers to adequate decision making about and performance of continuous sedation until death in nursing homes as experienced by the health care professionals.[22] A known problem within practice is the lack of conceptual clarity and even conceptual ambiguity among health care professionals about what sedation is, what is should be used for and how it should be used, even among palliative care physicians.[22] Physicians and nurses in our study indicated that is often unclear how continuous sedation relates to regular symptom control on the one hand and euthanasia on the other.[22] The international qualitative UNBIASED study has shown that continuous sedation may refer to different practices involved.[14,17,75] However, from the results of this dissertation this ambiguity seems to be even more complex in setting of residential care centres where a variety of actors with varying education and training in palliative care are involved in the care of the resident, each with their own emphasis and interpretation of the concept of sedation.[22] If there is no agreement as to which practices do and do not fall under the term, there is a great risk that discussion becomes meaningless as different narratives become indistinguishable from each other. Clear and well implemented guidelines and protocol could partially improve this.[22,47]

Specific attention can also be paid to the coordination of care with a clear division of roles and responsibilities.[22] In Belgium, nursing homes provide skilled nursing care to older persons with limitations in activities of daily living who do not need constant medical supervision.[22,76] There is no structural partnership between GPs and nursing homes as no regular GP is associated with the institution, while medical supervision is mostly provided by each resident's regular GP.[22]

Additionally, each nursing home is legally required to have one coordinating and advisory physician, a GP, preferably experienced and trained in gerontology and palliative care, who is responsible for the coordination of medical activities, for the training of staff and for the development of and training for palliative care.[22] However, the health care professionals in our study indicate that this role is rather unclear in practice and there is still a serious lack of coordination, communication, and continuity of care and it is often very unclear who should take the leading role,[22] which has been consistently shown in the literature to be a barrier for healthcare professionals.[77,78]

The needs of the patient and his/her family are paramount in palliative care.[79] The anxiety and fear regarding death may assume such dramatic forms for the patient and his family that the physician must attach considerable weight to them. The physician can be expected to adopt an open attitude and to raise any differences of opinion with the patient in good time.[80] A final major barrier found in this dissertation concerned, however, the way to handle and involve family members as physicians and nurses consider themselves insufficiently prepared and trained for this.[22] As mentioned earlier, guidelines on the use of sedation include recommendations to protect the well-being of relatives.[18,22] According to them, relatives should be involved in decision making and might benefit from being involved in monitoring and the waking state of the resident and providing light care such as mouth moistening.[18,22,81] The review of Bruinsma and colleagues[18] indicates discrepancies between the recommendations made in guidelines and the actual experience of relatives with the practice of continuous sedation until death. Despite the fact that the majority were reported to be comfortable with the use of sedation, their review showed that they may express distress before and during the process.[18,22]

Our results have suggested that that existing recommendations on continuous sedation are not always adapted to the complex reality of a nursing home. Although high-quality guidelines may be seen as necessary for reducing variations in practice, customizing a clinical practice guideline to a particular organization or context may further improve acceptance and adherence.[22,82]

Therefore, in this dissertation we developed an evidence-based practice protocol adapted to the specific needs of nursing homes to support healthcare profession in their decision-making, communication and performance of continuous sedation until death in nursing homes. It focuses on the main barriers mentioned earlier: achieving a shared understanding among all involved, designating a coordinator of care and a fixed contact point for the family through whom all communication takes place, offering a list of topics that can be used in communicating with the family, a clear role and division of tasks among professional caregivers, but it also tries to pay attention to small details that can make a world of difference taking for instance into account the unique life community and the way to inform and involve co-residents. Before implementing this protocol in daily clinical practice, it is important to develop a thorough implementation strategy taking into account multiple preconditions at micro, meso and macro level, related to successfully implementing the protocol in the complex nursing home setting. Gilissen and colleagues[83] emphasize the importance of engaging nursing home management in order to be better implementable and more sustainable. Based on our expert panels, short information sessions could be organized for all nursing home staff and general practitioners to alert them to the existence of the protocol and the way how to use it in daily clinical practice. In the next step, we should focus on the preconditions for implementing our practice protocol on continuous sedation and taking into account specific barriers to guideline/protocol implementation such as personal factors of the involved professional caregivers (knowledge and attitude) as for instance users have to be motivated to effectively use them, guideline-related factors (for instance poor layout or poor access) and external factors such as lack of resources, heavy workload, and so on.[84]

8.5. Recommendations for practice, policy and future research

8.5.1. Recommendations for clinical practice

While it is commonly argued that the adoption of a single, clear-cut, and well-defined term for the use of continuous sedation until death, and a clear definition of the practice, would greatly improve its quality, simply using a common term does not guarantee a shared concept, let alone

a common practice.[22,57] Not knowing, in end of life situations, what one is involved in and contributing to, because of lack of clarity regarding what is being done can be very distressing for healthcare professionals involved.[38,85,86] Thus, apart from the term being used, it seems more important to make clear what continuous sedation entails and what its modalities are and to come to a shared understanding and even shared terminology used among all professionals involved in the care of the dying person. The practice would benefit from interprofessional training and even team training, for instance within nursing homes, where, in addition to a shared understanding, attention is also paid to the specific role and tasks of the different involved healthcare professionals, how to deal for instance with conflict situations within the team or with and within the family of the dying person and with sufficient attention to reflection of one's own actions and lessons that can be learned from each unique case. To this extent, continuous training of (new) staff is important. In case of questions or doubts, we recommend to consult specialist palliative care practitioners and services within and beyond nursing homes when needed as this will help physicians and nurses to further develop expertise in continuous sedation and will lead to continuous sedation administered more safely and appropriately.[45,47,68]

To ensure that relatives' concerns are addressed, their needs should be properly monitored.[22] Providing full information and regular updates about, for example, the level of consciousness, clinical symptoms, and lack of potential alternatives is important. It is important that there is a common understanding of terms and phrases used and common expectations for all involved (relatives and health care professionals) and that checks are made to ensure this understanding is maintained throughout the process.[22] Relatives might benefit from being involved in the care of their loved one and in providing light care such as mouth moistening.[18] As several healthcare professionals in our study reported feeling uncomfortable and even not sufficiently prepared and trained in dealing with family and how to handle their emotions, more guidance seems needed on how to best involve relatives in the sedation process and how to support them before, during, and after it.[22]

8.5.2. Recommendations for policymakers

The findings of this dissertation have indicated that continuous sedation is often suboptimally performed and that professional caregivers are not always well acquainted with generally recommended indications for continuous sedation, leading to uncertainty whether and when to start continuous sedation and how to use it. Based on all currently available evidence on existing quality improvement initiatives and in-depth qualitative data from 141 involved health care professionals, we have developed a practice protocol for the use of continuous sedation until death in nursing homes adapted to its specific needs. The results of this dissertation point to a possible impact of guidelines corroborating with research from the Netherlands. Additional steps are needed to promote awareness, acceptance, adoption, and adherence to these initiatives, including wide dissemination and the use of thorough implementation strategies.[87,88] For example, our protocol, after it has been tested and validated, could also be a common point of reference for prospective and retrospective audits of clinicians' practices with the recommendations providing readily available process measures or review criteria for rating compliance with best care practices or for the formulation of useful educational approaches.

As mentioned earlier, some policy makers and clinicians call for some form of control and/or monitoring of the practice, whether organized by the legislator or within the profession of physicians.[51] The main question is the extent to which these control measures are effective in solving the problem they are aimed at and what are the possible side-effects that accompany them. As a government it is important not to make hasty decisions and to develop the measures in close consultation with the relevant authorities, taking into account the intended goal and target group, the effect that is expected the measures are expected to have and especially considering possible side effects of the measures in a wider context of other end-of-life practices. With this in mind, issuing practice recommendations and context-specific protocols like the one in this dissertation and specific training sessions are perhaps with the current scientific knowledge the best and most acceptable options. An additional step forward could be made by

enhancing health care professionals' knowledge on palliative care in the basic curriculum, in post-graduate training programs, through training courses, workshops and seminars. It is important that training programs sufficient attention is paid to reflection of one's own actions as well as to dialogue with other professional care providers about specific cases.

Developing, investing and implementing a palliative care strategy in nursing homes could enhance a general palliative care approach with e.g. assessment and treatment of pain and other symptoms, patient-centred communication and decision-making, interprofessional cooperation, better communication on all levels and more inclusion of relatives in a patient's care from the early stages of the disease could enhance quality of end-of-life care for nursing home residents. Physicians and nurses in our study indicated that the role of the coordinating and advisory physician, who is responsible implementing a palliative care approach, is insufficiently taken up, does not meet expectations and should be further developed and refined.[22]

8.5.3. Implications and suggestions for further research

The findings described in this dissertation point to several avenues of future research which could greatly contribute to our understanding of, and to improving, continuous sedation until death. First and perhaps in the context of this dissertation the most important one, having developed and modelled this specific intervention for the nursing home setting (e.g. our practice protocol), it will be important to – before implementing it in daily clinical practice - to develop a thorough implementation strategy taking into account multiple preconditions at micro, meso and macro level related to successfully implementing the protocol in the complex nursing home setting. It will then be important to test its feasibility and acceptability to residents dying in nursing homes and their primary carers as well as to all health care professionals involved in their care, and to evaluate its effectiveness thoroughly in a Phase II trial which will allow us to optimize the intervention model for further implementation.

Furthermore, given the considerable dissonance between guidelines and practice,[89] there is increasing concern on the quality of continuous sedation nationally as well as internationally. In

order to further monitor and improve the practice of continuous sedation, developing a gold-standard core outcome set reflecting its overall quality is an essential next step and will be fundamental to facilitating meaningful evaluations and comparisons between different clinical improvement studies and will be crucial for clinical practice to make more informed health decisions. The selection of a gold-standard core outcome measurement set will facilitate our understanding of which quality improvement initiatives are worth implementing in real-world applications, practice, and policy and will be fundamental for evidence-informed societal debate on possible control measures for continuous sedation. These outcomes should 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.

Also, differences in frequency and characteristics of the practice of continuous sedation until death between countries and between settings should be further monitored, quantitatively as well as qualitatively. It could yield evidence of differing medical cultures when it comes to end-of-life care. Finally, patients at the end of life are often viewed as too ill, clinically unstable, or otherwise unable to complete requirements for study participation.[90] We know from previous research that patient/relative reported outcomes may be underrepresented in existing knowledge.[18] Future research should supplement the current scientific knowledge by identifying outcome measures that deems to be essential to patients and their loved ones and in this way by including their perspectives in the evaluation of the practice. This would contribute to a better understanding of the problems of continuous sedation and to the formulation of useful educational approaches.[22] End-of-life research provides numerous potential benefits for subjects and family members, such as sharing their stories, reflecting upon experiences and contributing to research, thereby creating a need to successfully meet these challenges.[91]

8.6. References chapter 8

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Samenvatting van de belangrijkste bevindingen

9.1. Inleiding

Ook bij optimale palliatieve zorg komen situaties voor waarin ernstig lijden bij terminale patiënten niet langer verlicht kan worden door middel van normale medische behandelingen. In dergelijke situaties kan het doelbewust en het continue verlagen van het bewustzijn van de patiënt tot aan het levenseinde een laatste uitweg bieden zodat die zich niet langer bewust is van de symptomen die zijn/haar lijden veroorzaken. Hoewel continue sedatie een algemeen aanvaarde therapie is binnen de palliatieve zorg, blijft het niettemin een veelbesproken en controversieel onderwerp van een heftig medisch en ethisch debat. Deze debatten gaan voornamelijk over de voorwaarden waaronder deze vorm medisch geïndiceerd is, de manier waarop een arts de sedatie het beste kan uitvoeren en de ethische aanvaardbaarheid van de praktijk aangezien het door sommige artsen en zorgverleners soms werd en wordt gebruikt met de intentie om het leven te verkorten.

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 ter bevordering der Geneeskunst (KNMG) in Nederland in 2005 (en herzien in 2009), de 'European Association for Palliative Care' (EAPC) in 2009 en de Federatie Palliatieve Zorg Vlaanderen in 2010 (en herzien in 2012). Een samenvatting van de belangrijkste aanbevelingen van de Vlaamse, Nederlands en EAPC richtlijnen zijn weergegeven in tabel 1. Algemeen gezien wordt continue sedatie tot aan het overlijden door deze richtlijnen gezien als normaal medisch handelen waarbij het doel is om het lijden te verlichten en waarbij het verlagen van het bewustzijn een middel is om dat te bereiken. Continue sedatie die *lege artis* wordt toegepast, verkort het leven niet en in tegenstelling tot bijvoorbeeld euthanasie komt de patiënt te overlijden aan de onderliggende ziekte.

Tabel 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 dienst 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 symptoomcontrole.
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 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 heel wat studies blijkt dat in de praktijk de uitvoering niet altijd in overeenstemming is met de aanbevelingen uit die richtlijnen. De richtlijnen geven bijvoorbeeld 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 inschatten of een symptoom werkelijk refractair of onbehandelbaar is, vereist een zekere kennis en ervaring in pijn- en symptoomcontrole als ook in palliatieve zorg.

Verder geven de richtlijnen ook aan dat de levensverwachting van de patiënt kort moet zijn vooraleer continue sedatie tot aan het levenseinde opgestart kan worden. Uit onderzoek blijkt echter dat clinici in het algemeen de neiging hebben om de levensverachting van hun patiënt te overschatten. Zo is er aangetoond dat de overlevingsduur van patiënten doorgaans 30% korter is dan voorspeld door artsen, maar dat de nauwkeurigheid van de voorspelling toeneemt naarmate de dood nadert. Vaak wordt ook niet de aanbevolen geneesmiddelen (benzodiazepines) gebruikt. In richtlijnen en discussies over continue sedatie wordt vaak het proportionaliteitsbeginsel genoemd, in die zin dat de arts de sedativa individueel titreert totdat adequate symptoomverlichting wordt bereikt. Hierbij wordt het bewustzijn niet meer verlaagd dan nodig is en wordt dus een juiste balans gezocht tussen onder- en over medicatie. De evaluatie ervan dient gericht te zijn op het comfort van de patiënt, maar is nog steeds gebaseerd op subjectieve beoordelingen en de mate waarin de persoon al dan niet comfortabel en vredig oogt. Het is echter in veel gevallen niet duidelijk in hoeverre patiënten zich nog bewust zijn van hun situatie. Een recente prospectieve studie waarbij gebruik werd gemaakt van Bispectrale-indexmonitoring (BIS) om het niveau van bewustzijn van gesedeerde patiënten na te gaan dat een aantal van de patiënten bij bewustzijn was volgens BIS (>60%) in tegenspraak met klinische observatie (RSS 4-6). Continue sedatie tot aan het overlijden is nog steeds een heel complexe en soms omstreden praktijk. Het is belangrijk dat de incidentie van medische levenseindepraktijken zoals continue sedatie, de socio-demografische kenmerken en besluitvormingskenmerken moeten verder opgevolgd worden. Trends in levenseindepraktijken verschaffen inzicht in de kwaliteit van deze praktijken en maken het mogelijk om praktische en ethische prioriteiten voor de medische praktijk aan het levenseinde te identificeren.

Een ander aspect is de mate waarin patiënten en familieleden dienen betrokken te worden in het besluitvormingsproces. Hoewel medisch geïndiceerd dient de beslissing in de mate van het mogelijke in overleg te gebeuren met de patiënt en familieleden. Uit studies blijkt echter dat ze echter niet altijd betrokken zijn bij de besluitvorming en dat ze bovendien vaak slecht geïnformeerd zijn over wat ze kunnen verwachten bijvoorbeeld tijdens de sedatie, hetgeen

uiteindelijk leidt tot een slechte kwaliteit van sterven en problemen met rouwverwerking. En hoewel richtlijnen sterk aanraden om alle voorkeuren van de patiënt te gaan exploreren zijn richtlijnen niet duidelijk hoe je dat dan concreet doet. Vandaar dat binnen dit proefschrift ook zal gekeken worden welke rol patiënten opnemen in de besluitvorming voorafgaand continue sedatie en de rol van de Vlaamse patiënten te kaderen binnen een internationale context.

Uit verschillende internationale studies blijkt dat de uitdagingen met de besluitvorming en uitvoering van continue sedatie nog groter zijn in een setting van woonzorgcentra aangezien verschillende specifieke individuele en contextuele factoren goede praktijken verder compliceren. Bijvoorbeeld, een grote meerderheid van de bewoners in woonzorgcentra sterven aan aandoeningen die complexer en onvoorspelbaarder zijn wat betreft diagnose en prognose, wat het oordeel over de nog resterende levensverwachting en de geschiktheid van continue sedatie tot aan het overlijden verder bemoeilijkt. Ook kan het zijn dat de communicatie met de bewoner voorafgaand de sedatie moeilijk verloopt of zelfs onmogelijk is in geval van dementie. Verder blijkt uit epidemiologische studies dat in 35% van de sedatie patiënten in woonzorgcentra men enkel en alleen opiaten gebruikt in plaats van benzodiazepines, hetgeen kan gezien worden als zowel een indicatie van inefficiënte als problematische sedatie. Een bevraging door Rys en collega's bij huisartsen die allen betrokken waren geweest bij een overlijden in een woonzorgcentrum waaraan continue diepe sedatie was voorafgegaan, laat zien dat zij 37.8 % van die interventies catalogeren als 'intentioneel levensbekortend'. Het ging in een aantal gevallen ook om patiënten met een langere levensverwachting, een grotere wilsbekwaamheid en een grote wens om te overlijden. Ook had een aantal onder hen gevraagd naar euthanasie. Ten slotte blijken woonzorgcentra in vergelijking met ziekenhuizen en palliatieve eenheden minder technisch uitgerust en hebben ze vaak minder specialisten ter zake ter beschikking. De huidige praktijk van continue sedatie tot aan het overlijden garandeert niet altijd een optimale kwaliteit van sterven en is mogelijks vatbaar voor verbetering. Om die reden zullen we binnen dit proefschrift nagaan welke barrières professionele zorgverleners ervaren in het gebruik van continue sedatie tot aan het overlijden in woonzorgcentra. Op basis van deze informatie en alle beschikbare

wetenschappelijke evidentie zullen we binnen dit proefschrift een praktijkprotocol ontwikkelen dat inspeelt op de specifieke noden en kwaliteiten van woonzorgcentra met als doel professionele hulpverleners te ondersteunen in de besluitvorming voorafgaand, communicatie voor, tijdens en na en uitvoering van continue sedatie tot aan het overlijden in Vlaamse woonzorgcentra.

Het proefschrift heeft twee centrale doelstellingen: ten eerste het monitoren en verder bestuderen van de praktijk van continue sedatie tot aan het overlijden in Vlaanderen, België, en ten tweede om een praktijkprotocol te ontwikkelen die professionele zorgverleners ondersteunt in het gebruik van continue sedatie tot aan het overlijden in Vlaamse woonzorgcentra. Vijf verschillende studies werden gebruikt in dit proefschrift: vragenlijststudie bij artsen gebruik makend van overlijdensattesten (ELD), kwalitatieve interviewstudie met artsen, verpleegkundigen en naasten in Vlaanderen, Nederland en UK (UNBIASED), een kwalitatieve focusgroepsstudie met professionele zorgverleners die allen betrokken zijn bij de zorg van residenten in woonzorgcentra en bij het gebruik van sedatie in woonzorgcentra om de ervaren barrières te bestuderen bij het gebruik van de praktijk in woonzorgcentra, een systematisch literatuuronderzoek naar bestaande initiatieven ter verbetering van continue sedatie tot aan het overlijden en tot slot maakten we gebruik van experts betrokken bij de zorg van residenten in woonzorgcentra om ons praktijkprotocol verder te ontwikkelen en te verfijnen. De verschillende studies en methoden worden in de desbetreffende hoofdstukken uitvoering beschreven.

9.2. De praktijk van continue sedatie tot aan het levenseinde

Hoofdstuk 2 beschrijft de resultaten van een vragenlijststudie bij artsen gebruikmakend van overlijdensattesten in 2013 en vergelijkt de resultaten ervan met die uit 2007. Na de aanvankelijke stijging van het aantal continue diepe sedaties tussen 2001 en 2007 van 8.2 % naar 14.5%, daalde het gebruik ervan tot 12% van alle overlijdens in 2013. Deze daling deed zich voornamelijk voor bij vrouwen, weduwen, diegene die stierven in woonzorgcentra en bij hoger opgeleiden. Vergeleken met 2007, werden opiaten minder vaak gebruikt als enig middel en werd de beslissing vaker voorafgegaan door een expliciet verzoek van de patiënt. De resultaten uit

2013 tonen een praktijk die veel dichter aanleunt bij de praktijk zoals die omschreven wordt in richtlijnen, al is er nog ruimte voor verdere verbetering, vooral in het gebruik van aanbevolen medicatie, het verkrijgen van geïnformeerde toestemming en in het gebruik van continue sedatie met de intentie om het levenseinde te bespoedigen. Daarnaast vergeleken we de besluitvormings- en uitvoeringskenmerken ook naar de mate waarin de behandeld arts palliatieve zorg opleiding had gevolgd. Daaruit blijkt dat vergeleken met niet Palliatieve Zorg experten, artsen die opleiding genoten in Palliatieve zorg vaker benzodiazepines gebruikten en minder vaak opiaten, dienden minder kunstmatige voeding en vocht toe en voerden vaker sedatie uit na verzoek of na geïnformeerde toestemming van de patiënt of familie. Uit de studie blijkt dat wanneer artsen een opleiding genoten binnen Palliatieve Zorg, zij binnen hun praktijk veel dichter aanleunen tegen de aanbevelingen zoals ze in richtlijnen worden omschreven.

In **hoofdstuk 3** maakten we gebruik van interviews met 28 artsen en 22 verpleegkundigen waarin werd gekeken hoe zij hun gebruik van continue sedatie tot aan het overlijden rechtvaardigen en welke factoren een rol spelen bij de beslissing om continue sedatie tot aan het overlijden te starten. Artsen en verpleegkundigen verwezen naar de aanwezigheid van een breed scale aan klinische indicaties, al wezen ze ook op een aantal moeilijkheden in de beoordeling van deze klinische indicaties. Ten eerste vonden respondenten het moeilijk om het ondraaglijke karakter te beoordelen, omdat dit enkel door patiënten kan worden ervaren. De resultaten uit deze studie suggereren dat de beslissing om continue sedatie te starten niet altijd uitsluitend gebaseerd is op het actueel lijden, maar vaak ook op de noodzaak om toekomstig lijden te voorkomen. Ten tweede werd continue sedatie tot aan het overlijden enkel maar geschikt geacht als een de patiënt een korte levensverwachting had, maar het inschatten van de nog resterende levensverwachting van een patiënt hangt van heel wat elementen af die de beoordeling verder bemoeilijken. De resultaten uit deze studie wijzen er verder op dat de beslissing om sedatie te starten niet alleen gebaseerd zijn op klinische indicaties, maar dat ook de sociale context en de persoonlijke kenmerken van individuele patiënten het besluitvormingsproces beïnvloeden. Zo gaven artsen en verpleegkundigen aan dat ze bijvoorbeeld gevoelig zijn voor hoe patiënten hun

leven hebben geleefd en ze meldden vaak dat ze worden geconfronteerd met patiënten die de afhankelijk echt niet aankunnen. Een laatste opmerkelijk resultaat is dat continue sedatie tot aan het overlijden in sommige gevallen werd gebruikt wanneer euthanasie geen optie was, hetzij doordat de patiënt niet langer wilsbekwaam was of vanwege praktische zaken.

Hoofdstuk 4 beschrijft het besluitvormingsproces voorafgaand aan continue sedatie tot aan het overlijden, met bijzondere aandacht voor de betrokkenheid van de stervende en we vergeleken de betrokkenheid in Vlaanderen met de betrokkenheid van de stervende in het besluitvormingsproces in Nederland en het Verenigd Koninkrijk. Er konden vier stadia binnen de besluitvorming worden geïdentificeerd: de initiatiefase (wie haalt het aan?), de uitwisseling van informatie, de deliberatiefase waarin besloten wordt om continue sedatie te gebruiken wanneer de situatie zich voordoet en de beslissing om continue sedatie te starten. Het doel was steeds om het lijden van de patiënt te verlichten, toch blijkt uit de resultaten van dit onderzoek dat er een aanzienlijke variatie is in de timing en de specifieke rol van patiënten bij de besluitvorming. Aan de ene kant van het spectrum was de besluitvorming voornamelijk klinisch en arts gestuurd: de arts besprak het mogelijke gebruik van sedatie met de patiënt, maar het was uiteindelijk de arts die de beslissing nam. Deze gevallen kwamen vooral voor in het Verenigd Konikrijk, waar de respondenten een geleidelijk proces rapporteerden van het verstrekken van lage dosissen sedativa tot de meer zelden gebruikte continue diepe sedatie. Aan de andere kant van het spectrum begon de patiënt het gesprek over het gebruik van sedatie, terwijl de rol van de arts voornamelijk beperkt was tot het beoordelen of en wanneer de toestand van de patiënt aan de medische criteria voldeed. Deze gevallen kwamen voornamelijk uit België en Nederland, waar patiënten soms zelfs de 'keuze' van sedatie hadden.

9.3. Het verbeteren van de praktijk van continue sedatie tot aan het overlijden in woonzorgcentra

Hoofdstuk 5 geeft een systematisch literatuuroverzicht van 21 bestaande initiatieven ter verbetering en/of ondersteuning van de praktijk in levenseindezorg. Er konden drie soorten bestaande initiatieven worden geïdentificeerd: negen initiatieven waren gericht op beoordelingsinstrumenten voor bewustzijn, acht initiatieven waren gericht op het gebruik van een algemene richtlijn of setting-specifieke protocollen en drie initiatieven waren gericht op het consulteren van experten en collega's bij de klinische besluitvorming. Zowel de op waarnemers gebaseerde sedatieschalen als het gebruik van monitoringapparaten die het bewustzijn beoordelen werden gezien als nuttig, acceptabel en haalbaar voor zowel patiënten, familieleden als het medisch personeel. Onderzoek naar het gebruik van monitoringapparaten toonden aan dat een klein deel van de patiënten bewust was, ondanks het feit dat de patiënt niet meer reageerden en dus niet meer bewust waren volgens de op waarnemers gebaseerde sedatieschalen. Alleen het ontbreken van relevante normwaarden voor continue sedatie en het brede scala aan waarden van deze monitoringapparaten voor comfortabele en voldoende gesedeerde patiënten lijkt de algehele implementatie ervan in de dagelijkse klinische praktijk te belemmeren. Richtlijnen en setting-specifieke protocollen worden als ondersteunend beschouwd, al zijn niet alle artsen op de hoogte van hun bestaan. In het algemeen werden deze in hoge mate nageleefd en rapporteerden artsen veranderingen in hun praktijk conform de aanbevelingen, al was de verschuiving vrij beperkt. Overleg met deskundigen wordt als ondersteunend en nuttig beschouwd, vooral wanneer de behandeld arts zelf onvoldoende kennis en ervaring heeft. Deze studies suggereren dat overleg met deskundigen ervoor kan zorgen dat alle andere opties zeker uitgeput zijn en dat de voorwaarden voor sedatie volledig zijn opgehelderd, om op die manier mogelijke onnodige sedaties te vermijden.

In **hoofdstuk 6** identificeerden we mogelijke belemmeringen voor de besluitvorming, communicatie en uitvoering van continue sedatie tot aan het overlijden in woonzorgcentra volgens professionele zorgverleners die betrokken zijn bij de zorg van personen in woonzorgcentra. Barrières werden ingedeeld op drie niveaus, waaronder persoonlijke barrières met betrekking tot kennis en vaardigheden, relationele barrières met betrekking tot

communicatie en samenwerking tussen professionele hulpverleners onderling en met de familie, en contextuele barrières die betrekking hebben tot de organisatie van de zorg binnen woonzorgcentra. We vonden een gebrek aan conceptuele duidelijkheid en conceptuele ambiguïteit over wat sedatie is, waarvoor het moet worden gebruikt en hoe het moet worden gebruikt. Zo is er veel verwarring over hoe continue sedatie zich verhoudt tot enerzijds reguliere symptoomcontrole en anderzijds euthanasie. Deze studie toont aan dat deze ambiguïteit nog complexer kan zijn in de setting van woonzorgcentra waar een grote verscheidenheid aan actoren betrokken is bij de zorg voor de bewoner, elk met hun eigen nadruk en interpretatie van het concept sedatie. Zelfs zonder deze conceptuele ambiguïteit laten onze resultaten zien dat de besluitvorming en het uitvoeren van sedatie veel complexer is in deze populatie, zowel wat betreft de beoordeling van kwetsbare ouderen (bijvoorbeeld om te bepalen of een symptoom refractair is, het schatten van de resterende levensverwachting of het vinden van de juiste dosis bij bewoners die erg oud en kwetsbaar zijn en vaak gewend zijn aan medicatie) en van samenwerking en communicatie tussen zorgverleners. Ons onderzoek laat duidelijk zien dat artsen en verpleegkundigen zichzelf niet voldoende voorbereid en opgeleid zien in het omgaan met familie. Ze weten bijvoorbeeld niet hoe ze hen moeten betrekken bij de besluitvorming en hoe ze met hun emoties of tegenstrijdige opvattingen moeten omgaan. Onze bevindingen suggereren dus dat er aanzienlijke uitdagingen zijn voor het nemen van goede beslissingen over en het uitvoeren van continue sedatie tot de dood in woonzorgcentra.

Hoofdstuk 7 gaat in op de ontwikkeling van een praktijkprotocol ter ondersteuning van professionele zorgverleners in woonzorgcentra aangepast aan de specifieke noden en kwaliteiten van woonzorgcentra. De ontwikkeling was gebaseerd op de resultaten uit onze focusgroepsstudie waarin we de verschillende barrières geïdentificeerd hebben en verder aangevuld door de huidige wetenschappelijke kennis betreffende initiatieven ter verbetering van de praktijk. Een preliminair ontwerp werd voorgelegd aan 10 expertpanels bestaande uit 71 professionele zorgverleners die werkzaam zijn in en rond woonzorgcentra. Dit leidde met een aantal kleine aanpassingen tot een protocol bestaande uit 7 stappen met aandacht voor de conceptuele

verduidelijking van sedatie, het aanstellen van een coördinator, het uitklaren van de medisch-sociale situatie, het inplannen van een formeel overleg met alle betrokken hulpverleners en eventueel ook familie waarin afspraken worden vastgelegd onder meer rond bereikbaarheid, taakverdeling, het bespreken van de situatie met de patiënt en zijn/haar omgeving met daarin een lijst van mogelijke onderwerpen die zeker aan bod dienen te komen, de voorbereiding van de sedatie met oog bijvoorbeeld voor het organiseren van een afscheidsmoment ook voor medebewoners, de uitvoering van sedatie, de zorg voor de familie en hulpverleners tijdens de sedatie en de nazorg.

9.4. Algemene discussie en conclusie

Hoewel algemeen wordt beweerd dat het gebruik van één enkele, duidelijke en goed gedefinieerde term voor het gebruik van continue sedatie tot de dood, en een duidelijke definitie van de praktijk, de kwaliteit ervan aanzienlijk zou verbeteren, garandeert een gemeenschappelijke term nog geen gedeeld concept, laat staan aan gangbare praktijk. Afgezien van de term die wordt gebruikt, lijkt het ons belangrijker om duidelijk te maken wat continue sedatie inhoudt en wat de modaliteiten ervan zijn, en om te komen tot een gedeeld begrip en zelfs een gedeelde terminologie die wordt gebruikt door alle professionals die betrokken zijn bij de zorg voor de stervende.

De praktijk zou baat hebben bij interprofessionele training en zelfs teamtraining, bijvoorbeeld in verpleeghuizen, waar naast een gedeeld begrip ook aandacht wordt besteed aan de specifieke rol en taken van de verschillende betrokken zorgprofessionals, hoe om te gaan met bijvoorbeeld conflictsituaties binnen het team of met en binnen de familie van de stervende en met voldoende aandacht voor reflectie op eigen handelen en lessen die uit elk uniek geval kunnen worden geleerd. In dit opzicht is continue opleiding van (nieuwe) medewerkers belangrijk. In geval van vragen of twijfels raden we aan om specialistische palliatieve zorgverleners en diensten binnen en buiten verpleeghuizen te raadplegen wanneer dat nodig is, omdat dit artsen en

verpleegkundigen zal helpen om hun expertise op het gebied van continue sedatie verder te ontwikkelen en zal leiden tot continue sedatie die veiliger en beter wordt toegediend.

De behoeften van familieleden moeten goed worden bewaakt. Het is belangrijk dat er een gemeenschappelijk begrip is van de gebruikte termen en uitdrukkingen en dat de verwachtingen van alle betrokkenen (familieleden en beroepsbeoefenaars in de gezondheidszorg) gemeenschappelijk zijn en dat er controles worden uitgevoerd om ervoor te zorgen dat dit begrip gedurende het hele proces wordt gehandhaafd. Familieleden kunnen er baat bij hebben om betrokken te zijn bij de zorg voor hun geliefde en bij het geven van lichte zorg, zoals het bevochtigen van de mond. Aangezien heel wat praktijkmensen in onze studie aangaven dat ze zich niet comfortabel voelden en voldoende voorbereid zijn om met de familie om te gaan en de daarmee gepaarde emoties, raden we aan om zorgverleners beter te begeleiden in hoe ze familieleden het beste bij het sedatieproces kunnen betrokken en hoe ze hen daarvoor, tijdens en na kunnen ondersteunen.

De bevindingen van dit proefschrift hebben verder aangetoond dat continue sedatie vaak suboptimaal wordt uitgevoerd en dat professionele zorgverleners niet altijd goed bekend zijn met algemeen aanbevolen indicaties voor continue sedatie, wat leidt tot onzekerheid of en wanneer continue sedatie moet worden gestart en hoe deze moet worden gebruikt. Op basis van alle momenteel beschikbare gegevens over bestaande initiatieven voor kwaliteitsverbetering en diepgaande kwalitatieve gegevens van 141 betrokken zorgprofessionals, hebben we een oefenprotocol ontwikkeld voor het gebruik van continue sedatie tot de dood in verpleeghuizen aangepast aan zijn specifieke behoeften. De resultaten van dit proefschrift wijzen op een mogelijke impact van richtlijnen die aansluiten bij onderzoek uit Nederland. Er zijn aanvullende stappen nodig om de bewustwording, acceptatie, acceptatie en naleving van deze initiatieven te bevorderen, waaronder een brede verspreiding en het gebruik van gedegen implementatiestrategieën. Ons protocol kan bijvoorbeeld, nadat het is getest en gevalideerd, ook een gemeenschappelijk referentiepunt voor prospectieve en retrospectieve audits van de

praktijken van clinici met de aanbevelingen die gemakkelijk beschikbare procesmaatregelen bieden of criteria herzien om de naleving van de beste zorgpraktijken te beoordelen of voor het formuleren van nuttige educatieve benaderingen.

Zoals eerder vermeld, pleiten sommige beleidsmakers en clinici voor een vorm van controle en / of monitoring van de praktijk, hetzij georganiseerd door de wetgever, hetzij binnen het beroep van arts. De belangrijkste vraag is in hoeverre deze controlemaatregelen effectief zijn in het oplossen van het probleem waarop ze zijn gericht en wat zijn de mogelijke bijwerkingen die daarmee gepaard gaan. Als overheid is het belangrijk om geen overhaaste beslissingen te nemen en de maatregelen in nauw overleg met de relevante autoriteiten te ontwikkelen, rekening houdend met het beoogde doel en de doelgroep, het verwachte effect van de maatregelen en vooral met het oog op mogelijke kanten effecten van de maatregelen in een bredere context van andere praktijken op het gebied van levenseinde. Met dit in gedachten zijn het geven van richtlijnen en context specifieke protocollen zoals in dit proefschrift en specifieke trainingen misschien gezien de huidige wetenschappelijke kennis de beste en meest acceptabele opties. Kennis van palliatieve zorg moet verder in het basiscurriculum, in postdoctorale trainingsprogramma's, door middel van trainingen, workshops en seminars worden opgenomen om de praktijk op korte en lange termijn verder te verbeteren. Het is daarbij belangrijk dat er in de opleidingen voldoende aandacht is voor reflectie op het eigen handelen en voor dialoog met andere professionele hulpverleners over specifieke gevallen.

Onze bevindingen wijzen op verschillende wegen van toekomstig onderzoek die enorm zouden kunnen bijdragen tot ons begrip van en tot verbetering van continue sedatie tot de dood. Ten eerste en misschien in het kader van dit proefschrift de belangrijkste aanbeveling voor verder onderzoek focust zich op het ontwikkelen van een grondige implementatiestrategie voor het implementeren van ons protocol in de dagelijkse klinische praktijk waarbij rekening wordt gehouden met meerdere voorwaarden op micro-, meso- en macroniveau met betrekking tot het succesvol implementeren van het protocol in de complexe verpleeghuisomgeving. Het zal dan

belangrijk zijn om de haalbaarheid en aanvaardbaarheid ervan te testen voor bewoners die sterven in verpleeghuizen en hun primaire verzorgers, evenals voor alle beroepsbeoefenaren in de gezondheidszorg die bij hun zorg betrokken zijn, en om de doeltreffendheid ervan grondig te evalueren in een fase II-studie die ons in staat zal stellen om het interventiemodel optimaliseren voor verdere implementatie. het zal belangrijk zijn om in een fase II-proef de effectiviteit grondig te evalueren.

Bovendien is er, gezien de grote dissonantie tussen richtlijnen en praktijk, steeds meer bezorgdheid over de kwaliteit van continue sedatie, zowel nationaal als internationaal. Om de praktijk van continue sedatie verder te monitoren en te verbeteren, is het ontwikkelen van een set met 'kernuitkomsten' die de algehele kwaliteit weerspiegelt van de kwaliteit van sedatie, een essentiële volgende stap en zal deze van fundamenteel belang zijn voor het vergemakkelijken van zinvolle evaluaties en vergelijkingen tussen verschillende klinische verbeteringsonderzoeken en zal cruciaal zijn voor klinische praktijk om beter geïnformeerde gezondheidsbeslissingen te nemen. De selectie van een set met kernuitkomsten voor metingen van kernresultaten zal ons begrip vergemakkelijken van welke kwaliteitsverbeteringsinitiatieven de moeite waard zijn om geïmplementeerd te worden en zal fundamenteel zijn voor wetenschappelijk onderbouwd debat over mogelijke controlemaatregelen voor continue sedatie . Deze resultaten moeten verder worden gebruikt als basis voor de ontwikkeling en verbetering van de opleiding en training van professionele zorgverleners in de gezondheidszorg, afgestemd op een adequate sedatiepraktijk in verschillende klinische omgevingen.

Ook moeten verschillen in frequentie en kenmerken van de praktijk van continue sedatie tot de dood tussen landen en tussen instellingen verder worden gecontroleerd, zowel kwantitatief als kwalitatief. Het kan bewijzen opleveren van verschillende medische culturen als het gaat om zorg aan het levenseinde. Ten slotte worden patiënten aan het einde van hun leven vaak gezien als te ziek, klinisch onstabiel of anderszins niet in staat om aan de vereisten voor deelname aan het onderzoek te voldoen.81 We weten uit eerder onderzoek dat patiënt / relatieve gerapporteerde

resultaten mogelijk ondervertegenwoordigd zijn in bestaande kennis. Toekomstig onderzoek moet de huidige wetenschappelijke kennis aanvullen door uitkomstmaten te identificeren die essentieel worden geacht voor patiënten en hun dierbaren en op deze manier hun perspectieven te betrekken bij de evaluatie van de praktijk. Dit zou bijdragen tot een beter begrip van de problemen van continue sedatie en tot het formuleren van nuttige educatieve benaderingen.

Curriculum vitae Lenzo Robijn

10.1. About the author

Lenzo Robijn, born 5 august 1988, is a Social Worker and holds a master's degree in Sociology (2013, Ghent University). He joined the End-of-Life Care Research Group at the Vrije Universiteit Brussel (VUB) in 2013. In 2016, Lenzo obtained a PhD Fellowship from the Research Foundation Flanders. His PhD project entailed the monitoring of continuous sedation until death in daily clinical practice and the development of a practice protocol adapted to the specific needs in nursing homes. He further claims to be an excellent father of Oona and Ellis.

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Robijn L, Vissers S, Chambaere K. Maatregelen ter controle van continue diepe sedatie. 2019. Rapport voor Ministerie Sociale Zaken en Volksgezondheid.

10.3. Oral presentations

Oral presentations at international conferences and seminars

8-10.5.15, Reasons for Continuous Sedation until Death in Cancer Patients: A qualitative Interview study. 14th World Congress of the European Association for Palliative Care (EAPC), Kopenhagen, Denmark [Poster presentation]

9-11.6.16, Trends in Continuous Deep Sedation until Death between 2007 and 2013: A Repeated Nationwide Survey. 9th World Research Congress of the European Association for Palliative Care (EAPC), Dublin, Ireland [Poster presentation]

18.5.17, The role of patient preferences in the decision-making process of continuous deep sedation until death in cancer patients: Findings from the UNBIASED study. 15th World Congress of the European Association for Palliative Care (EAPC), Madrid, Spain [Oral presentation].

13-15.9.17, An international perspective on patient preferences in the decision-making of continuous sedation until death. 2nd International Conference on End of Life Law, Ethics, Policy, and Practice (ICEL2), Halifax, Canada [Oral presentation, presented by Agnes Van der Heide].

30.11.17, De verschillende fasen van besluitvorming in continue sedatie tot aan het overlijden en de rol van kankerpatiënten in de besluitvorming. Nederlands-Vlaamse Wetenschapsdagen Palliatieve Zorg 2017, Amsterdam, the Netherlands [Oral presentation].

19.03.18, Results and methodological aspects of the UNBIASED study. State of the Art Workshop 'From anxiolysis to deep continuous sedation: development of recommendations for sedation in specialist palliative care', Frankfurt, Germany [Oral presentation, invited speaker].

23.05.18, Methodological challenges in the development of a complex intervention for the improvement of palliative sedation practice in nursing homes: a phase 0-1 study. EAPC RN & PACE pre-congress seminar, Bern, Switzerland [Oral presentation, presented by Naomi Dhollander].

02.10.18, The Involvement of Cancer Patients in the Four Stages of Decision-making in Continuous Sedation Until Death. 22nd International Congress on Palliative Care, Montreal, Canada [Oral presentation, plenary session for best abstract].

02.10.18, Barriers for the Early Integration of Palliative Home Care Into the Disease Trajectory of Advanced Cancer Patients: A Focus Group Study with Palliative Home Care Teams. 22nd International Congress on Palliative Care, Montreal, Canada [Oral presentation on behalf of Naomi Dhollander].

08.03.19, Palliative sedation at the end of life: challenges and opportunities for improvement. 3th International Conference on End of Life Law, Ethics, Policy, and Practice (ICEL3), Ghent, Belgium [Oral presentation, invited speaker].

23.05.19, The complexities of the use of continuous sedation until death in nursing homes: a qualitative exploration of healthcare professionals' experiences. 16th World Congress of the European Association for Palliative Care (EAPC), Berlin, Germany [Oral presentation].

22.11.19, Barrières voor de besluitvorming en uitvoering van continue sedatie tot aan het overlijden in Vlaamse woonzorgcentra vanuit het perspectief van zorgpr ofessionals. Nederlands-Vlaamse Wetenschapsdagen Palliatieve Zorg 2019, Antwerpen, Belgium [Oral presentation].

Oral presentations at national conferences and seminars

10.12.15, Palliative Sedation: the what, when and how. Open seminar of the End-of-life Care Research Group, Jette, Belgium [Oral presentation, Invited speaker].

8.12.18, Palliatieve sedatie vanuit een onderzoeksmatig perspectief. Basisopleiding 'Palliatieve Zorg' Artsen, Hasselt, Belgium [Oral presentation, Invited speaker].

28.02.19, Het verleden, heden en toekomst van Palliatieve Sedatie. Open seminar of the End-of-life Care Research Group, Jette, Belgium [Oral presentation, Invited speaker].

14.05.19, Who needs euthanasia when you have palliative sedation? The existence of a grey area. Open research seminar of the End-of-Life Care Research Group, Ghent, Belgium [Oral presentation, Invited speaker].

12.12.19, Palliatieve sedatie: uitdagingen voor de toekomst. Studiedag 'Palliatieve sedatie: naar een betere praktijk', Brussels, Belgium [Oral presentation, invited speaker].

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