

**The experiences of bereaved relatives  
with palliative sedation and other  
end-of-life care practices**

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**The Experiences of Bereaved Relatives  
with Palliative Sedation and other  
End-of-life Care Practices**

**De ervaringen van naasten  
met palliatieve sedatie en andere vormen  
van zorg rond het levenseinde**

**PROEFSCHRIFT**

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# CHAPTER 1

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## General introduction

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## 1.1 STATE OF THE ART

### End of life care and decision-making

During the past century, the circumstances in which people die have changed substantially. Acute deaths due to infectious diseases have been gradually replaced by more prolonged dying trajectories (1). One third of all deaths in The Netherlands occur suddenly and unexpectedly (2, 3). The increasing importance of chronic diseases as a cause of death and the attention currently being paid to patient-centred care at the end of life have created interest in the role of medicine in the timing and mode of death and dying (1). In many instances, death is not merely the result of the natural course of a lethal disease: medical decision-making often has an active role (2, 4-6). Such decision-making may concern the use of medical treatment to prolong the life of seriously ill patients (7). However, there is increasingly recognition that extension of life might not always be the most appropriate goal of medicine. Other goals have to guide medical decision-making at the end of life, such as improvement of quality of life of patients and their families by prevention and relief of suffering (8).

### Palliative sedation

Sometimes, patients who are nearing death have symptoms that cannot be relieved with conventional medical care, such as intractable pain, dyspnoea, and delirium (9, 10). This sometimes requires a treatment of last resort: 'palliative sedation'. Palliative sedation is defined as the deliberate lowering of a patient's level of consciousness in the last stages of life (11). The term palliative sedation may refer to several subtypes: temporary or intermittent sedation and continuous sedation until death. The degree of sedation necessary to relieve suffering may vary from superficial to deep (11). Continuous sedation is always administered in the final stages of life to patients who are dying and are experiencing unbearable suffering. Guidelines state that the aim of palliative sedation is to relieve suffering; lowering the level of consciousness is the means to that end. The aim should not be to lengthen or cut short the patient's life (11). Guidelines further record that palliative sedation can only be used for patients whose death will ensue in the reasonably near future, that is, within one to two weeks (12-14). Studies have shown that palliative sedation is used in all settings where patients die and for patients with all kinds of diagnoses, but most often in hospitals and for patients with cancer (15, 16).

### How often is continuous sedation until death used?

Findings from surveys of physicians suggest that continuous sedation until death has a rather high frequency of use (15). Within palliative care settings, estimates of the incidence of the use of sedatives range from 15 to more than 60% (17-23). However, these estimates are difficult to compare due to differences in the settings studied and the



definitions used. In 2001, in six European countries with comparable epidemiology of terminal diseases, there was a variation in prevalence of continuous deep sedation until death of between 2.5 and 8.5% of deaths (15). Italy and Belgium reported the highest percentages of continuous deep sedation: 8.5 and 8.2% of all deaths, respectively, were preceded by the use of continuous deep sedation. A survey in the UK conducted in 2007 found a frequency of 16.5% of continuous deep sedation until death (24). In a more recent study, it was estimated that in The Netherlands in 2010, 12.3% of all patients received continuous deep sedation until death (25). This is a clear increase compared to the figures of 5.6% for 2001 and 8.2% for 2005 (25, 26). In Flanders (Belgium), a similar increase in the use of continuous deep sedation was demonstrated, from 8.2% in 2001 to 14.5% in 2007 (27).

## **Guidelines**

In several countries, national or local guidelines have been developed for the use of sedatives in the last phase of life. Procedural guidelines are helpful for educating medical practitioners, setting standards for best practice, and promoting optimal care (28). In 2009, the European Association for Palliative Care (EAPC) published a framework of recommendations for the use of sedation in palliative care comparable with earlier published international recommendations (28). In 2005, in The Netherlands, the Royal Dutch Medical Association launched a nationwide guideline. This guideline was revised in 2009 (11). A summary of the main recommendations of the Dutch guideline is presented in textbox 1. Guidelines have been published in several other countries, for example, in 2005, a clinical guideline for continuous sedation was prepared in Japan (29), and, in 2010 in Flanders (Belgium), a guideline was presented by the Federation for Palliative Care Flanders (30).

## **The debate about continuous sedation until death**

The benefits and drawbacks of palliative sedation are frequently discussed by caregivers, and legal and ethical experts. The use of continuous sedation until death is the most controversial in this respect. On the one hand, it is often praised as an easy, innovative and indispensable technique to alleviate suffering, which is one of the most important goals of end of life care. On the other hand, it may be applied too easily (31). Lowering a patient's consciousness until death is a far-reaching intervention that has an important impact on the patient, the relatives and the caregivers. It deprives patients in their very last days of the possibility to communicate and to say goodbye, and many patients consider being mentally aware very important at the end of life (32). Relatives and caregivers have also been found to consider this procedure to be distressing (33-35). Another important issue that is often debated is whether the use of continuous sedation until death may shorten life. It is assumed in guidelines that continuous sedation

**Textbox 1:** Main recommendations Dutch guideline (11)

- Continuous sedation should always be administered in the final stages of life to patients who are dying and are experiencing unbearable suffering.
- Indications for sedation are present when one or more intractable or 'refractory' symptoms are causing the patient unbearable suffering. The physician will have to decide whether a symptom is treatable or not on the basis of 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 the patient is capable of making a conscious decision, the patient must agree with sedation; if the patient is no longer competent to make an informed decision, the physician must consult her representative.
- The advice of a consultant is mandatory if the attending physician possesses insufficient expertise and/or is in doubt about key issues such as medical indications and life expectancy.
- The sedation is aimed at the relief of the patient's suffering and not at hastening or postponing death.
- 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 as is regarded bad practice, morphine should only be given or continued (alongside sedatives) to relieve pain and/or dyspnoea.
- In cases of continuous, deep sedation until the moment of death, there should be no artificial administration of fluids.
- Relatives play an important role, both when sedation is being considered and while it is being carried out. Relatives should be involved in the decision-making process, they can assist in monitoring and caring for the patient, and that they should be clearly informed and supported. Further, it is important not only to provide the best possible information and emotional support for the patient and her family, but also to care for the various professionals involved in the case.

until death has no life- shortening effect when used for patients with an estimated life expectancy of at most two weeks and when sedatives are properly dosed (14, 26). Several empirical studies have suggested that sedation as used in clinical practice has no significant life-shortening effect (17, 23, 36-39). However, physicians may have a different perspective. A Dutch study in 2005 revealed that physicians estimated that continuous sedation until death might have had a life-shortening effect in 26% of the cases (26). Further, a substantial number of studies show that physicians declared to

have used continuous sedation until death with a (co)intention to hasten death (16, 40-43). Further, while some argue that it should be clearly distinguished from euthanasia (11, 44, 45), others argue that it may become similar to euthanasia or even being considered it as 'slow euthanasia' (46).

### **International differences**

Existing comparative international evidence suggest that there are systematic differences according to the country in which practice occurs. A study carried out in Belgium, the Netherlands and the UK demonstrated that 'country' is an important factor in predicting the probability of reporting use of continuous deep sedation (47, 48). A qualitative study conducted in the US and the Netherlands suggested that the justification for sedation and the openness with which it is discussed differ between the countries (49). Further, findings from a qualitative study in Belgium, the Netherlands and the UK among clinicians and academic researchers working in the field of palliative care (50) indicated that Dutch and Belgian respondents position continuous sedation until death as an 'alternative' choice to euthanasia (legalized in 2002). This alternative should be presented to patients to enhance their autonomy. In contrast, respondents from the UK (where euthanasia has not been legalized) appeared to be strongly influenced by a discourse of palliative care, placing more emphasis on careful medical management of symptoms. A qualitative study in 2012 demonstrated a systematic variation in end-of-life care sedation practice and its conceptualization in the UK, Belgium and the Netherlands (48). UK physicians and nurses reported a continuum of practice from the provision of low doses of sedatives to control terminal restlessness to rarely encountered deep sedation. In contrast, Belgian respondents predominantly reported the use of deep sedation, emphasizing the importance of responding to the patient's request for relief of suffering. Dutch respondents emphasized a 'formal' medical decision to initiate sedation based on a process of consultation and discussion with the patient and/ or their family depending on the patient's capacity and with professional colleagues. Sedation was used once it was established that a refractory symptom was present and it was clear that a patient was in the last days of life (48).

### **Caring for the relatives**

Professionals working in palliative care stress the importance of good care for the patient's relatives (51). The World Health Organization's definition of palliative care incorporates a support system to help the relatives to cope during the patient's illness and during their own bereavement (52). Patient and relatives together are 'the unit of care'. Being a close relative of someone who is in the final phase of life is often complicated. Relatives must handle both their own sorrow and that of the dying person, in addition to addressing a multitude of practical issues (53). Relatives often

perceive being involved in the care for a dying person as burdensome (53). This could potentially increase the vulnerability to the loss experience or slow down adjustment to bereavement (54). Although the majority of adults recover after the loss of a loved one, a portion continues to grieve for an extended period of time and develops symptoms of a state known as complicated grief (55).

Palliative sedation is a far-reaching intervention that may have a significant impact on the experience of the dying process both for patients and their relatives. The start of sedation may be the time at which it dawns on the family that the patient's death is imminent and the intimacy of family care may be disrupted by the introduction of technologies such as sedation (11). Relatives play an important role, both when sedation is being considered and while it is being carried out. However, there has been little research exploring the perceptions and experiences of bereaved relatives with palliative sedation and its impact on their wellbeing after the patient's death.

## 1.2 THIS THESIS

This thesis aims to provide a comprehensive view of bereaved relatives' experiences with the practice of palliative sedation. Because 'palliative sedation' is the term most commonly used in guidelines and research papers (11, 28, 29, 56), this term will be used throughout this thesis. Throughout this thesis, attention will be paid to one of the subtypes of palliative sedation, namely continuous sedation until death. Further, we aim to gain more insight in the potential life-shortening effect of palliative sedation and the risk factors for complicated grief in older adults. To achieve these goals, several research questions will be addressed.

*Research question 1: What are the experiences of bereaved relatives with the practice of continuous palliative sedation?*

*Research question 2: What is the prolonged impact of palliative sedation on relatives' experience of the dying phase and their wellbeing after the patient's death?*

To answer these research questions, data were used from the UNBIASED study.

### UNBIASED study

The 'UNBIASED' study (UK - Netherlands - Belgium International SEDation study), which started in 2009, is a collaboration between research teams in UK, Belgium and the Netherlands with funding from the Economic and Social Research Council (UK),

Research Foundation Flanders (BE), the Flemish Cancer Association (BE), the Research Council of Ghent University (BE), the Netherlands Organisation for Scientific Research (NL) and the Netherlands Organisation for Health Research and Development (NL). The aim of the study is to explore decision-making surrounding the application of therapeutic (or palliative) sedation in contemporary clinical practice, experiences of clinical staff and decedents' companions of its use and their perceptions of its contribution to the management of death. A mixed-method approach has been used, consisting of a literature review, focus groups with bereaved informal caregivers (NL); qualitative interviews with informal caregivers closely involved in the care of cancer patients who received continuous sedation until death (UK, BE, NL); and a survey among bereaved relatives (NL).

### **1. Systematic literature review**

To review the existing evidence on the experiences of relatives with the practice of palliative sedation, a systematic literature review was performed in 2010. Several databases were searched for empirical studies on relatives' experiences with palliative sedation. We investigated relatives' involvement in the decision-making and sedation processes, whether they received adequate information and support, and their positive and negative emotions (for more details, see chapter 2).

### **2. Focus groups**

To explore relatives' experiences with palliative sedation and to gain more insight in positive and negative elements in their evaluation of palliative sedation, between October 2010 and March 2011 three focus groups were held with a total of 10 relatives of patients who received palliative sedation in various care settings in the Netherlands. In addition, four individual interviews were carried out. The decision-making process, information and communication, the process of sedation, and the overall evaluation of the relatives of the use of sedation were addressed during the focus groups and interviews with the use of an aide-memoire (for more details, see chapter 3).

### **3. Interviews**

To explore relatives' descriptions and experiences of continuous sedation in end-of-life care for cancer patients and to identify and explain differences between respondents from the Netherlands, Belgium and the UK, face-to-face interviews were held with bereaved relatives. Interviews were held between January 2011 and May 2012 with 38 relatives of 32 cancer patients who received continuous sedation until death in hospitals, the community, and hospices/ palliative care units. The interviews were semi-structured, supported with the use of aide memoires. The aide memoire focused on relatives' recollection of the care for the patient and of the use of sedation in particular.

Relatives were asked to describe the decision-making process, the information received and how the sedation was carried out. Finally, relatives were asked how they in general looked back on the use of sedation.

#### **4. Survey**

To study the impact of palliative sedation on relatives' experience of the dying phase and their wellbeing after the patient's death, we conducted an observational study among bereaved relatives of consecutive patients who had died an expected death in the Erasmus Medical Centre-Daniel Den Hoed Rotterdam or hospice Laurens Cadenza Rotterdam, between 2010 and 2013. We included patients that died after the use of palliative sedation or died without the use of palliative sedation. Bereaved relatives of both groups of patients were asked to fill in a questionnaire about the possible use of palliative sedation, their experience of the dying phase, and their wellbeing after the patient's death. In total, 241 bereaved relatives answered a questionnaire (sedation n=151, no sedation n=90). The total response rate was 44% (for more details, see chapter 5).

*Research question 3: How accurately do physicians' estimate the potential life-shortening effect of continuous sedation until death?*

To get insight in the accuracy of estimates of the life-shortening effect of continuous sedation until death, data of the AMROSE study were analysed.

#### **AMROSE study**

The goal of the AMROSE-study is to describe the practice of palliative sedation and to establish to what extent this practice is in accordance with the RDMA-guideline (57, 58). For that purpose 370 physicians were required to answer a questionnaire. Data collection took place between February 2008 and September 2008. The potential life shortening effect of continuous sedation was estimated through a direct approach (question: Did continuous sedation, according to your estimation, hasten the patients' death?; if yes: by how much time?) and an indirect approach (estimated life expectancy minus duration of sedation). The two approaches to estimate the potential life shortening effect of continuous sedation until death were compared. In total, 370 Dutch physicians answered a questionnaire and reported about their last patient who received continuous sedation until death. The total response rate was 61% (for more details, see chapter 6).

*Research question 4: What are risk factors for complicated grief among older adults?*

To answer this research question, data from the Rotterdam study were used.

## Rotterdam study

The Rotterdam Study is a prospective cohort study that started in 1990 in Ommoord, a suburb of Rotterdam, among 10,994 men and women aged 55 and over. The main objective of the Rotterdam Study is to investigate the prevalence and incidence of and risk factors for chronic diseases in the elderly. The chronic diseases of interest are cardiovascular, neurological, locomotor and ophthalmologic diseases. The findings from the Rotterdam Study will contribute to a better prevention and treatment of chronic diseases in the elderly.

The aim of the study was to find out whether personal characteristics of the patient and the bereaved partner, the patient's illness, end-of-life care and the nature of death are risk factors for complicated grief in older adults. To gain more insight in these risk factors for complicated grief, a nested case-control study was performed within the Rotterdam Study. 100 couples of which one person had deceased and the other person experienced 'complicated grief' were selected, and 100 control couples of which one person had deceased and the other person experienced 'normal grief'. Complicated grief was assessed with a 17-item Inventory of Complicated Grief. Determinants were assessed using several sources of information that were available for all participants of the Rotterdam Study. Additionally, medical files of the deceased were manually screened (for more details, see chapter 7).

## 1.3 OUTLINE OF THIS THESIS

In **chapter 2** the results of a systematic review on the experiences of relatives with the practice of palliative sedation are presented in the light of the recommendations in guidelines on palliative sedation to protect the wellbeing of relatives involved in the use of sedation. **Chapter 3** describes relatives' experiences with palliative sedation and positive and negative elements in their evaluation of palliative sedation. **Chapter 4** explores relatives' descriptions and experiences of continuous sedation in end-of-life care for cancer patients and potential differences between respondents from the Netherlands, Belgium and the UK. **Chapter 5** examines the prolonged impact of palliative sedation on bereaved relatives' satisfaction with the dying phase and their wellbeing after the patient's death. **Chapter 6** reports on the accuracy of physicians' estimates of the life-shortening effect of continuous sedation until death. **Chapter 7** explores potential risk factors for complicated grief in older adults. Finally, in **chapter 8**, the key findings of the study and the scientific and policy consequences are discussed.

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## CHAPTER 2

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# **The experiences of relatives with the practice of palliative sedation: A systematic review**

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## ABSTRACT

**Context.** Guidelines about palliative sedation typically include recommendations to protect the wellbeing of relatives.

**Objectives.** The aim of this study was to systematically review evidence on the experiences of relatives with palliative sedation.

**Methods.** PubMed, Embase, Web of Science, PsychInfo and Cinahl were searched for empirical studies on relatives' experiences with palliative sedation. We investigated relatives' involvement in the decision-making and sedation process, whether they received adequate information and support, and relatives' emotions.

**Results.** Of the 564 studies identified, 39 were included. The studies (30 quantitative, six qualitative and three mixed methods) were conducted in 16 countries; three studies were based upon relatives' reports, 26 on physicians' and nurses' proxy reports, seven on medical records and three combined different sources. The 39 studies yielded a combined total of 8791 respondents or studied cases. Caregivers involved relatives in the decision-making in 69-100% of all cases (19 quantitative studies) and in 60-100% of all cases, relatives were reported to have received adequate information (five quantitative studies). Only two quantitative studies reported on relatives' involvement in the provision of sedation. Despite the fact that the majority of relatives were reported to be comfortable with the use of palliative sedation (seven quantitative studies, four qualitative studies), several studies found that relatives were distressed due to the use of sedation (five quantitative studies, five qualitative studies). No studies reported specifically about the support provided to the relatives.

**Conclusion.** Relatives' experiences with palliative sedation are mainly studied from the perspective of proxies, mostly professional caregivers. The majority of relatives seems to be comfortable with the use of palliative sedation; however, they may experience substantial distress due to the use of sedation.

## INTRODUCTION

During the last decades, death as the result of acute diseases largely has been replaced by death from chronic diseases (1), resulting in an increased need for end-of-life care. In some cases, patients who are approaching death experience refractory symptoms that are difficult to alleviate despite intensive medical treatment (2-3). This sometimes requires a treatment of last resort: palliative sedation (3). This entails the use of sedating drugs to induce a state of decreased consciousness until death (4).

It is known that palliative sedation is frequently used in end-of-life care. A study in six European countries reported that it was used in 2.5%-8.5% of all deaths (5). Dutch nationwide studies showed that palliative sedation is increasingly used in the Netherlands, up to 8.2% of all deaths in 2005(6-7). Palliative sedation is used in all settings where patients die, but most often in hospitals and for patients with cancer (5, 8-11). Within palliative care settings, incidence estimates of the use of sedatives prior to death range from 15% up to more than 60% of patients (12-16). It is usually recommended that for the use of palliative sedation, the patient's disease should be irreversible and advanced, with a life expectancy of, at most, two weeks; benzodiazepines should be the drug of first choice; artificial hydration should only be offered to sedated patients when the benefit will outweigh the harm; the sedation should not be intended to hasten death; and advice from palliative care specialists should be sought before initiating the use of sedation (4, 17).

To guide caregivers, several international, national and local guidelines for the use of palliative sedation have been published (18). These guidelines typically also include recommendations to protect the wellbeing of relatives of patients who receive palliative sedation. In 2009, the European Association for Palliative Care introduced a 10-item framework for the development of institutional guidelines for the use of palliative sedation (17). In 2005, the Royal Dutch Medical Association (RDMA) published a national guideline for palliative sedation in the Netherlands, which was revised in 2009 (4). Guidelines have been published in other countries also, for example, in 2005, a clinical guideline for palliative sedation was constructed in Japan (19). According to these guidelines, relatives should be involved in the decision-making, for example, by discussing the decision to sedate. Furthermore, relatives can be involved in the provision of the sedation, for example by spending time with and observing the patient and to provide physicians and nurses with information about the patient. The relatives should be kept informed, at various points in the course of palliative sedation, of the patient's wellbeing and what to expect; and the care team should communicate with the relatives in a language they can understand. The care team also must provide supportive care to the relatives by comforting and lending a sympathetic ear to help them cope with the experience.

How these recommendations relate to the actual experiences of relatives has never been systematically investigated. The aim of this study is to systematically review evidence on the experiences of relatives with the practice of palliative sedation.

## **METHODS**

### **Search strategy**

A search strategy was developed for finding relevant publications in electronic literature databases. In November 2010, five electronic databases were searched (PubMed, Embase, Web of Science, PsychINFO, and CINAHL) using the following search string (“palliative sedation” OR “terminal sedation” OR “continuous deep sedation” OR “continuous sedation”) AND (“end of life” OR palliat\* OR terminal\* OR death OR dying\*). The search string was initially developed in PubMed and later adapted for the other databases. Because “experiences of relatives” with palliative sedation were not always the primary objective of the studies found and information about this topic was sometimes only provided in tables or text, these and other related keywords were not included in the search string. To retrieve all the relevant literature, the search string was not restricted by language or date of publication. The search covered the literature published between 1991 and 2010. In addition, reference lists of the eventually selected studies were manually screened.

### **Selection criteria**

Studies were included when they met the following inclusion criteria: the study concerned empirical research (quantitative or qualitative); the study was about palliative sedation, not sedation in the context of surgical procedures; the study included information about the experiences of relatives with palliative sedation; the experiences of relatives were either directly measured or found through medical records or via a proxy (e.g., physicians, nurses); and the study was about the provision of palliative sedation in adults (older than 18). Studies were excluded when they did not meet these inclusion criteria. Reviews, studies reporting duplicate data, comments, case studies, ethical analysis, and conference abstracts were also excluded.

Relatives were not necessarily restricted to family members, but could also include others (friends, etc.).

### **Inclusion and evaluation process**

The studies identified were entered into EndNote and duplicates were removed. Ten percent of the of the publications were independently assessed by SMB (first author) and JACR (second author) using the inclusion criteria. Cohen’s Kappa was calculated



to determine the degree of agreement:  $\kappa=0.78$ , indicating a substantial agreement. The remaining titles were assessed by SMB. This procedure was repeated for the assessment of the abstracts ( $\kappa=0.78$ ). Of all the studies that did not pass the selection process, the reasons for noninclusion were listed.

### **Data extraction**

Data were extracted using a standard form that included as themes: general information, decision-making process, information/communication, involvement in the sedation therapy, feelings/emotions towards sedation, and support. SMB extracted the data from the studies and discussed the results with JACR.

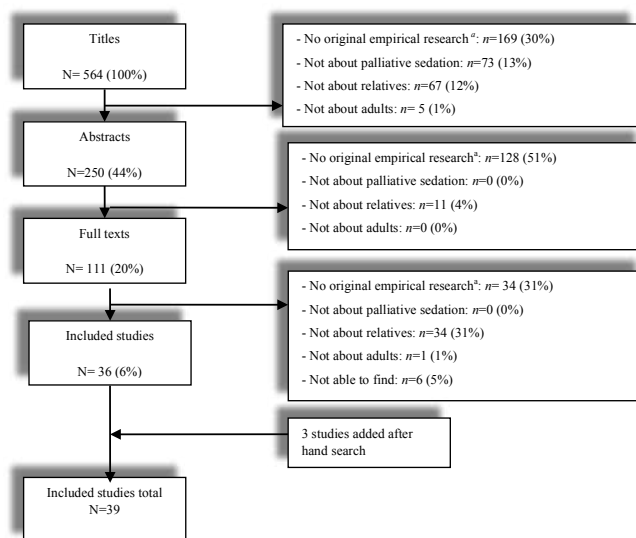
### **Quality assessment**

Because the review included qualitative, quantitative, and mixed methods studies, a multi-methods assessment tool, devised by Hawker et al (20) was used to evaluate the quality of individual studies. An assessment form was used, which covered nine areas; each area was rated on a four-point scale, from 1 (very poor) to 4 (good). The areas covered were abstract and title; introduction and aims; method and data; sampling; data analysis; ethics and bias; results; transferability or generalizability; and implications and usefulness. For each paper, it was possible to calculate a total score (9= very poor to 36= good) that indicated its methodological rigour. As the studies used different methods, outcome measures, and samples, it was not appropriate to combine data across studies for meta-analysis (21). The methodological quality of the selected publications was assessed by SMB; JACR assessed a 10% random sample of studies. Both authors agreed on the quality assessment of all the studies.

## **RESULTS**

### **Characteristics of the studies**

Searching the electronic databases, 564 studies were identified (excluding duplicates). After scanning the titles, abstracts, and full texts, 36 studies were included (6%) (Fig.1). After manually screening the reference lists of the selected studies, three studies were added, resulting in 39 studies. The 39 studies included 30 quantitative studies, six qualitative studies and three mixed-method studies. The studies used different methods to gather data: questionnaires (23 studies), medical records (seven studies), interviews (five studies), and focus groups (one study). Three studies used several methods. The studies were conducted in different care settings: palliative care unit (eight studies), hospital (four studies), home (two studies), hospice (two studies), and a nursing home (one study). Most studies were conducted in multiple settings (21 studies); and in one



**Figure 1** Inclusion- and evaluation process. a Including reviews, case studies, ethical analysis, studies reporting duplicate data, comments, and conference abstracts

study, the setting was not restricted. Three studies concerned relatives' reports about their experiences and 26 studies concerned proxy reports, mainly from physicians and/or nurses (23 studies) (in three studies, researchers and pharmacists were included as respondents). Seven studies concerned reports from content analysis of medical records. Three studies combined several sources. Because the data gathered from relatives, proxies, and medical records did not show substantial differences, the results will not be broken down for these groups. The studies originated from 16 different countries, most often from The Netherlands (10 studies) and Japan (eight studies). Thirteen studies were published between 1999 and 2005 and 26 studies between 2005 and 2010. The 39 studies yielded a combined total of 8791 respondents or studied cases (see Table 1 for a full description of the included studies).

In this study, the concept of relatives was not necessarily restricted to family members. Because the included studies did not always provide a clear definition of "relatives", it remains unclear to whom the concept of relatives exactly relates.

### Decision-making process

Of the 39 studies included, 30 provided information about relatives' involvement in the decision-making process. Of these, 25 were quantitative (11, 16, 22-44), two were qualitative (18, 45) and three used mixed methods (46-48). The 30 studies yielded a

**Table 1** Characteristics included studies

First author (reference)	Year of publication	Country	Study design	Data collection method	Setting	Respondents	Number of respondents/ studied cases	Methodological appraisal: Total score <sup>a</sup>
Seale (11)	2010	U.K.	Quantitative study, retrospective	Questionnaire	Home, elder care, hospital	Physicians	519 respondents	32
Chiu (16)	2001	Taiwan	Quantitative study, prospective	Medical records <sup>b</sup>	Hospice and palliative care unit hospital	-	70 cases	26
Rietjens (18)	2007	United States	Qualitative study, retrospective	Interviews	Palliative care unit, medical intensive care unit hospital	Nurses	16 respondents	33
Alonso-Babarro (22)	2010	Spain	Quantitative study, retrospective	Medical records	Home	-	29 cases	25
Chambaere (23)	2010	Belgium	Quantitative study, retrospective	Questionnaire	Home, hospital, care home	Physicians	561 cases	31
Classens (24)	2010	Belgium	Quantitative study, prospective	Questionnaire	Palliative care units in hospitals and hospice	Nurses, researchers	20 cases	28
De Graeff (25)	2008	The Netherlands	Quantitative study, retrospective	Medical records <sup>b</sup>	E.g. hospital, nursing home, hospice, home	-	138 cases	20
Eckerdal (26)	2008	Sweden	Quantitative study, retrospective	Questionnaire <sup>c</sup>	Hospital	Physicians, nurses	22 cases	19
Forde (27)	2001	Norway	Quantitative study, retrospective	Questionnaire	Hospital	Physicians	47 respondents	27
Hasselaar (28)	2008	The Netherlands	Quantitative study, retrospective	Questionnaire	Hospitals, home, nursing homes	Physicians	304 cases	29
Marin (29)	2003	Spain	Quantitative study, prospective	Medical records <sup>b</sup>	Hospital	-	36 cases	24

**Table 1** Characteristics included studies (*continued*)

First author (reference)	Year of publication	Country	Study design	Data collection method	Setting	Respondents	Number of respondents/ studied cases	Methodological appraisal: Total score <sup>a</sup>
Morita (30)	2004	Japan	Quantitative study, retrospective	Questionnaire	Palliative care units	Physicians	29 respondents	25
Morita (31)	2004	Japan	Quantitative study, retrospective	Questionnaire	Palliative care units	Physicians	29 respondents	27
Morita (32)	2005	Japan	Quantitative study, prospective	Questionnaire <sup>c</sup>	Palliative care units	Physicians	102 cases	28
Parker (33)	2008	Australia	Quantitative study, cross-sectional	Questionnaire <sup>c</sup>	Hospital, home	Physicians	1478 respondents	28
Pomerantz (34)	2004	United States	Quantitative study, cross-sectional	Questionnaire	Not restricted	Physicians	135 respondents	29
Porzio (35)	2009	Italy	Quantitative study, retrospective	Medical records <sup>b</sup>	Home	-	16 cases	19
Rietjens (36)	2006	The Netherlands	Quantitative study, retrospective	Interviews	Home, nursing home and hospital	Physicians	211 respondents	31
Rietjens (37)	2004	The Netherlands	Quantitative study, retrospective	Interviews	Home, nursing home and hospital	Physicians	211 respondents	31
Rietjens (38)	2008	The Netherlands	Quantitative study, retrospective	Medical records	Palliative care unit hospital	-	68 cases	29
Van Dooren (39)	2009	The Netherlands	Quantitative study, retrospective	Medical records <sup>b</sup>	Palliative care unit hospital	-	45 cases	28
Van Deijck (40)	2010	The Netherlands	Quantitative study, retrospective	Questionnaire	Nursing homes	Physicians	316 cases	30
Mercadante (41)	2009	Italy	Quantitative study, prospective	Medical records, interviews	Palliative care unit	-, relatives	42 cases/ respondents	23

**Table 1** Characteristics included studies (*continued*)

First author (reference)	Year of publication	Country	Study design	Data collection method	Setting	Respondents	Number of respondents/ studied cases	Methodological appraisal: Total score <sup>a</sup>
Morita (42)	2004	Japan	Quantitative study, retrospective	Questionnaire	Palliative care units	Relatives	185 respondents	30
Morita (43)	2004	Japan	Quantitative study, cross-sectional	Questionnaires	Cancer centres, hospitals palliative care units	Nurses	2607 respondents	28
Swart (44)	2010	The Netherlands	Quantitative study, retrospective	Questionnaire	Home, nursing homes, hospices, and hospitals	Physicians, nurses	555 respondents	26
Blondeau (45)	2009	Canada	Qualitative study, retrospective	Interviews	Hospitals, hospices, long-term-care facilities, home	Physicians	19 respondents	28
Blondeau (46)	2005	Canada	Mixed methods study, cross-sectional	Questionnaire <sup>c</sup>	Hospitals, hospices, home	Physicians, pharmacists	124 respondents	29
Chater (47)	1998	Canada, U.K., Ireland, Italy, United States, Australia, New Zealand, South Africa	Mixed methods study, retrospective	Questionnaire	Inpatient palliative care facility, hospital, home, outpatient care	Physicians, nurses	53 respondents	32
Venke Gran (48)	2008	Norway	Mixed methods study, cross-sectional	Questionnaire	Hospitals and palliative unit nursing home	Nurses	73 respondents	30

**Table 1** Characteristics included studies (*continued*)

First author (reference)	Year of publication	Country	Study design	Data collection method	Setting	Respondents	Number of respondents/ studied cases	Methodological appraisal: Total score <sup>a</sup>
Morita (49)	1999	Japan	Quantitative, prospective	Questionnaire <sup>c</sup>	Hospice	Physicians	87 cases	26
Brajtman (50)	2003	Israel	Qualitative study, retrospective	Interviews, focus groups	Hospice	Relatives, clinical staff (nurses, physicians, social worker)	32 respondents	17
Morita (51)	2004	Japan	Qualitative study, retrospective	Questionnaire	Palliative care units	Relatives	185 respondents	32
Forde (52)	2006	Norway	Quantitative study, retrospective	Questionnaires	Hospital	Physicians	12 respondents first questionnaire, 116 respondents second questionnaire	26
Van den Block (53)	2009	Belgium	Quantitative study, retrospective	Questionnaire <sup>c</sup>	Home, care home (elderly or nursing home), hospital, inpatient palliative care unit	Physicians	177 cases	33
Maessen (54)	2009	The Netherlands	Quantitative study, retrospective	Questionnaire	Hospital, outpatient care	Physicians, informal caregivers	31 cases	29
Miyashita (55)	2008	Japan	Quantitative study, retrospective	Questionnaire, medical records	Cancer center, palliative care unit	Relatives	32 cases	28
Rietjens (56)	2009	The Netherlands	Qualitative study, cross-sectional	Focus groups	Home, nursing home and hospital	Physicians	24 respondents	31

Table 1 Characteristics included studies (continued)

First author (reference)	Year of publication	Country	Study design	Data collection method	Setting	Respondents	Number of respondents/ studied cases	Methodological appraisal: Total score <sup>a</sup>
Seymour (57)	2007	U.K., the Netherlands, Belgium	Qualitative study, cross-sectional	Interviews	Hospices, hospitals, palliative care unit, community setting	Physicians, nurses, researchers	35 respondents	31

<sup>a</sup> Scoring system: 9=very poor, 18=poor, 27=fair, 36=good

<sup>b</sup> Medical records also refer to assessment forms, recording forms, consult records, clinical investigation records, charts, and notations in multidisciplinary records

<sup>c</sup> Questionnaires also refer to surveys, clinical vignettes, data collecting sheets and registration forms.

combined total of 8060 respondents or studied cases (quantitative,  $n=7775$ ; qualitative,  $n=35$ ; mixed methods,  $n=250$ ).

The involvement of relatives in the decision-making process was variously described in the studies. Some studies reported about involving the relatives in the decision-making process in general terms, whereas other studies reported specific types of involvement, such as discussing the decision, obtaining consent, or informing the relatives about the decision. Quantitative studies found that relatives were involved in the decision-making process in 81-100% of all cases of palliative sedation (22, 28, 32, 36, 44, 47). Specific aspects of the use of palliative sedation (e.g., the indication, goal, or the expected course of the sedation) were discussed with the relatives in 90%-93% (27, 32, 37-38). Relatives gave their consent to use palliative sedation in 69%-100% (16, 23, 29-31, 35-36, 39-41). Consent was sometimes not obtained from relatives, e.g. because it was already obtained directly from patients (29). The relatives were informed about the decision in 95%-100% (26, 44). Further, studies showed that the relatives proposed or requested the use of palliative sedation in 9%-41% (11, 32, 34, 41). One study provided information about the phase before the proposal to use sedation and showed that in, 70%, the relatives were involved in the assessment of intolerable suffering (24). According to one study, physicians were more willing to provide palliative sedation on their own initiative than at the request of relatives (33). Another study showed that 38% of the physicians and pharmacists attributed an important role to the family in the process of deciding whether to choose sedation or not (46). Further, the wellbeing of relatives was an indication for the use of palliative sedation in 12%-22% (25, 31). Disagreement about the use of sedation was found among relatives in 10%-17%, between the patient and relatives in 8%-11% and between relatives and medical staff in 10% (32, 42-43). According to one study, 14% of the physicians and 3% of the nurses reported that they felt pressure to start sedation from patients and/or relatives (44) (Table 2).

The qualitative data additionally showed that physicians acknowledge the importance of involving the relatives in the process of deciding whether to use sedation or not, but that the patient typically remains top priority (45). Nurses sometimes felt that patients and/or their relatives should decide when suffering is intolerable and palliative sedation is necessary, instead of the physicians (48) (Table 3).

### **Information/communication**

Eight studies reported specifically on the information relatives received about palliative sedation or about communication issues. Of these, five were quantitative (31-32, 39, 42, 49), two were qualitative (50-51) and one used mixed methods (48). The eight studies yielded a combined total of 738 respondents or studied cases (quantitative,  $n=448$ ; qualitative,  $n=217$ ; mixed methods,  $n=73$ ).



**Table 2** Results quantitative data (n=32)

Core themes	No. (%) of studies reporting	Range of answers	References
<b>Decision-making process</b>	27 (84%)		(11, 16, 22-44, 46-47) <sup>a</sup>
<i>Involvement in decision-making process</i>			
Relatives involved in decision-making process	6 (19%)	81%-100%	(22, 28, 32, 36, 44, 47) <sup>b</sup>
Relatives consent	10 (31%)	69%-100%	(16, 23, 29-31, 35-36, 39-41)
Decision discussed with relatives	4 (13%)	90%-93%	(27, 32, 37-38)
Relatives informed of decision	2 (6%)	95%-100%	(26, 44)
<i>Other findings</i>			
Sedation proposed (requested) by relatives	4 (13%)	9%-41%	(11, 32, 34, 41)
Well-being of relatives indication for sedation	2 (6%)	12%-33%	(25, 31)
Conflicts about the use of sedation between people involved	3 (9%)	8%-17%	(32, 42-43)
<b>Information/communication sufficient for relatives</b>	5 (16%)		(31-32, 39, 42, 49)
Information provided to relatives (about indication, goal, expected course; reduction in consciousness, ability to communicate, life-threatening complications; effects on survival, life-supporting functions, treatment options other than PS; physical changes and physical status, and prognosis if PS not induced; risks, benefits)	5 (16%)	60%-100%	(31-32, 39, 42, 49)
Relatives understood the information	2 (6%)	89%-100%	(39, 42)
Prior discussion about end-of-life issues between relatives and medical staff	2 (6%)	75%-82%	(32, 42)
Information sufficient for relatives	1 (3%)	75%	(42)
<b>Involvement in the sedation process</b>	2 (6%)		(52-53)
Monitoring patient by relatives	1 (3%)	42%	(52)
Involvement relatives in caring patient	1 (3%)	17%	(53)

**Table 2** Results quantitative data (n=32) (*continued*)

Core themes	No. (%) of studies reporting	Range of answers	References
<b>Emotions and evaluation</b>	9 (28%)		(16, 39, 41-42, 44, 49, 52, 54-55)
<i>Positive emotions or evaluation</i>			
Satisfied (or “fair”) with PS	3 (9%)	78%-93%	(42, 44, 49)
PS decreased symptom distress patient	1 (3%)	88%	(42)
Decision to start sedation in accordance with families’ wish	1 (3%)	100%	(52)
PS is appropriate for relatives	1 (3%)	98%	(41)
Timing of PS is appropriate for relatives	1 (3%)	77%	(42)
Ethical acceptable (right or might be right to use sedation)	1 (3%)	93%	(16)
Peaceful death because of PS	1 (3%)	91%	(54)
<i>Negative emotions or evaluation</i>			
Relatives experienced distress	1 (3%)	25%	(42)
Relatives expressed concerns	1 (3%)	51%	(39)
Relatives unsatisfied with PS	1 (3%)	5%	(42)
Relatives asked to stop the sedation	1 (3%)	5%	(41)
PS neg. associated with good death	1 (3%)	-	(55)
Delirium, ambivalence of patients’ wishes, and lack of objectivity of distress associated with difficulty in making decision for family members	1 (3%)	-	(49)
<b>Support</b>	0 (0%)		

PS= palliative sedation

<sup>a</sup> Not all the reporting studies are discussed in table, some only in text<sup>b</sup> Mixed methods studies (46-47)

**Table 3** Results qualitative data ( $n=7$ )

Core themes	No. (%) of studies reporting (%)	Aspects	References
Decision-making process	3 (43%)	Importance of role relatives, but patient's top priority	(45)
		Well-being relatives was an indication sedation	(18)
		Relatives should decide whether or not to use PS	(48) <sup>a</sup>
Information/communication	3 (43%)	Kind of information relatives received (clinical aspects and physical aspects of dying process)	(48) <sup>a</sup>
		Relatives reported desire to know that the maximum efforts had been made, to prepare for the patient's death, to tell the patient something important before sedation, to understand the nature of the patient's suffering, and wishes that medical professionals treat the patient with dignity	(51)
		Relatives differ in type of information they need	(50)
Involvement in sedation process	0 (0%)		
Emotions and evaluation	5 (71%)	<i>Positive emotions or evaluation</i>	
		Sedation made relatives feel more comfortable, because it offered them sense of peace and closure	(18)
		Relatives wanted the patient's suffering to end	(50-51, 57)
		Relatives are grateful for caregivers who treated patient with respect	(50)
		<i>Negative emotions or evaluation</i>	
		Relatives experienced distress, e.g., anger, frustration, disappointment, concerns, struggles, guilt, helplessness, and physical and emotional exhaustion	(18, 50-51, 56-57)
		Distress as a result of: inability to interact with patient, feelings that sedation possibly hastened death, longer duration sedation, well-being of the patient, information not easily obtained or not relevant to needs at that moment	(18, 50-51, 56-57)
Support	0 (0%)		

<sup>a</sup> Mixed methods study: (48)

Overall, the quantitative data showed that relatives received information from professional caregivers in 60%-100% (31-32, 39, 42, 49). In these studies, the type of information ranged from explanations about the reduction in consciousness, patients' inability to communicate, life-threatening complications, physical changes, physical status, and the prognosis of the patient. Relatives were reported to understand the information in 89%-100% (39, 42) and one study found that relatives experienced the provided information as sufficient in 75%, slightly insufficient in 22%, and insufficient in 2% (42). Further, prior discussions about end-of-life issues and/or the choice of sedation between medical staff and relatives took place in 75%-82% (32, 42) (Table 2).

The qualitative data additionally showed that relatives have needs for specific types of information concerning the patient's symptom distress and treatment, the dying process and when the patient was expected to die (50). Also, relatives reported a desire to know that the maximum efforts have been made and that there were no other methods available for symptom relief; to prepare for the patient's death; to tell the patient something important before the start of sedation; to understand the nature of the patient's suffering; and expressed wishes that medical professionals treat the patient with dignity (51) (Table 3).

### **Involvement during the provision of sedation**

Only two studies (both quantitative) reported on the involvement of relatives in the provision of sedation (N=305): one study reported that patients were monitored by relatives in 42% (but under supervision of professional caregivers) (52), and another that relatives were involved in the care for the patient in 17% (53) (Table 2).

### **Emotions and evaluation**

Of the 39 studies included, 14 studies provided information about relatives' emotions regarding sedation. Of these, nine were quantitative (16, 39, 41-42, 44, 49, 52, 54-55) and five were qualitative (18, 50-51, 56-57). The 14 studies yielded a combined total of 2022 respondents or studied cases (quantitative,  $n=1730$ ; qualitative,  $n=292$ ).

According to seven quantitative studies, the majority of the relatives were reported to have positive feelings regarding the use of palliative sedation (16, 41-42, 44, 49, 52, 54). Relatives seemed to be satisfied with the use of palliative sedation in 78%-93% (42, 44, 49). One study found that 88% of relatives felt that palliative sedation helped to decrease patient's symptom distress (42). Another study showed that relatives reported that palliative sedation was appropriate in 93%, because it ended the patients' suffering (41), and one study showed that the timing of the sedation was seen as appropriate in 77% (42). In another study, relatives described palliative sedation as "ethically acceptable" in 93% (16), and results from another study showed that palliative sedation was associated with a peaceful death in 91% (54). According to one study, the decision to

start sedation was in accordance with relatives' wishes in 100% (52). However, five quantitative studies showed that relatives also experienced negative emotions due to the use of sedation (39, 41-42, 49, 55). According to one study, relatives were unsatisfied with the sedation therapy in 5% (42). Low-level satisfaction was significantly associated with poor symptom palliation after sedation, insufficient information giving, concerns that sedation might shorten the patient's life, and the feeling that there might be other ways to provide symptom relief. In the same study, relatives expressed high levels of emotional distress about sedation in 25%: 10% of the relatives reported to be very distressed and 15% to be distressed (42). This distress was significantly associated with poor symptom palliation, feeling the burden of responsibility for the decision after sedation, feeling unprepared for changes of patient conditions, feeling that the physicians and nurses were not sufficiently compassionate with the patient, and a shorter interval to the patient's death (42). One other study found that relatives expressed concerns between the start of the sedation and the death of their loved ones in 51% (39). It concerned concerns regarding the aim of the sedation, the well-being of the patient, and the well-being of the relatives themselves (feelings of exhaustion because of sleep deprivation, or unbearable feelings of watching their loved one die) (39). Another study showed that relatives asked to stop the sedation in 5% because they wanted to communicate with the patient before death and wanted to take the patient home (41) (Table 2).

The qualitative data provided more insight in the type of negative emotions relatives experienced due to the sedation. "Distress" was described in terms of anger, frustration, disappointment, concerns, struggles, guilt, helplessness, and physical and emotional exhaustion (18, 50-51, 56-57) (Table 3).

### **Support**

No studies reported specifically about the support provided to the relatives.

### **Quality assessment**

The total scores are presented in Table 1. One article was rated between "very poor" and "poor"; 11 articles were rated between "poor" and "fair"; and 27 articles were rated between "fair" and "good".

## **DISCUSSION AND CONCLUSIONS**

Professionals working in palliative care stress the importance of good care for the patient's relatives because they are the ones who are often present during the last period of the patient's life, and obviously, the most closely involved with the patient (39). The

World Health Organization's definition of palliative care incorporates providing a support system to help the relatives cope during the patient's illness and during their own bereavement (58). Patient and relatives together are "the unit of care". The importance of relatives is also reflected in guidelines, which stress that relatives should be involved in the decision-making process, that they can assist in monitoring the patient, and that they should be clearly informed and supported (4, 17, 19). The results from this review suggest that the majority of relatives are adequately involved in the decision-making and receive adequate information, although there seems room for improvement. However, hardly any information is available about relatives' involvement in the provision of sedation and no studies report specifically about the support provided to relatives. Furthermore, despite the fact that the majority of relatives reported to be comfortable with the use of palliative sedation, our review shows that relatives may express distress before or during the application of sedation.

Several findings deserve particular attention. The first finding concerns the role of relatives in the decision making. Guidelines recommend that physicians actively involve relatives in this process, but because palliative sedation is a medical procedure, it is the physician who bears final responsibility for assessing the indications (4). According to the results of this review, relatives sometimes seem to play a rather decisive role in the decision to use sedation, sometimes even more decisive than guidelines recommend. Relatives are, for instance, often involved in the assessment of intolerable suffering (24) and quite often propose or request the use of palliative sedation (11, 32, 34, 41). On the one hand, caregivers sometimes feel that it should be possible or necessary for relatives to decide when suffering is intolerable and palliative sedation is necessary (48). On the other hand, physicians and nurses sometimes feel pressured by relatives to start sedation (44). However, it is shown that relatives sometimes feel the burden of responsibility for the decision to use sedation which may lead to feelings of distress (42).

Secondly, there is a large variation in the "needs" relatives express. Relatives want specific types of information; the information needs to be easily available and relevant to their needs at a particular moment in time. The nature of the desired information shows that it includes many facets of the sedation process, concerning both patients' well-being as relatives' well-being, and that provision of information is important during the whole process of sedation.

Finally, it was striking that although the majority of relatives reported to be comfortable with the use of sedation, a substantial amount of relatives expressed distress as a result of its use. On the one hand, relatives want the patients' suffering to end; on the other hand, they express concerns regarding the aim of sedation, the patients' well-being and their own well-being. Apparently, both emotions can exist simultaneously. This is in line with findings that relatives generally report to be satisfied with the care

received at the end of life, even when they have unmet needs (59). Relatives express anger, frustration, disappointment, concerns, struggles, guilt, helplessness, and physical and emotional exhaustion. The reasons for such distress were the inability to interact with the patient, concerns about a possibly hastened death, a longer duration of the sedation, and the fact that information about the sedation was not easily obtained or less relevant to needs of the relatives at that moment. The fact that relatives experience distress due to the use of sedation is not surprising. Being a close relative of someone in the final phase of life in general is often complicated in general. Relatives must handle both their own sorrow and that of the dying person, in addition to solving a multitude of practical problems (60). Aside from these difficulties, relatives of patients who receive palliative sedation also face issues such as the inability to communicate with the patient because of the patient's reduced consciousness; being awake for several days, leading to exhaustion; the unfamiliarity with sedation, after sometimes an extended period of severe suffering and functional decline of the patient.

Our study has some limitations. In the literature, several terms are used for palliative sedation, for example, continuous deep sedation and terminal sedation, potentially limiting full comparison and extrapolation of the studies. Second, "experiences" is not a clearly definable entity. Third, whether presented facts about e.g. relatives involvement in the decision-making can be interpreted as "experiences of relatives" can be debated. We interpreted the concept of experience broadly and also included, for instance, relatives' views on palliative sedation. Fourth, not all the included studies appeared to be of "good" quality. Finally, the majority of papers analyzed did not have as a main aim to investigate on relatives' experiences with palliative sedation. If the focus of research had been this, data could have been different.

The results of this review show that there seem to exist some discrepancies between the recommendations made in guidelines and the actual experiences of relatives with the practice of palliative sedation. First, it seems that recommendations are not always followed. For instance, relatives not always perceive the provision of information as sufficient (39). Second, there obviously is a lack of evidence about some aspects of the recommendations made in guidelines. Considering the fact that all the guidelines about palliative sedation stress the importance of involving relatives in the sedation process and supporting the relatives before, during, and after the sedation of their loved ones, it is a remarkable finding that there is no evidence about these issues. In conclusion, we found that relatives' experiences with the practice of palliative sedation are mainly studied from the perspective of proxies, mostly professional caregivers. Studies show that the majority of relatives is involved in the decision-making process. The majority of relatives receives adequate information, although there is room for improvement. Hardly any information is available in the literature about relatives' involvement in the sedation process and no studies report specifically about the support provided to the

relatives. Despite the fact that the majority of relatives seem to be comfortable with the use of palliative sedation, there are indications that several of them experience substantial distress with its use.

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## CHAPTER 3

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# **Palliative sedation: a focus group study on the experiences of relatives**

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## ABSTRACT

**Background.** Most studies that have investigated the practice of palliative sedation have focused on physicians' practices and attitudes.

**Objective.** The aim of this study was to explore relatives' experiences with palliative sedation and to gain more insight in positive and negative elements in their evaluation of palliative sedation.

**Design.** Focus groups and individual interviews.

**Setting.** Various care settings in the Netherlands.

**Subjects.** A total of 14 relatives of patients who received palliative sedation until death participated.

**Results.** Most relatives evaluated the provision of palliative sedation of their dying family member positively. Positive experiences were related to: the beneficial impact of palliative sedation on the patient's suffering, the opportunity that was offered to prepare for the patient's death, their involvement in the decision-making and care for the patient, and the pleasant care environment. However, the majority of the relatives were unsatisfied with one or more aspects of how information was being provided for. Some relatives were frustrated about the fact that nurses were not authorized to make decisions about the care for the patient and about the absence of physicians during weekends. None of the relatives mentioned the loss of the ability to communicate with the patient during the sedation and the possibility of "hastening death" as disadvantages of palliative sedation.

**Conclusion.** Relatives tend to evaluate the provision of palliative sedation to their severely suffering family member positively because it contributes to a peaceful dying process. However, relatives indicated discontent with how information was being provided and with the communication in general.

## INTRODUCTION

At the end of life, many patients suffer from severe symptoms. Sometimes, sedation until death is needed to control symptoms that cannot be relieved with conventional measures. This practice is often referred to as palliative sedation (1). The degree of sedation necessary to relieve suffering may vary from superficial to deep. Dutch nationwide studies showed that palliative sedation is increasingly used in The Netherlands in up to 8.2% of all deaths in 2005 (2,3). Palliative sedation is used in all settings in which patients die, but most often in hospitals and for patients with cancer (4-8). Within palliative care settings, estimates about the frequency of palliative sedation vary from 15% to more than 60% of all deceased patients, depending on the type of setting and the definitions used (9).

Being a close relative of someone who is in the final phase of life is often complicated. Relatives must handle both their own sorrow and that of the dying person, in addition to addressing a multitude of practical issues (10). Professionals working in palliative care stress the importance of good care for the relatives of the patient (11). This can also be seen through the World Health Organization's definition of palliative care, in which providing a support system to help relatives cope during the patient's illness and during their own grief is incorporated (12). The importance of relatives' well-being is also reflected in guidelines about palliative sedation, which stress that relatives should be involved in the decision-making process, that they can assist in monitoring and caring for the patient, and that they should be clearly informed and supported (13-15).

Most studies that have investigated the practice of palliative sedation have focused on physicians' practices and attitudes (16-23). The aim of this qualitative study was to explore relatives' experiences with palliative sedation and to gain more insight into positive and negative elements in their evaluation of palliative sedation.

## METHODS

As part of a larger study about the practice of palliative sedation and its role in end-of-life care, the UNBIASED study' (UK-Netherlands-Belgium InternAtional SEDation study), we held focus groups and interviews with relatives of patients who received palliative sedation until death. Because of the exploratory nature of the study, focus groups were deemed most suitable. In the focus groups, the group processes were particularly useful in clarifying relatives' views on palliative sedation (24). Interviews were held when relatives were not able to attend a focus group. The term palliative sedation was systematically used throughout the study, since this is the most commonly used term

in guidelines and research papers (1, 13-15). We followed the criteria for qualitative research to ensure rigour in our research (25).

### **Recruitment of participants**

Because palliative sedation is used in all settings in which patients die, we focused on a variety of settings (23). Purposive sampling was used for the selection of participants to make sure different settings were represented, and to achieve variation in relatives' experiences and in types of sedation used. Inclusion criteria of the patients were that they were older than 18 and that their death had been a maximum of 1.5 years ago. Inclusion criteria of relatives of patients who had received palliative sedation until death were: frequent contact with the patient in his/her last phase of life, both prior to and during the sedation, and being Dutch-speaking and residents of The Netherlands. Relatives were not necessarily restricted to family members, but could also include friends. We included one relative per patient. Relatives were contacted no sooner than 3 months and no later than 12 months after the patient's death.

Relatives were recruited using both professional and personal contacts of members of the research team. The professional contacts concerned both nurses and physicians working in the home, hospital, or hospice setting. They were asked to identify the most involved relative of a patient who had received palliative sedation and to contact the relative by sending an information letter from the research team. In the hospice and hospital setting, 25 cases were identified. The relatives of these 25 cases were approached by the health care professional and 8 relatives agreed to participate. Two relatives of all relatives who have been approached by a general practitioner agreed to participate. It is unknown how many relatives were approached by general practitioners in total. Furthermore, we identified cases through our personal contacts. Five relatives were approached and 4 agreed to participate.

Ten relatives were willing and able to participate in a focus group (two focus groups with three participants and one focus group with four participants). Four additional interviews were held with relatives who were willing to participate, but were not able to attend a focus group because of practical reasons. The focus groups and interviews took place between October 2010 and March 2011.

### **Procedures**

A semistructured questionnaire was developed, based on the recommendations described in the Dutch nationwide guideline for palliative sedation and a systematic review on the experiences of relatives with palliative sedation, to ensure consistency in topics addressed across groups (26). The questionnaire was piloted in three interviews. This led to some small changes in the formulation of the questions. The questionnaire covered several topics: background information of patient and relatives, the decision-



making process, information and communication, the process of sedation, and the overall evaluation of the relatives of the use of sedation.

All focus group and interview participants filled in a short questionnaire on socio-demographic data and signed a consent form before the start of the focus groups. The focus groups were led by experienced moderators (A.H., J.R.) and lasted approximately 2 hours. An assistant moderator (S.B.) was present to take notes. The interviews were conducted by S.B. and lasted approximately 60 minutes. Participants consented to the discussion or interview being audiotaped. The Erasmus MC Medical Ethical Research Committee approved the study. The procedure followed the Helsinki Declaration.

### **Data analysis**

The audiotaped discussions were transcribed verbatim and analyzed by constant comparative analysis. We removed names and other information that could lead to identification. After completing all focus groups and interviews, we (S.B., J.R., A.H.) read through all transcripts. Data were analyzed by S.B. using the themes from the questionnaire. Attention was paid to issues that were not explicitly addressed in the questionnaire. As a next step, the results were discussed with J.R. and A.H. until consensus was reached. A professional translator translated the quotes that are presented in the results. Each quote is followed by information on the gender of the respondent (F = female, M = male), the nature of the relationship with the patient, and the setting in which the patient died. When there is more than one respondent with the same characteristics, the gender of the respondent is followed by a number to distinguish the different respondents.

## **RESULTS**

### **Characteristics patients and relatives**

The characteristics of relatives and patients are presented in tables 1 and 2.

### **Decision-making process**

Different issues came up while discussing the decision-making process.

### ***Reason(s) for the use of sedation***

Relatives believed that the patient's suffering was the most important reason to start palliative sedation. Pain, respiratory problems, fatigue, restlessness, anxiety, confusion, delirium, inability to drink and eat, and nausea were mentioned as decisive factors. Furthermore, although relatives believed that patients' suffering was the main reason

to start sedation, their descriptions of “suffering” also included their own suffering as a result of the patients’ suffering.

**Table 1** Characteristics relatives

Gender	Male	6
	Female	8
Age		41-69
Nature of relationship with patient	Partner	8
	Child	3
	Grandchild	1
	Daughter in law	1
	Parent	1
Time passed since patient passed away		2-16 months

**Table 2** Characteristics patients

Sex	Male	8
	Female	6
Age		33-89
Primary diagnose	Cancer <sup>a</sup>	12
	Alzheimer/dementia	1
	No specific diagnose <sup>b</sup>	1
Setting	Home	7
	Institution <sup>c</sup>	7
Duration illness		4 weeks-2,5 years
Time spent in setting were patient passed away		4 days-3 months

<sup>a</sup> Skin cancer (two patients), colon cancer (two patients), lung cancer (two patients), peritoneum cancer, breast cancer, cervical cancer, oesophagus cancer, brain tumour, liver cancer, pleural cancer

<sup>b</sup> Advanced age

<sup>c</sup> Hospice (4), nursing home (1), psychiatric/geriatric institution (1), hospital (1).

*‘My two children and I said, we are going to propose this [sedation], it couldn’t go on like this. And it was the same for him - at least we think it was - but of course you can’t ever really know that. But it was so awful for us to be there: to see how he was fighting to breathe, oh and his hallucinations... it is so hard just to stand by and watch. You don’t know what is going on inside his head’ [F1, partner, home].*

### **Making the decision**

The decision to start sedation was either initiated by the patient, the relative, or the physician. Sometimes it was the patient who specifically asked for sedation. In these cases, patient and relatives had previously discussed the option of sedation with the physician. In the end, the physician made the final decision to start sedation and the relatives gave their consent.

*'So the general practitioner explained it to him. Yes (...) that it was possible just to be put to sleep and to let the body itself take over. And he (the patient) said that he would prefer palliative sedation. He really wanted to sleep through the very last bit. He consciously wanted to say goodbye and then go to sleep. He made the choice himself, and we had talked about it a few times. (...) I supported his decision, well rationally I did, but emotionally you would rather it had gone differently' [F2, partner, home].*

In a couple of cases, relatives asked for the sedation. Again, the physician made the final decision to start sedation. The relatives were positive about physician's involvement.

*'Yes it was at our own request. (...) We talked to him (the patient) about sedation, well we talked about it a bit but he didn't express any particular opinion about it. But he did say that he didn't want to have to fight for breath, or be in any pain – that sort of thing. (...) He was so thirsty all the time and he was given morphine for it. But then he began to hallucinate and became very restless, and then we got to the point that we said.... (...) to the doctor, I said "well it's time to give him some strong sedating medication' [F1, partner, home].*

The majority of the relatives stated, however, that the physician was the one who proposed the use of sedation. This proposal was in most cases preceded by a discussion between physician and relatives about the need to relieve the patients' suffering.

*'The night before he died he was given injections to calm him but they didn't help at all. (...) The doctor said that it was inhuman to go on like this. (...) The doctor discussed this with me and the boys. (...) And then the next day they brought a pump.... and then he went to sleep and he didn't wake up again' [F3, partner, home].*

A few relatives mentioned, however, that the physician made the decision without involving them at all. The reason to start the sedation was not always clear for these relatives.

*'We assumed that if sedation was going to be given, then it would be the patient that made the decision. That the patient would say that he couldn't stand to go on like this (...). But in reality....we left on Sunday morning, change of shift, and we came back in the evening and we heard that she had been given an injection that had knocked her out and you think, well, you think what's going on? What on earth has happened? And that's..., well you think "this just isn't right". (...) So it meant my mother wasn't in pain. And that's..., but I still don't understand. Why did it have to happen like that?' [F, child, hospice]*

*'And then the telephone call came that the bodily functions were beginning to shut down (...) Then of course you ask "Well, what now?" Is he in pain? No he is not in pain. And, well he is slowly dying. I don't know what they did to him, no idea. The only thing I am sure of is that the last 2 or 3 days, that the well-known 'pain pump' was attached. And then you assume that sedation has in fact begun' [F, child, nursing home].*

### **Negative emotions regarding the decision-making process**

Some respondents mentioned their frustration regarding the fact that nurses were not authorized to make decisions about the care for the patient, whereas they were most of the times the only ones that were available. Another point of critique that was mentioned was that the physician was not available during the weekend.

*'So I always had a problem with the fact that medical care is from 9:00 am to 5:00 pm and not during/in the weekend. So I thought "Here we go again, its the weekend again." And you have to fight so hard to get care; you have to knock on so many doors. So I said to the doctor, I said "Listen, if you start that and then go home, I want it started properly because nurses aren't allowed to make decisions on their own' [F, grandchild, hospice].*

### **Information and communication**

Adequate information and communication between the patient, relatives, physicians and other professional caregivers were considered as very important by the relatives. In all cases but one, the relatives mentioned that professional caregivers had discussed end-of-life issues with them and (when possible) with the patient. These conversations took place at different phases in the disease process.

*'We had already talked about euthanasia at an earlier stage, and about palliative sedation—with the general practitioner. He (the patient) also had a written*

*declaration of intent regarding euthanasia and a do-not-resuscitate statement. We got all that sorted out. Also because we had no idea what was going to happen'* [F2, partner, home].

*'Two days after we knew he was sick we went to the general practitioner and we discussed the possibilities (...). And we discussed sedation. And he (the patient) made clear he wanted that'* [F4, partner, home].

Nine relatives were, at least at one point in time, dissatisfied with the amount of information they had received. Some of these relatives expressed a lot of criticism, while others only briefly mentioned this. Relatives' were discontent with (insufficient) information about: sedation in general, the early start of the sedation, the drugs that were used, further treatment (e.g., artificial nutrition and hydration), the well-being of the patient during the sedation, the expected duration of the sedation, the time of death, and/or the possible symptoms or reactions of the patient during the sedation.

*'And (they didn't) tell us what sort of symptoms to expect and what the patient's reaction could be. There you are then (sighs). All on your own, you have to go through it all on your own'* [F5, partner, home].

*'No. Everything was lumped under one heading—pain relief. The words euthanasia or palliation—I can hardly bring myself to say them—they were never mentioned'* [M, child, psychiatric/geriatric institution].

*'Yes, what's it really about? Yes...communication....of course. They didn't say "We are going to start morphine now and we are going to add some midazolam and then you can expect..." because they just don't think that way...it's not what they do'* [M, child, psychiatric/geriatric institution].

*Interviewer: 'How do you think things could have been done better?' Respondent: 'Yes - communication. Clearly say what is going to happen, say what you are going to do and what the consequences will be - not only for the person it is being given to, but also for the people around them - say what can happen'* [F, child, nursing home].

Sometimes the content of the information was unclear.

*'I mean they did not tell us what it practically means. (...) OK. My daughter-in-law knew about these things, yes but that wasn't really - maybe that is why it was*

*not explained, because they automatically assumed that we would know too. And we didn't ask, didn't ask what is going to happen because ... well, again all the time we were only thinking how much longer does this have to go on. Please let it be over as soon as possible' [M, parent, hospital].*

Sometimes relatives received conflicting information from different professional caregivers.

*'They weren't a team. They were all working individually and sometimes against each other. It just makes you so uncertain about everything (...). Sometimes we had to make the decisions about what to do. (...) And I was confronted with more than one way of working; and that shouldn't be allowed' [F5, partner, home].*

Some relatives had the feeling that they were not being taken seriously by the physicians.

*'As a family, we just weren't taken seriously. Information about him and the care and so on, it really wasn't taken seriously. And I think it is a real shame, and I also think that it is wrong. After all who knows the person better than those who are with him all the time? The nurses took us seriously, but the others didn't' [F5, partner, home].*

### **Euthanasia**

Although the issue of euthanasia was not explicitly addressed in the focus groups or interviews, almost all respondents referred to it in some way. Some relatives distinguished sedation and euthanasia as clearly different options, whereas others referred to sedation as "slow euthanasia."

*'Yes, if you stop that treatment, then they wake up again. In that respect it has nothing to do with euthanasia' [F, daughter-in-law, home].*

*'Actually I think... to me palliative sedation is also a form of euthanasia. You send someone to sleep, and then instead of it all being over in five minutes like it would be with euthanasia, it takes 2 days' [M, partner, hospice].*

Some patients were admitted to a care setting that had a no-euthanasia policy. The attending physicians had been clear about this and in most cases, the patients and relatives accepted or agreed with this policy.

*'I am still a supporter of euthanasia. (...) But we had taken this into consideration (...) and in a very pleasant care environment, then you accept palliative sedation because, well, I'll put it this way, it is still a humane - you know what I mean - solution' [M, partner, hospice].*

Some relatives mentioned that the patient had expressed a wish for euthanasia and that the physician had offered sedation as an alternative.

*'Actually, she (the patient) wanted active euthanasia (...). And the general practitioner was willing to perform euthanasia. But then he came with the option to put her to sleep (...) He explained that performing active euthanasia is very burdensome. And she didn't want that for us, and the children. And then she decided she wanted to be put to sleep' [M1, partner, home].*

### **Relatives' involvement in the process of sedation**

The involvement of relatives in the sedation process varied. All relatives visited or stayed with the patient during the sedation. Most relatives provided the physicians and nurses at some point with information about the well-being of the patient. Some relatives provided (most of) the care for the patient process varied. All relatives visited or stayed with the patient during the sedation. Most relatives provided the physicians and nurses at some point with information about the wellbeing of the patient. Some relatives provided (most of) the care for the patient themselves (e.g. the administration of the medication).

*'We were with her a lot, also when she was receiving professional care. So there came a point when although the carers didn't see it, we did and we said "She's in pain' [M, child, psychiatric/geriatric institution].*

*'The pump was connected on Thursday and on Wednesday he passed away. All this time at home, we provided all the care' [F5, partner, home].*

### **Overall evaluation of the provision of palliative sedation**

Eleven relatives evaluated the provision of sedation to their dying family member overall as positive. The start of the sedation was most of the times seen as a relief, both for the patient and for the relatives themselves. During the sedation the patient seemed comfortable. According to most relatives, sedation had been the best solution.

*'But you have to—otherwise something like this is just unbearable for him. And that would be terrible. We, the people around him, couldn't have coped otherwise*

*because he didn't know what he was doing any more and he needed to relax. He was so wound up, he kept trying to get out of bed and that just wasn't possible. That's not good for you and certainly not for the patient. And this is a very nice way of doing it. Yes, it is' [F5, partner, home].*

*'I think it is a good process in that you actually allow your body to go its own way, that you are no longer interfering with the natural process. And it means that the last battle can be fought unconsciously, that you no longer have to experience it actively. I can see that from the patient's point of view it can be a relief, but also for us' [F2, partner, home].*

Overall, the relatives were positive about professional caregivers.

*'I am full of praise for them. Both the doctor and the nurse, they did everything, you just had to ask and they did everything in their power' [M, parent, hospital].*

The place of death was in all cases in agreement with the wishes of the patient. The relatives were glad they could fulfil the wish of the patient.

*'Well, then she expressed the wish to die here at home. And that is what I did... I helped. (...) A hospice would have been easier for me of course. But that is not the point, it's what she wanted' [M2, partner, home].*

Some relatives also mentioned their satisfaction with and the importance of the care environment.

*'We are really full of praise about the way it went, (...) and really I mean that. (...) We were very lucky that he was put into a room that was quite large. (...) There were fold-up beds so we could be there day and night. (...) The experience of wanting to and being able to do that was really marvellous. They also provided us with food like it was the most normal thing. I mean, it was really fantastic. (...) They gave us a room where we could go and talk privately. Oh - it was... yes, really. I keep saying it but I can't praise them enough' [M, parent, hospital].*

The respondents knew that death was near. The sedation provided an opportunity to prepare, to some extent, for the loss of their loved one.



*'The advantage of something like this, I mean euthanasia - and this as well - is that you know roughly when it is going to happen and you can say goodbye to each other in a conscious way, it is a good way to part' [M1, partner, home].*

A few relatives had a more negative experience with the provision of sedation. Sometimes this had to do with symptoms or reactions of the patient during the sedation. The relatives were concerned about the patient's wellbeing.

*'The time finally came to start sedation, with a pump. That meant that we knew the time would come (...) when she would no longer regain consciousness. And then the moment came when the last words had been said. We had embraced each other for the last time and were waiting for her to fall asleep. (....). For me that was confirmation that I knew that once she went under, she would indeed go peacefully. But, looking back she woke up twice, oh what a situation was that. When she had to go back to sleep it didn't work. .(....). She was in so much pain' [F, child, hospice].*

The duration of the sedation varied from five hours to one week. The duration of the sedation had consequences for the relatives' wellbeing. The longer the sedation process, the higher the burden for the relatives.

*'On Friday she was started on morphine (...), and you just mentioned Dormicum, I think that she received that too at some point (....), and she died on Wednesday. We thought that this was really a very long time to go on - and a time that has had a really big impact. I don't use the word "traumatic" lightly, but the experience of going through the last phase from say, Friday to Wednesday - it's a very long time. It was a very difficult time' [M, child, psychiatric/geriatric institution].*

## DISCUSSION

Information about the concerns and needs of relatives of patients who receive palliative sedation can assist health care professionals in providing information and support to relatives during this difficult time in their lives (11). The aim of this study was to explore how relatives evaluate palliative sedation and to gain more insight into positive and negative elements of their experiences. We found that many relatives had positive experiences with the provision of sedation for their dying family member. The start of the sedation was a relief for relatives because the patient's suffering was finally alleviated. Relatives often appreciated having an active role in decision-making process

and the provision of the sedation. Other positive experiences related to the degree of involvement of professional caregivers, the appropriateness of the place of death, and the care environment. On the other hand, several relatives indicated that they were dissatisfied with the information they received and about communication in general. Other negative experiences were related to concerns about the wellbeing of the patient during sedation, especially when the sedation process lasted long, the lack of authority of nurses to make decisions, and the absence of physicians during the weekends.

A few findings deserve particular attention. First, although relatives believed that patients' suffering was the main reason to start sedation, their descriptions of "suffering" also included their own suffering. According to the guideline, the indication consists of one or more refractory symptoms experienced by the patient (13). Although in palliative care the patient and the relatives together are "the unit of care," relatives' suffering is not mentioned as an indication for sedation. This issue needs further attention in research.

Second, it was striking that the majority of relatives in our study expressed dissatisfaction with one or more aspects of communication and the provision of information. For instance, the physician sometimes made the decision to start sedation without involving relatives, although the guideline on palliative sedation recommends physicians to actively involve relatives in the decision-making, despite the fact that they bear final responsibility for the decision (13). Many studies about end-of-life care report that the provision of information and communication are inadequate and insufficient (10). A Japanese study on relatives' experiences with palliative sedation showed that insufficient information can lead to low levels of satisfaction and high levels of distress (27). Our results support the findings from previous studies, i.e., that relatives experience distress due to a lack of information or unclear information. Such distress may be diminished by discussing the patient's situation openly; providing full information, e.g., about the moment of the start of sedation, the drugs used, and/or possible symptoms or reactions of the patient during sedation. Furthermore, proper communication between the different caregivers can enhance clarity of the situation for the relatives.

Although the majority of relatives seemed to experience distress due to a lack of information or unclear information, they generally evaluated the sedation of their loved ones positively. Such positive evaluation of palliative sedation was mostly related to patient's symptom relief. Before the start of the sedation, patients presented multiple distressing physical symptoms, such as severe pain, fatigue, and restlessness. During the sedation most patients seemed comfortable. Relatives indicated that they appreciated the fact that the patient could die "naturally," without burdening medical interventions. Previous studies have also shown that adequate symptom relief is key to the experience of a "good death" (28-31). Furthermore, palliative sedation makes relatives themselves

feel more comfortable because it allows them a sense of peace and closure after a difficult period of suffering.<sup>9</sup>

Additionally, several relatives mentioned that the use of palliative sedation provided them with the time necessary to prepare for the loss of their loved one. They knew that death was near and could say goodbye to the patient in a conscious way. None of the relatives in our study mentioned loss of the ability to communicate during the sedation with the patient as a disadvantage of palliative sedation. This is in contrast with the frequency with which loss of communication is discussed as a problematic aspect of palliative sedation in the literature (27, 32-33). Findings from the current study suggest that the benefits of palliative sedation outweighed the loss of the ability to communicate with the patient before death.

Almost all relatives talked about the issue of euthanasia. Some relatives considered palliative sedation as "slow euthanasia," others as a terminal intervention that is sharply distinguished from euthanasia. The ethical debate about palliative sedation often focuses on its presumed potential to hasten death (23). However, none of the relatives in our study mentioned the possibility of "hastening death" as a disadvantage of palliative sedation. A possible resemblance of palliative sedation to euthanasia seems to be no issue for these relatives, which may be related to the public and legal acceptance of euthanasia in The Netherlands.

Both our focus groups and personal interviews appeared to be successful methods for exploring relatives' experiences with palliative sedation. The relatives appreciated the opportunity to share their stories, and felt that it helped them to deal with their grief. Nevertheless, our study has some limitations. The number of respondents was small. Therefore, the study can only be seen as explorative and not as conclusive. However, the number of respondents included was appropriate for answering the research question. Second, because the anonymity of the respondents had to be guaranteed, the results could not be specified by setting. Third, to be sensitive to the early phases of grieving, relatives were contacted no sooner than 3 months after the death of the patient. The data could be influenced by recall bias. Furthermore, a focus group usually consists of six to eight participants. Our focus groups included three or four relatives. Possibly, this diminished the dynamic interchange between the group members. Because of the sensitivity of the issue discussed, we chose to use smaller focus groups, which worked well. Finally, sedation occurs in all settings in which patients die but most often in hospitals (15). Unfortunately, we were not able to recruit more relatives of patients who received sedation until death in a hospital.

In conclusion, the relatives involved in this study seem to agree that palliative sedation is a beneficial intervention for patients who are severely suffering at the end of their lives. It relieves patient's suffering and provides relatives with a sense of peace and closure after a difficult period. Also, communication with relatives seems a challenge

for physicians and nurses involved in this practice. The loss of the ability to communicate with the patient during the sedation and the possibility of “hastening death” do not seem to be issues for the relatives.

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## CHAPTER 4

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# **Making sense of continuous sedation in end-of-life care for cancer patients: an interview study with bereaved relatives in three European countries**

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## ABSTRACT

**Purpose.** The purpose of the study was to explore relatives' descriptions and experiences of continuous sedation in end-of-life care for cancer patients and to identify and explain differences between respondents from the Netherlands, Belgium, and the UK.

**Methods.** In-depth interviews were held between January 2011 and May 2012 with 38 relatives of 32 cancer patients who received continuous sedation until death in hospitals, the community, and hospices/palliative care units.

**Results.** Relatives' descriptions of the practice referred to the outcome, to practical aspects, and to the goals of sedation. While most relatives believed sedation had contributed to a 'good death' for the patient, yet many expressed concerns. These related to anxieties about the patient's wellbeing, their own wellbeing, and questions about whether continuous sedation had shortened the patient's life (mostly UK), or whether an alternative approach would have been better. Such concerns seemed to have been prompted by relatives witnessing unexpected events such as the patient coming to awareness during sedation. In the Netherlands and in Belgium, several relatives reported that the start of the sedation allowed for a planned moment of 'saying goodbye'. In contrast, UK relatives discerned neither an explicit point at which sedation was started nor a specific moment of farewell.

**Conclusions.** Relatives believed that sedation contributed to the patient having a good death. Nevertheless, they also expressed concerns that may have been provoked by unexpected events for which they were unprepared. There seems to exist differences in the process of saying goodbye between the NL/BE and the UK.

## INTRODUCTION

Sometimes, patients who are nearing death have symptoms such as dyspnea, pain, nausea, and delirium that cannot be relieved with conventional therapeutic interventions (1, 2). One option for relieving such symptoms entails the continuous use of drugs with a sedative effect to induce a state of unconsciousness, so that the patient's perception of symptoms is removed. Continuous sedation is used for patients with a life expectancy of 2 weeks or less (3–5). There is some discussion about these recommendations. Estimating life expectancy of patients with advanced disease is known to be very difficult (6–8). Moreover, some argue that palliative sedation may be indicated for patients with a longer life expectancy if the benefit of palliation outweighs the harm of an earlier death, if there are no other alternatives, and if dosages are titrated according to the patient's need (9). Sedation is frequently used in end-of-life care. A European study undertaken in six countries in 2001/2 reported that continuous deep sedation until death was used in the management of 2.5–8.5 % of all deaths (10). Subsequent studies suggest the use of sedation in the management of 15 % of all deaths in Flanders, Belgium (11), 12 % of deaths in The Netherlands (12), and 17 % of deaths in the UK (13, 14). Ethical concerns and practical issues surrounding the practice have resulted in the publication of a number of guidelines or frameworks for clinical practice (3–5, 15, 16).

Most studies investigating the use of sedation have focused on physicians' practices and attitudes (10, 17–23). There has been little research exploring the perceptions and experiences of bereaved relatives. Rendering patients unconscious until death is a far-reaching intervention that may have a significant impact on the experience of the dying process both for the patient and their relatives. The intimacy of family care may be disrupted by the introduction of technologies such as sedation (5), with relatives experiencing a loss of contact with the patient. A review of the literature conducted in 2012 showed that what little research has been conducted to try to understand relatives' experiences has been primarily accessed from the perspective of proxies, usually clinical staff (24). The latter review showed that while the majority of relatives perceive positive benefits to be associated with the use of sedation, some experience its use to be associated with substantial distress (24). In this paper, we report results from the UNBIASED study (UK-Netherlands-Belgium International Sedation Study) (25) conducted in the UK, Belgium, and the Netherlands to gain insights into the experiences of clinical staff and relatives with the use of continuous sedation until death for cancer patient and their perceptions of its contribution to the dying process in different countries. A previous UNBIASED paper showed that there is systematic variation in end-of-life care sedation practice between the three countries (26). UK respondents reported a continuum of practice from the provision of low doses of sedatives to control terminal restlessness to rarely encountered deep sedation. In contrast, Belgian respondents predominantly

described the use of deep sedation, emphasizing the importance of responding to the patient's request. Dutch respondents emphasized making an official medical decision informed by the patient's wish and establishing that a refractory symptom was present. Usual practice in the Netherlands was described as involving starting with low doses of sedatives and then—if necessary—cautiously increasing the dosage until the patient was in a quiet and peaceful state (26). This paper addresses the following specific questions: What are relatives' understandings of the practice of continuous sedation at the end of life? How do relatives experience the dying process of the patient who has sedation administered continuously? What are the differences in relatives' experiences between the Netherlands, Belgium, and the UK?

## **METHODS**

Between January 2011 and May 2012, in-depth interviews were held with bereaved relatives of patients with cancer who died after the use of continuous sedation until death in the Netherlands, Belgium, and the United Kingdom (UK). In total, 84 deceased patients were included as case studies. Full details of the methods employed in the UNBIASED study are available in a published study protocol (25); we provide a summary here.

### **Settings**

To reach maximum variation (27), the study explored the care of patients who died in hospitals (oncology wards), palliative care units (PCU) (in Belgium), hospices (in the UK and the Netherlands), and in the community (at home).

### **Recruitment of relatives**

In all countries, senior clinical staff identified eligible decedents: patients aged over 18 who had died of cancer and to whom sedating medications (benzodiazepines or propofol, but not morphine), with the intention to decrease awareness, were administered continuously to alleviate otherwise uncontrollable symptoms (either physical or psychological/existential), and for whom the sedation was in place at the time of death. As a next step, they identified eligible relatives. The person identified as their closest relative was invited to take part in the study via a letter and information sheet sent on behalf of the research team by patient's physician. Relatives were invited at least 3 months after the death of the patient (with a maximum of 18 months). Relatives contacted the research team if they were willing to take part in the study. When relatives did not respond within 1 month, physicians were asked to send a reminder. Most

physicians were willing to do this. The relative could invite one or two other relatives to participate in the interview if they wished and five chose to do so.

### **Procedure**

The interviews were undertaken by trained interviewers and lasted approximately 60 min. All participants consented to the interview being audiotaped. At the beginning of each interview, socio-demographic information was obtained through a short questionnaire and all participants signed a consent form. The interviews were semi-structured, supported with the use of aide-memoire to ensure that all areas of interest were explored. The aide-memoire was piloted in focus groups and interviews prior to use in the Netherlands and small changes in the formulation of the questions were made (28). The aide-memoire focused on relatives' recollection of the care for the patient and of the use of sedation in particular. If relatives actively referred to the use of sedation, this became the focus of the interview. If not, they were asked 'Did anyone ever give him/her something to help him/her to relax?' The term(s) that relatives used to describe the use of sedation were used by the interviewer throughout the interview.

### **Data analysis**

All audiotaped interviews were transcribed verbatim, and all data that could identify patients or relatives were removed to preserve anonymity. The Belgian and Dutch interviews were translated into English by a professional translation bureau and checked for accuracy by the researchers. SB and JR read through all transcripts. Qualitative analysis software (NVIVO 9) was used to organize the data. Main themes relating to relatives' experiences were identified. A coding tree was developed and agreed upon by all authors. The interviews were reread and coded with the use of the coding tree by SB. The codes were independently studied by SB and JR and discussed until consensus about the further refinement and content of the coding tree was reached. Finally, quotes were selected by SB and JR and approved by all authors. Each quote is followed by information on the country of origin of the relative (NL, BE, UK), and the setting where the patient died. When there is more than one respondent with the same characteristics, this is followed by a number to distinguish the different respondents.

## **RESULTS**

In 32 of the 84 cases (13 NL; 11 BE; 8 UK), one or more relatives volunteered to be interviewed. In total, 38 relatives participated in 32 interviews (17 NL; 13 BE; 8 UK). In five cases, there was no contact information available. In seven cases, the physician was not willing to contact the relative because he/she was afraid that the invitation would

**Table 1** Characteristics patients (n=32)

		BE	NL	UK	Total
Sex	Male	6	7	6	19
	Female	5	6	2	13
Age		30-92	43-83	51-81	30-92
Primary diagnose	Lung cancer	1	4	1	6
	Pancreatic cancer	2	1	1	4
	Prostate cancer	1	1	1	3
	Melanoma	1	2	-	3
	Other types of cancer	6	5	5	16 <sup>a</sup>
Setting	Community	4	5	4	13
	Specialist palliative care setting/ hospice	3	3	4	10
	Hospital	4	5	-	9

<sup>a</sup> Leukemia (2), peritoneal (2), renal (2), abdominal/stomach (1), bladder (1), brain (1), colon (1) facial maxillary (1), esophageal (1), unknown primary (2), and uterus (1)

**Table 2** Characteristics relatives (n=32<sup>a</sup>)

		BE	NL	UK	Total
<b>Sex</b>	Male	5	4	1	10
	Female	6	9	7	22
<b>Nature of relationship with patient</b>	Partner	5	9	4	18
	Child	3	2	4	9
	Sibling	1	1	-	2
	Parent	-	1	-	1
	Grandchild	1	-	-	1
	Daughter in law	1	-	-	1

<sup>a</sup> Results from the relatives that were identified by the physician as the 'most involved relative'

stir up a lot of difficult issues, or the physician did not respond to the request to invite the relative. In 72 cases, the relatives were contacted by the physician. Of these cases, 29 did not reply to the invitation; 10 declined participation, mostly because they considered participation too upsetting; and in one case there was no relative. Characteristics of the deceased patients are presented in Table 1 and of the relatives in Table 2.

Several main themes that were raised during the interviews will be discussed: relatives' understandings of continuous sedation at the end of life, the contribution of sedation to the quality of dying, concerns related to the use of sedation, and the process of saying goodbye.

### Relatives' understandings of continuous sedation at the end of life

Some relatives from the Netherlands and Belgium indicated that they had previous experience of the use of sedation in the care of another close relative, while others had 'heard about it' through the media. Some relatives, especially those from the Netherlands and Belgium, indicated that the physician caring for the patient had explained the concept of sedation to them. Relatives from the UK were particularly unsure about what its use entailed, although this uncertainty was shared by some relatives from the Netherlands and Belgium. This uncertainty sometimes led to feelings of distress for relatives.

*'Well, I don't know what they actually,...to be honest, I don't know what they gave him that last week' (UK, hospice, 1)*

Most of the relatives from the Netherlands and Belgium used the term 'sedation' or 'palliative sedation' during the interviews, while others, particularly those from the UK, tended to use phrases such as 'making the patient more relaxed', 'sleeping', 'calming the patient down' or 'coma'.

*'She was in like a semi-coma' (UK, hospice, 2)*

Relatives used three distinct ways of describing the practice of sedation, the *outcome*, the *practical issues*, and the *goals* of sedation. The *outcome* of sedation related to the effects that relatives were expecting; for instance, terms were used such as 'sleeping' or 'a coma'.

*'To put him to sleep with the knowledge that he couldn't come out of that by himself' (NL, hospice)*

Several relatives from all three countries focused on the *practical aspects* of using sedation. For instance, they referred to the drugs that were used and the mechanics of administering the sedatives. Terms were used such as: 'the injection', 'a morphine pump', 'a pump with a sedative', 'a syringe driver', 'a cassette with sleeping stuff', or 'a sleeping pill'.

*'Yes the doctor explained what would happen again (...). That he [the patient] would get a pump with a sedative' (NL, community, 1)*

Relatives also referred to the duration of the sedation, the use of food and fluids, and the proportionality of sedation.

*'Yes you don't know how long it would have taken you know. Maybe it might have taken five days, I don't know. But with the sedation it was a maximum of five days'* (NL, hospital, 1)

Finally, some relatives referred to the *goals* of sedation, primarily in terms of preventing or decreasing the (physical or psychological/existential) suffering of the patient. Sometimes specific symptoms were mentioned, such as pain and nausea. In other cases, relatives did not use such specific terms, but described the goal of sedation as 'treating the discomfort'. Other goals were associated with allowing the patient to be peaceful and to die with dignity.

*'So they changed the medication (...) and hopefully it'll, erm, make him more, more relaxed'* (UK, community, 1).

*'The reason why they gave X those drugs was... yes... doctors shared the opinion that it wasn't possible anymore and that this was really it for X... this really was not dignified, no one deserves that'* (NL, hospital, 2)

Some Dutch and Belgian relatives compared sedation with other practices such as surgical anesthesia, and euthanasia.

*'So it's just, like an operation, you don't wake up'* (BE, hospital, 1)

*'In contrast to, to euthanasia, uh, yes, that is, they give an injection and one, two, three, poof and it's done huh'* (BE, hospital, 2).

### **Contribution to the quality of dying**

Relatives from all three countries positively evaluated the provision of sedation to their dying family member. Many reported that the sedation contributed to the patient having a good death and described sedation as effective in achieving symptom relief for the patient, making them more comfortable, and/or allowing them to die in peace and with dignity. Some relatives used descriptions like 'beautiful', 'peaceful', 'wonderful', or 'dignified' to describe the death.

*'Erm ... he [the patient] was very reluctant, he was afraid he would have a lot of pain and that he would choke and stuff like that. And because he was just asleep and it was actually painless, I think that for him it had additional advantage....so*



*he actually had assurance for himself that no crazy things would happen (...) That was the contribution for him' (NL, community, 1)*

*Interviewer: 'Yeah. And how did you feel about that?' Respondent: 'Yeah, I think I thought it was better than trying to...seeing him in distress when we'd had to move him and do all of that...to see him sleeping what looked like peacefully... that was fine' (UK, community, 1)*

Several relatives also felt that sedation had contributed to the patient's quality of dying because it allowed for their wishes to be honored.

*'Because of the palliative sedation (...) we knew: look, she still got what she wanted at the very end' (BE, hospital, 3).*

## **Concerns**

In many cases relatives (mostly, although not solely from the Netherlands and Belgium) also expressed concerns, relating to the wellbeing of the patient and themselves, possible alternatives to the use of sedation, and the possibility of hastening death.

### ***Wellbeing of the patient during the sedation***

Concerns were often related to the wellbeing of the patient during sedation. Several relatives felt that when sedation was commenced, the patient did not 'fall asleep' as quickly as they had anticipated and some relatives described the patient 'waking' during sedation. Others expressed concerns that either the patient was not sufficiently sedated to relieve the suffering, or that the level of sedation led patients to be more deeply unconscious than they needed to be (the latter concerned mainly UK respondents), or they died sooner than expected.

*'And when he was dying he was constantly pulling, always pulling. (...) And he started to vomit.(...) Gosh yes, how should I say this? I'm very content that we had those last 14 days together, but in those final hours, I wouldn't even wish that on my worst enemy. The agony.'* (BE, community)

*Erm... I thought that perhaps the medications maybe had dosed him up too, too much... of course, probably (...) So even, although they put him on some medication that you thought was perhaps making him a bit-, or he was a little bit over-medicated...(UK, community, 2)*

### **Wellbeing of relatives**

Some relatives described concerns regarding the use of sedation that were specifically related to their own wellbeing. These were sometimes related to the (long) duration of the sedation.

*'I thought that was so cruel hey, that was awful (...) because he was in a coma for eleven days, which is really very long (...) and they warned us (...) And we said "yeah we can handle that and we are aware of it and so on, hey, that's no problem". But as the days progressed and the sleep, I began to realize it" yes doctor, you have indeed warned us, but you cannot know how we feel (...)". That was something they could not prepare me for' (BE, PCU, 1)*

### **Alternatives to the use of sedation**

Consideration of whether an alternative approach to sedation of the patient would have been more appropriate was also a source of concern for some relatives in all three countries. Several questioned whether it would have been more appropriate for sedation to have started earlier or whether euthanasia would have been a more appropriate option. One relative (UK) felt it would have been more appropriate for the sedation to have been deeper; another (NL) questioned whether sedation had been necessary and reflected on who benefitted from its use.

*'My feeling is that it [the death of the patient] probably would not have gone otherwise, apart from the fact that we now have the feeling that we still have done something for her, (...) because that's what I just say, seeing suffering is worse than suffering itself. So I wonder if that last hour when she slept on those drugs was it for our benefit or hers' (NL, hospital, 2)*

### **Hastening death**

There were few concerns about whether or not sedation had shortened the patient's life in the Netherlands and Belgium. However, in the UK, the issue of hastening death was a concern raised by some relatives.

*'I mean, I did think to myself, 'Have we actually killed him? ... Well, it was obviously something very powerful...' (UK, hospice, 1)*

### **Sedation and the process of saying goodbye**

In descriptions of the dying process that relatives gave, there were marked differences between the countries in relation to the process of saying goodbye.

### **Netherlands and Belgium: a planned farewell**

In the Netherlands and Belgium, the opportunity to say goodbye was highly appreciated by many relatives and patients who knew that death was inevitable and were able, to some extent, to prepare for it. Saying goodbye was frequently a planned event occurring either before sedation began, or as it commenced. However, some relatives had less positive experiences. For example, one relative described the gathering of everyone around the patients' bed for a planned goodbye as a 'carnival'. Unexpected events, as described above, such as the patient regaining consciousness, were perceived as distressing and interfered with the process of saying goodbye. A further stressor for relatives was the time between saying goodbye and the patients' death with some describing this as a 'vacuum' where they were 'waiting' for the patient to die.

*'But they did give us the time to say goodbye. They said...because we had that conversation in the morning, like, we are going to do that [start the sedation] in the afternoon, like they slowly came to prepare her and they kept on saying like, she can still hear you now. So you can still talk to her now. But once we've put her to sleep later then contact isn't possible anymore' (NL, hospital, 1)*

*'It's difficult to put it into words, but as you said, you have indeed already said goodbye when the sedation is administered. You can say a fancy goodbye hey, right that's how it should be, what really helps in placing death, huh, but then there...(...) You cannot leave the man there at the palliative unit without going there huh. Just the idea of 'I'm leaving my father behind, I'm not going... That is not good; my brother said "I'm sorry; I'm not going to go anymore. I'm no longer going, because I already said goodbye..."' (BE, PCU, 1)*

### **United Kingdom: gradual process**

A discrete moment of parting was less dominant in the accounts of relatives from the UK. Here, the use of sedation was generally described as a gradual process with increasing sedative doses and accompanying loss of consciousness occurring over time during symptom management rather than being a planned single event. Relatives therefore did not usually describe a specific planned moment of goodbye. Some relatives in all three countries described occasions where patients had regained consciousness once sedation had been commenced, however, in the UK such situations were not typically described as distressing; rather, they were welcomed and greatly appreciated by some.

*'Erm, but, erm...the thing was, they like, when he woke up and you had some communication, these were golden moments, because these were the times...these were all I had left' (UK, hospice, 3).*

## DISCUSSION

This was the first study to gain in-depth understanding of relatives' experiences of continuous sedation until death in three European countries. Most relatives were able to provide a description of the concept of sedation; nevertheless, several were unsure about what it entailed. Although relatives generally believed sedation contributed to the patient having a good death, they also expressed some concerns about its use and experienced some unexpected events for which they were unprepared. According to relatives from the Netherlands and Belgium, the start of the sedation allowed for a planned moment of 'saying goodbye'. In contrast, relatives from the UK described the process of saying goodbye as a more gradual and less explicit process.

### **Relatives' understandings and descriptions of the concept of sedation**

Most relatives in this study were aware of, and used, the term 'sedation' or 'palliative sedation'. Relatives had three distinct ways of describing the practice, referring to the goals, practical aspects, and outcomes of sedation. In contrast, a study among the general population of Dutch citizens showed that the majority were unfamiliar with the concept of sedation, describing it as similar to dehydration or euthanasia (29). While this seems initially incongruent with the findings of this study, this may be because the sample had no personal experience of the use of sedation. However, it was also evident that some relatives from all three countries in this study continued to be unsure about the use of sedation. Reflecting on the death of their family member, some relatives still had questions and certain misunderstandings about what sedation entailed. For example a few relatives thought morphine was the predominant drug used to sedate the patient, although benzodiazepines were the sedatives used for all patients included in this study.

Although relatives from all three countries in this study generally appeared to be satisfied with the provision of information regarding sedation, lack of knowledge or understanding for some appeared to be related to concerns they experienced as a result of its use. Many studies have highlighted inadequate provision of information and poor communication in end-of-life care which may result in feelings of isolation, disillusion, and distress (30) and it is evident from this study that giving of information, regularly over time, and checking of understanding could be important in fostering patients and relatives' satisfaction with the use of sedation.

Finally, relatives in our study described the goal of sedation primarily in terms of preventing or decreasing the physical or psychological/existential suffering of the patient. There is general consensus regarding the use of continuous sedation for the management of physical symptoms such as delirium or dyspnea that are refractory to palliative treatments. The use of sedation to treat uncontrolled psychosocial or existen-

tial suffering is, however, considered controversial (31, 32). It has to be kept in mind that relatives may have different experiences in case of different refractory symptoms needs.

### **Quality of dying and relatives' concerns**

Relatives from all three countries evaluated the use of sedation for their dying family member as being positive overall. This positive evaluation was largely related to the decrease in patients' physical or psychological/existential suffering (33), and previous studies have shown that adequate symptom relief is key to the experience of a 'good death' (34–37).

However, it has been argued in the literature that consciousness is a fundamental part of being alive; therefore, deliberate reduction of consciousness by the use of deep sedation may contribute to a loss of dignity for the patient (15). Nevertheless, according to the relatives in this study patient dignity was threatened by overwhelming symptoms and sedation contributed to a dignified death by offering some relief from those symptoms. As with other studies (38–39), this research demonstrated the importance of care being in line with patient's wishes and, in this study, the use of sedation was perceived as contributing not only to the patient's quality of dying but also as a means of honoring their wishes and allowing them to die with dignity.

Although the majority of relatives reported that they were comfortable with the use of sedation, many also expressed concerns about its use which related to the wellbeing of the patient and the relative themselves, possible alternatives to the use of sedation, and the hastening of death. The type of concerns that relatives expressed differed between the three countries. Concerns regarding the potential hastening of death were for instance mostly expressed by relatives from the UK. Previous results from the UNBIASED study showed that in the UK, an overarching concern exists among professional caregivers to avoid hastening death, while most of the Dutch and Belgian health care professional did not perceive that sedation hastened death or accepted that it may, to some extent (26). Concerns regarding the potential hastening of death were for instance mostly expressed by relatives from the UK. For relatives from the Netherlands and Belgium, unexpected events, such as the time it took the patient to become unconscious or patients coming to awareness during sedation, were an important cause of concern. This suggests two things, on the one hand some relatives may have not have been sufficiently informed by their professional caregivers about what can occur at the start of, and during sedation. On the other hand, it raises questions about the effectiveness of the sedative drugs, the dosages used, echoing previously published concerns (40–42), while at the same time demonstrating the complexities of administering appropriate dosage to induce unconsciousness.

### **Sedation and saying goodbye**

Saying goodbye to the patient as an event or particular moment was an important theme in the Netherlands and Belgium, but less so in the UK. In the Dutch and Belgian cases, the start of sedation was often a distinguishable and planned moment, in which an 'orchestrated farewell' was created. It is striking that relatives' descriptions of such a planned 'goodbye' have many similarities with the practice of euthanasia, (which is legalized in the Netherlands and Belgium) (43, 44) where relatives gather around the bed of the patient and say goodbye, and the physician administers drugs. One of the key differences though seems to be the trajectory thereafter. Patients who receive euthanasia typically die within several seconds to minutes, in contrast, in patients who receive sedation, death typically follows after one or more days (45), and as such a 'social death' precedes the 'physical' death of the patient (15). Swarte et al. (46) found that bereaved relatives of cancer patients who died by euthanasia coped better with respect to grief and post-traumatic stress reactions than the bereaved of comparable patients who died a natural death, and that this was predominantly related to the opportunity to say goodbye to the patient. The importance of saying goodbye and the beneficial effects on the risk of experiencing traumatic grief have been described by others (35, 47).

However, in this study, it took time for some patients to lose consciousness, others unexpectedly regained consciousness, or lived longer than expected, all of which provoked concerns in some relatives and potentially compromised the expectation in Belgium and the Netherlands for planned moment of parting, although not necessarily for relatives in the UK. This highlights the influence of cultural norms and expectations in influencing perceived experiences of continuous sedation and the subsequent death. For example, while the use of sedation may sometimes be considered as hampering the process of saying goodbye, and as a result could complicate relatives' grieving process in one context, this may not apply in another. It is clear that such cultural expectations should be taken into consideration when explaining sedation and giving information to relatives.

It was striking that saying goodbye was a less dominant theme in the account of the UK relatives. If described at all, they described saying goodbye as a more gradual process rather than a planned single moment in time. This is in line with the finding of a previous study that in the UK, usual sedation practice entails starting with a low dose of sedatives which can be gradually increased when necessary, with less emphasis placed on making an official medical decision (26).

### **Limitations**

As this is a qualitative study based on the intense exploration of a relatively small number of cases, it is not possible to generalize in a statistical sense from our findings. Secondly, to be sensitive to the early phases of grieving, relatives were contacted

no sooner than 3 months after the death of the patient, introducing potential recall bias. Thirdly, the data could be influenced by selection bias, because it is possible that relatives with relatively strong positive or negative experiences agreed to participate in the study. Fourth, due to the small number of cases included in the study, comparison between countries is difficult. Therefore, our results should be interpreted with some caution. Finally, the response rate was rather low among bereaved relatives. It is highly likely that the impact of bereavement following a death where the patient had severe symptoms may have influenced this low response rate, but we do not have any firm evidence about this.

### **Recommendations for practice and directions for future research**

Understanding relatives' experiences with continuous sedation until death is of value in developing effective care strategies (48). Both the nature and extent of the concerns that relatives experience suggest that relatives are in need of continuous information and professional guidance at the beginning and throughout continuous palliative sedation of their family members (49). Providing full information and regular updates about e.g., the level of consciousness, clinical symptoms, and (the 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. To ensure that relatives' diverse concerns are addressed, and to reduce the risk of potential adverse health outcomes for them, the needs of relatives should be continuously monitored. Guidelines on the use of sedation in end-of-life care state that families should be allowed and encouraged to be with the patient before and during the sedation, and should be given an opportunity to say goodbye (4). Further studies should investigate in more depth how the use of sedation affects grief, and how saying goodbye could be best incorporated in the varying contemporary sedation practices at the end of life.

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# CHAPTER 5

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## **No negative impact of palliative sedation on relatives' experience of the dying phase and their wellbeing after the patient's death**

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Submitted

## ABSTRACT

**Background.** Palliative sedation hampers communication and this may affect the quality of the dying process negatively, both for patients and their relatives.

**Objective.** To study whether relatives of patients who received palliative sedation differ in their experience of the dying phase and their wellbeing after the patient's death from relatives of patients who died a non- sudden death without the use of sedation.

**Methods.** We conducted an observational study among relatives of a consecutive sample of patients who died an expected death in the Erasmus MC Cancer Institute or hospice Laurens Cadenza in Rotterdam, between 2010 and 2013. Relatives were asked to fill in a questionnaire about the possible use of palliative sedation, their experience of the dying phase, and their wellbeing after the patient's death. The association of the use of sedation with relatives' experiences and their wellbeing was assessed with a multivariate linear regression analysis, controlling for socio-demographics and care characteristics.

**Results.** Relatives filled in questionnaires for 151 patients who had been sedated and 90 patients who had not been sedated. The median time since the patient had passed away was 21 months (IQR 14-32). Relatives of sedated patient more often stated that the professional caregivers could have done more to make the period before the death of the patient more bearable ( $n=31$ , 20%) than relatives of non-sedated patients ( $n=7$ , 8%) ( $p=.013$ ). No significant differences were found in relatives' assessments of the quality of end-of-life care (a median score of 9 in both groups on a 0-10 scale), patients' quality of life in the last week before death (a median score of 4 and 3 on a 0-10 scale), and their quality of dying (a median score of 8 in both groups on a 0-10 scale), between relatives of patients who did not and did receive sedation. Further, no significant differences were found in relatives' satisfaction with their own life 3 months after the patient's death (a median score of 6 in both groups on a 0-10 scale) and at the time of the survey (a median score of 8 and 7 on a 0-10 scale), their general health (a median score of 3 in both groups on a 1-5 scale) and their mental wellbeing (a median score of 11 and 12 on a 0-25 scale).

**Conclusion.** The use of sedation does not seem to have a negative influence on bereaved persons' experience of the dying phase of their deceased relative or their wellbeing after the patient's death.

## BACKGROUND

A frequently used last resort intervention in end-of-life care is palliative sedation, that is, the administration of sedating drugs to induce a state of unconsciousness to take away a dying patient's perception of symptoms (1-3). A European study undertaken in 6 countries in 2001/2 reported that continuous deep sedation until death was used for 2.5%-8.5% of all dying patients (2). Subsequent studies suggested that sedation was used for 15% of deceased persons in Flanders, Belgium in 2007 (4), in 12% of all deceased persons in The Netherlands in 2010 (5), and 17% of all deceased persons in the U.K. in 2007 (6, 7). Palliative sedation is used in all settings where patients die, but most often in hospitals and for patients with cancer (2, 8-10). While palliative sedation is often seen as an indispensable intervention to alleviate severe suffering in the dying phase, it is also heavily being criticized for depriving patients of the ability to communicate, where many patients consider being conscious until death important (11), and its resemblance to euthanasia (12). Further, its use can be disturbing for patients' relatives (13, 14). The start of sedation may be the time at which it dawns on the family that the patient's death is imminent and the intimacy of family care may be disrupted by the introduction of technologies such as sedation (1).

There has been little research exploring the experiences of relatives with palliative sedation. Relatives' experiences have mainly been understood from the perspective of professional caregivers. A review of the literature showed that despite the fact that the majority of relatives seems to be comfortable with the use of sedation, several studies found that relatives may experience the use of sedation distressing (15). The reasons for such distress are e.g. the feeling that the patient still suffers while receiving sedation, the inability to interact with the patient after the start of sedation, feeling the burden of responsibility for the decision to start sedation, concerns about a possibly hastened death, the (long) duration of the sedation, the fact that information about the sedation cannot easily be obtained, and the idea that there might be more appropriate ways to provide symptom relief (14-17). As a result, sedation potentially negatively influences relatives' experience of the patient's dying phase and their wellbeing after the patient's death. Insight in these potential consequences of the use of palliative sedation can support the development of evidence-based care strategies to improve the death experience for terminally ill patients and their relatives. Although most palliative care efforts focus on assessing and improving quality of life and quality of care for patients, many studies also highlight the importance of taking good care of the patient's relatives (18-20).

The aim of this study is to assess whether relatives of patients who received sedation differ in their experience of the dying phase and their wellbeing after the patient's death compared to relatives of patients who died a non- sudden death without the use of palliative sedation.

## METHODS

### Study population and recruitment of participants

We conducted an observational study among relatives of a consecutive sample of 564 patients who had died an expected death in the Erasmus MC Cancer Institute or hospice Laurens Cadenza Rotterdam, between 2010 and 2013. The relative who was registered as the contact person of the patient in the medical file, was invited to take part in the study via an information letter that was sent by a senior clinical staff member of the participating settings. If the relative was willing to take part in the study, he/she was asked to fill in the questionnaire. If the relative was not willing to participate, he/she was asked to inform the research team via an answering sheet, or to ignore the invitation. When the relative did not respond within six weeks, he/she received a reminder.

### Questionnaire

The questionnaire was based on several validated questionnaires (21-28).

To assess whether or not the patient had received sedation prior to death, relatives were asked: 'Has your relative been brought to sleep with medication prior to death?' (yes/no/don't know).

Relatives' experience of the dying process was assessed in three items that were derived from the Quality of Death and Dying questionnaire (21): ratings on a 0-10 scale of (1) the patient's quality of life in the last week before death, (2) their quality of dying and (3) the quality of end-of-life care. On these scales, 0 represented a 'terrible experience' and 10 an 'almost perfect experience'.

Relatives' satisfaction with life three months after the patient's death and at the time of the survey was measured by the 'Cantril Ladder' (22), i.e. a picture of a ladder numbered from 0 on the bottom rung (worst possible life) to 10 on the top rung (best possible life). Relatives' general health was assessed with a single item from the Short Form 36 Health Survey (SF-36) (23). A score of 1 indicates poor health and a score of 5 excellent health. Mental wellbeing in the four weeks prior to the survey was assessed with the SF-36, which includes 5 items about mental health (23). Scores were linearly transformed from a 1-6 to a 0-5 scale. The sum score had a minimum of 0 and a maximum of 25. A low score indicates poor mental wellbeing (feelings of nervousness and depression all the time), and a high score implies excellent mental wellbeing (feels peaceful, happy, and calm all the time).

Questions about the socio-demographic characteristics of the deceased person and the relative were added by the research team (24, 25). Items on relatives' involvement in the care for the patient and the decision-making process, and the provision of information were based on the VOICES questionnaire (26). The severity of patient's

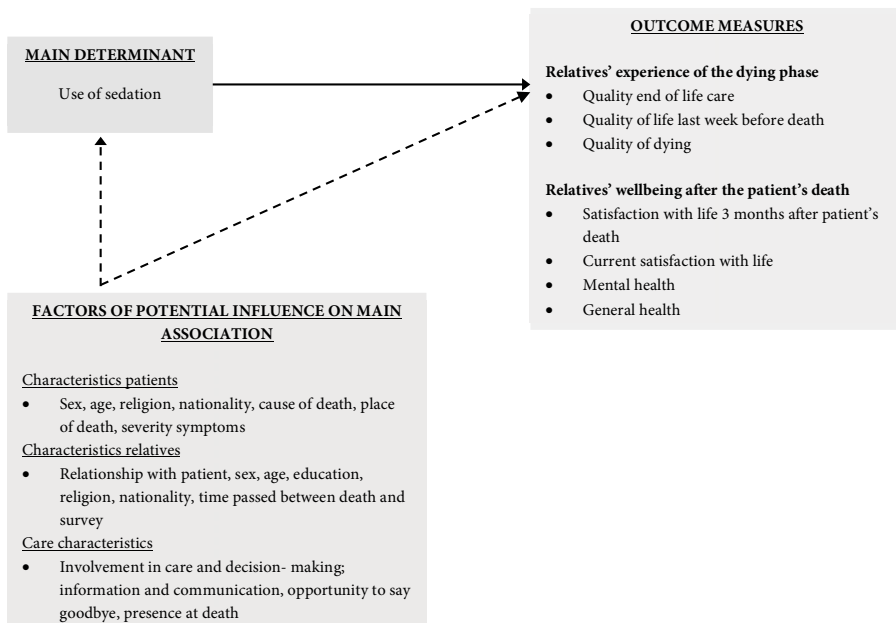


symptoms during the last week of life was assessed using items from the ESAS and the SISC questionnaire (27, 28).

The content of the questionnaire was piloted among five respondents. This led to some small changes in the formulation of the questions. In July and August 2013, 564 questionnaires were sent to potential participants.

## Data analyses

To assess whether relatives of patients who received sedation differed in their experience of the dying phase and their wellbeing after the patient's death from relatives of patients who had died a non- sudden death without the use of palliative sedation, univariable linear regression analyses were performed. The variance of some dependent variables varied across the data (heteroscedasticity), therefore the bootstrap method was used (29). Bootstrapping is a method for deriving robust estimates of standard errors and confidence intervals for point estimates such as the regression coefficient. To be consistent, this method was used for all dependent variables. Logistic regression was used to assess the association between personal and care characteristics, and the use of sedation. Those variables that showed a p-value of 0.30 or less in this analysis, were included in the main multivariable linear regression model (figure 1).

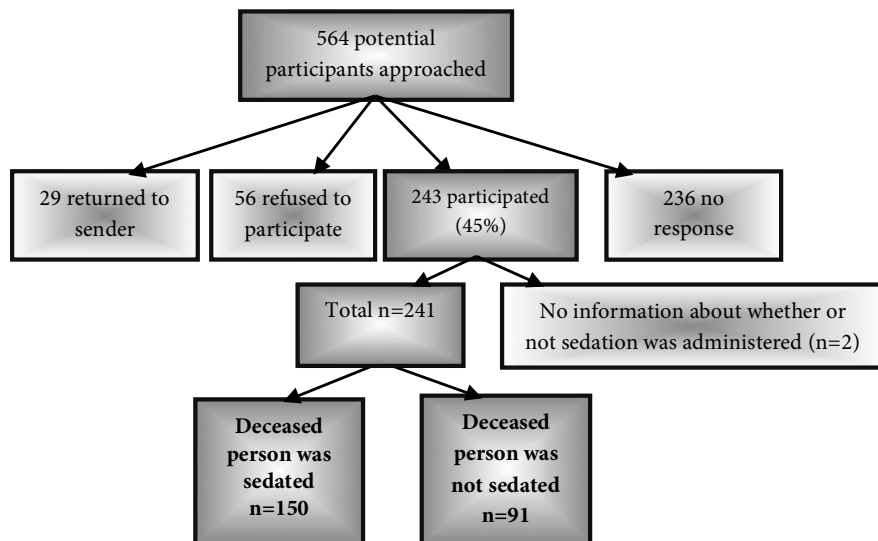


**Figure 1** Model analyses

## RESULTS

In total, 243 of 564 relatives who were approached were willing to participate (45%). Two relatives did not answer the question on whether sedation had been administered. Therefore, a total of 241 cases were included in the study, 151 of whom concerned relatives of patients who had died after the use of palliative sedation. For a full description of the inclusion of cases, a flowchart is presented in figure 2.

The characteristics of the deceased patients and relatives are presented in table 1. The median age at death of non-sedated patients was somewhat higher (77 years (IQR 70-86)) than the age of sedated patients (71 years (IQR 62-81)) ( $p=.002$ ). Patients who received sedation prior to death more often died of cancer (92%) than patients who did not receive sedation (77%) ( $p=.002$ ). Further, the median score for severity of symptoms during the last week of life was slightly higher (worse) for sedated patients (42 (IQR 34-52)) than for non-sedated patients (38 (IQR 30-46)) ( $p=.008$ ). No significant differences were found with regards to sex, religion and place of death. Relatives of sedated patients were more often female (68%) than relatives of non-sedated patients (51%) ( $p=.007$ ). No significant differences were found between both groups with regards to relatives' relationship to the patient, age, education, religion, and time since bereavement.



**Figure 2** Flowchart inclusion participants

Table 1 Characteristics deceased and relatives (n=241)

		No sedation (n=90)	Sedation (n=151)	P value of difference <sup>a</sup> Unadjusted
<i>Deceased</i>				
<b>Sex</b>	<i>Female</i>	50 (56%)	71 (47%)	.187
	<i>Male</i>	39 (44%)	79 (53%)	
	<i>Missing</i>	1	1	
<b>Age</b> (median (IQR) (n=228)		77 (70-86)	71 (62-81)	.002
<b>Religion</b>	<i>Catholic</i>	17 (22%)	22 (17%)	.338
	<i>Christian</i>	21 (28%)	31 (23%)	
	<i>Other<sup>b</sup></i>	6 (8%)	23 (17%)	
	<i>No religion</i>	32 (42%)	57 (43%)	
	<i>Missing</i>	14	18	
<b>Cause of death</b>	<i>Cancer</i>	62 (77%)	133 (92%)	.002
	<i>Other<sup>c</sup></i>	19 (23%)	12 (8%)	
	<i>Missing</i>	9	6	
<b>Place of death</b>	<i>Hospice</i>	83 (92%)	138 (91%)	.821
	<i>Hospital</i>	7 (8%)	13 (9%)	
<b>Severity of symptoms during last week of life<sup>d</sup></b> (median (IQR)) (n=201)	<i>Overall score</i>	38 (30-46)	42 (34-52)	.008
<i>Relatives</i>				
<b>Relatives relationship to patient</b>	<i>Married/partner</i>	24 (27%)	51 (36%)	.581
	<i>Child</i>	42 (48%)	54 (38%)	
	<i>Parent</i>	5 (6%)	12 (8%)	
	<i>Other<sup>e</sup></i>	17 (19%)	26 (18%)	
	<i>Missing</i>	2	8	
<b>Sex</b>	<i>Male</i>	44 (49%)	47 (32%)	.007
	<i>Female</i>	45 (51%)	101 (68%)	
	<i>Missing</i>	1	3	
<b>Age</b> (median (IQR)) (n=237)		57 (49-66)	59 (50-65)	.465
<b>Education<sup>f</sup></b>	<i>Missing</i>	1	3	.400
	<i>Low</i>	37 (44%)	43 (31%)	
	<i>Intermediate</i>	18 (21%)	55 (39%)	
	<i>High</i>	29 (35%)	43 (31%)	
	<i>Missing</i>	6	10	
<b>Religion</b>	<i>Catholic</i>	10 (13%)	15 (12%)	.132
	<i>Protestant</i>	20 (25%)	33 (25%)	
	<i>Other<sup>g</sup></i>	5 (6%)	19 (15%)	

**Table 1** Characteristics deceased and relatives (n=241) (continued)

	No sedation (n=90)	Sedation (n=151)	P value of difference <sup>a</sup> Unadjusted
<i>No religion</i>	44 (56%)	63 (48%)	
<i>Missing</i>	11	21	
<b>Time since bereavement (in months)</b> (median (IQR)) (n=234)	20 (14-31)	22 (15-32)	.592

<sup>a</sup> Difference test is based on logistic regression analysis (univariable). Reference group is no sedation.

<sup>b</sup> E.g. Buddhism, Hinduism, Judaism

<sup>c</sup> CVA, respiratory diseases, dementia, heart failure and other diseases

<sup>d</sup> Scale consisting of 15 items with range: 1-5. Total scale score with a minimum of 15 (not severe) and a maximum of 75 (very severe). Symptoms: pain, nausea/ vomiting, dyspnea, confusion, restlessness, depression, anxiety, consciousness, fatigue, loss of control, loss of dignity, burden for environment, loss of interest, hopelessness, longing for death.

<sup>e</sup> Sibling, grandchild, cousin, family in law, aunt/uncle

<sup>f</sup> Low= primary education + lower vocational education + lower secondary education; Intermediate= intermediate vocational education + upper secondary education; High= higher vocational education or university

Relatives of sedated patients more often stated that the professional caregivers could have done more to make the period *before* the death of the patient more bearable (n=31, 20%) than relatives of non-sedated patients (n=7, 8%) (p=.013). Such statements included suggestions to provide 'more information', e.g. regarding the drugs that were administered and the duration of the sedation, to provide 'more compassionate care', e.g. by being more attentive to relatives or offering a listening ear when needed, and general suggestions to provide 'better care'. Otherwise, we found no statistically significant differences between both groups in the characteristics of the care that was provided during the last week of life (table 2). Relatives of non-sedated patients were involved in the care for the patient in 74% of the cases, and relatives of sedated patients in 83% (p=.093). Relatives perceived the degree of their involvement as sufficient in 84% and 88% of the cases, respectively (p=.357). In case relatives did not perceive the degree of their involvement as sufficient, all except one would have preferred more involvement. Relatives of non-sedated patients perceived the amount of information they received from professional caregivers about the patient's situation and care during the last week of life as sufficient in 82% of the cases, compared to 88% of the relatives of sedated patients (p=.191). All relatives who did not perceive the amount of information as sufficient wished they had received more information. Relatives of non-sedated patients had had the opportunity to say goodbye to the patient in 53% of the cases and they had 'more or less' had the opportunity in 30%, versus 66% and 24% of relatives of sedated patients, respectively. Relatives of non-sedated patients were present at

**Table 2** Care characteristics (n=241)

		No sedation (n=90)	Sedation (n=151)	Total	P value <sup>a</sup>
Relative was involved in the care for the patient by the professional caregivers in last week of life	Yes	67 (74%)	126 (83%)	193 (80%)	.093
	No	23 (26%)	25 (17%)	48 (20%)	
Relative perceived the degree of involvement in care for the patient by the professional caregivers in last week of life as sufficient	Yes	72 (84%)	132 (88%)	204 (86%)	.357
	No	14 (16%)	18 (12%)	32 (14%)	
	Missing	4	1	5	
Relative perceived the amount of information received from professional caregivers about situation patient and care for patient during last week of life as sufficient	Yes	72 (82%)	132 (88%)	204 (86%)	.191
	No	16 (18%)	18 (12%)	34 (14%)	
	Missing	2	1		
Relative had the opportunity to say goodbye to the patient <sup>b</sup>	Yes	48 (53%)	98 (65%)	146 (61%)	.200
	More or less	27 (30%)	36 (24%)	63 (26%)	
	No	14 (16%)	15 (10%)	29 (12%)	
	Missing	1	2	3	
Relatives was present at the death of the patient	Yes	50 (56%)	91 (60%)	141 (58%)	.473
	No	40 (44%)	60 (40%)	100 (42%)	
Professional caregivers could have done something to make the period <u>before</u> the death of the patient more bearable for the relative	Yes	7 (8%)	31 (20%)	38 (16%)	.013
	No	81 (92%)	120 (80%)	201 (84%)	
	Missing	2	-	2	
Professional caregivers could have done something to make the period <u>after</u> the death of the patient more bearable for the relative	Yes	5 (6%)	7 (5%)	12 (5%)	.700
	No	81 (94%)	143 (95%)	224 (95%)	
	Missing	4	1	5	

<sup>a</sup> Difference test is based on logistic regression analysis (univariable). Reference group is no sedation.

<sup>b</sup> Variable has been dichotomized for the logistic regression analysis

the patient's death in 56%, compared to 60% of the relatives of sedated patients. In all cases where the relative was not present at the death of the patient, they indicated that another relative had been present. In total, 6% of the relatives of non-sedated patients stated that the professional caregivers could have done something for them to make the period *after* the death of the patient more bearable, compared to 5% of the relatives of sedated patients ( $p=.700$ ).

**Table 3** Experience of the dying phase and wellbeing after the patient's death: Differences between relatives of patients who received sedation and relatives of patients who had died a non- sudden death without the use of palliative sedation ( $n=241$ )

	No sedation ( $n=90$ )	Sedation ( $n=151$ )	Univariable regression <sup>a</sup>		Multivariable regression <sup>b</sup>	
	Median (IQR)	Median (IQR)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)
<i>Relatives' experience of the dying phase</i>						
<b>Quality end of life care<sup>c</sup></b> ( $n=241$ )	9 (8-9)	9 (8-10)	.808	0.06 (-0.43-0.52)	.888	0.04 (-0.57-0.66)
<b>Quality of life patient last week before death<sup>c</sup></b> ( $n=241$ )	4 (2-7)	3 (2-7)	.356	-0.35 (-1.12-0.30)	.818	-0.13 (-1.21-0.96)
<b>Quality of dying<sup>c</sup></b> ( $n=239$ )	8 (6-8)	8 (6-8)	.324	0.31 (-0.32-0.99)	.273	0.46 (-0.37-1.28)
<i>Relatives' wellbeing after the patient's death</i>						
<b>Life satisfaction 3 months after the death of the patient<sup>c</sup></b> ( $n=241$ )	6 (4-8)	6 (4-7)	.082	-0.51 (-1.06-0.09)	.970	0.01 (-0.74-0.77)
<b>Current life satisfaction<sup>c</sup></b> ( $n=241$ )	8 (7-8)	7 (6-8)	.268	-0.26 (-0.67-0.19)	.581	-0.20 (-0.90-0.51)
<b>General health<sup>d</sup></b> ( $n=236$ )	3 (3-4)	3 (3-3)	.742	-0.39 (-2.69-1.92)	.288	1.62 (-1.38-4.62)
<b>Mental health<sup>e</sup></b> ( $n=232$ )	11 (9-14)	12 (12-14)	.204	0.59 (-0.37-1.50)	.371	0.61 (-0.73-1.95)

<sup>a</sup> Linear regression (univariable)

<sup>b</sup> Linear regression (multivariable). Adjusted for sex patient, age patient, cause of death, severity symptoms, religion relative, sex relative, involvement relative in care for patient, satisfaction relative with information from caregivers, opportunity to say goodbye to patient and care for relative before the death of the patient ( $p<.30$ )

<sup>c</sup> Range 0-10 (0= terrible experience, 10= almost perfect experience)

<sup>d</sup> Range 1-5 (1= poor health, 5= excellent health)

<sup>e</sup> Mental wellbeing four weeks before questionnaire. Scale with 5 items. The sum score had a minimum of 0 (low mental wellbeing) and a maximum of 25 (excellent mental wellbeing)

Table 3 presents relatives' experience of the dying phase and relatives' wellbeing after the patient's death for non-sedated and sedated patients. We found no significant differences between both groups in univariable analyses and multivariable models that controlled for characteristics of patients, relatives and care. The median score for the quality of end-of-life care was 9 in both groups and the median score for quality of life was 4 for non-sedated and 3 for sedated patients. The median score for quality of dying was 8 in both groups. Relatives' satisfaction with their own life three months after the patient's death was rated at a median of 6 in both groups, and at the time of the survey the median scores were 8 and 7, respectively. The median scores on the general health scale were 3 in both groups and the median scores on mental health were 11 and 12.

## DISCUSSION

The aim of this study was to assess whether relatives of patients who received sedation differ in their experience of the dying phase and in their wellbeing after the patient's death compared to relatives of patients who died a non-sudden death without the use of palliative sedation. No significant differences were found in relatives' assessments of the quality of end-of-life care, patients' quality of life in the last week before death, and their quality of dying. Further, no significant differences were found in relatives' satisfaction with their own life, their general health and their mental wellbeing after the patient's death. Apparently the use of sedation does not have a negative influence on bereaved persons' experience of the dying phase of their deceased relative or their own wellbeing after the patient's death, despite the fact that it is known that relatives may experience the use of sedation as distressing (15, 17, 30).

Previous studies have shown that adequate symptom relief is key to the experience of a 'good death' (11, 31-33). Many relatives have been demonstrated to evaluate the provision of palliative sedation to their severely suffering family member positively because the patient's suffering is finally alleviated (34). The benefit of palliation could explain why no differences were found in relatives' experience of the dying phase and wellbeing after the patient's death, despite the fact that relatives of sedated patients report significantly more severe symptoms in the last week of life than relatives of non-sedated patients, which has also been found in other studies (9). Further, the loss of the ability to communicate with the patient during the sedation, also sometimes referred to as a social death (35), and a potential life-shortening effect are often considered to be key drawbacks of the use of palliative sedation by health care professionals, ethical and legal experts (11, 12). However, in the evaluation of relatives, adequate symptom relief apparently outweighs these possible drawbacks. It has been well established that the wellbeing of the patient is a crucial factor for the health and welfare of the patient's

relatives (36). Adequate symptom relief for the patient might therefore also benefit the wellbeing of relatives.

It is known that providing information to family members and involving them in discussions about medical care and interventions reduces symptoms of post-traumatic stress, anxiety, and depression (37, 38). Our study showed that a large majority of the relatives experienced the amount of information they received from caregivers as sufficient, which might have been an important determinant of their wellbeing after the patient's death. These findings are not fully in line with other studies highlighting inadequate provision of information and poor communication in end of life care in general (19), or with palliative sedation in particular (34, 39). One explanation could be that our study predominantly concerned relatives of patient who were cared for in a hospice (91%) which has been found to be the place of care where bereaved family members have relatively few unmet needs for information (40).

The World Health Organization's definition of palliative care incorporates a support system to help the relatives to cope during the patient's illness and during their own bereavement (41). Previous studies have shown that relatives need support for their own wellbeing as well as to enable them to be close to and support the patient (42). The majority of the relatives in our study was satisfied with the support that was provided to them by the professional caregivers before and after the death of the patient. However, one in five relatives of sedated patients stated that the professional caregivers could have done something to make the period *before* the death of patient more bearable for them. Since palliative sedation is a far-reaching intervention that often follows a trajectory of intense suffering for the patient, caregivers should specifically focus on comforting, supporting and providing continuous information to the patient's family when palliative sedation is being considered and while it is being administered.

This study has several strengths. Since we conducted a study among relatives of *consecutive* patients, it is not possible that the senior clinical staff members made a specific selection of patients or relatives. A large sample was employed which enhances the generalizability of the findings. However, our study also has some limitations. Non-response may have influenced our findings. For instance, people with more severe feelings of grief are more prone to non-response than persons with less feelings of grief (43, 44). Also, relatives may differ in their interpretation of the question "Has your relative been brought to sleep with medication prior to death". Nevertheless, we think that this descriptive definition is less ambiguous than the term "palliative sedation". Previous studies have shown that "lay persons" have different notions about what this term entails (45). Further, most relatives were recruited via a hospice. The quality of hospice care is generally rated higher than the quality of hospital care (46, 47), also by relatives (26). However, when we corrected the analysis for place of death the results were similar. Therefore, it is not expected that the results with regard to the comparison



between the two groups were influenced. Finally, heterogeneity in the investigated population, such as variability in causes of death, may have lowered the power to find differences between the two patient groups.

We conclude that the use of sedation does not, in itself, seem to have a negative influence on bereaved persons' experience of the dying phase of their deceased relative or on their own wellbeing after the patient's death. This can probably be explained by the benefit of relieving severe suffering of a dying patient. Still, palliative sedation is a far-reaching and ethically complex intervention that requires caregivers to focus on providing comfort, support and continuous information both to the patient and to the patient's family.

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## CHAPTER 6

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# **Estimating the potential life-shortening effect of continuous sedation until death: a comparison between two approaches**

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## ABSTRACT

**Context.** In some cases, physicians estimate that continuous sedation until death may have a life-shortening effect. The accuracy of these estimations can be questioned.

**Aim.** The aim of this study is to compare two approaches to estimate the potential life-shortening effect of continuous sedation until death.

**Methods** In 2008, 370 Dutch physicians filled out a questionnaire and reported on their last patient who received continuous sedation until death. The potential life-shortening effect of continuous sedation was estimated through a direct approach (question: Did continuous sedation, according to your estimation, hasten the patient's death? If yes: by how much time?) and an indirect approach (estimated life expectancy minus duration of sedation). The intrarater agreement between both approaches was determined with a weighted  $\kappa$ .

**Results.** According to the direct approach, sedation might have had a life-shortening effect in 51% of the cases and according to the indirect approach in 84%. The intrarater agreement between both approaches was fair (weighted  $\kappa=0.38$ ). In 10% of all cases, the direct approach yielded higher estimates of the extent to which life had been shortened; in 58% of the cases, the indirect approach yielded higher estimates.

**Conclusions.** The results show a discrepancy between different approaches to estimate the potential life-shortening effect of continuous sedation until death.



## INTRODUCTION

A significant minority of dying people experience serious symptoms that are unresponsive to conventional therapies. In such circumstances, palliative sedation may be considered. Palliative sedation is the deliberate lowering of a patient's level of consciousness in the last stages of life (1). Sedation can be used intermittently or continuously until death, and the degree of sedation necessary to relieve suffering may vary from superficial to deep (2). Continuous sedation is most frequently used in patients suffering from physical symptoms such as delirium, dyspnoea, pain and nausea (3, 4). The moral status of continuous sedation until death has been the subject of fierce ethical debate (5). This debate mostly focuses on whether continuous sedation may hasten death. It is stated in guidelines that physicians should use sedation with the intention to relieve suffering, and not with the intention to shorten the patient's life (1, 6). Further, to preclude a potential life-shortening effect, it is recommended to restrict the use of continuous sedation to patients with an estimated life expectancy of at most 2 weeks (1, 7, 8). When the patient's life expectancy is within this limit and when sedatives are properly dosed, continuous sedation until death has presumably no life-shortening effect (1, 3, 8).

The underlying assumption in guidelines is that physicians can estimate a patient's life expectancy with sufficient accuracy. However, estimating life expectancy of patients with advanced disease is known to be very difficult (7, 9, 10). Physicians tend to overestimate survival: it has been shown that survival of patients is typically 30% shorter than predicted by physicians, but that the accuracy of physicians' predictions increases when death approaches (10).

Although it is assumed in guidelines that continuous sedation until death has no life-shortening effect when used proportionally (1), physicians may have a different perspective. In a large-scale nationwide follow-up study, performed in 2005 in the Netherlands, physicians estimated that continuous sedation until death might have had a life-shortening effect in 26% of the cases (3). In 20% of these cases, it was estimated that sedation had shortened the patient's life by less than one week, in 4% of the cases by less than one month and in 2% by more than one month. These estimates should be interpreted cautiously. On the one hand, physicians might be cautious when they are directly asked to estimate the potential life-shortening effect of continuous sedation until death. The sensitivity of the topic might have led to socially desirable answers and physicians might have been reluctant to state their true opinions (11). For instance, because they might feel that a life-shortening effect is undesirable and morally complex, and because acknowledging such an effect may suggest that a patient's death was actively hastened. On the other hand, physicians are known to be inclined to overestimate the life expectancy of patients with advanced disease (9). It has been shown that

survival of patients is typically 30% shorter than predicted by physicians, but that the accuracy of physicians' predictions increases when death approaches.<sup>9</sup> The fact that physicians commonly have difficulty in estimating life expectancy and often are inclined to overestimation might also hold true for the life-shortening effects of sedative medication in patients with a limited life expectancy (12). Obviously, estimating the true life-shortening effect of continuous sedation would require an experimental study, which is, however, not an option for this patient group.

The aim of this study therefore is to get insight in the accuracy of estimates of the life-shortening effect of continuous sedation until death by comparing two different approaches. We compare a direct approach, where we ask physicians to estimate the life-shortening effect of continuous sedation until death, and an indirect approach, where we ask the physicians to estimate the patient's life expectancy and relate that to the duration of the sedation.

## METHODS

### Study Design and Data Collection

A secondary analysis was performed of data that were collected among physicians in a study that evaluated the practice of palliative sedation after the introduction of the Royal Dutch Medical Association guideline (13-14). Data collection took place between February 2008 and September 2008. For this study, a structured questionnaire was sent to a random sample of 1580 physicians: 1128 in the north-western and south-western regions of the Netherlands (general practice,  $n=466$ ; nursing home,  $n=195$ ; and hospital,  $n=467$ ) and 452 general practitioners in the north-eastern region (13). Physicians were asked to report on the last patient for whom they had been responsible for providing continuous sedation until death. One of the issues addressed was the potential life-shortening effect of continuous sedation until death. Physicians were asked whether or not the use of continuous sedation until death might have had a life-shortening effect ('Did continuous sedation, in your estimation, hasten the patients' death?'); to estimate the patient's life expectancy at the start of sedation ('What, in your estimation, was the patient's life expectancy, at the time continuous sedation was started?'); and to assess the actual duration of the sedation (question: 'How long after the start of continuous sedation did the patient die?') (table 1).

### Analysis

We used a direct and an indirect approach to estimate the potential life-shortening effect of continuous sedation until death. The direct approach was based on the direct question about the life-shortening effect of sedation. Response categories ranged

**Table 1** Two approaches of estimating the life-shortening effect of continuous sedation until death

Direct approach		-		=		Indirect approach
	Life expectancy		Duration sedation			
"Did the use of continuous sedation in your estimation shorten life?"	"What was in your estimation the patient's life expectancy at the start of continuous sedation"		"How long after the start of the sedation did the patient pass away?"			Life expectancy <i>MINUS</i> duration
<ul style="list-style-type: none"> <li>• &lt; 1 day shortened</li> <li>• 1-2 days shortened</li> <li>• 3-6 days shortened</li> <li>• 1-2 weeks shortened</li> <li>• 2 weeks- 1 month shortened</li> <li>• &gt; 1 month shortened</li> <li>• Don't know</li> <li>• Contradictory</li> </ul>	<ul style="list-style-type: none"> <li>• &lt; 1 day shortened</li> <li>• 1-2 days shortened</li> <li>• 3-6 days shortened</li> <li>• 1-2 weeks shortened</li> <li>• 2 weeks- 1 month shortened</li> <li>• &gt; 1 month shortened</li> <li>• Contradictory</li> </ul>		<ul style="list-style-type: none"> <li>• Weeks, days and/or hours</li> </ul>			<ul style="list-style-type: none"> <li>• &gt; 3 days prolonged</li> <li>• 3 days prolonged</li> <li>• 2 days prolonged</li> <li>• 1 day prolonged</li> <li>Combined: no life shortening</li> <li>• &lt; 1 day shortened</li> <li>• 1-2 days shortened</li> <li>• 3-6 days shortened</li> <li>• 1-2 weeks shortened</li> <li>• 2 weeks- 1 month shortened</li> <li>• &gt; 1 month shortened</li> <li>• Don't know</li> <li>• Contradictory</li> </ul>

between 'no life-shortening' and 'more than one month shortened'. With the indirect approach, the duration of the sedation until death was subtracted from the estimated life expectancy at the start of sedation. The estimated life expectancy consisted of categories varying from 'less than one day' to 'more than one month'. The question about the duration of the sedation was answered in weeks, days and/or hours. To make statistical calculations possible, life expectancy was recoded into hours by taking the middle of categories: for example, 'less than one day' was recoded as '12 h'. The difference between the recoded estimated life expectancy and the duration of the sedation was calculated (table 1).

A total of 606 physicians (38%) filled out the questionnaire. Response rates were 43% for general practitioners, 50% for nursing homes physicians and 24% for clinical specialists. Of the responding physicians, 370 (61%) reported about their last case (11). Physicians were on average 49-years-old (range 28–64). A majority of the physicians were men (64%). Of all physicians, 15% worked in a hospital, 17% in a nursing home or hospice and 68% were general practitioners. Physicians had on average 19 years work experience (range 1–38). The patients physicians reported on were on average 70 years old (range 3–99) at the time of their death. The majority of the patients (71%) had cancer as their main diagnosis. The majority of the patients were male (52%) (table 2).

Physicians were excluded from the analyses if the answer to one of the questions was 'unknown', 'don't know' or uninterpretable (more than one answer). The intra-rater agreement between the direct and indirect approaches was determined by calculating a weighted  $\kappa$ : quadratic weights were used to take into account the size of differences between both approaches. The scores were interpreted using the Landis and Koch criteria: <0.00=poor agreement, 0.00–0.20=slight agreement, 0.21–0.40=fair agreement, 0.41–0.60=moderate agreement, 0.61–0.80=substantial agreement and 0.81–1.00=almost perfect agreement (13). We also calculated weighted  $\kappa$  values for two subgroups to see whether the level of agreement was different for patients with a relatively long estimated life expectancy and patients with a relatively short estimated life expectancy. A cut-off point of 1 week was used for this analysis, based on the median value of the estimated life expectancy. The significance level was set at 5%. For the analysis, Excel and SPSS V.22.0 were used.

## RESULTS

In 269 cases (74%), physicians estimated that the patient had a life expectancy of less than 1 week, in 84 cases (23%) between 1 and 2 weeks, and in 10 cases (3%) more than 2 weeks at the start of sedation. The duration of the sedation varied between less than 1 day, and 1 and 2 weeks (table 2).

**Table 2** Characteristics of responding physicians and patients and sedation characteristics (N=370)

Variable	Categories	Mean, range	N	%
<b>Respondents</b>				
Age		49 (28-64)		
Sex				
	Male		237	64
	Female		132	36
Work experience		19 (1-38)		
Setting				
	Home		250	68
	Nursing home/hospice		64	17
	Hospital		56	15
<b>Patients</b>				
Age		70 (3-99)		
Sex				
	Male		189	52
	Female		175	48
Primary diagnoses	Cancer		251	71
<b>Sedation characteristics</b>				
Life expectancy at start of sedation <sup>a</sup>				
	< 1 day		14	4
	1-2 days		116	32
	3-6 days		139	38
	1-2 weeks		84	23
	2 weeks–1 month		9	3
	> 1 month		1	0
Duration sedation <sup>b</sup>				
	< 1 day		115	32
	1-2 days		116	32
	3-6 days		115	32
	1-2 weeks		15	4
	2 weeks – 1 month		0	0
	> 1 month		0	0

<sup>a</sup> Missing: n=7<sup>b</sup> Missing: n= 9

**Table 3** Estimated life-shortening effect (direct approach), life expectancy, duration of sedation and the estimated life-shortening effect (indirect approach) (N=370)

	Estimated life- shortening effect according to the direct approach (N, %) <sup>a</sup>	Estimated life- shortening effect according to the indirect approach (N, %) <sup>b</sup>
No life-shortening effect	148 (41)	56 (16)
< 1 day	38 (11)	78 (22)
1-2 days	54 (15)	50 (14)
3-6 days	31 (9)	105 (30)
1-2 weeks	23 (6)	58 (16)
2 weeks – 1 month	5 (1)	8 (2)
> 1 month	0 (0)	0 (0)
Don't know	64 (17)	NA

<sup>a</sup> Missing: n=7<sup>b</sup> Missing: n=15**Table 4** The estimated life-shortening effect of continuous sedation (direct en indirect approach) (n=289<sup>a,b</sup>)

Life shortening effect of continuous sedation until death (direct approach)								
		Not shortened	< 1 day shortened	1-2 days shortened	3-6 days shortened	1-2 weeks shortened	2 weeks- 1 month shortened	Total
<b>Life shortening effect of continuous sedation until death (indirect approach)</b>	Not shortened	35 (12%)	7 (2%)	3 (1%)	0 (0%)	1 (0%)	1 (0%)	47 (16%)
	< 1 day shortened	40 (14%)	11 (4%)	9 (3%)	2 (1%)	0 (0%)	0 (0%)	62 (22%)
	1-2 days shortened	21 (7%)	8 (3%)	9 (3%)	2 (1%)	0 (0%)	1 (0%)	41 (14%)
	3-6 days shortened	32 (11%)	11 (4%)	17 (6%)	17 (6%)	6 (2%)	0 (0%)	83 (29%)
	1-2 weeks shortened	13 (5%)	0 (0%)	13 (5%)	9 (3%)	14 (5%)	0 (0%)	49 (17%)
	2 weeks- 1 month shortened	1 (0%)	1 (0%)	0 (0%)	0 (0%)	2 (1%)	3 (1%)	7 (2%)
	Total	142 (49%)	38 (13%)	51 (18%)	30 (10%)	23 (8%)	5 (2%)	289 (100%)

<sup>a</sup> After excluding cases where the answer to one of the questions was 'don't know', uninterpretable or missing<sup>b</sup> Weighted  $\kappa$  (intra-rater agreement): 0.38 (p=0.000)

When asked directly, 148 physicians (41%) stated that continuous sedation did not have a life-shortening effect, 151 physicians (42%) stated that there might have been a life-shortening effect and 64 physicians (17%) did not know. Using the indirect approach, the use of sedation might have had a life-shortening effect in 84% and no such effect in 16% of the cases (table 3).

After excluding cases where the answer to one of the questions was 'don't know', uninterpretable or missing, 289 cases remained available for analysis of the level of agreement between the direct and indirect approaches of assessing the estimated life-shortening effect of sedation. When asked directly, 147 physicians (51%) estimated a potential life-shortening effect of continuous sedation (table 4). In 13% of these cases, it was estimated that sedation might have shortened the patient's life by less than 1 day; in 28% of the cases, between 1 day and 1 week; in 8% between 1 and 2 weeks; and in 2% by more than 1 month. The duration of the sedation was shorter than the estimated life expectancy at the start of sedation according to 242 physicians (84%). So, following this indirect approach, it was estimated that the use of sedation might have had a life-shortening effect in 84% of the cases (table 4). In 22% of these cases, it was estimated that sedation might have shortened the patient's life by less than 1 day; in 43% of the cases, between 1 day and 1 week; in 17% between 1 and 2 weeks; and in 2% by more than 1 month. In 10% of these cases, the direct approach yielded higher estimates of the extent to which life had been shortened than the indirect approach; in 58% of the cases, the indirect approach yielded higher estimates and there was no difference in 31% of the cases. The level of agreement between the direct and indirect approaches as assessed by weighted  $\kappa$  was 0.38, indicating 'fair' agreement (table 4). Further analysis showed that the level of agreement was somewhat higher for patients with an estimated life expectancy of less than a week (weighted  $\kappa=0.26$ ) as compared with patients with a life expectancy of more than 1 week (weighted  $\kappa=0.10$ ).

## DISCUSSION

In this study, we found that in 51% of the cases Dutch physicians estimate that the use of continuous sedation until death might have had a life-shortening effect when they are directly asked about such an effect. In contrast, on the basis of physicians' estimations of patients' life expectancy at the start of sedation and the duration of sedation until death, it can be estimated that such an effect occurs in 84% of cases. The finding of this substantial discrepancy between the two approaches to estimate the life-shortening effect of continuous sedation until death confirms the difficulty of predicting the life expectancy of patients with advanced disease, and of estimating the potential life-shortening effect of end-of-life interventions. However, our finding

that there is 'fair' agreement between both approaches suggests that this discrepancy is not merely the result of random inaccuracy. In general, physicians might be relatively cautious when they are directly asked to estimate the potential life-shortening effect of continuous sedation until death, because they feel that such an effect is undesirable and morally complex, and because admitting such an effect may suggest that a patient's death was actively hastened. On the other hand, physicians are known to be inclined to overestimate the life expectancy of patients with advanced disease (10), which may extend to patients who are provided with continuous sedation until death. Such inclination could explain the high proportion of cases in which sedation might have shortened life, when the estimate is based on our 'indirect' approach.

Our finding that the agreement between the two approaches to estimate the potential life-shortening effect of continuous sedation was higher for patients with a life expectancy of less than 1 week confirms findings from previous studies that estimations of life expectancy become more accurate when death approaches (10). An implication could be, if physicians indeed consistently overestimate their patients' life expectancy, that in some cases where sedation would be a beneficial intervention, it is started too late or not at all, which would involve unnecessary suffering.

It is striking that, according to both approaches, physicians often think that continuous sedation until death can have a (mostly limited) life-shortening effect. Several empirical studies have suggested that sedation as used in clinical practice has no significant life-shortening effect (15-20). It can, in either of the approaches, be questioned if physicians tend to overestimate the life-shortening potential of sedation, but our data allow no firm conclusion here. The importance of a potential life-shortening effect of continuous sedation until death can also be questioned. The Royal Dutch Medical Association guideline argues that the life expectancy of a maximum of 2 weeks is conditional for palliative sedation (1). The authors of the European Association of Palliative Care framework even stated that sedation should only be contemplated if the patient is hours or days from death (6). However, one could hold the position that palliation with life-shortening side effects is morally justified, as long as proportionately consequential reasons are present. The indication for sedation originates from the presence of one or more refractory symptoms that lead to severe and unbearable suffering. In such circumstances, the life expectancy criterion can be weighed against the severity of refractory symptoms (21). If the benefit of palliation outweighs the harm of an earlier death, if there are no other alternatives and if dosages are titrated according to the patient's need, palliative sedation may be indicated, even if death is not imminent (22). In some cases where the conditions for continuous sedation until death are not met, brief or intermittent sedation may be a possible alternative (1).

Our study had some limitations. First, the physicians in our study provided information retrospectively. The data could therefore be influenced by recall bias. Further,



we asked about the physician's most recent case, which may not always represent physicians' usual practices or approaches (13). Third, the risk that physicians matched their answers and estimations in the questionnaire cannot be ruled out. The true differences between the two approaches might therefore be larger than suggested in our study. To improve accuracy, it might be useful to include patients prospectively in a future study: life expectancy could then be estimated before the start of sedation, and the duration of sedation could be timed. For this study, a secondary analysis was performed of data that were collected in 2008. Therefore, this approach could not be followed in the present study. It can be concluded that estimating the life expectancy of patients who are provided with continuous sedation until death is difficult. Recommendations in guidelines that continuous sedation until death should only be used for patients with a life expectancy of less than 1 or 2 weeks may therefore be difficult to translate to clinical practice. In research, the type of question that is used to estimate the life-shortening effect of sedation and other end-of-life interventions has to be taken into account when interpreting the results. Based on this study, we cannot conclude whether a direct question or a more veiled approach is preferable.

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# CHAPTER 7

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## **Risk factors for complicated grief in older adults**

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## ABSTRACT

**Background.** Older adults grieving the death of a spouse have been found to have a higher risk of complicated grief compared with younger adults.

**Objective.** To find out whether personal characteristics of the patient and the bereaved partner, or characteristics of the patient's illness, end-of-life care and the nature of death are risk factors for complicated grief in older adults.

**Design.** We performed a nested case-control study within the Rotterdam Study.

**Subjects.** We selected 100 couples of which one person had deceased and the other person experienced 'complicated grief', and 100 control couples of which one person had deceased and the other person experienced 'normal grief'.

**Measurements.** Complicated grief was assessed with a 17-item Inventory of Complicated Grief. Determinants were assessed using several sources of information that were available for all participants of the Rotterdam Study. Additionally, medical files of the deceased were manually screened. Logistic regression analysis was performed.

**Results.** Only depression at baseline was significantly associated with complicated grief. Bereaved partners with depression at baseline had a higher risk of complicated grief compared to bereaved partners without depression (OR=3.48; 95% CI=1.40-8.68).

**Conclusions.** Our results suggest that complicated grief in older adults is not clearly related to the circumstances of dying of the deceased partner. Pre-existing conditions such as depression seem to be more important in explaining the occurrence of complicated grief.

## INTRODUCTION

Bereavement is a common experience in older adults. Although the majority of adults recover after the loss of a loved one, a portion continues to grieve for an extended period of time and develops symptoms of a state known as complicated grief (1) or Prolonged Grief Disorder (2). This type of grief is distinct from normal grief as the person cannot accept the death and instead experiences disbelief and preoccupations with the deceased person (1, 3). Complicated grief can be associated with a number of negative health outcomes, such as hypertension, sleep impairment and suicidality (4-6). Among older adults, complicated grief is under diagnosed, minimized as a factor affecting mental health and function, and undertreated (3, 7, 8). Although the bereavement experience of older adults has been associated with less mourning (9), secondary consequences such as social isolation may lead to grief of longer duration and poorer health and mental health outcomes than observed in younger persons. Older adults grieving the death of a spouse have been found to have a higher risk of complicated grief compared with younger adults (7, 8). A Dutch study showed that the prevalence of complicated grief in older adults in the general population is 4.8% (1).

Knowledge about vulnerability to complicated grief can provide opportunities to target care and resources appropriately (10). The literature abounds with factors that are considered useful in identifying who is at risk of complicated grief (10-14). A great deal of attention is paid to the characteristics of the bereaved, such as age, sex and physical and mental illness (10). Another area of interest is the deceased's illness, the characteristics of end of life care and the nature of the patient's death.(10) It has been shown that there is an increased risk of complicated grief if the duration of the patient's terminal illness was either very short or very long (12); if the patient had suffered from a cognitive impairment (12); if the patient died in a hospital setting (13); if the patient died after euthanasia (14); and if death occurred suddenly or unexpectedly (10). Multiple care transitions and hospitalisations in the last phase of life could also influence grief experiences (15). However, little is known about these characteristics as potential risk factors for complicated grief in older adults. Since the bereavement experience of older adults is different from younger adults, this potentially also holds true for factors that contribute to this bereavement experience. To examine whether complicated grief in older adults can be explained by predeath information, this study includes both personal and situational factors in a comprehensive analysis. The aim of the present study is to find out whether personal characteristics of the patient and the bereaved partner, or characteristics of the patient's illness, end-of-life care and the nature of death are risk factors for complicated grief in older adults.

## DESIGN AND METHODS

This study was based upon the Rotterdam Study, an ongoing prospective cohort of older adults to examine the occurrence and risk factors of chronic diseases (16).

### The Rotterdam Study (1)

The Rotterdam Study comprises two cohorts. The first stems from the original study which commenced in 1990–1993. At this time all inhabitants aged over 55 years living in the Ommoord district of Rotterdam were invited to participate; 7983 persons (78%) participated. In 2000, people who had become 55 years of age, or who were 55 years or over and had moved into the study district after the start of the study, were added as a second cohort; 3011 (67%) participated. A detailed description of the design of the Rotterdam study has been published elsewhere (17).

### Nested case-control

Loss of a spouse is very common and accounts for a large proportion of losses among older adults (18). Therefore, we selected 200 (married/partnership) from the Rotterdam cohorts, in a nested case-control design (19): 100 couples of which one person had deceased and of which the other experienced complicated grief, and 100 control couples of which one person had deceased and the other person experienced ‘normal’ grief. Group matching was used to increase statistical power.

### Case definition

In case a participant has lost a spouse, grief was assessed in the original cohort in the fourth follow-up examination (2002–2004) and in the added cohort in the second follow-up examination (2004–2005) (1). Complicated grief was assessed with a 17-item Dutch version of the Inventory of Complicated Grief (ICG), constructed by Prigerson et al. (1995) (20). The ICG is the most widely used instrument to measure complicated grief and items represent the array of symptoms attributed to complicated grief. The measure has high internal consistency and convergent and criterion validity and it is considered the ‘gold standard’ for measurement of complicated grief in older adults (1). A summary score for the ICG was calculated by adding up each individual item score (responses from 0=never to 4=always) across the 17-items, providing a potential total score range of 0 to 68. Participants with a total score greater than 21 and with symptoms reported to have been present for at least six months were considered to have complicated grief. In total, 1089 (19%) participants reported that they were experiencing grief at the time of the assessment and of these, 277 participants were assessed as having complicated grief. A detailed description of the measurement of complicated grief has been published elsewhere (1).



### **Assessment of determinants**

Several sources of information were available for all participants of the Rotterdam Study: home interviews, examinations at the research center, Nationwide Medical Registry, and general practitioners' records. A detailed description of the methods for data collection of the Rotterdam study has been published elsewhere (21). These sources were used for the assessment of personal characteristics as well as characteristics of patient's illness, end-of-life care and the nature of death as potential risk factors for complicated grief.

#### ***Personal characteristics at baseline***

Information was gathered on sex, age and ethnicity (Caucasian or non-Caucasian). Working status was recorded and recoded into retired from full-time work/unemployed or working. Education was grouped according to the Dutch Standard Classification of Education (Dutch Central Bureau of Statistics (CBS), 1989) (22). The ratings for low (1) to high education (6) were recoded into low, intermediate and high education. Cognitive capacity was assessed with the Mini Mental State Examination, which assesses six broad areas of daily cognitive functions (23). Activities of daily living performance was assessed with the Stanford Health Assessment Questionnaire (24) and the Instrumental Activities of Daily Living scale (25). Depression was evaluated with the use of the Centre for Epidemiological Studies Depression Scale (score  $\geq 16$ ) (26).

#### ***Patient's illness, end-of-life care and the nature of death***

Health events were coded according to the tenth edition of the International Classification of Disease (ICD) (27). The underlying causes of death were recorded and classified as neoplasms, diseases of the circulatory system and other causes of death. Information was gathered on the date and place of death. Place of death was recorded as at home, in hospital, community living (i.e. home for the elderly/ nursing home) or other places. Further, information was obtained on hospital admissions in the last year of life (number and median number of days).

Medical files of the deceased were manually screened for additional information on the patient's illness, characteristics of end of life care and the nature of the patient's death. Based on the literature, a check list was developed by the research team. The checklist was piloted before use: 10 files were independently assessed by Sophie Bruinsma (SB) and Judith Rietjens (JR) and discussed. This led to some small changes in the checklist. A second pilot was performed to test these changes; no disagreement was found. As a next step, all medical files were checked by SB with the use of this checklist. Several topics were covered. The duration of the illness that was the underlying cause of death was registered as a continuous variable. The nature of death was classified as 'completely unexpected', 'patient was ill, but death occurred unexpectedly' and

‘expected’. ‘The number of transitions between care settings in the last three months of life’ was registered. End of life decision-making was classified as ‘withholding or withdrawal of potential life-prolonging treatments’, ‘euthanasia’ and ‘other end of life decisions’.

### Data analysis

To increase the comparability of analyses and reduce bias, missing values (if >5%) were imputed with Randomized single imputation (28). This was the case for ‘the duration of the illness’ (30%), ‘the expected nature of death’ (9%), and ‘the number of transitions between care settings in the last three months of life’ (14%). To determine the association between the potential risk factors ‘personal characteristics, and characteristics of deceased person’s illness, end of life care and nature of death and the grief response, logistic regression was performed. Those variables that showed a p-value of 0.20 or smaller in the univariate regression analysis were included in the multivariate regression model.

## RESULTS

The characteristics of the deceased and the bereaved partner are presented in appendix 1. The majority of the deceased persons were male (66%). They were on average 74 years old at the time of death. Almost all were Caucasian (99%). At baseline, most deceased persons had been retired or unemployed (85%) and the highest education attained was predominantly low or intermediate (91%). Bereaved partners were predominantly female (66%). They were on average 73 years old at time of their spouse’s death. All partners were Caucasian (100%). At baseline, 89% of the partners had been unemployed or retired, and the highest education attained was predominantly low or intermediate (93%). Of all partners, 19% suffered from a depression at baseline. On the activities of daily living scale, partners scored on average 24 (= little difficulties) and on the cognitive status scale on average 28 (= normal cognition). The median of the time passed between a person’s death and the interview with the bereaved partner was 34 months (IQR 14-68).

Table 1 describes the characteristics of deceased persons and the bereaved partners in relation to the occurrence of normal and complicated grief. Very few differences were found between the types of grief with regards to personal characteristics. Of the bereaved partners with normal grief, 9% suffered from depression at baseline, compared to 25% of the bereaved partners with complicated grief. The median of the time passed between a person’s death and the interview with the bereaved partners was 39 months (IQR 16-67) for normal grief, compared to 33 (IQR 13-68) for complicated

**Table 1** Differences between older adults experiencing normal grief or complicated grief: Characteristics deceased and bereaved partners (n=200)

	Normal grief (n=100)	Complicated grief (n=100)	Difference between groups Unadjusted <sup>d</sup>	Difference between groups Adjusted for sex and age <sup>e</sup>	
				Overall p-value	OR ( 95% CI)
<b>Deceased</b>					
Sex					
Male	65 (65%)	67 (67%)	.765	1.00 (ref)	.148
Female	35 (35%)	33 (33%)		0.92 (0.51+1.64)	
Age at death (mean ± SD) (n=200)	74.88 ± 7.11	74.08 ± 7.21	.428	0.98 (0.95-1.02)	.064
Working status (baseline)					
Working	14 (14%)	16 (16%)	.626	1.00 (ref)	.702
Unemployed or retired	86 (86%)	81 (81%)		0.82 (0.38-1.80)	
Missing	-	3			
Education (baseline)					
Low	49 (49%)	51 (51%)	.864	1.00 (ref)	.314
Intermediate	40 (40%)	38 (38%)		0.91 (0.51+1.65)	
High	11 (11%)	8 (8%)		0.70 (0.25-1.88)	
Missing	-	3			
<b>Bereaved partners</b>					
Sex					
Male	36 (36%)	33 (33%)	.655	1.00 (ref)	.580
Female	64 (64%)	67 (67%)		1.14 (0.64+2.05)	
Age at death deceased (mean ± SD) (n=198)	72.98 ± 6.76	72.94 ± 6.48	.966	0.99 (0.96-1.04)	.949
Working status (baseline)					
Working	11 (11%)	10 (10%)	.818	1.00 (ref)	.750
Unemployed or retired	89 (89%)	90 (90%)		0.90 (0.36-2.22)	
Education (baseline)					
Low	63 (63%)	62 (62%)	.645	1.00 (ref)	.787
Intermediate	28 (28%)	34 (34%)		1.23 (0.67+2.27)	
High	9 (9%)	4 (4%)		0.45 (0.13-1.54)	

**Table 1** Differences between older adults experiencing normal grief or complicated grief: Characteristics deceased and bereaved partners (n=200) (continued)

	Normal grief (n=100)	Complicated grief (n=100)	Difference between groups Unadjusted <sup>d</sup>	OR ( 95% CI)	Overall p-value	Difference between groups Adjusted for sex and age <sup>e</sup>	OR ( 95% CI)
Depression (CESD) (baseline )							
No depression	81 (81%)	66 (66%)	.004**	1.00 (ref)	.003**	1.00	
Depression	9 (9%)	25 (25%)		3.49 (1.49-7.81)			3.86 (1.60-9.33)
Missing	10	9					
ADL <sup>a</sup> At baseline (n=190)	24.44 ± 3.03	24.08 ± 3.41	.444	0.97 (0.88-1.06)	.441		0.97 (0.88-1.06)
Cognitive status <sup>b</sup> (MMSE) At baseline (n=194) (mean ± SD)	28.24 ± 1.40	27.93 ± 1.46	.130	0.85 (0.70-1.05)	.132		0.85 (0.70-1.05)
Time since death of partner months <sup>c</sup> (n=196) (median (IQR)	39 (16-67)	33 (13-68)	.812	0.99 (0.99-1.01)	.678		1.00 (0.99-1.01)

<sup>a</sup> Total score with a minimum of 0 (much difficulties with ADL) and 27 (little difficulties with ADL)

<sup>b</sup> Any score greater than or equal to 27 points (out of 30) indicates a normal cognition. Below this, scores can indicate severe (≤9 points), moderate (10-18 points) or mild (19-24 points) cognitive impairment.

<sup>c</sup> Time in months between death of the deceased and the interview where type of grief was assessed

<sup>d</sup> Difference test is based univariate logistic regression. Reference group is normal grief (\*\* p<0.01)

<sup>e</sup> Difference test is based multivariate logistic regression. Reference group in normal grief (\*\* p<0.01)

**Table 2** Differences between normal grief and complicated grief: characteristics illness, end of life care and nature of death

	Normal grief (n=100)	Complicated grief (n=100)	Difference between groups Unadjusted <sup>e</sup>		Difference between groups Adjusted for sex and age <sup>f</sup>	
			Overall p-value	OR (95% CI)	Overall p-value	OR (95% CI)
<b>Cause of death (ICD-10)</b>	Neoplasms	35 (35%)	45 (45%)	1.00 (ref)	.042*	1.00
	Diseases of the circulatory system	32 (32%)	35 (35%)	0.80 (0.42-1.55)		0.76 (0.39-1.49)
	Other <sup>d</sup>	32 (32%)	21 (21%)	0.51 (0.25-1.03)		0.47 (0.23-0.97)
<b>No. of co- morbidity</b>	Missing	1	1			
	0	7 (7%)	5 (5%)	1.00 (ref)	.438	1.00
	1	27 (27%)	28 (28%)	1.45 (0.41-5.14)		1.51 (0.42-5.39)
	2	18 (18%)	25 (25%)	1.94 (0.53-7.12)		2.02 (0.54-7.59)
	3	14 (14%)	18 (18%)	1.80 (0.47-6.90)		1.87 (0.47-7.47)
	4	13 (13%)	10 (10%)	1.07 (0.26-4.43)		1.22 (0.29-5.16)
	>=5	20 (20%)	14 (14%)	0.98 (0.26-3.73)		1.02 (0.26-4.00)
	Home	36 (36%)	37 (37%)	1.00 (ref)	.918	1.00
	Hospital	42 (42%)	40 (40%)	0.93 (0.49-1.74)		0.91 (0.48-1.75)
	Community living	16 (16%)	16 (16%)	0.97 (0.42-2.23)		1.00 (0.42-2.38)
<b>Place of death</b>	Other <sup>b</sup>	3 (3%)	3 (3%)	0.97 (0.18-5.14)		0.91 (0.17-4.86)
	Missing	3	4			
	0	20 (20%)	24 (24%)	1.00 (ref)	.975	1.00
<b>No. of hospitalizations last year of life</b>						

**Table 2** Differences between normal grief and complicated grief: characteristics illness, end of life care and nature of death (continued)

	Normal grief (n=100)	Complicated grief (n=100)	Difference between groups Unadjusted <sup>e</sup>		Difference between groups Adjusted for sex and age <sup>f</sup>	
			Overall p-value	OR (95% CI)	Overall p-value	OR (95% CI)
1	26 (26%)	21 (21%)		0.64 (0.28-1.47)		0.64 (0.28-1.48)
2	16 (16%)	14 (14%)		0.64 (0.27-1.77)		0.69 (0.27-1.77)
3	10 (10%)	11 (11%)		0.87 (0.31-2.48)		0.88 (0.31-2.50)
4	5 (5%)	11 (11%)		1.74 (0.52-5.88)		1.75 (0.52-5.96)
>=5	22 (22%)	19 (19%)		0.68 (0.29-1.62)		0.70 (0.29-1.65)
<b>Duration hospitalizations last year of life</b> (n=156) (median (IQR))	25 (9-49)	26 (14-50)	.827	1.01 (0.99-1.01)	.950	1.00 (0.99-1.01)
<b>Duration illness<sup>a</sup></b>	0- 6 months	40 (40%)	42 (42%)	1.00 (ref)	.247	1.00
	6 months- 1 year	23 (23%)	27 (27%)	1.12 (0.55-2.26)		1.14 (0.56-2.31)
	1 year-4 years	17 (17%)	22 (22%)	1.23 (0.57-2.65)		1.21 (0.56-2.61)
	> 4 years	17 (17%)	22 (22%)	0.45 (0.18-1.11)		0.44 (0.18-1.10)
	Missing	2	0			
<b>Sudden death<sup>b</sup></b>	Completely unexpected	20 (20%)	14 (14%)	1.00 (ref)	.155	1.00
	Deceased ill, but death unexpected	29 (29%)	26 (26%)	1.28 (0.54-3.04)		1.34 (0.56-3.19)
	Expected	51 (51%)	60 (60%)	1.68 (0.77-3.66)		1.73 (0.79-3.80)

**Table 2** Differences between normal grief and complicated grief: characteristics illness, end of life care and nature of death (continued)

		Normal grief (n=100)	Complicated grief (n=100)	Difference between groups Unadjusted <sup>e</sup>		Difference between groups Adjusted for sex and age <sup>f</sup>	
				Overall p-value	OR (95% CI)	Overall p-value	OR (95% CI)
<b>Number of transitions last 3 months<sup>c,n</sup></b>	0	26 (26%)	25 (25%)	.243	1.00 (ref)	.222	1.00
	1	35 (35%)	30 (30%)		0.93 (0.45-1.92)		0.91 (0.43-1.91)
	2	21 (21%)	19 (19%)		0.98 (0.43-2.23)		0.96 (0.42-2.21)
	>=3	17 (17%)	26 (26%)		1.65 (0.73-3.74)		1.71 (0.74-3.93)
	No/not in file	76 (76%)	81 (81%)	.390	1.00	.367	1.00
<b>End of life decision-making</b>	Withholding or withdrawal of potential life-prolonging treatments						
	Euthanasia	No/not in file	19 (19%)		0.74 (0.38-1.46)		0.73 (0.37-1.45)
		99 (99%)	92 (92%)	.044*	1.00	.047*	1.00
	Yes	1 (1%)	8 (8%)		8.61 (1.06-70.17)		8.38 (1.02-68.49)
	Other <sup>d</sup>	No/not in file	90 (90%)	.211	1.00	.179	1.00
	Yes	16 (16%)	10 (10%)		0.58 (0.25-1.36)		0.56 (0.24-1.31)

<sup>a</sup> Other causes of death: Diseases of the respiratory system; diseases of the nervous systems, mental and behavioral disorders; certain infectious and parasitic diseases; diseases of the digestive system; diseases of the genitourinary system; symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified; injury, poisoning and certain other consequences of external causes; external causes of morbidity and mortality

<sup>b</sup> Other= e.g. outside on the street, family's home

<sup>c</sup> First transition mainly from home to hospital; second transition mainly from hospital to home

<sup>d</sup> Palliative sedation, intensified alleviation of symptoms, DNR

<sup>e</sup> Difference test is based univariate logistic regression. Reference group is normal grief (\* p<0.05)

<sup>f</sup> Difference test is based multivariate logistic regression. Reference group in normal grief (\* p<0.05)

<sup>n</sup> Imputed results

grief. Univariate regression analysis showed that bereaved partners with depression at baseline had a higher risk of complicated grief (OR=3.86; 95% CI=1.60-9.33).

Table 2 describes the characteristics of deceased person's illness, end of life care and nature of death in relation to the occurrence of normal and complicated grief. For normal griever, in 35% of the cases the partner had died from cancer, in 32% from diseases of the circulatory system, and in 32% from other causes. For complicated griever, this was respectively 45%, 35% and 21%. Out of 9 partners of patients who had died from euthanasia, 8 experienced complicated grief. Univariate analysis showed that partners of patients who had died from cancer had a higher risk of complicated grief than partners of patients who had died from diseases of the circulatory system (OR=0.76; 95% CI=0.39-1.49) or other diseases (OR=0.47; 95% CI=0.23-0.97). Further it showed that if the deceased died after the use of euthanasia, complicated grief was more likely (OR=8.38; 95% CI= 1.02-68.49).

Following the univariate analyses (table 1 and 2), multivariate logistic regression was performed (for all variables with  $p < .02$ ) (no table presented). The underlying cause of death; the nature of death; end-of-life decisions (euthanasia and other end of life decisions); sex and the age at death of the deceased person, and depression (CESD) and cognitive status (MMSE) at baseline were included in the model. Only depression was significantly associated with type of grief. Bereaved partners with depression at baseline had a higher risk of complicated grief compared to bereaved partners without depression (OR=3.48; 95% CI=1.40-8.68).

## DISCUSSION

In the present study we found that complicated grief in older adults is significantly associated with depression, and not with characteristics of the patient's illness, end-of-life care and the nature of death.

Multivariate analysis showed that only depression at baseline was significantly associated with an increased risk of complicated grief. Apparently, complicated grief in older adults cannot be explained by circumstances surrounding the patient's death (situational factors), but predominantly by factors related to the bereaved itself (personal factors). Depression has been closely associated with grief in the literature. While studies have focused on depression as an outcome of grief (29), or as a syndrome following a spousal death (30), there are few studies that examined the etiologic relevance of depression for the onset of complicated grief (31-33). Horowitz et al., who studied 70 individuals who had experienced the death of a spouse when they were between the ages of 21 and 55 years, found that those bereaved with a history of major depressive disorder were more vulnerable to complicated bereavement (31). This may be explained



by a lack of ability to cope with loss (34). Apparently, this especially holds true for older bereaved partners.

Social support is important in the bereavement period, because it protects against physical and psychological illness and helps to maintain quality of life (35). A study performed among older adults who experienced complicated grief showed that they often rely on available interpersonal support to help them manage their grief, but that such support is not always experienced as sufficient (36). Professional support may therefore be especially important for older persons seeking bereavement support (35, 36). Health care professionals who care for terminal patients and their partners should pay particular attention to partners with pre-loss depression (11). Potentially, physicians could be trained to perform evidence-based assessments for depression and to link those who could benefit to bereavement or mental health specialists (37).

In the present study, 8 out of 9 relatives of patients who had died from euthanasia experienced complicated grief. A previous Dutch study showed that the bereaved family of patients with cancer who died by euthanasia coped better with respect to grief symptoms and post-traumatic stress reactions than the bereaved of patients with cancer who died a natural death (14, 38). Our results should be interpreted with caution due to the small numbers, but the difference with the previous study may be explained by the fact that patients receiving euthanasia in our study may have had a relatively difficult and protracted dying process, whereas in the previous study patients who received and did not receive euthanasia died from comparable disorders. Van den Boom (39) who described the consequences of euthanasia on grief among the bereaved family and friends, previously found that a complicated euthanasia process was associated with complicated grief and added distress to the bereaved family and friends.

No associations were found between socio- demographic characteristics of the bereaved and the type of grief they experience. While demographic factors are consistently identified as relating to bereavement outcomes, it is likely that they are of little importance in determining an individual's specific risk of complicated bereavement outcomes (10). Demographic factors such as age, gender and socio-economic status may affect health independently of bereavement (10, 40). Age, for instance, may be more of an indicator of differences in grieving style than a specific indicator of risk (41). Also the (younger) age of the deceased is often cited as a risk factor for complicated bereavement in surviving relatives.(10) However, this counts particularly in relation to the death of child (10). As the current study focuses on spousal loss, this could potentially explain the lack of a significant association.

Our study has several strengths. First, it was conducted within a population-based setting (1). Second, a large sample was employed which enhances the generalizability of the findings (1). However, the study also has some limitations. First, grief was dichotomized. Dichotomization of a continuous outcome variable may lead to a loss of power.

However, complicated grief is designated as a disorder with distinct characteristics and adverse outcomes. Unfortunately, no information was found in the medical files on relatives' involvement in the patient's care. Intensity of care provided has been found to be a risk for complicated grief (12). Future studies should assess whether characteristics of the care giving experience result in distinctive risk factors for developing complicated grief in older adults (12). This also holds true for other bereaved related characteristics, such as a history of previous losses and high pre-death distress, or factors concerning interpersonal relationships, such as the availability of social support and the level of family functioning (10). Social support has been shown to be an important protective factor against the negative effects of complicated grief' (42-45). Finally, other mental health factors than depression were not taken into account but may have been of influence, such as anxiety and panic disorders.

In conclusion, our results suggest that complicated grief in older adults is not related to the circumstances of dying of the deceased spouse. Pre-existing conditions such as depression seem to be more important in explaining the occurrence of complicated grief.

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**Appendix 1** Characteristics of deceased and bereaved partners (n=200)

		N (%)
<b>Deceased</b>		
<b>Sex</b>	<i>Male</i>	132 (66%)
	<i>Female</i>	68 (34%)
<b>Age at death (mean ± SD)</b>		74.48 ± 7.15
<b>Ethnicity</b>	<i>Caucasian</i>	192 (99%)
	<i>Non- Caucasian</i>	1 (1%)
	<i>Missing</i>	7
<b>Working status</b> (baseline)	<i>Working</i>	30 (15%)
	<i>Unemployed or retired</i>	167 (85%)
	<i>Missing</i>	3
<b>Education<sup>a</sup></b> (baseline)	<i>Low</i>	100 (50%)
	<i>Intermediate</i>	78 (40%)
	<i>High</i>	19 (10%)
	<i>Missing</i>	3
<b>Bereaved partners</b>		
<b>Sex</b>	<i>Male</i>	69 (34%)
	<i>Female</i>	131 (66%)
<b>Age at death deceased</b> (mean ± SD)		72.96 ± 6.60
<b>Ethnicity</b>	<i>Caucasian</i>	194 (100%)
	<i>Non- Caucasian</i>	0
	<i>Missing</i>	6
<b>Working status</b> (baseline)	<i>Working</i>	21 (11%)
	<i>Unemployed or retired</i>	179 (89%)
<b>Education<sup>a</sup></b> (baseline)	<i>Low</i>	125 (62%)
	<i>Intermediate</i>	62 (31%)
	<i>High</i>	13 (17%)
<b>Depression (CESD)</b> (baseline) (n=181)	<i>No depression</i>	147 (81%)
	<i>Depression</i>	34 (19%)
	<i>Missing</i>	
<b>ADL<sup>b</sup></b> (baseline) (n=192)		24.26 ± 3.22
<b>Cognitive status<sup>c</sup> (MMSE)</b> (baseline) (mean ± SD) (n=194)		28.08 ± 1.43
<b>Time since death of partner<sup>d</sup></b> (in months) (median (IQR))		34 (14-68)

<sup>a</sup> Highest education attained (completed or not completed): Low=primary education; primary education, plus higher not completed education; lower vocational education; lower secondary education. Intermediate= intermediate vocational education; general secondary education. High= higher vocational education; university

<sup>b</sup> Total score with a minimum of 0 (much difficulties with ADL) and 27 (little difficulties with ADL)

<sup>c</sup> Any score greater than or equal to 27 points (out of 30) indicates a normal cognition. Below this, scores can indicate severe (≤9 points), moderate (10-18 points) or mild (19-24 points) cognitive impairment.

<sup>d</sup> Time between the death of deceased and the interview where type of grief was assessed







A faint, light-colored background illustration depicting two figures in a landscape. On the left, a figure is seated or kneeling, facing right. On the right, a taller figure stands, facing left. The style is sketchy and painterly, with visible brushstrokes. The overall tone is muted and artistic.

# CHAPTER 8

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## Discussion

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The aim of this thesis is to provide a comprehensive overview of bereaved relatives' experiences with the practice of palliative sedation. Further, we aim at getting insight into the potential life-shortening effect of palliative sedation and the risk factors for complicated grief in older adults. First, the key findings of the studies will be summarized in this chapter. Next, the strengths and weaknesses of the studies will be explored. Third, a number of findings will be discussed in more detail. This chapter will be concluded with implications and recommendations for clinical practice, policy and for future research.

## 8.1 KEY FINDINGS

In the introduction of this thesis, several research questions were formulated. In this section, the main answers to each of these research questions are summarized.

### **Research question 1: What are the experiences of bereaved relatives with the practice of palliative sedation?**

We studied the experiences of relatives with the practice of continuous palliative sedation in a systematic literature review (chapter 2), by interviewing focus groups of Dutch bereaved relatives (chapter 3) and by interviewing bereaved relatives of cancer patients from Belgium, the Netherlands and the UK (chapter 4). The in-depth interviews with bereaved relatives from the Netherlands, Belgium and the UK showed that many relatives were able to provide a description of the concept of sedation. All studies showed that relatives in general seem to be comfortable with the use of palliative sedation. This was predominantly related to their impression that the patient's suffering was finally alleviated. Relatives generally believed that the sedation contributed to the patient having a 'good' death. Positive experiences are also related to an active role of relatives in the decision-making. The results of the focus groups also suggested that relatives were positive about having an active role in the application of the sedation, the degree of involvement of professional caregivers in caregiving and decision-making, and that they thought that the place of death was in agreement with the wishes of the patient. According to the participants of the focus groups, the sedation had offered them an opportunity to prepare themselves for the patient's death. The interview study provided more insight into the what seems to be rather typically Dutch and Belgian process of 'saying goodbye'. According to the relatives from the Netherlands and Belgium, the start of the sedation allowed for a planned moment of saying goodbye, which most of them appreciated. In contrast, saying goodbye was a less dominant theme in the account of the UK relatives. If described at all, they said that saying goodbye was a gradual process

rather than a planned single moment in time. Relatives seemed to consider this as an acceptable way of proceeding.

However, all studies also pointed at relatives expressing distress before or during the application of sedation. Although our literature review suggests that the majority of relatives receives adequate information, the focus group study and the interview study revealed that some relatives indicated dissatisfaction with the received information, and about communication with professional caregivers in general. Further, concerns existed about patients' wellbeing during the sedation. Sometimes relatives felt that the patient was not sufficiently sedated to relieve his/her suffering. Also, concerns were expressed about relatives' own wellbeing, especially if sedation was of a longer duration than anticipated. The focus groups suggested that relatives were sometimes frustrated about the lack of authority of nurses to make decisions in the absence of the physician. The interview study additionally showed that relatives sometimes questioned whether there were other alternatives to continuous sedation, such as euthanasia or a different type of sedation. Although the loss of the ability to communicate during the sedation with the patient and a potential life-shortening effect are frequently discussed as possible disadvantages of the use of sedation by caregivers, legal and ethical experts, the relatives in general did not experience these issues as important disadvantages. The interview study indicated that some respondents from the UK expressed the potential hastening of death as a main concern. In contrast, there were few concerns about whether or not sedation had shortened the patient's life in the Netherlands and Belgium.

**Research Question 2: What is the prolonged impact of palliative sedation on relatives' experience of the dying phase and their wellbeing after the patient's death?**

In chapter 5 we report on the results of a survey among bereaved relatives of patients who received and did not receive palliative sedation. Relatives of sedated patient more often stated that the professional caregivers could have done more to make the period before the death of the patient more bearable than relatives of non-sedated patients. Relatives of patients who received and did not receive sedation did not significantly differ in their assessment of the quality of end-of-life care, patients' quality of life in the last week before death and their quality of dying. No significant differences were found in relatives' satisfaction with their own life three months after the death of the patient and at the time of the survey, their general health and their mental wellbeing. It can be concluded that the use of sedation does not seem to have a negative influence on bereaved persons' experience of the dying phase of their deceased relative or their wellbeing after the patient's death.

### **Research Question 3: How accurately do physicians estimate the potential life-shortening effect of continuous sedation until death?**

Our study indicated a substantial discrepancy between two approaches to estimate the life-shortening effect of continuous sedation until death by physicians (chapter 6). The direct approach (question: Did continuous sedation, according to your estimation, hasten the patients' death?) led to the finding that sedation might have had a life shortening effect in 51% of the cases and the indirect approach (the duration of the sedation was subtracted from the patient's life expectancy as estimated by the physician) to 84%. These varying results confirm the difficulty of predicting the life expectancy of patients with advanced disease, and of estimating the potential life-shortening effect of end-of-life interventions.

### **Research Question 4: What are risk factors for complicated grief in older adults?**

Chapter 7 provides insight into risk factors for complicated grief in older adults. We studied the influence of personal characteristics of the patient and the bereaved partner on the one hand, and characteristics of the dying process, such as the patient's illness, end-of-life care and the nature of death on the other hand. Only pre-existing depression (that was already present before the death of the patient) was significantly associated with complicated grief. No significant associations were found for characteristics of deceased person's illness, end of life care and the nature of death. These results suggest that complicated grief in older adults is not clearly related to the circumstances of dying of the deceased partner. Pre-existing conditions such as major depression seem to be of more importance in explaining the occurrence of complicated grief.

## **8.2 STRENGTHS AND WEAKNESSES**

End-of-life care is generally considered to be a complex research topic that requires multidimensional and multidisciplinary studies. Yet, the majority of research focused on the medical aspects solely from perspectives of healthcare providers, while important opportunities for understanding and improving patients' dying experiences can be found among care professionals from other disciplines as well. Because it is known that professional caregivers and relatives often have different views on what constitutes a good death (1-3) and have different views on the ethical and moral considerations involved in the use of sedation (4), our study included the perspectives of both physicians and nurses, as well as bereaved relatives. The WHO considers the wellbeing of relatives as an explicit aim of end-of-life care (5). So far, however, relatives received

surprisingly little attention in end-of-life research. When researching end of life care, it is important to consider the complex interaction between different groups and the wider context within which they operate. This thesis made a useful contribution to this field of research.

Further, another strength of this thesis is that it combines findings from multiple countries (the Netherlands, Belgium and the United Kingdom). Palliative care has evolved across the globe in different contexts and in different ways, although many of the challenges faced are similar (6). Comparison between countries helps to identify the best solutions for patients and their families, who have complex needs and problems (6). By aforementioned reasons and by applying multiple methods (both qualitative and quantitative) and using multiple data sources, it was possible to generate a more comprehensive and balanced picture of the experiences of bereaved relatives with palliative sedation at the end of life. To our knowledge, this is the first time that such a comprehensive approach has been used to understand the experiences of relatives in end-of-life care. Further, this thesis contributes to the ethical debate by supplying evidence-based arguments for assessing the benefits and drawbacks of palliative sedation.

The different methods used in this thesis will be discussed more in depth.

## **Review**

The review provided the reader with an exhaustive summary of the existing literature on the experiences of relatives with the practice of palliative sedation. Systematic review are widely regarded as credible sources of evidence, and are often recommended as among the highest levels of evidence that can be located on a topic (7). It is important to recognize that there is not a shared language or understanding of what palliative sedation is across or within health and care services. This variety in the terms and definitions used (i.e. variety in the terminology regarding palliative sedation and an apparent lack of a consistent operational definition of palliative sedation) potentially limited full comparison and extrapolation of the studies. Further, not all studies included appeared to be of 'good' quality.

## **Qualitative studies: focus groups and interview**

By using focus groups, we elicited relatives' multiplicity of views, beliefs, knowledge about and experiences with the practice of palliative sedation (8). The group processes were particularly useful in clarifying relatives' views on palliative sedation. In the interviews we could examine the issues raised by the relatives in detail and in depth. In this way, the focus groups and interviews complemented each other. Death, dying and bereavement are all sensitive and potentially upsetting topics to discuss. However, relatives highly appreciated the opportunity to share their stories, and felt that it helped

them to deal with their grief. Nevertheless, some limitations were encountered. As these were qualitative studies based on the in depth exploration of relatively small numbers of cases, it is not possible to generalize in a statistical sense from our findings. Second, the quality of the research partly depended on the individual skills of the interviewer and could be influenced by the interviewer's personal and/or cultural biases. The use of an aide-memoire with questions and nonspecific prompts such as "tell me more" were used to avoid interviewer bias. Further, interviews were rehearsed with experts in research, field tested, and adjusted before final use. Third, to be sensitive to the early phases of grieving, relatives were contacted no sooner than three months after the death of the patient, introducing potential recall bias. Memories can also have been disturbed by the strong emotions they experienced at that time. However, the effect of bereavement on the accuracy of surrogates' responses is an unexplored area (9). This is probably due to the difficulties in conducting this type of research and in identifying which factors from the complex emotions associated with grief impinge on the memories of bereaved relatives (9). Finally, the data could be influenced by selection bias, because it is possible that relatives with relatively strong positive or negative experiences agreed to participate in the studies. Also, selection bias could have been introduced because clinical staff members were asked to identify eligible decedents and relatives.

### **Quantitative studies: the surveys**

The strength of quantitative research is that the data are standardized and numerical. Statistical analysis allowed us to infer important insights in research data, including differences between groups (e.g. sedation versus no-sedation) (chapter 5), and to control for the effects of extraneous variables that might result in confounding interpretations of data analyses, more specifically of causality (chapter 7). Quantitative studies nowadays encounter more often that all kinds of information are difficult to obtain through structured survey instruments (by high non-response for instance), particularly on sensitive topics such as death, dying and bereavement. Although the questionnaire was developed using existing scales (e.g. for quality of dying) it was not examined whether the scales performed well in terms of concurrent validity, internal consistency, and reliability (chapter 5). For the development of the questionnaire, validated measurement tools were used such as the SF-36 (chapter 5). However these have not been validated with bereaved relatives. Furthermore, as explained earlier, recall bias could have influenced the data and selection bias cannot be ruled out (chapter 5 and 6). Finally, the response rates in both questionnaire studies were moderate, although this is not uncommon (10-12).

### **Mixed methods**

Structured questionnaires and semi-structured interviews/focus groups are often used in mixed method studies to generate more complete knowledge, despite differences in methods of data collection, analysis, and interpretation. The integration of quantitative and qualitative data in the form of a mixed methods study has great potential to strengthen the accuracy and may enrich the analysis and conclusions. Nevertheless, integrating qualitative and quantitative data during analysis is complex and challenging (13). One of the main problems facing many mixed methods researchers is the question of how to weigh and to integrate the various data, with the particular problem of 'contradictory' findings (14). It has to be kept in mind that such conflicts may be merely the outcome of the fact that social reality (including memories of respondents) is complex and can at times be conflicting (14). However, results do not necessarily have to exclude each other. For instance, in the survey we found that relatives are in general satisfied with the information they received from caregivers (chapter 5), and in the interviews and focus groups, many relatives seemed to be dissatisfied with the provision of information (chapter 3 and 4). These differences could simply be the result of differences in sample, since it is possible that relatives with relatively strong negative experiences agreed to participate in the qualitative studies. Different techniques were also mixed in the study on complicated grief among older bereaved adults (chapter 7). We used data of home interviews with older adults, physical examinations at the research center, Nationwide Medical Registry, GPs' records of the older adults, and medical files of the deceased. This mixture of methods has complementary strengths and non-overlapping weaknesses, such as incomplete medical files (chapter 7).

## **8.3 INTERPRETATION OF THE FINDINGS**

### **8.3.1 Relatives' evaluation of the practice of palliative sedation**

#### ***Positive experiences***

One of the key findings of this thesis is that relatives in general reflect positively on palliative sedation for their dying relative. Many relatives believed the sedation contributed to the patient having a 'good' death. Some relatives even used descriptions like 'beautiful', 'peaceful', 'wonderful' or 'dignified' to describe the death of the patient.

#### ***A 'good' death***

A 'good' death is an important aim for health services and for us all. Although relatives may differ in their understanding of a 'good death', this thesis showed that, in the opinions of bereaved relatives, palliative sedation contributed to the patient having



a 'good death'. In several studies we found that the most important element of the positive evaluation of continuous sedation from the perspectives of relatives is related to the beneficial impact of palliative sedation on the patient's suffering (chapter 2-4). Before the start of the sedation, patients suffer from multiple distressing symptoms. After the start of the sedation these symptoms seem to have been relieved and most patients seem comfortable. The results from our survey suggest that adequate symptom relief possibly explains why there are no differences in relatives' experience of the dying phase for patients who died either with or without sedation (chapter 5). Another element of relatives' positive evaluation is the opportunity that the sedation offers them to say goodbye to the patient. This especially holds true for relatives from the Netherlands and Belgium, who often describe saying goodbye as a planned event, occurring either before sedation begins or at the moment it commenced (chapter 4).

Our results are in line with previous studies that adequate symptom relief is key to the experience of a 'good' death (2, 15-17). The importance of 'providing desired physical comfort' is widely recognized in expert guidelines and confirmed in research among patients, families, and health care providers. A study by Steinhäuser et al (2) that focused on determining important factors at the end of life as reported by patients, their families, physicians, and other care providers revealed that the large majority of respondents endorsed the importance of pain and symptom management. A study by Teno et al (17) showed that for bereaved family members, providing the desired level of physical comfort was paramount to their perception of the quality of care provided by health care professionals. Family members emphasized the importance of health care providers anticipating the needs for physical comfort and responding quickly to their reports of pain. The importance of saying goodbye has also been described by others (16, 18). Rietjens et al (16), who studied the preferences of the Dutch general public for a good death, found that the possibility to say goodbye to loved ones was considered important for a good death by the large majority of respondents. The reasons why relatives tend to evaluate the provision of sedation to their dying overall as positive are consistent with the factors that generally are considered important at the end of life.

### ***The decision-making process***

The importance of involvement of relatives of sedated patients in the decision-making process is stressed in the existing literature. Caregivers reported that relatives are involved in the decision-making about sedation in 81%-100% of all cases (chapter 2). The questionnaire study demonstrated that almost all relatives are actively involved in the decision-making process and appreciate this active role very much (chapter 5). The qualitative studies (chapter 3 and 4) additionally showed that caregivers sometimes discussed the decision to start sedation with the relatives, sometimes they asked for

their consent to begin sedation, and sometimes they informed them about the decision (chapter 3). Although the physician bears the final responsibility by determining whether the medical indications are present, it is recommended by guidelines that, if possible, the patient, his family and the health care staff should be involved in all stages of the decision-making process (19). This process is referred to as a shared decision-making: an interactive, collaborative, and ongoing process in which health-care professionals, patients and relatives are mutually engaged by sharing information, wishes and decisions (20-22). Multiple descriptive studies show that increased shared decision-making is associated with greater family satisfaction (23). Our results support the implementation and the importance of this interactive and collaborative process.

It has to be kept in mind too that relatives vary in the extent to which they want to be involved in decision-making. The literature review indicated that relatives sometimes feel the responsibility for the decision to start sedation as a burden (chapter 2). A previous study also concluded that family members sometimes feel that they alone are responsible for decisions at the end of life (17). Relatives can play a decisive role in drawing attention to a patient's situation and care needs because of their regular close contact with the patient. The Dutch national guideline for palliative sedation states that determining whether there are indications for palliative sedation is a medical decision (19). It should be kept in mind that relatives may sometimes experience this differently and sometimes assume responsibility for the decision to start sedation. Although the decision-making should be an interactive, collaborative and on-going process in which healthcare professionals, patients and relatives mutually engage (if possible), clinical practice involves clear boundaries between the relatives' responsibilities and those of the medical caretakers. It should not be possible or necessary for relatives to decide if palliative sedation is necessary. This boundary should be explicitly discussed with the relatives.

### ***Other positive elements***

Some topics were mentioned less often by the respondents, but they can also be considered as significant elements in relatives' evaluation of patients' end of life care. For instance, as with other studies (1, 24), the interview study underlined the importance of care being in line with the patient's wishes (chapter 4). Sedation was perceived as contributing not only to the patient's quality of dying but also as a means of honoring the patient's wishes. Physicians are strongly encouraged to address end-of-life care preferences of all patients with progressive terminal illnesses (25). When possible, the manner of relief of extreme distress should be discussed before entering the palliative sedation process. This should include discussions regarding the indication of sedation (25). This thesis highlighted the importance of discussing patient's preferences and

wishes in advance. It is known that both professionals and relatives fear entering a medical crisis without knowledge of patient preferences (3). However, it has to be kept in mind that sometimes acute sedation has to take place for medical reasons. In such cases, the attending physician has to make the decision to use palliative sedation on the basis of the patient's condition, and it is sometimes impossible to consult with all concerned (19).

### **Concerns**

Relatives in general reflect positively on palliative sedation for their dying relative, but this thesis also revealed a wide variety in concerns that relatives express due to sedation. These related for instance to anxieties about the patient's wellbeing, their own wellbeing, and questions about whether continuous sedation had shortened the patient's life (mostly UK), or whether an alternative approach would have been better. Many of the aforementioned concerns seem to be related to a lack of information and/or communication with health care professionals. Communication is one of the key elements of quality of end of life care for seriously ill patients and their family members (26), and effective communication is therefore recognized as a priority in healthcare (27). Communication has been identified as the most important factor to explain variance in relatives' satisfaction with end of life care (28, 29).

### **Information and communication**

Our literature review (chapter 2) demonstrated that relatives in general seem to receive adequate information, although there is room for improvement. In the survey we found that relatives are in general satisfied with the information they receive from caregivers about patient's situation and care during the last week of life and they seem to understand the information they receive (chapter 5). The percentage that was not satisfied with the received information was relatively small, namely 14%. The interviews and focus groups provided more insight in these negative experiences (chapter 3 and 4). Some relatives specifically mentioned the lack of information or communication (chapter 3 and 4). The nature of the concerns and the questions relatives had regarding the concept of sedation suggest that these relatives indeed received too little information regarding the use of sedation, or that they were not able to make sufficient sense of the information that was provided to them (chapter 3 and 4). Issues surrounding communication in health care are not uncommon. Many studies have highlighted inadequate provision of information and poor communication in end of life care (30-36). For instance, patients sometimes receive less information and involvement in their care than they desire (36). Further, relatives were found to be dissatisfied with communication and information (32), relatives had to make great efforts to get information, they had to be obstinate and continue to ask questions (33) or information was difficult to get (32, 33).

It seems that relatives often agree with the decision to start sedation to relieve the patient's severe suffering. They are relieved that there is a solution available ('something has to be done'). However, not all relatives understand or are able to oversee the implications of this decision. In the interview study it was shown that some relatives from all three countries continued to be unsure about the use of sedation (chapter 4). Reflecting on the death of their family member, some relatives still had questions and certain misunderstandings about what sedation had entailed. It is known that physicians frequently fail to assess patients' degree of understanding (12, 37). On the other hand, patients sometimes seem to overestimate their own understanding (37). The same could hold true for the patient's family.

Whereas communication in health care in general is difficult, this especially holds true for communication in end of life care. Dealing with death involves a multitude of complex issues for patients, health professionals, and family members (38). Research has attempted to clarify the nature and problems of these communication issues. Some of the reasons why doctors and nurses have problems with communication in palliative medicine are having inadequate skills, not knowing how to handle an emotional outburst of relatives and patients, worries about containing one's own emotions, fear of provoking emotional distress, fear of being blamed by patients and relatives for (possible) failure, over identification with certain patients and, having to confront one's own fears about death (39, 40). Conversations about care goals are often conducted by physicians who do not know the patient, do not routinely address patients' nonmedical goals, and often fail to provide patients with sufficient information about prognosis to allow appropriate decisions; and, in addition, they tend to occur so late in the patient's illness that their impact on care processes is reduced (38). Also, relatives themselves sometimes experience difficulties. They can be reluctant to start the conversation with the physician or nurse about the sensitive subject of death and dying. A study performed in 2005 showed that family caregivers sometimes express ambivalence about what they want to know, and they sometimes have difficulties in comprehending and accepting "bad news" (41). Further, the amount of information a person wants can differ, and this can vary and change over time (30). Our review confirmed this large variation in the 'needs' of relatives. Relatives want specific types of information regarding the use of sedation; the information needs to be easily available and relevant to their needs at a particular moment in time (chapter 2). Difficulties in communication about end-of-life issues are likely to result from both physicians' lack of communication, but also from family caregivers' difficulty with hearing the news (41).

It is known in end of life care that inadequate information may result in feelings of isolation, disillusion and distress for the relatives involved (30). Our results support the findings from previous studies. Relatives expressed anger, frustration, disappointment, concerns, guilt and helplessness, partly due to the fact that information about the sedation was not easily obtained or less relevant to needs of the relatives at that moment (chapter 2).

### **8.3.2 The potential life-shortening effect of palliative sedation**

As continuous sedation until death has become routine part of common medical practice, it has also turned into a very relevant topic in medical-ethical discussions (42, 43). A topic that has often been debated in the literature is whether continuous sedation shortens life. The official guidelines assume that continuous sedation until death has no life-shortening effect for patients with an estimated life expectancy of at most two weeks and when sedatives are properly dosed (44, 45). Our survey indicated that physicians often have the opinion that continuous sedation until death has a (mostly limited) life-shortening effect (chapter 6). It has to be noted that estimating life expectancy of patients with an advanced disease is difficult (46-48). Physicians tend to overestimate survival: it has been assessed elsewhere that survival of patients is typically 30% shorter than predicted by physicians, but that the accuracy of physicians' predictions increases when death approaches (47). Recommendations in guidelines that continuous sedation until death should only be used for patients with a life expectancy of less than one or two weeks, may therefore be rather difficult to translate to clinical practice. But even if sedation can shorten the patient's life, many physicians do not consider this as problematic. It has been held that this is justifiable under what is known as the doctrine of double effect (49). This doctrine stresses that a harmful effect of treatment (e.g. the shortening of life), even resulting in death, is permissible if it is not intended and occurs as a side effect of a beneficial action (the relief of suffering) (49).

#### ***Relatives' perspective***

Very few relatives in our studies mentioned the potential life-shortening effect as an important disadvantage of palliative sedation (chapter 3 and 4). In most cases relatives did not raise this issue at all, but sometimes relatives specifically stated that this was not seen as a problematic result of sedation. Some relatives in our focus group study referred to sedation as 'slow euthanasia' (chapter 3). However, a possible resemblance of palliative sedation to euthanasia, in the sense of hastening death, seems to be no issue for these relatives. More in general, we found no significant differences in relatives' satisfaction with the dying phase between relatives of sedated and non-sedated patients in the survey (chapter 5). Apparently, in the views of relatives, the importance of adequate symptom relief outweighs the potential life shortening effect as a result of sedation. In

other words, if the goal of relatives is a 'good' death, symptom management is pursued vigorously, even when that pursuit has the unintended consequence of compromising survival. A Dutch study from 2013 showed that most of the general public accept the use of palliative sedation at the end of life to alleviate refractory symptoms (50). Like in our studies, they found that the suffering and wishes of the patient are considered of greater importance than life expectancy and the potential hastening death. Relatives in our focus groups and interview study perceived a long duration of the sedation often as burdensome (chapter 3 and 4), and a short interval between the start of the sedation and the death of the patient was sometimes even appreciated. Some relatives described the time between saying goodbye and the patients' death as a 'vacuum' where they were 'waiting' for the patient to die (chapter 4). Another recent publication revealed that during the sedation, family members sometimes become agitated and start to put pressure on the doctor to end the dying process (51). Some physicians reported elsewhere that they indeed hastened the dying process, in order to relieve the family's suffering (51). These findings are in contrast with the frequency with which the potential life-shortening effect is discussed as a problematic aspect of palliative sedation in the literature (43, 45, 52, 53). Whereas this issue tends to evoke rather heated debates, the opinions of bereaved relatives suggest that the benefit of palliation should perhaps have a more prominent place in the moral evaluation than the harm of a potentially hastened death (50).

### ***International differences***

In the Netherlands and in Belgium, a potential life-shortening effect of palliative sedation the resemblance of palliative sedation to euthanasia seems to be no issue for most of the relatives. However, some concerns regarding the potential hastening of death were expressed by relatives of the UK. Previous results from the UNBIASED study found that in the UK, an overarching concern exists among professional caregivers to avoid hastening death, while most of the Dutch and Belgian health care professionals had no concerns that sedation hastened death, or accepted that it may have such an effect (54). Belgian and Dutch doctors and nurses are working in a culture where deliberately ending a patient's life is a rather acceptable procedure in law and in professional codes, as long as certain conditions are met, and this is also publically accepted, with patients and relatives clearly used to considering euthanasia as an option (55). It seems likely that legalizing euthanasia both influences care practices and perceptions of what is important in ethical debates about sedation. However, it might also be possible that cultural norms in these countries affect people's positive judgments of the acceptability of these end-of-life care practices. The UK medical culture of end-of-life care, on the other hand, is one that is deeply influenced by the hospice movement which, although it contains secular components, has significant religious overtones (55). This means

that the view that life has intrinsic value, even when it involves suffering, is perhaps a stronger guiding principle than it is in Belgium and the Netherlands. With the addition of a legal prohibition against assisted dying (euthanasia or physician-assisted dying), the use of sedatives in UK end-of-life care has a very different ethical complexion for care providers. Again, this highlights the influence of cultural norms and expectations on experiences of continuous sedation and the subsequent death.

### **8.3.3 Relatives' wellbeing after the patient's death**

Bereavement can influence every aspect of wellbeing, from physical and mental health to feelings of connectedness and the ability to function at work (56). A death has a huge effect on those left behind. For instance, relatives have to take on new responsibilities, move, or adjust to different living standards (56). Although the loss of someone close is one of the most painful experiences we can encounter, researchers rarely study relatives before the death of the patient in order to assess the effects of bereavement (57). Since the deaths of most persons are preceded by chronic disease, disability, and family involvement in caregiving, it is important to assess responses to bereavement when end-of-life care is provided up to the patient's death (57).

Study among bereaved older adults suggested that complicated grief in older adults is not clearly related to the circumstances of dying of the deceased partner (chapter 7). Only pre-existing conditions such as depression seem to be associated with the occurrence of complicated grief in this population. This is a surprising outcome, since the circumstances of dying of a partner (e.g. duration of the lethal illness and the nature of death) have been considered useful in identifying who is at risk of complicated grief in other studies (59). A recent study among 217 family caregivers of persons with dementia demonstrated that bereaved family members' perceptions of the quality of end-of-life care are associated with complicated grief (57). It was made clear that when death was preceded by a protracted and stressful period of caregiving, caregivers reported considerable relief at the death itself. The intensity of caregiving was not considered in our analysis, which could potentially explain these conflicting findings. Understanding bereavement requires close attention to the context in which the death occurs.

It is often assumed that the use of palliative sedation is particularly burdensome for the relatives of dying patients, e.g. because it hampers communication between them and the patient in the very last phase of life. Our studies (chapter 2-4) clearly show that relatives may experience distress due to sedation. Reasons for this distress were e.g. the feeling that the patient still suffered during the sedation, the (long) duration of the sedation, or the fact that information about the sedation was not easily obtained. However, the results of our survey pointed to the fact that the use of sedation does not

seem to have a negative influence on bereaved persons' experience of the dying phase of their deceased relative or their wellbeing after the patient's death (chapter 5). Relatives have been demonstrated to tend to evaluate the provision of palliative sedation for their severely suffering family member positively because the patient's suffering is finally alleviated (60). Probably, relatives seem to perceive sedation as an 'appropriate solution', because it managed the distress of the patient and relieved the burden placed upon themselves by having to deal with the sometimes overwhelming patient care needs.

We conclude that not the specific circumstances of dying, nor the use of palliative sedation at the end of life (in comparison to other end-of-life practices) seem to have a considerable long-term impact on relatives' wellbeing after the patient's death. On the one hand, these results suggest that other factors seem to be more significant or meaningful for relatives' long-term experiences with the care for their loved one at the end of life. The fact that the patient's wellbeing is preserved and that the patient receives the best care possible considering the circumstances seem to be prerequisites for a positive evaluation. Further, this thesis showed that pre-existing conditions such as depression seem to be of importance as well. It is therefore necessary to find ways to assess carers who are at risk of depression. On the other hand, the fact that relatives sometimes experienced concerns during the use of sedation but do not experience long term consequences for their wellbeing after the patient's death suggests that clinicians and scientists should view bereavement not only as a phenomenon that affects relatives after the death of the patient, but mainly as one that affects many relatives before the death occurs (57). It is possible that when relatives know that the death of their loved one is approaching and are aware of the patient's suffering, they grieve for the loss of the patient before the death (57). This type of grief is also known as anticipatory grief. The concept of anticipatory grieving could play an important role in palliative sedation, since the patient has already been brought to sleep and death is anticipated within short period of time. By providing a supportive and safe environment, physicians and nurses can help the relatives understand that their feelings are common and are experienced by others in similar situations and assist them with developing coping strategies (61).

## **8.4 Implications for practice, policy and future research**

### **8.4.1 Practice**

This thesis provides a strong basis for developing strategies for evidence-based use of palliative sedation and for enhancing the wellbeing of patients' relatives.

To help relatives to cope with their distress, an important task for physicians is to provide family members with appropriate and clear information, clear, and to provide this information in a compassionate manner.



Healthcare professionals should focus on providing full information to relatives before sedation begins and after it commenced about sedation in general, (the lack of) potential alternatives to the use of sedation, the patient's life expectancy (although estimating life expectancy is known to be very difficult), the drugs that will be used, further treatment (e.g. artificial nutrition and hydration), the wellbeing of the patient during the sedation, the expected duration of the sedation, and/or the possible symptoms or reactions of the patient during the sedation.

Relatives are, however, not always able to make sufficient sense of the information that is provided to them. This could be because the information is communicated to them in a language that they cannot understand, they receive conflicting information from different professional caregivers, or they simply have trouble understanding the information due to the fact that it is provided to them in a situation where they are extremely distressed (chapter 3). Providing extended information and regular updates is important and needs more attention in practice. Our data show that it is crucial that there is a common understanding of terms and phrases for all actors involved (patient, relatives and health care professionals) and that checks should be made systematically to ensure this understanding is maintained throughout the process.

However, the coordinated sharing of vital information among patients, patients' families, and the professional care team is sometimes difficult to accomplish (62). Several successful interventions have been identified to improve communication in end of life such as the team approach to communication, the formal family meeting, and use of advanced practice nurses (63). Also, communication and assessment strategies are available for care providers that facilitate end-of-life decision-making (64). Communication strategies include: being clear, avoiding euphemisms, spelling out the goals and expectations of treatment, using words such as "death" and "dying," and being specific when using such words as "hope" and "better." Assessment strategies include: assessing patients' physical conditions and end-of-life wishes, patients' and family members' understandings of the disease and prognosis, and their expectations and goals (64). Health care professionals should examine which strategies are available and might be useful to solve the potential communication and information issues that they are experiencing with relatives in the use of palliative sedation.

Since the provision of well-communicated care requires significant staff time and effort, and one of the most frequently endorsed barriers for physicians is a continuous lack of time, nurses too should have a significant role and time in identifying, observing, measuring and reporting on developments. Palliative care nursing is a key component

in the multidisciplinary approach necessary to meet the complex needs of individuals and their families facing a life threatening illness. Nurses have more frequent contact with patients and their families than physicians, and may be more likely to observe changes in patient and family needs.

Physicians seem to be reluctant to consult experts about palliative sedation (65). Whereas many physicians have only little experience with providing palliative sedation and communicating it patients and their relatives, increased consultation of an expert palliative care team may be helpful here.

To support patients, physicians, nurses and relatives in initiating end of life care discussions; advance care planning is encouraged (66, 67). Early discussions about goals of care are associated with better quality of life, reduced use of non- beneficial medical care near death, enhanced goal-consistent care, positive family outcomes, and reduced costs (68). Especially since, looking back, relatives underline the importance of care being in line with the patient's wishes. Ongoing discussions with patients and their families are needed to ensure their current wishes for end-of-life care are both known and followed. A recent review showed that best practices in discussing goals of care include the sharing prognostic information, eliciting decision-making preferences, understanding fears and goals, exploring views on trade-offs and impaired function, and wishes for family involvement (68). However, in practice, acute situations always can arise in which carrying out effective advance care planning is hampered. Advance directives represent one method to provide patients with the means to proactively determine their future care (69). However, advance directives do not and should not take the place of ongoing discussions with patients and their families regarding wishes for end-of-life care (69).

Finally, since relatives emphasize the importance of being prepared for the patient's death and particularly highlight the importance of saying goodbye, it is strongly recommended that professionals should coordinate the process in a way that patients and their family members always have a 'last' chance to communicate about their feelings or thoughts before patients receive sedation (70). When the patient is hospitalized, every effort should be made to provide room for privacy for emotional and physical intimacy to give patients and their relatives an opportunity to say goodbye (25).

#### **8.4.2 Policy**

This thesis provided insight into the experiences of relatives with palliative sedation, and the effect of palliative sedation on the wellbeing of relatives after the patient's

death and characteristics that are associated with this. Implementing these findings in guidelines is an excellent means to improve care for the dying and their loved ones.

According to guidelines on palliative sedation (19, 25, 71, 72), relatives should be involved in the decision-making, e.g. by discussing the decision to sedate. Furthermore, relatives can be involved in the provision of the sedation, e.g. by spending time with and observing the patient and to provide physicians and nurses with information about the patient. The relatives should be kept informed at various points in the course of palliative sedation, about e.g. patient's wellbeing and what to expect, and the care team should communicate to the relatives in a language they can understand. In line with recommendations in current guidelines, relatives seem to be adequately involved in the decision-making process of sedation and in the care for the dying patient. Further, relatives seem to receive sufficient support from caregivers. However, this thesis made clear that the information provided by caregivers is not always sufficient. As said, relatives need more information on e.g. the patient's wellbeing during sedation, possible alternatives to continuous sedation and the patient's life expectancy. However, guidelines already recommend this type of information. Following up on relatives' main concerns, no major changes or modifications of the guidelines seem to be necessary. It should be noted that the Dutch guideline can serve as an example for other guidelines, which are often far less comprehensive with regards to care for the patient's relatives.

However, the fact that many relatives do experience concerns due to the use of sedation cannot be ignored. Apparently some kind of tension exists between what the guideline recommends and how this works out in practice. The focus in policy should therefore merely be on improving the quality of the application of the guideline with respect to the care for patients' relatives. Clinical audits of the practice and documentation (e.g. of the decision-making process and consultation with the patient's family) of palliative sedation performed by health professionals or external organizations will for instance be an effective tool to recognize learning opportunities, and to foster practice change (73).

Guidelines highlight best practices in treating the array of problems patients and their relatives face at the end of life. However, it has to be kept in mind that personal perspectives often emphasize diverse elements, and those perspectives will never be perfectly integrated in one policy. Healthcare professionals should be aware of these diverse needs and act flexible in this respect to best promote and protect the interests of patients and their families. Ultimately, the response to a difficult clinical situation is born in practice, taking into account legal, medical and ethical regulations, guidelines

or principles (74). By providing a practical and legal framework, guidelines offer a starting point for such responses.

The main premise of the Royal Dutch Medical Association's (RDMA) guideline on palliative sedation is that palliative sedation, contrary to euthanasia, is normal medical practice (19). One of the crucial propositions of the guideline is that the patient's life expectancy should not exceed two weeks. This thesis showed that in the views of bereaved relatives, the benefit of palliation should have a more prominent place in the moral evaluation of palliative sedation than the harm of a potentially hastened death. Is the relief of suffering the most important goal of sedation and is it therefore ethically acceptable that guideline recommendations on life expectancy are not always strictly followed? One could wonder whether relatives' perspective on this particular issue is the most relevant one to follow. It is difficult to balance the different considerations involved in deciding whether to start continuous sedation. Both physicians, patients and relatives have roles to play in the decision-making process. However, determining whether there are indications for palliative sedation is a medical decision.

#### **8.4.3 Future research**

Improving the quality of health care for patients at the end of life and their relatives should be a major clinical and research objective. This should not be limited to the practice of palliative sedation. Reviews of the literature have consistently highlighted a lack of research on family caregivers within the context of palliative care (75). Priority research areas include: intervention development and testing; under researched caregiver groups; access to services; unmet needs; bereavement; experience and implications of the caregiver role; and development of assessment tools (75).

This thesis made an important contribution to research on family caregivers within the context of palliative care. More insight was gained in areas such as relatives' unmet needs, bereavement and experiences and implications of the caregiver role. However, empirical research in other areas is still lacking. For instance, although selection bias was limited in our studies, certain groups were not included in our samples, such as young caregivers and ethnic minorities (e.g. Turkish and Moroccan). Further, most of our studies focused on the experiences of relatives of cancer patients, although future studies should also be conducted among other patient populations, for instance patients with dementia. Finally, to contribute to the improvement of care for the vulnerable group of suffering dying patients and their relatives, patients' perspectives could potentially also be included in future research. Of course, research among patients that ultimately need palliative sedation is challenging and there has been controversy about the appropriateness of involving palliative care patients in research (76, 77). However,

research to date in the palliative care setting has suggested that patients are interested in participating in research, and may actually benefit from doing so (78).

The findings in this thesis also revealed several new areas of research. First, studies should aim to map and understand the perceived barriers and facilitators affecting the provision of information and communication processes. Another key area that warrants comprehensive attention is 'bereavement'. Since this thesis showed that pre-existing conditions, such as depression, can be important in explaining complicated bereavement after the patient's death, studies should be aimed to assess carers who are at risk of poor psychological wellbeing. Further, attention should be paid to the development of care strategies that deal with pre-loss/anticipatory grief among relatives.

One of the major strengths of this thesis is that combines findings from multiple methods (both qualitative and quantitative) and multiple data sources. However, several weaknesses were encountered. For instance, it is not always entirely clear whether participants refer to the same type of sedation, which potentially limits full comparison and extrapolation of the studies. Therefore a case-based approach, such as used in the interview study, would be highly recommended for future research. This design could be solidified using elements from the other designs, such as the use of validated questionnaires. Second, a prospective longitudinal design would be recommended. Since only a minority of patient receives palliative sedation at the end of life (79), the focus in this type of study should therefore be on relatives in end-of-life care in general. One of the strengths of this design is that it can be used in order to study changes in e.g. communication processes and relatives' behavior. This design could be further extended with an observational element, which is also a very suitable way to find out more about relatives' attitudes, beliefs, expectations, and knowledge. Although the prospective element deals with issues such as recollection bias, there are potentially medical ethical challenges associated with this design. Efforts to protect the rights and welfare of patients and their relatives should balance the need for protections against the ethical imperative to improve care.

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# CHAPTER 9

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**Summary**

**Samenvatting**

**Dankwoord / Acknowledgements**

**About the author**

**Publications**

**PhD portfolio**

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## SUMMARY

Palliative sedation is the deliberate lowering of a patient's consciousness in the last stage of life. It may be administered continuously until death, or temporarily/intermittently. In this thesis the focus is on continuous sedation until death. Continuous sedation is administered in the final stages of life to patients who are dying and are experiencing unbearable suffering.

In the first chapter, current knowledge of the practice of palliative sedation based on empirical research and guidelines is discussed. We present an overview of research reporting the frequency of the use of continuous sedation until death and discuss guidelines on palliative sedation, with special attention to the Dutch national guideline. Further, we summarize findings regarding clinical characteristics of the practice of continuous sedation, for example aspects of the decision-making.

Relatives play an important role in the trajectory when sedation is being considered and while it is carried out. This thesis aims to provide a comprehensive overview of bereaved relatives' experiences with the practice of palliative sedation. Further, the aim is to gain more insight into the potential life-shortening effect of palliative sedation and in the risk factors for complicated grief in older adults. To achieve these goals, several research questions will be addressed.

- Research question 1: What are the experiences of bereaved relatives with the practice of palliative sedation?*
- Research question 2: What is the impact of continuous sedation on relatives' experience of the dying phase and their wellbeing after the patient's death?*
- Research question 3: Can physicians' accurately estimate the potential life-shortening effect of continuous sedation until death?*
- Research question 4: What are risk factors for complicated grief among older adults?*

To guide caregivers, several international, national, and local guidelines for the use of palliative sedation have been published. These guidelines typically also include recommendations to protect the wellbeing of relatives of patients who receive palliative sedation. According to these guidelines, relatives should be involved in the decision making and they can be involved in the provision of the sedation, for example by spending time with and observing the patient and providing physicians and nurses with information about the patient. Further, relatives should be kept informed, and the care team must provide supportive care to the relatives.

In chapter 2 the results of a systematic review on the experiences of relatives with the practice of palliative sedation are presented in the light of the recommendations in guidelines. Most studies report that the majority of relatives are adequately involved in the decision-making and receive adequate information, although there seems room for improvement. However, hardly any information is available about relatives' involvement in the provision of sedation and no studies report specifically about the support provided to relatives. Despite the fact that the majority of relatives were reported to be comfortable with the use of palliative sedation, our review shows that the relatives may express distress before or during the application of sedation.

Chapter 3 reports on the results of the focus group study conducted among bereaved relatives. A total of 14 relatives of patients who received palliative sedation until death participated in focus groups and individual interviews. A semi-structured questionnaire was used. Many relatives had positive experiences with the provision of sedation for their dying family member. The start of the sedation is a relief for relatives because the patient's suffering is finally alleviated. Relatives often appreciated having an active role in decision-making and the provision of the sedation. Other positive experiences relate to the degree of involvement of professional caregivers in caregiving and decision-making, and that they thought that the place of death was in agreement with the wishes of the patient. On the other hand, several relatives indicated that they were dissatisfied with the information they received, and about communication in general. Other negative experiences relate to concerns about the wellbeing of the patient during sedation, especially when the sedation process lasts long, the lack of authority of nurses to make decisions, and the absence of physicians during the weekends.

In chapter 4 we describe an interview study among bereaved relatives from the UK, Belgium and the Netherlands. It shows that most relatives are able to provide a description of the concept of sedation. Nevertheless several of them were unsure about what it entails. Although relatives generally believed sedation contributes to the patient having a good death, they also expressed some concerns about its use and experienced some unexpected events for which they were unprepared. These relate to anxieties about the patient's wellbeing, their own wellbeing, and questions about whether continuous sedation had shortened the patient's life, or whether an alternative approach would have been better. According to relatives from the Netherlands and Belgium, the start of the sedation allows for a planned moment of 'saying goodbye'. In contrast, relatives from the UK described the process of saying goodbye as a more gradual and less explicit process.

It is often assumed that the use of palliative sedation is burdensome for the relatives of dying patients because it hampers communication in the very last phase of life. In chapter 5, we examined whether bereaved relatives of patients who received sedation and bereaved relatives of patients who had died a non-sudden death without the use of palliative sedation differ in their experience of the dying phase and their wellbeing after the patient's death. An observational study was conducted among relatives of consecutive patients who died an expected death in the Erasmus MC Cancer Institute or hospice Laurens Cadenza in Rotterdam, between 2010 and 2013. No significant differences were found in relatives' assessments of the quality of end-of-life care, patients' quality of life in the last week before death, and their quality of dying, between relatives of patients who received and did not receive sedation. Further, no significant differences were found in relatives' own satisfaction with life, their general health, mental wellbeing and detachment levels. The use of sedation does not, in itself, seem to negatively influence bereaved persons' experience of the dying phase of their deceased relative or their wellbeing after the patient's death.

In chapter 6 we aim to get insight into the accuracy of estimates of the life-shortening effect of continuous sedation until death by comparing two different approaches. We compare a direct approach, where we ask physicians to estimate the life-shortening effect of continuous sedation until death, and an indirect approach, where we ask the physicians to estimate the patient's life expectancy and relate that to the duration of the sedation. There is a substantial discrepancy between the two approaches. When directly asked, physicians estimated that the use of continuous sedation until death might have had a life shortening effect in 51% of the cases. In contrast, on the basis of physicians' estimations of patients' life expectancy at the start of sedation and the duration of sedation until death such an effect had occurred in 84% of cases. The finding of this substantial discrepancy between two approaches confirms the difficulty of predicting the life expectancy of patients with advanced disease, and of estimating the potential life-shortening effect of end-of-life interventions.

Although the majority of adults recover after the loss of a loved one, a portion continues to grieve for an extended period of time and develops symptoms of a state known as complicated grief. The prevalence of complicated grief in older adults in the general population is considerable (namely 4,8%), however, research on complicated grief in older adults is scarce. In chapter 7, we aimed to assess whether characteristics of the patient and the bereaved relative, the patient's illness, end-of-life care and the nature of death are risk factors for developing complicated grief in older adults. A nested case-control study was conducted within the Rotterdam Study. 100 couples of which one person had deceased and the other person experienced 'complicated grief' and 100

control couples of which one person had deceased and the other person experienced 'normal grief' were selected. Only pre-existing depression was significantly associated with complicated grief. Bereaved partners with pre-existing depression had a higher risk of complicated grief compared to bereaved partners without depression. It can be concluded that complicated grief in older adults is not related to the circumstances of dying of a deceased relative. Pre-existing conditions such as depression seem to be more important in explaining the occurrence of complicated grief.

In the final chapter (8), we summarize and discuss the main findings of the studies. We conclude that, despite that relatives express several concerns due to the use of sedation, they generally evaluate its use positively. Concerns that relatives express are mostly related to a lack of information or communication. A potential life shortening effect, which is an important issue in the ethical debate on palliative sedation, does not seem to play an important role in their evaluation of sedation, at least not in the Netherlands and Belgium. The chapter concludes with implications for clinical practice and recommendations for policy and future research.



## SAMENVATTING

Palliatieve sedatie is het opzettelijk verlagen van het bewustzijn van een patiënt in de laatste levensfase. Er kunnen twee verschillende situaties worden onderscheiden: continu sederen tot het moment van overlijden en kortdurend of intermitterend sederen. De focus in dit proefschrift ligt op continu sederen tot aan het overlijden. Continue sedatie vindt plaats bij patiënten die stervende zijn en ondraaglijk lijden.

In hoofdstuk 1 wordt een overzicht gegeven van onderzoek naar de frequentie waarmee sedatie wordt toegepast. Richtlijnen voor palliatieve sedatie worden besproken, met specifieke aandacht voor de Nederlandse richtlijn die in 2009 door de KNMG werd uitgebracht. Daarnaast worden bevindingen uit onderzoek samengevat ten aanzien van de klinische kenmerken van sedatie, zoals betrokkenheid van patiënten, naasten en palliatieve zorg experts bij de besluitvorming.

Zowel in het traject dat leidt tot palliatieve sedatie als ook gedurende de uitvoering daarvan, spelen de naasten van de patiënt een belangrijke rol. Doel van dit proefschrift is om inzicht te geven in de ervaringen van naasten van patiënten die aan het einde van hun leven worden gesedeerd. Daarnaast wordt het mogelijke levensbekortende effect van palliatieve sedatie onderzocht en wordt er gekeken naar mogelijke risicofactoren voor gecompliceerde rouw bij ouderen. De onderzoeksvragen zijn:

- Onderzoeksvraag 1: Wat zijn de ervaringen van naasten met palliatieve sedatie?*
- Onderzoeksvraag 2: Wat is de invloed van continue sedatie op de beleving van naasten van de stervensfase en het welzijn van naasten na het overlijden van de patiënt?*
- Onderzoeksvraag 3: Hoe nauwkeurig kunnen artsen het mogelijk levensbekortende effect van palliatieve sedatie inschatten?*
- Onderzoeksvraag 4: Wat zijn de risicofactoren voor gecompliceerde rouw bij ouderen?*

Richtlijnen voor palliatieve sedatie bevatten aanbevelingen gericht op het welzijn van de naasten. Naasten moeten betrokken worden in het besluitvormingsproces en naasten kunnen betrokken worden bij de toepassing van sedatie, door bijvoorbeeld het monitoren van de patiënt en helpen bij de verzorging. Daarnaast moeten naasten duidelijk worden geïnformeerd en waar nodig ondersteund door zorgverleners.

In hoofdstuk 2 worden de ervaringen van naasten met palliatieve sedatie zoals beschreven in de empirische wetenschappelijke literatuur systematisch in kaart gebracht. We zien dat naasten over het algemeen adequaat worden betrokken in het besluitvorm-

ingsproces en adequate informatie ontvangen, al lijkt er ruimte te zijn voor verbetering. Er is echter weinig bekend over de betrokkenheid van naasten in het zorgproces en er is er geen onderzoek gedaan naar de steun die naasten ontvangen van zorgverleners. Hoewel de meerderheid van de naasten aangeeft de toepassing van sedatie positief te hebben ervaren, laat deze studie zien dat naasten voorafgaand aan of tijdens de sedatie ook stress kunnen ervaren.

In hoofdstuk 3 worden de resultaten gepresenteerd van een focusgroep studie onder naasten van gesedeerde patiënten. Tussen oktober 2010 en maart 2011 zijn drie focusgroepen gehouden met in totaal 10 naasten en vier individuele interviews. Voor deze gesprekken werd gebruik gemaakt van een semi-gestructureerde vragenlijst. De start van de sedatie bleek vaak een opluchting voor naasten te zijn, omdat het lijden van de patiënt eindelijk werd verlicht. Naasten vonden het prettig actief betrokken te worden bij het besluitvormingsproces en de toepassing van sedatie. Andere positieve ervaringen betroffen de betrokkenheid van zorgverleners, de plaats van overlijden die in overeenstemming was met de wens van de patiënt en de prettige zorgomgeving met goede faciliteiten. Sommige naasten waren minder tevreden met de informatie die zij hadden ontvangen en met de communicatie in het algemeen. Andere negatieve ervaringen betroffen zorgen omtrent het welzijn van de patiënt tijdens de sedatie, met name wanneer de sedatie lang duurde, het feit dat verpleegkundigen geen beslissingen konden nemen over de medicatie en de afwezigheid van artsen in de weekenden.

In hoofdstuk 4 presenteren we de resultaten van een interview studie uitgevoerd onder naasten van gesedeerde patiënten uit Nederland, België en Engeland. We zien dat de meeste naasten begrepen wat het concept sedatie inhoudt. Hoewel de meeste naasten meenden dat de sedatie had bijgedragen aan een 'goede dood', hadden zij ook vragen en hadden er zich soms onverwachte situaties voorgedaan (zoals het wakker worden van de patiënt tijdens de sedatie) waarop zij niet waren voorbereid. Hun vragen betroffen het welzijn van de patiënt of hun eigen welzijn, of het mogelijk levensbekortende effect van sedatie. Sommigen vroegen zich af of sedatie wel de meest geschikte interventie was geweest om het lijden van de patiënt te verlichten. Volgens veel naasten uit Nederland en België betekende de start van de sedatie een 'afgebakend' moment, waarop ze afscheid konden nemen van de patiënt. Naasten uit Engeland hadden die ervaring veel minder: het proces van afscheid nemen was voor hen meer een geleidelijk proces geweest.

Er wordt vaak verondersteld dat palliatieve sedatie belastend is voor de naasten van patiënten omdat het de communicatie belemmert in de allerlaatste fase van het leven. In hoofdstuk 5 is nagegaan of naasten van gesedeerde patiënten en naasten van niet-

gesedeerde patiënten verschillen in hun tevredenheid met de stervensfase en hun welzijn na het overlijden van de patiënt. Tussen 2010 en 2013 werd een vragenlijst afgenomen bij 151 naasten van gesedeerde patiënten en 90 naasten van niet-gesedeerde patiënten. Het gebruik van sedatie op zichzelf bleek geen negatieve invloed te hebben op de tevredenheid met de stervensfase of op het welzijn van de naaste.

In hoofdstuk 6 worden verschillende methoden om het mogelijk levensbekortende effect van sedatie in te schatten vergeleken. Bij de 'directe' benadering werd een arts gevraagd het levensbekortende effect van continue sedatie tot aan het overlijden te schatten. Bij de 'indirecte' benadering werd een arts gevraagd om de levensverwachting van de patiënt te schatten en werd deze vergeleken met de daadwerkelijke duur van de sedatie. Er was een aanzienlijke discrepantie tussen de twee benaderingen. Wanneer artsen direct werden gevraagd of continue sedatie een levensbekortend effect had gehad, gaven zij in 51% van de gevallen aan dat dit het geval was geweest. In 84% van de gevallen was de duur van de periode vanaf de start van de sedatie tot aan het overlijden van de patiënt korter dan de door de arts ingeschatte levensverwachting. De discrepantie tussen deze twee benaderingen bevestigt de complexiteit van het inschatten van de levensverwachting van patiënten en van het mogelijk levensbekortend effect van medische interventies.

Er wordt gesproken van gecompliceerde rouw als iemand gedurende ten minste 6 maanden intense rouwreacties ervaart die gepaard gaan met ernstige problemen in het normale alledaagse functioneren. Hoewel de prevalentie van gecompliceerde rouw onder ouderen vrij hoog is, is er nog weinig onderzoek naar gedaan. In hoofdstuk 7 is onderzocht of kenmerken van de patiënt of diens ziekte, kenmerken van de naaste, of kenmerken van de zorg rond het levenseinde en het overlijden invloed hebben op het ontwikkelen van gecompliceerde rouw bij ouderen. Binnen de Rotterdam studie zijn 100 echtparen waarvan de een was overleden en de ander 'normale rouw' ervoer vergeleken met 100 echtparen waarvan de een was overleden en de ander 'gecompliceerde rouw' ervoer. De aanwezigheid van gecompliceerde rouw bleek niet samen te hangen met kenmerken van het overlijden. Reeds bestaande condities zoals de aanwezigheid van depressie speelden wel mee bij het verklaren van het bestaan van gecompliceerde rouw.

In het laatste hoofdstuk (8) worden de belangrijkste bevindingen samengevat. We concluderen dat, hoewel naasten soms vragen hebben en zorgen ervaren bij de toepassing van palliatieve sedatie, zij er over het algemeen positief op terugkijken. Hun zorgen hebben veelal te maken met een gebrek aan informatie of communicatie. Een mogelijk levensbekortend effect van sedatie (volgens artsen vaak het geval) of het gebrek aan communicatie met de gesedeerde patiënt voor het overlijden, twee belangrijke onder-

werpen in het ethische debat rondom sedatie, lijken geen belangrijke rol te spelen in hun beoordeling van sedatie. De toepassing van sedatie heeft geen negatieve invloed op de tevredenheid van naasten met de stervensfase van de patiënt en hun welzijn na het overlijden. Het hoofdstuk wordt afgesloten met een bespreking van de implicaties voor de klinische praktijk en aanbevelingen voor beleid en onderzoek.

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De hoofdstukken in dit proefschrift, waarvan de meeste inmiddels zijn gepubliceerd in internationale peer-reviewed journals, zouden niet van deze kwaliteit zijn geweest zonder de inbreng van de co-auteurs. Hartelijk dank voor jullie kritische en waardevolle feedback op mijn manuscripten. I would also like to thank my foreign co-authors for their critical and valuable feedback on my manuscripts.

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Tot slot Vincent, te allen tijde een luisterend oor. Dank je wel lieverd.





## ABOUT THE AUTHOR

Sophie Marringje Bruinsma was born in Enschede on September 7, 1984. She obtained her Gymnasium diploma at the Jacobus College in Enschede in 2002. After secondary school, she started studying Dutch Law, at the University of Groningen and obtained her propaedeutic degree in 2005. In 2005, she switched to studying Sociology at the University of Groningen. She specialized in 'Health, care and wellbeing'. Her thesis was about the wellbeing of residents in a nursing home. She obtained her Masters of Science degree in 2010. In 2010, she started as a PhD candidate at the Department of Public Health of Erasmus MC, the Netherlands. She was involved in an international study (the UNBIASED study) that explores the perspectives of clinical staff and bereaved informal caregivers on the use of continuous sedation until death for cancer patients. In the same period, she also completed her master's degree in Epidemiology at the Netherlands Institute for Health Sciences in Rotterdam. In February 2014, she was a visiting researcher at the Brocher Foundation in Geneva, Switzerland. In that same year, she started working as a postdoctoral researcher at the Department of Urology of Erasmus MC, the Netherlands, where she is involved in an international study (GAP3) on active surveillance for low-risk prostate cancer.

Sophie Marringje Bruinsma werd op 7 september 1984 geboren. Ze behaalde haar Gymnasium diploma aan het Jacobus College te Enschede in 2002. Na haar middelbare school is ze begonnen met de studie Nederlands Recht aan de Rijksuniversiteit Groningen. Na het behalen van haar propedeuse is ze Sociologie gaan studeren, met als specialisatie Medische Sociologie. Haar afstudeeronderzoek richtte zich op het welbevinden van bewoners in verzorgingstehuizen. In 2010 behaalde ze de titel 'Master of Science'. Vanaf 2010 werkte ze als PhD op de afdeling Maatschappelijke Gezondheidszorg van het Erasmus MC te Rotterdam. Ze was betrokken bij een internationale studie over de ervaringen van artsen, verpleegkundigen en naasten met palliatieve sedatie. Tijdens haar PhD periode behaalde zij ook haar master titel in Epidemiologie aan het NIHES te Rotterdam. In februari 2014 werkte zij tijdelijk als onderzoeker bij de Brocher Foundation in Geneve, Zwitserland. In datzelfde jaar is zij begonnen als postdoctoraal onderzoeker op de afdeling Urologie van het Erasmus MC en is zij betrokken bij een internationale studie (GAP3) over 'active surveillance' bij prostaatkanker.



## LIST OF PUBLICATIONS

### International

Bruinsma SM, Tiemeier HW, Verkroost- van Heemst J, van der Heide A, Rietjens JAC. Risk factors for complicated grief in older adults. *J Palliat Med* 2015 (in press).

Bruinsma SM, Brown J, van der Heide A, Deliens L, Anquinet L, Payne SA, Seymour JE, Rietjens JA, on behalf of UNBIASED. Making sense of continuous sedation in end of life care for cancer patients: An interview study with bereaved relatives in three European countries. *Support Care Cancer* 2014;22(12):3243-52.

Bruinsma SM, Rietjens JA, Swart SJ, Perez RS, van Delden JJ, van der Heide A. Estimating the potential life-shortening effect of continuous sedation until death: a comparison between two approaches. *J Med Ethics* 2014;40(7):458-62.

Bruinsma S, Rietjens J, van der Heide A. Palliative sedation: a focus group study on the experiences of relatives. *J Palliat Med* 2013;6(4):349-55.

Bruinsma SM, Rietjens JA, Seymour JE, Anquinet L, van der Heide A. The experiences of relatives with the practice of palliative sedation: a systematic review. *J Pain Symptom Manage* 2012;44(3):431-45.

Seymour J, Rietjens J, Bruinsma S, Deliens L, Sterckx S, Mortier F, Brown J, on behalf of UNBIASED. Continuous sedation in end of life care for cancer patients: A qualitative interview study of physicians' and nurses' practice in three European countries. *Palliat Med* 2015;29(1):48-59.

Anquinet L, Rietjens JAC, van der Heide A, Bruinsma S, Janssens R, Deliens L, Addington-Hall J, Smithson WH, Seymour J, on behalf of UNBIASED. Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life. *Psycho-Oncology* 2014;23(5):539-46.

Raus K, Brown J, Seale C, Rietjens J, Janssens R, Bruinsma S, Mortier F, Payne S, Sterckx S. Continuous sedation until death: The everyday moral reasoning of physicians, nurses and family caregivers in the UK, The Netherlands and Belgium. *BMC Med Ethics* 2014;15:14.

Seale C, Raus K, Rietjens J, Bruinsma S, van der Heide A, Sterckx S, Mortier F, Payne S, 1. Mathers N, on behalf of UNBIASED. The language of sedation in end-of-life care: The ethical reasoning of care providers in three countries. *Health* 2014. pii 1363459314555377 (epub ahead of print).

Bruinsma SM, van der Heide A, van der Lee ML, Vergouwe Y, Rietjens JAC. No negative impact of palliative sedation on relatives' experience of the dying phase and their wellbeing after the patient's death (submitted).

### **National**

Bruinsma S, Rietjens J, Janssens R, Van Zuylen L, Van der Heide A. Een internationale studie naar de praktijk van palliatieve sedatie. *Nederlands Vlaams Tijdschrift van Palliatieve Zorg* 2011;11(1):22-26.

### **Book contribution**

Bruinsma SM, Rietjens JAC, van der Heide A (2013). Continuous sedation until death: state of the art. In: Sterckx S, Raus K, Mortier F (Eds). *Continuous Sedation at the End of Life: Ethical, Clinical and Legal Perspectives* (pp.29-46). Cambridge University Press.

## PHD PORTFOLIO- SUMMARY OF PHD TRAINING

Name	Sophie Bruinsma
PhD period	April 2010- March 2014
Erasmus MC department	Public Health
Promotor	Prof. Dr. A. van der Heide
Supervisor	Dr. J.A.C. Rietjens

	Year	Workload (ECTS/ hours)
<b>1. PhD training</b>		
<b>General academic skills</b>		
Computer course/ literature search, Erasmus MC	2010	6 hours
Qualitative research in healthcare, Antwerp, Belgium	2010	40 hours
<b>Research skills</b>		
Master Epidemiology, NIHES	2010-2013	70 ECTS
<b>In depth courses</b>		
Suffering, Death and Palliative Care, Nijmegen, the Netherlands	2013	1 ECTS
<b>Presentations- International</b>		
Oral presentation: The experiences of relatives with palliative sedation. Bioethics conference. Rotterdam, the Netherlands	2012	1 ECTS
Oral presentation: Estimating the potential life-shortening effect of continuous sedation until death: a comparison between two approaches. International Collaborative for End-of-Life Care Research (ICER). Amsterdam, the Netherlands.	2012	1 ECTS
Poster-presentation: Palliative sedation: a focus group study on the experiences of relatives. Conference of the European Association of Palliative Care (EAPC). Trondheim, Norway	2012	1 ECTS
Poster-presentation: The experiences with the practice of palliative sedation: a systematic review. Conference of the European Association of Palliative Care (EAPC). Lisbon, Portugal.	2011	1 ECTS
<b>Presentations- National</b>		
Experiences of relatives with the practice of palliative sedation: the UNBIASED study, Erasmus MC, Rotterdam, the Netherlands	2013	1 ECTS
Oral presentation: Estimating the potential life-shortening effect of continuous sedation until death: a comparison between two approaches. Nationaal Congres Palliatieve Zorg. Lunteren, the Netherlands.	2012	1 ECTS
Oral presentation: Care and decision- making at the end of life. Post- EAPC congress. Leiden, the Netherlands.	2012	1 ECTS
Oral presentation: Experiences of relatives with palliative sedation. Flemish Dutch Research Forum Palliative Care. Rotterdam, the Netherlands.	2012	1 ECTS
Oral presentation: Relatives in end-of- life care research. Agora. Nijmegen, the Netherlands.	2011	1 ECTS

<b>(Inter) national conferences</b>		
Nationaal Congres Palliative Zorg, Lunteren, the Netherlands	2010	1 ECTS
European Association of Palliative Care conference, Lissabon, Portugal	2011	1 ECTS
Conference: Continuous sedation at the end of life: Ethical perspectives, Ghent, Belgium	2011	1 ECTS
Nationaal Congres Palliative Zorg, Lunteren, the Netherlands	2012	1 ECTS
European Association of Palliative Care conference, Trondheim, Norway	2012	1 ECTS
World Congress of Bioethics	2012	1 ECTS
<b>Workshops and seminars</b>		
Seminars department of Public Health, Erasmus MC	2010-2014	3 ECTS
Flemish Dutch Research Forum Palliative Care, Rotterdam, the Netherlands	2012	1 ECTS
PhD dag (2x)	2011, 2013	8 hours
Symposium 'Evidentie en beslissen in de gezondheidszorg: Stand van de wetenschap en praktijk'	2010	4 hours
Post EAPC symposium, De Bilt, the Netherlands	2011, 2013	4 hours
Symposium 'Als botsen raken wordt'	2010	4 hours
International Collaborative for End-of-Life Care Research (ICER) (2x)	2011, 2013	8 hours
<b>2. Teaching activities</b>		
Supervising medical students theme 3.C.4 (community project)	2011, 2013	32 hours
Supervising nurses literature review, Sophia, Erasmus MC	2011	20 hours
<b>Total</b>		90 ECTS, 126 hours