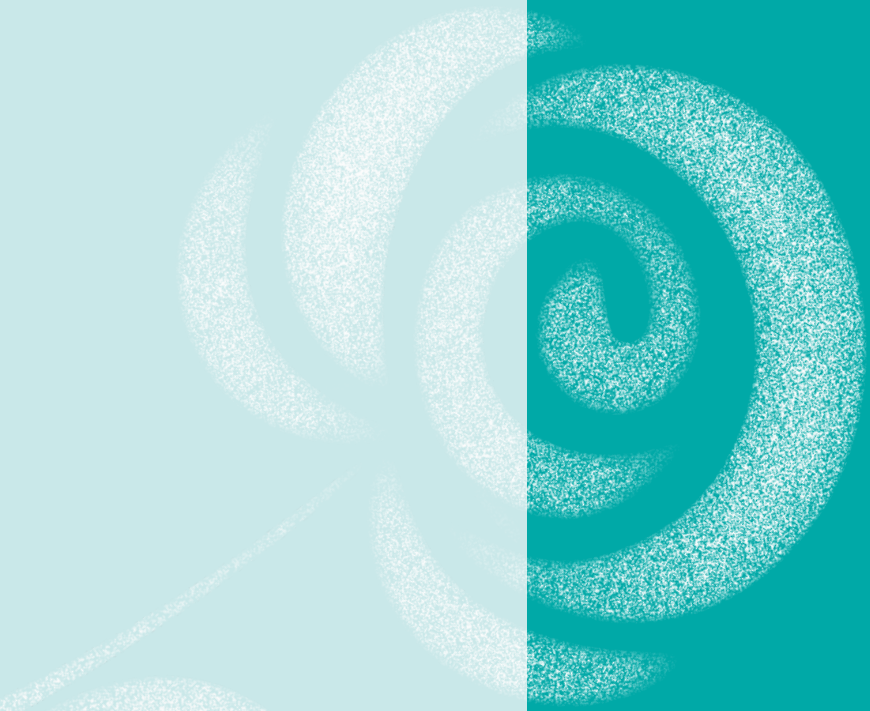
Siebe Swart

The practice of palliative sedation in the Netherlands after the launch of the national guideline



AMROSE

Siebe Swart

The practice of palliative sedation in the Netherlands after the launch of the national guideline

The Practice of Palliative Sedation in the Netherlands after introduction of the National Guideline. Thesis, Erasmus MC University Medical Centre Rotterdam.

ISBN 978-94-6169-376-1

Cover illustration: pringletta@iStockphoto.com
Cover and interior design: Anna Bosselaar | Zoiets Communicatie (anna@zoiets.com)
Printed by Optima Grafische Communicatie BV (www.ocg.nl)

The studies presented in this thesis were carried out within the framework of the AMsterdamROtterdamSedation-project (AMROSE) and performed at the department of Public Health, Erasmus MC. Logistical support was kindly offered by the Comprehensive Cancer Centre Rotterdam (IKNL).

The AMROSE-project has been funded by the Dutch Organisation for Health Research and Development (ZonMw 1150.0004). The PhD-trajectory would not have been possible without the financial support of Stichting Laurens Fonds Rotterdam and Stichting Palliatieve Zorg Dirksland Calando.

The printing of this thesis was financially supported by the department of Public Health, Erasmus MC and the Erasmus Univerity Rotterdam.

The practice of palliative sedation in the Netherlands after the launch of the national guideline

De praktijk rond palliatieve sedatie in Nederland na het verschijnen van de landelijke richtlijn

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de rector magnificus

Prof.dr. H.G. Schmidt

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 26 juni 2013 om 9.30 uur

door

Siebe Jan Swart

geboren te Apeldoorn.

Promotiecommissie

Promotoren:	Prof.dr. A. van der Heide Prof.dr. J.J.M. van Delden
Overige leden:	Prof.dr. P.J.E. Bindels Prof.dr. C.C.D. van der Rijt Prof.dr. D.L. Willems
Copromotoren:	Dr. J.A.C. Rietjens Dr. C. van Zuylen

What's in a name?
That which we call a rose
by any other name would smell as sweet

Uit: *Romeo and Juliet,*
William Shakespeare
(1554-1616)

TABLE OF CONTENTS

1

General introduction

INTRODUCTION

Palliative sedation is a medical intervention aimed at relieving intractable suffering by inducing decreased awareness of symptoms. It is typically considered a palliative option for patients suffering unbearably in the last days of life.[1-3] The estimated frequency of palliative sedation varies considerably in scientific literature, partly due to differences in definition and research setting and differences in terminology. Whereas in the English medical scientific literature the first descriptions of palliative sedation referred to 'terminal sedation'[4], in Dutch medical literature palliative sedation was first described as 'deep sedation in the dying phase'.[5] Although terminology still varies – e.g. continuous deep sedation[6], continuous sedation until death[7], continuous deep sedation until death[8], continuous sedation at the end of life[9], palliative sedation at the end of life[10], palliative sedation therapy[2], palliative sedation to unconsciousness[11], terminal sedation[12-14], continuous palliative sedation[15] – the most frequently used general term for this treatment in the literature nowadays is palliative sedation.[16]

Palliative sedation refers to several subtypes: intermittent or continuous sedation and deep or mild sedation.[2] Comparable nationwide studies show frequencies of continuous deep sedation in Europe of 2.5% up to 16% of all deaths.[17,18] In the Netherlands the estimated frequency of continuous deep sedation has risen from 5,6% of all deaths in 2001 to 12,3% in 2010.[6,19] The benefits and drawbacks of continuous palliative sedation (CPS), including both deep and superficial sedation, are frequently debated.[20-23] Continuous palliative sedation is regarded as an indispensable treatment to alleviate intolerable refractory symptoms in the last days of life, but it diminishes the patients' ability to communicate.[2,21,24-26] Also, concerns have been voiced that forgoing artificial nutrition or hydration may reflect an intention to hasten death in deeply sedated patients.[27,28] However, for people in the last weeks of their lives, evidence concerning the effects of continuing or withdrawing artificial nutrition and hydration is still lacking and little is known regarding life-shortening or life prolonging effects.[29]

FROM PRACTICE TO GUIDELINE

Although it is argued that continuous sedation does not shorten life when administered properly[30-33], controversies may arise in clinical practice. This was illustrated in the Netherlands, in 2003, in the case of Dr Vencken, a trainee anaesthesiologist who, while on duty as a casualty doctor, palliated breathing difficulties in a patient who had had a large cerebral stroke. This treatment was applied after it was agreed with the family to offer palliative care. His act led to a legal test case that lasted for two years.[34] He was accused of 'having given purposefully and with malice aforethought a lethal injection to a terminal patient'. With this test case the public prosecutor wanted to create clarity with respect to the grey area between hastening death and 'normal' medical treatment. The fact that Dr Vencken was taken into preventive custody for 9 days caused great agitation within the medical community. Eventually, in 2006, the court acknowledged that dr Vencken's use of morphine and midazolam had been clearly aimed at relieving his dying patient's symptoms and not at

ending his life. His treatment was considered normal medical treatment within professional standards.[35,36]

Meanwhile research regarding medical decisions at the end of life had shown that in about two thirds of cases in which continuous deep palliative sedation had preceded death, physicians indicated that in addition to alleviating symptoms, they had intended to hasten death.[37] These circumstances led the government to urge the medical profession to draft a national palliative sedation guideline, which was launched in 2005 and updated in 2009. Later, other countries (e.g Belgium and Canada) followed in developing national guidelines or frameworks for palliative sedation.[38,39]

Dutch national guideline

The Dutch national guideline defines palliative sedation as 'the intentional lowering of the consciousness of a patient in the last phase of life'[2,5,40,41] and provides recommendations regarding decision making and procedures (box 1).

At the launch of the guideline, the Royal Dutch Medical Association (RDMA) stated that it would actively monitor its content and the debate on palliative sedation. The main reasons for an update of the guideline in 2009 related to areas of continuing debate. First, research had shown that physicians had not always acted in accordance with earlier regional guidelines that formed the basis for the national RDMA-guideline.[42] Second, specific elements of the guideline (e.g. refractory symptoms, life expectancy criterion and consultation of expert opinion) and the relation between continuous deep sedation and euthanasia needed further elaboration.[3,6,20,43] Although the text of the guideline on these issues was adjusted, the principal criteria for applying palliative sedation, remained similar in the updated guideline:

Box 1 Most important criteria and recommendations regarding the use of continuous palliative sedation (CPS) in the Dutch national guideline.

Guideline recommendation

Regarding decision making

- Indication: one or more refractory symptoms, leading to unbearable suffering in the patient
- 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 his 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

Regarding procedure

- 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
- Accurate records must be kept of the decision-making process, the way palliative sedation is being administered and the effect of the intervention

1. An indication for palliative sedation is present when one or more intractable or 'refractory symptoms are causing the patient unbearable suffering. A symptom is or, becomes 'refractory', when none of the conventional modes of treatment is effective or fast-acting enough, and/or if these modes of treatment are accompanied by unacceptable side-effects
2. Besides the presence of medical indications in the form of one or more refractory symptoms, a precondition for the use of continuous sedation is the expectation that death will ensue in the reasonably near future – that is, within one to two weeks
3. In situations where it is hard to judge whether the patient actually is in the final stages of life, particular care needs to be taken in establishing whether a particular symptom is permanently refractory and deciding on that basis to initiate continuous sedation. In such cases, the committee considers the advice of a consultant, preferably a palliative specialist, to be mandatory.

The guideline explicates that continuous deep palliative sedation can be clearly distinguished from euthanasia.[3,44] This explication followed after intensive debates within politics, society and amongst physicians, ethicists and lawyers on this distinction and addresses relevant differences between palliative sedation and euthanasia, in view of the regulation by law of euthanasia in the Netherlands in 2002. This regulation by law confirmed that euthanasia is not considered normal medical practice, and also that it is not considered a criminal act when physicians apply strict criteria of due care when they comply with a patients' request for euthanasia.[45,46] In the national guideline, palliative sedation is considered a normal medical procedure, meaning that the indication and its use in medical practice are determined by current standards within the medical profession. However, distinguishing normal medical practice from non-normal medical practice in guidelines does not necessarily imply that such distinctions are easily made in clinical practice, as shown in the case of Dr Vencken.

FROM GUIDELINE TO PRACTICE

The launch of the guideline in 2005 resulted in increased attention for the practice of palliative sedation. Although the guideline provided clues to distinguish palliative sedation from euthanasia, associations of palliative sedation with 'slow euthanasia' were still heard.[14] Others voiced a fear that palliative sedation could be used by physicians to avoid euthanasia, thus letting physicians' considerations override patients' considerations and patient autonomy.[47] Also palliative sedation was associated with 'medicalization of dying'.[48,49] Since a proper implementation strategy for the national guideline had not been developed and many questions related to practical and moral aspects of palliative sedation continued to be raised, many initiatives for teaching and symposia addressing important topics in the guideline were initiated. For example, the RDMA organised a repeated symposium on: 'Suffering: discussion on the boundaries of medical treatment'.[50] With respect to palliative sedation questions were discussed such as: Is it possible for physicians to precisely predict a life expectancy of two weeks? Is it possible for patients to choose for palliative sedation? This illustrates that launching a guideline on palliative sedation cannot easily solve all questions on this topic, as was already anticipated by the guideline committee, stating that 'a guideline inevitable leads to differences in interpretation and cannot describe all specific

situations'. The guideline also states that 'a decision to start palliative sedation is part of a trajectory and process of palliative care'. Thus, it is very important to have information about palliative sedation practice and how a guideline works out in that practice.

THIS THESIS

The studies described in this thesis were aimed at providing insight in the practice of continuous palliative sedation (CPS) after the launch of the national guideline, focusing on decision making. First we analysed physicians' experiences in different settings (home, nursing home and hospital) in relation to the main recommendations of the national guideline (box 1). Although physicians are legally responsible for making medical decisions[51], it has been shown that nurses contribute to the decision making and prefer to be involved also.[52,53] Nurses interact more continuously with patients and relatives than physicians, and are often involved in assessing the patients' symptoms and administering the sedating medication.[54] Therefore we also studied their perspectives.

CPS can be applied when suffering becomes refractory.[2,3,55-58] It is known that CPS is most frequently used in patients suffering from physical symptoms such as delirium, dyspnoea and pain.[6,37] Psychological and existential distress may add to the suffering of terminal patients, but their acceptability as a single indication for CPS is more controversial.[2,56,59-61] We performed an in-depth study to get more insight in healthcare providers' considerations concerning the indications for CPS, focussing on the refractoriness of symptoms and the life expectancy criterion.

Other important questions associated with CPS concern the depth of sedation, i.e. how deep the sedation must be to relieve suffering and how important it is for patients and their families to maintain a certain level of consciousness.[2] This is also reflected in literature where proportional palliative sedation is distinguished from palliative sedation until death.[62] 'Proportional palliative sedation' is described as sedation at the end of life, in which the minimum dosage of sedatives is used necessary to relieve refractory symptoms, while maintaining consciousness if possible. 'Palliative sedation until death' is described as a more controversial practice with unconsciousness until death as an intended outcome.[62] Palliative sedation guidelines often advise titrating sedatives[3,42,56], meaning that the dosages of sedatives are adjusted to the level needed for proper symptom relief. We investigated the arguments physicians use for choosing the depth of CPS and how these relate to palliative sedation guidelines.

Finally we wanted to address possible differences in the practice of palliative sedation between cancer patients and non-cancer patients. It is known that the quality of dying and death is determined by the type of disease the patient is suffering from.[63] Knowledge about the practice of palliative sedation is predominantly based on research in cancer patients.[22] However, in a nationwide Dutch study continuous deep sedation was in 53% used for non-cancer patients. Furthermore, in a European study the probability of receiving continuous deep sedation was only 15% larger for cancer patients than for non-cancer patients[6,17], illustrating that continuous deep sedation is also quite common among non-cancer patients.

As little information is available about palliative sedation for patients with non-malignant diseases and the importance of palliative care for non-malignant disease is increasingly acknowledged[64,65], we compared the practice of continuous sedation for non-cancer patients and cancer patients.

RESEARCH QUESTIONS

1. Is physicians' practice of CPS in accordance with the main recommendations of the Dutch national guideline on palliative sedation?
2. Do the perspectives of nurses regarding palliative sedation practice differ from those of physicians?
3. What considerations do physicians and nurses have regarding the indications for CPS and what factors influence these considerations?
4. What arguments do physicians use for choosing the depth of CPS?
5. Does the practice of CPS differ between cancer and non-cancer patients?

METHODS

We performed our studies in the context of the AMROSE-project (AMsterdam ROtterdam studies on SEdation). We started our research in 2007, 2 years after the launch of the national guideline, but before the update in 2009.

Study design

We followed a mixed methods design, focusing on the type of sedation that is most extensively described in the national guideline and that has been the main focus of the medical-ethical, social and political debate that has taken place in the Netherlands: continuous palliative sedation (CPS), which includes both deep and mild sedation.

Quantitative studies

An anonymous structured questionnaire study was performed amongst physicians and nurses from February - September 2008.

- Physicians: a paper version of the questionnaire was sent to a random sample of 1128 physicians working in three settings in the northwest and southwest of the Netherlands: general practice, n=466, nursing home, n=195 and hospital, n=467. Furthermore, the questionnaire was sent to all general practitioners (n=452) working in the northeast of the Netherlands. The response total response rate was 38%: general practitioners 43%, nursing home physicians 52%, and medical specialists 24%.
- Nurses: it was not possible to draw a random sample of nurses because a comprehensive database with contact information of nurses does not exist. We therefore approached contact persons in 6 professional home care organisations, 10 nursing homes/hospices and 7 hospitals in the northwest and southwest of the Netherlands. We asked the contact persons to distribute the questionnaire amongst all nurses who were likely to have been involved in the practice of continuous sedation. In total, 576 nurses received a questionnaire (home care, n=111, units for palliative care in nursing homes or in hospices, n=121,

and hospitals, n=344). The total response rate was 48%: home care 52%, nursing homes 55% and hospitals 45%.

Further details of the quantitative methods are described in chapters 2, 3 and 6.

Qualitative studies
In the questionnaire study, 370 physicians and 185 nurses reported about their most recent case of continuous palliative sedation.[15,44,57,66] Of these respondents, 51 physicians and 36 nurses indicated to be willing to participate in an additional qualitative interview. We added pilot interviews with one physician from each of the settings. We interviewed a total of 54 physicians (general practice, n=23, nursing home, n=23, hospital, n=8) and 36 nurses (home care, n=11, nursing home, n=10, hospital, n=15). Further details of the qualitative methods are described in chapters 4 and 5.

OUTLINE OF THIS THESIS

Chapter 2 portrays whether the practice of CPS as described by physicians is in accordance with the Dutch national guideline on palliative sedation.

Chapter 3 describes continuous palliative sedation practices in general practice, nursing homes and hospitals, focusing on differences in experiences between physicians and nurses.

Chapter 4 analyses physicians' and nurses' considerations concerning the indications for CPS and the factors that influence these considerations.

Chapter 5 explores the arguments physicians use for choosing the depth of CPS and how these relate to palliative sedation guidelines.

Chapter 6 concerns differences in continuous palliative sedation practices between cancer patients and non-cancer patients.

Chapter 7 contains the general discussion.

Chapter 8 summarizes this thesis.

References

1. Cherny N. The use of sedation to relieve cancer patients' suffering at the end of life: addressing critical issues. Ann Oncol. 2009 Jul;20(7):1153-5.
2. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. J Palliat Med. 2007 Feb;10(1):67-85.
3. KNMG. KNMG-richtlijn palliatieve sedatie 2009. http://knmgartsennetnl/Diensten/knmgpublicaties/KNMGpublicatie/Guideline-for-palliative-sedation-2009htm. 2009.
4. Enck RE. Drug-induced terminal sedation for symptom control. Am J Hosp Palliat Care. 1991 Sep-Oct;8(5):3-5.
5. Verhagen EH, Eliel MR, de Graeff A, Teunissen SC. [Sedation in the terminal phase of life] Sedatie in de laatste levensfase. Ned Tijdschr Geneeskd. 1999 Dec 25;143(52):2601-3.
6. Rietjens J, van Delden J, Onwuteaka-Philipsen B, Buiting H, van der Maas P, van der Heide A. Continuous deep sedation for patients nearing death in the Netherlands: descriptive study. BMJ. 2008 Apr 12;336(7648):810-3.
7. Seymour J, Rietjens J, Brown J, van der Heide A, Sterckx S, Deliens L, et al. The perspectives of clinical staff and bereaved informal caregivers on the use of continuous sedation until death for cancer patients: The study protocol of the UNBIASED study. BMC Palliat Care. 2011 Mar 4;10(1):5.
8. Inghelbrecht E, Bilsen J, Mortier F, Deliens L. Continuous deep sedation until death in Belgium: a survey among nurses. J Pain Symptom Manage. 2011 May;41(5):870-9.
9. Raus K, Sterckx S, Mortier F. Is continuous sedation at the end of life an ethically preferable alternative to physician-assisted suicide? Am J Bioeth. 2011 Jun;11(6):32-40.
10. Caraceni A, Zecca E, Martini C, Gorni G, Campa T, Brunelli C, et al. Palliative sedation at the end of life at a tertiary cancer center. Support Care Cancer. 2011 Jul 16.
11. AMA. Sedation to Unconsciousness in End-of-Life Care. 2008 [cited 2012 March 9]; Available from: http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2201.page.
12. Morita T, Akechi T, Sugawara Y, Chihara S, Uchitomi Y. Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: a nationwide survey. J Clin Oncol. 2002 Feb 1;20(3):758-64.
13. van Deijck RH, Rondas AA, Berghmans RL. [Terminal sedation in mentally competent patients: no overriding medical-ethical arguments against in the medical literature] Terminale sedatie bij wilsbekwame patienten: geen overwegende morele bezwaren in de medische literatuur. Ned Tijdschr Geneeskd. 2003 Dec 13;147(50):2479-83.
14. Gevers JK. Terminal sedation: between pain relief, withholding treatment and euthanasia. Med Law. 2006 Dec;25(4):747-51.
15. Swart SJ, Rietjens JA, van Zuylen L, Zuurmond WW, Perez RS, van der Maas PJ, et al. Continuous Palliative Sedation for Cancer and Noncancer Patients. J Pain Symptom Manage. 2011 Sep 17.
16. World Health Organization (WHO). WHO definition of Palliative Care. [cited 2009 10 June]; Available from: http://www.who.int/cancer/palliative/definition/en/.
17. Miccinesi G, Rietjens JA, Deliens L, Paci E, Bosshard G, Nilstun T, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage. 2006 Feb;31(2):122-9.
18. Seale C. End-of-life decisions in the UK involving medical practitioners. Palliat Med. 2009 Apr;23(3):198-204.
19. Onwuteaka-Philipsen BD, Brinkman-Stoppelenburg A, Penning C, de Jong-Krul GJ, van Delden JJ, van der Heide A. Trends in end-of-life practices before and after the enactment of the euthanasia law in the Netherlands from 1990 to 2010: a repeated cross-sectional survey. Lancet. 2012 Jul 10.
20. van Delden JJ. Terminal sedation: source of a restless ethical debate. J Med Ethics. 2007 Apr;33(4):187-8.
21. Materstvedt LJ, Bosshard G. Deep and continuous palliative sedation (terminal sedation): clinical-ethical and philosophical aspects. Lancet Oncol. 2009 Jun;10(6):622-7.
22. Hasselaar JG, Verhagen SC, Vissers KC. When cancer symptoms cannot be controlled: the role of palliative sedation. Curr Opin Support Palliat Care. 2009 Mar;3(1):14-23.
23. Claessens P, Menten J, Schotsmans P, Broeckaert B. Palliative sedation: a review of the research literature. J Pain Symptom Manage. 2008 Sep;36(3):310-33.
24. Hasselaar J, Verhagen S, Reuzel R, van Leeuwen E, Vissers K. Palliative sedation

is not controversial. Lancet Oncol. 2009 Aug;10(8):747-8.
25. Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. Jama. 2000 Nov 15;284(19):2476-82.
26. Steinhauser KE, Clipp EC, McNeilly M, Christakis NA, McIntyre LM, Tulsky JA. In search of a good death: observations of patients, families, and providers. Ann Intern Med. 2000 May 16;132(10):825-32.
27. Quill TE, Lee BC, Nunn S. Palliative treatments of last resort: choosing the least harmful alternative. University of Pennsylvania Center for Bioethics Assisted Suicide Consensus Panel. Ann Intern Med. 2000 Mar 21;132(6):488-93.
28. Jansen LA, Sulmasy DP. Sedation, alimentation, hydration, and equivocation: careful conversation about care at the end of life. Ann Intern Med. 2002 Jun 4;136(11):845-9.
29. Raijmakers NJ, van Zuylen L, Costantini M, Caraceni A, Clark J, Lundquist G, et al. Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects. Ann Oncol. 2011 Jul;22(7):1478-86.
30. Sykes N. End of life issues. Eur J Cancer. 2008 May;44(8):1157-62.
31. Sykes N, Thorns A. Sedative use in the last week of life and the implications for end-of-life decision making. Arch Intern Med. 2003 Feb 10;163(3):341-4.
32. Maltoni M, Pittureri C, Scarpi E, Piccinini L, Martini F, Turci P, et al. Palliative sedation therapy does not hasten death: results from a prospective multicenter study. Ann Oncol. 2009 Jul;20(7):1163-9.
33. Maltoni M, Miccinesi G, Morino P, Scarpi E, Bulli F, Martini F, et al. Prospective observational Italian study on palliative sedation in two hospice settings: differences in casemixes and clinical care. Support Care Cancer. 2012 Feb 24.
34. Bruntink R. [It was like in a story of Kafka (translation sjs)] Het is echt Kafkaesk geweest. Relevant. 2006;1:10-3.
35. Sheldon T. Doctor who was remanded for murder wins record damages. Bmj. 2006 Feb 25;332(7539):443.
36. Legemaate J. [Relief of symptoms and palliation versus ending a patient's life: looking back at the case against Vencken] Symptoombestrijding en palliatie versus levensbeëindiging: een terugblik op de zaak-Vencken. Ned Tijdschr Geneeskd. 2006 Jul 29;150(30):1689-92.
37. Rietjens JA, van der Heide A, Vrakking AM, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med. 2004 Aug 3;141(3):178-85.
38. Broeckaert B, Mullie A, Gielen J, Desmet M, Vanden Berghe P. Ethics Commission Federation Palliative Care Flanders. Palliative Sedation Guideline. 2010 [30 novembre 2011]; Available from: http://www.pallialine.be/template.asp?f=rl_sedatie.htm#page=page-1.
39. Dean MM, Cellarius V, Henry B, Oneschuk D, Librach Canadian Society Of Palliative Care Physicians Taskforce SL. Framework for continuous palliative sedation therapy in Canada. J Palliat Med. 2012 Aug;15(8):870-9.
40. Royal Dutch Medical Society. RDMS guideline palliative sedation. 2005; Available from: http://knmg.artsennet.nl/actueel/Nieuwsartikel/KNMG-richtlijn-palliatieve-sedatie-herzien-1.htm.
41. Verkerk M, van Wijlick E, Legemaate J, de Graeff A. A national guideline for palliative sedation in the Netherlands. J Pain Symptom Manage. 2007 Dec;34(6):666-70.
42. Hasselaar JG, Reuzel RP, Verhagen SC, de Graeff A, Vissers KC, Crul BJ. Improving prescription in palliative sedation: compliance with dutch guidelines. Arch Intern Med. 2007 Jun 11;167(11):1166-71.
43. Rietjens JA, van Delden JJ, van der Heide A, Vrakking AM, Onwuteaka-Philipsen BD, van der Maas PJ, et al. Terminal sedation and euthanasia: a comparison of clinical practices. Arch Intern Med. 2006 Apr 10;166(7):749-53.
44. Swart SJ, van der Heide A, Brinkkemper T, van Zuylen L, Perez RSGM, Rietjens JAC. Continuous Palliative Sedation until death: Practice after introduction of the Dutch national guideline. BMJ Support Palliat Care, in press. 2012.
45. Buiting HM, Gevers JK, Rietjens JA, Onwuteaka-Philipsen BD, van der Maas PJ, van der Heide A, et al. Dutch criteria of due care for physician-assisted dying in medical practice: a physician perspective. J Med Ethics. 2008 Sep;34(9):e12.

46. Rietjens JA, van der Maas PJ, Onwuteaka-Philipsen BD, van Delden JJ, van der Heide A. Two Decades of Research on Euthanasia from the Netherlands. What Have We Learnt and What Questions Remain? J Bioeth Inq. 2009 Sep;6(3):271-83.
47. van Dam H. Euthanasie en palliatieve sedatie verdienen gelijke waardering. Relevant. 2006;3(1):http://www.nvve.nl/nvve2/pagina.asp?pagkey=71922&metkey=375.
48. Bruntink R, van Leeuwen P. Wordt de juiste discussie gevoerd. Volop de debat over sedatie. Pallium. 2006;7(5):6-8.
49. Schuurmans J. Sedatie als antwoord op onvoldoende preventieve zorg. Pallium. 2006;8(1):23-4.
50. van Dijk G. KNMG: Lijden: discussie over de grenzen van het medisch handelen. Verslag van een sympsosium. Medisch Contact. 2008 26 november(48):2024-5.
51. Francke AL. Palliative Care for Terminaly Ill Patients in the Netherlands. Dutch Governmeent Policy. The Hague, the Nethelands: Ministry of Health, Welfare and Sports; 2003. 2003.
52. de Veer AJ, Francke AL, Poortvliet EP. Nurses' involvement in end-of-life decisions. Cancer Nurs. 2008 May-Jun;31(3):222-8.
53. Hilden HM, Honkasalo ML. Finnish nurses' interpretations of patient autonomy in the context of end-of-life decision making. Nurs Ethics. 2006 Jan;13(1):41-51.
54. Bruera E. Palliative sedation: when and how? J Clin Oncol. 2012 Apr 20;30(12):1258-9.
55. Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care. 1994 Summer;10(2):31-8.
56. Cherny NI, Radbruch L, Board of the European Association for Palliative C. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med. 2009 Oct;23(7):581-93.
57. Swart SJ, Rietjens JA, Brinkkemper T, van Zuylen L, van Burg-Verhage WA, Zuurmond WW, et al. [Palliative sedation largely in accordance with Dutch national guideline.] Palliatieve sedatie na introductie KNMG-richtlijn. Ned Tijdschr Geneeskd. 2011;155(6):A2857.
58. Hasselaar JG, Verhagen SC, Wolff AP, Engels Y, Crul BJ, Vissers KC. Changed patterns in Dutch palliative sedation practices after the introduction of a national guideline. Arch Intern Med. 2009 Mar 9;169(5):430-7.
59. Taylor BR, McCann RM. Controlled sedation for physical and existential suffering? J Palliat Med. 2005 Feb;8(1):144-7.
60. Cassell EJ, Rich BA. Intractable end-of-life suffering and the ethics of palliative sedation. Pain Med. 2010 Mar 1;11(3):435-8.
61. Jansen LA, Sulmasy DP. Proportionality, terminal suffering and the restorative goals of medicine. Theor Med Bioeth. 2002;23(4-5-):321-37.
62. Quill TE, Lo B, Brock DW, Meisel A. Last-resort options for palliative sedation. Ann Intern Med. 2009 Sep 15;151(6):421-4.
63. Hales S, Zimmermann C, Rodin G. The quality of dying and death. Arch Intern Med. 2008 May 12;168(9):912-8.
64. Gielen B, Remacle A, Mertens R. Patterns of health care use and expenditure during the last 6 months of life in Belgium: Differences between age categories in cancer and non-cancer patients. Health Policy. 2010 Mar 30.
65. Burt J, Shipman C, Richardson A, Ream E, Addington-Hall J. The experiences of older adults in the community dying from cancer and non-cancer causes: a national survey of bereaved relatives. Age Ageing. 2010 Jan;39(1):86-91.
66. Swart SJ, Brinkkemper T, Rietjens JA, Blanker MH, van Zuylen L, Ribbe M, et al. Physicians' and nurses' experiences with continuous palliative sedation in the Netherlands. Arch Intern Med. 2010 Jul 26;170(14):1271-4.

2

Continuous palliative sedation until death: practice after introduction of the Dutch national guideline

Siebe J. Swart
Agnes van der Heide
Tijn Brinkkemper
Lia van Zuylen
Roberto S.G.M. Perez
Judith A.C. Rietjens

BMJ Supportive & Palliative Care (2012)
doi:10.1136/bmjspcare-2011-000063

ABSTRACT

Background In 2005, a national palliative guideline was launched in The Netherlands. The authors describe the practice of continuous palliative sedation until death (CPS) after the introduction of this guideline.
Methods In 2008, a random sample of physicians (n=1580) were asked to fill out a questionnaire regarding the last patient in whom they had provided CPS until death.
Results The response was 38%. In all, 82% of the respondents were aware of the existence of the national guideline. Dyspnoea, pain and physical exhaustion were most often mentioned as decisive indications for continuous sedation. The decision to use sedation was discussed with all competent patients, but in 18% this merely involved informing the patient. Life expectancy at the start of continuous sedation was estimated to be less than 2 weeks in 97% of the cases. In 14%, the physicians had felt pressure to start the sedation, predominantly from patients and relatives. Physicians were present at the start of the sedation in 81% of the cases. Midazolam was used to induce the sedation in 92%. Overall, 41% of the physicians estimated that continuous sedation had hastened death to some extent. Most physicians thought that patients' complaints were adequately relieved by continuous sedation, that relatives were satisfied and that a good quality of dying was achieved.
Interpretation Continuous palliative sedation practice in The Netherlands largely reflects the recommendations from the national guideline. Issues needing further attention are the pressure felt by physicians to start continuous sedation and the potential life-shortening effect as mentioned by the physicians.

INTRODUCTION

In the Dutch national guideline, palliative sedation is defined as 'the intentional lowering of consciousness of a patient in the last phase of life'.[1,2] This refers to all subtypes of sedation: intermittent and continuous as well as deep and superficial. Continuous deep sedation until death is the most far-reaching subtype. The estimated frequency of the use of palliative sedation varies considerably in scientific literature, partly due to differences in definition and research setting. Comparable nationwide studies showed frequencies in Europe of 2.5% up to 16% of all deaths.[3-5] Continuous deep sedation was given up to the moment of death in 8.2% of all deaths in The Netherlands in 2005.[6]

The benefits and drawbacks of continuous sedation until death are frequently debated.[7-9] It is regarded as an indispensable treatment to alleviate intolerable refractory symptoms, but it diminishes the patient's ability to communicate in the last days of life.[8,10,11] Although it is argued that continuous sedation does not shorten life when its use is restricted to the patient's last days of life,[12,13] physicians sometimes indicate using it with the intention of hastening death.[14-16] These issues illustrate that the clinical decision-making about continuous sedation until death is very precarious, and have stimulated the development of frameworks and guidelines regarding this very delicate part of medical practice.[10,17-19]

In view of these developments, we present the results of a study regarding the practice of palliative sedation in The Netherlands after the introduction of a national guideline. Elsewhere we reported on differences in experiences with continuous sedation until death between physicians and nurses relating to decision-making, feelings of pressure and intention[20] and on differences in the practice of continuous sedation until death between cancer and non-cancer patients.[21] In this paper, we address the practice of continuous palliative sedation until death (CPS) in relation to the Dutch guideline on palliative sedation. This guideline was issued in 2005 by the Royal Dutch Medical Association (RDMA) and describes criteria and recommendations for palliative sedation.[22]

We focused on the type of sedation that is most extensively described in the guideline, which has been the main focus of the medical-ethical, social and political debate that has taken place in The Netherlands: CPS, which included both deep and mild sedation. The aim of our study is to study whether the practice of CPS is in accordance with the main recommendations of the Dutch guideline on palliative sedation. Furthermore, we investigated physicians' evaluations of, and experiences with, the RDMA guideline.

METHODS

In 2008, a cross-sectional survey was carried out among 1580 physicians. From a total population of 4127 physicians in the western part of The Netherlands we took a random sample of 1128 (466/2856 general practitioners, 195/292 nursing home physicians and 467/979 clinical specialists). Additionally, all 452 general practitioners in the north-eastern part of The Netherlands were included. The sample of clinical specialists was taken from all physicians working in internal medicine, cardiology, pulmonary disease, neurology and clinical geriatrics in the western part of The Netherlands. Within each specialty, physicians were classified as working in academic or non-academic hospitals and a third of the

Table 1 Most important criteria and recommendations regarding the use of continuous palliative sedation until death (CPS) in the Dutch national guideline.

Guideline recommendation	Questions in questionnaire
Regarding decision making	
Indication: one or more refractory symptoms, leading to unbearable suffering in the patient	* What was the decisive indication for the decision to start CPS? * To what extent was the symptom in the preceding question refractory? * Was the patient suffering unbearably when the decision for CPS was made?
The patient's life expectancy should not exceed one to two weeks	* What, according to your estimation, was the patients' life expectancy, at the time CPS was started?
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 his representative	* Was the patient competent at the time the decision for CPS was made? * Was the decision for CPS discussed with the patient? * Was the decision for CPS discussed with the patients' relatives? * Preceding CPS, did you feel being pressured to start continuous sedation?
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	* Did you consult a palliative care team preceding the decision to start CPS? * What was the goal of this consultation?
The sedation is aimed at the relief of the patient's suffering and not at hastening or postponing death	* CPS was used: - without the intention to hasten death - partly with the intention to hasten death - with the explicit intention to hasten death * Did CPS, according to your estimation hasten the patients' death?
Regarding procedure	
The attending physician must be present at the initiation of the sedation	* Who was present at the start of CPS? - physician responsible for decision - nurse - other physician - relatives - other
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	* What medication did the patient receive as from the start of CPS?
In cases of continuous, deep sedation until the moment of death, there should be no artificial administration of fluids	* Did the patient receive artificial fluids and/or food during CPS? * What was the depth of continuous sedation reached?
Accurate records must be kept of the decision-making process, the way palliative sedation is being administered and the effect of the intervention	* Did you keep a written document regarding the course of events on CPS? * Were according to your assessment symptoms adequately relieved by using CPS? * Were relatives satisfied about the course of CPS? * What according to your opinion was the quality of dying for this patient?

respondents were sampled from academic hospitals and two-thirds from non-academic hospitals.

The physicians received a questionnaire that addressed the main recommendations of the national guideline, inquiring about the last patient for whom they had used CPS (table 1). Additionally, we also asked respondents about their experiences with the national guideline (table 2).

CPS refers to the use of sedatives in patients, at the end of life, intended specifically for lowering consciousness continuously from a certain point in time until the patient dies, including both deep and mild sedation.[2] All questionnaires were sent by mail. If there was no response after 2 months a reminder was sent by mail and after 4 months by email. After this second reminder, all clinical specialists and a random selection of 20% of the general practitioners and nursing home physicians in the south-western region who did not respond were asked by email or telephone for their reasons for non-response. A pilot study was carried out in which a concept version of the questionnaire was tested among 55 general practitioners. The questionnaire was subsequently modified and submitted to 12 physicians who had been trained in palliative care. Their comments and suggestions resulted in the definitive version of the questionnaire. The questionnaire focused on the

Table 2 Experiences of 606 physicians with the Dutch national guideline on palliative sedation.

	General practitioners (n=399); N (%)	**Clinical specialists (n=110); N (%)**	**Nursing home physicians (n=97); N (%)**	**Total (n=606); N (%)**
Knows content of national guideline				
In general outline	273 (72)	72 (68)	66 (70)	411 (71)
Detailed	30 (8)	8 (8)	25 (27)	63 (11)
No	79 (21)	26 (25)	3 (3)	108 (19)
Missing; n	*17*	*4*	*3*	*24*
Has problems with aspects of the guideline*#†	**(n=303)**	**(n=80)**	**(n=91)**	**(n=474)**
Estimation of life expectancy	84 (30)	17 (23)	26 (30)	127 (29)
Determination of refractoriness of symptoms	39 (14)	10 (14)	7 (8)	56 (13)
Consultation of an expert	16 (6)	5 (7)	2 (2)	23 (5)
Withholding artificial fluids after the start of continuous sedation	13 (5)	10 (14)	0	23 (5)
Missing; n	*25*	*5*	*8*	*38*
Thinks that some aspects are missing†				
Yes	18 (6)	7 (10)	7 (9)	32 (7)
No	132 (48)	44 (61)	44 (55)	220 (51)
Don't know	127 (46)	21 (29)	29 (36)	177 (42)
Missing; n	*26*	*8*	*11*	*45*

* Several alternatives could be ticked off.

Score 4 and 5 on a 5-point Likert scale (1 = no problems; 5 = to a large extent having problems with aspects).

† data presented only for respondents knowing content of national guideline in general outline and detailed

characteristics of the respondent and the patient, decisionmaking and procedure regarding CPS, and experiences with the RDMA guideline. Statistical analyses were carried out using SPSS, V.15 (SPSS, Chicago, Illinois, USA).

RESULTS

Characteristics of physicians and patients

A total of 606 physicians (38%) returned the questionnaire. The response rate varied between specialties (general practitioners 43%, nursing home physicians 52% and medical specialists 24%). In the south-western part of The Netherlands, all non-responding clinical specialists (n=109) were asked by email and 20% of the non-responding general practitioners and nursing home physicians (n=39) were asked by telephone for their reasons for non-response. The most important reasons for non-response (clinical specialists (n=32) and general practitioners/nursing home physicians (n=39)) were: too busy with patient care (17%), no experience with continuous palliative sedation (14%), practised continuous sedation too long ago (11%), receive too many requests for participation in research (11%) and never participate in research (11%).

Of the 606 respondents, 69% had experience with continuous sedation, and 61% (n=370) provided information about their most recent sedated patient (table 3). In all tables, valid percentages are presented. The average age of these patients was 70; the most common diagnosis was cancer. In nursing homes, sedated patients relatively frequently had dementia (23%). Prior to the start of continuous sedation, 70% of patients were considered to be able to make a conscious decision. In the nursing home setting, this percentage was the lowest (39%).

Clinical practice was studied on guideline recommendations regarding decision-making and procedure, along with evaluation of CPS and experiences with the RDMA guideline.

Decisive symptoms

In all cases, the symptoms were considered to be refractory. In 88% of the cases, this was because of lack of effective treatment. Other reasons were unacceptable side effects (6%) and treatment having effect not quickly enough (6%). Most physicians (n=231) considered one refractory symptom decisive to the indication for CPS (table 4). Most frequently mentioned were dyspnoea (25%), pain (16%) and physical exhaustion (15%). Less frequently, nonphysical symptoms were considered as a decisive indication: existential suffering (7%), anxiety (3%) and psychological exhaustion (3%). A minority of the physicians (n=139) considered a combination of symptoms decisive, among which also pain (53%), physical exhaustion (53%) and dyspnoea (35%) were most frequently mentioned. The latter physicians mentioned existential suffering (22%), psychological exhaustion (27%) and anxiety (10%) more frequently than respondents mentioning only one decisive indication. Further study of cases in which existential suffering (n=17; 7%) was the only decisive indication revealed that most often this considered patients with cancer, who had a broad spectrum of severe physical as well as non-physical symptoms during the decision-making on CPS. Overall, 93% of the respondents indicated that the patient suffered unbearably when the decision for CPS was made.

Table 3 Characteristics of physicians participating in a study on palliative sedation, and of the last patient to whom they had given CPS.

	General practitioners (n = 399) N (%)*	Clinical specialists (n = 110) N (%)*	Nursing home physicians (n = 97) N (%)*	Total (n = 606) N (%)*
Physicians				
Gender ♂	262 (67)	74 (67)	37 (38)	373 (62)
♀	131 (33)	36 (33)	60 (62)	227 (38)
Missing n	*6*	*0*	*0*	*6*
Age, mean (SD), y	50 (8)	49 (8)	47 (8)	49 (8)
Missing; n	*7*	*1*	*2*	*10*
Work experience, median quartiles(25-75%), y	9 (5-10)	15 (10-20)	20 (15-40)	10 (5-20)
Missing; n	*9*	*1*	*2*	*12*
Amount of deaths in 2007, mean (SD)	10 (7)	20 (20)	28 (17)	15 (14)
Missing; n	*23*	*12*	*3*	*38*
Patients	***(n = 250)***	***(n = 56)***	***(n = 64)***	***(n = 370)***
Gender ♂	133 (54)	25 (44)	31 (49)	189 (52)
♀	112 (46)	31 (56)	32 (51)	175 (48)
Missing; n	*5*	*0*	*1*	*6*
Age, mean (SD), y	68 (14)	72 (14)	75 (13)	70 (14)
Missing; n	*7*	*1*	*2*	*10*
Diagnosis				
Cancer	204 (87)	39 (70)	33 (51)	276 (78)
Heart failure	7 (3)	5 (9)	6 (11)	18 (5)
COPD	4 (2)	2 (4)	2 (4)	8 (2)
Dementia	1 (0)	1 (2)	13 (23)	15 (4)
Neurologic disease	9 (4)	4 (7)	5 (7)	18 (5)
Other	11 (5)	4 (7)	4 (6)	19 (5)
Missing; n	*14*	*1*	*1*	*16*
Capable of making a conscious decision; %†				
Yes	188 (76)	45 (80)	25 (39)	258 (70)
Partly	43 (17)	8 (14)	7 (11)	58 (16)
No	19 (7)	3 (5)	32 (50)	54 (14)

* In all tables valid percentages are presented
† Variable without missing numbers
COPD, chronic obstructive pulmonary disease.

Decision-making

In 97% of cases, the life expectancy of the patient at the start of continuous sedation was estimated to be less than 2 weeks (table 4). All of the patients with a life expectancy of more than 2 weeks were deeply sedated. The physicians discussed the decision to use CPS with all patients who were capable of making a conscious decision: 82% of them were involved in the decision-making process, and 18% were only told of the decision. The decision

Table 4 Considerations regarding decision making for the last patient to whom physicians had given CPS.

	General practitioners, (n = 250); N (%)	Clinical specialists (n = 56); N (%)	Nursing home physicians (n = 64); N (%)	Total (n = 370); N (%)
Decisive refractory symptoms for starting CPS[#†]	**(n = 149)**	**(n = 37)**	**(n = 46)**	**(n =231)**
dyspnoea	29 (20)	17 (46)	11 (24)	57 (25)
pain	25 (17)	10 (27)	4 (9)	39 (16)
physical exhaustion	26 (17)	4 (11)	5 (11)	35 (15)
delirium	14 (9)	1 (3)	10 (22)	25 (11)
nausea/vomiting	16 (11)	0	2 (4)	18 (8)
existential suffering	14 (9)	1 (2)	2 (4)	17 (7)
motoric discomfort not related to delirium	3 (2)	0	4 (9)	7 (3)
anxiety	2 (1)	0	4 (9)	7 (3)
psychological exhaustion	6 (4)	0	0	6 (3)
bleeding	3 (2)	0	1 (2)	4 (2)
cachexia	2 (1)	0	0	2 (1)
depression	1 (1)	0	0	1 (0)
other	8 (6)	3 (8)	3 (7)	14 (6)
Life expectancy at the start of sedation	**(n = 250)**	**(n = 56)**	**(n = 64)**	**(n = 370)**
Less than a day	7 (3)	2 (4)	5 (8)	14 (4)
between 1-2 days	75 (30)	18 (32)	25 (39)	118 (32)
between 3-6 days	95 (39)	21 (38)	24 (38)	140 (38)
between 1-2 weeks	62 (25)	13 (23)	10 (16)	85 (23)
between 2-4 weeks	7 (3)	2 (4)	0	9 (3)
Missing; n	*4*	*0*	*0*	*4*
Decision for CPS discussed with competent[&] patient?	**(n = 188); %**	**(n = 45); %**	**(n = 25); %**	**(n = 258); %**
yes, only told	36 (19)	9 (20)	1 (4)	46 (18)
yes, patient was involved in decision making	151 (81)	36 (80)	24 (96)	211 (82)
no	0	0	0	0
Missing; n	*1*	*0*	*0*	*1*
Decision for CPS discussed with relatives?	**(n = 250)**	**(n = 56)**	**(n = 64)**	**(n = 370)**
yes, only told	49 (20)	10 (19)	9 (14)	68 (19)
yes, relatives were involved in decision making	199 (80)	42 (81)	55 (86)	296 (81)
No	0	0	0	0
Missing; n	*2*	*4*	*0*	*6*
Consultation of palliative care team preceding decision[†]	71 (29)	4 (7)	6 (9)	81 (22)
Missing; n	*3*	*1*	*0*	*4*
Physicians felt themselves under pressure to start sedation?[†]				
felt no pressure	209 (84)	49 (88)	59 (92)	317 (86)
felt pressure, namely from*				
- patient	19 (8)	2 (3)	2 (3)	23 (6)
- relatives	26 (10)	2 (3)	2 (3)	30 (8)
- other physicians	1 (0)	1 (2)	0	2 (1)
- nurses	2 (1)	2 (4)	1 (2)	5 (2)

Table 4 Continued

	General practitioners, (n = 250); N (%)	Clinical specialists (n = 56); N (%)	Nursing home physicians (n = 64); N (%)	Total (n = 370); N (%)
CPS was used				
without the intention to hasten death	206 (83)	46 (82)	62 (97)	312 (85)
partly with the intention to hasten death	38 (15)	10 (18)	2 (3)	50 (14)
with the explicit intention to hasten death	4 (2)	0	0	4 (1)
Missing; n	*2*	*0*	*0*	*2*
Estimation of life shortening				
no life shortening	106 (43)	14 (25)	28 (44)	148 (41)
less than a day	21 (9)	10 (18)	7 (11)	38 (10)
1–2 days	33 (14)	12 (21)	9 (14)	54 (15)
3–6 days	22 (9)	5 (9)	4 (6)	31 (9)
1–2 weeks	20 (8)	3 (5)	0	23 (6)
2–4 weeks	5 (2)	0	0	5 (1)
don't know	37 (15)	12 (21)	15 (24)	64 (18)
Missing; n	*6*	*0*	*1*	*6*

only data from respondents reporting one decisive indication are listed.
† Variable without missings.
* Several alternatives could be ticked off.
& n refers to last variable in table 3: capable of making a conscious decision, answer yes
CPS, continuous palliative sedation until death.

to use CPS was always discussed with relatives. In one out of five patients (22%), advice from a palliative care consultation team was sought prior to initiating continuous sedation; general practitioners did so significantly more often than other physicians. The most important reasons for consultation were advice on medication (52%), 'general information on CPS' (32%), anticipating advice (29%) or advice regarding refractoriness of symptoms (21%). In 14% of patients, physicians experienced pressure to start sedation. The pressure was reported to come predominantly from patients and their relatives. Whereas 85% of the physicians used continuous sedation without the intention of hastening death, 14% indicated that they partly had an intention to hasten death and 1% an explicit intention to hasten death. In all, 41% of physicians estimated that as a result of sedation life had been somewhat shortened.

Procedure

In 81% of patients, physicians were present when continuous sedation was started (table 5). CPS was usually induced using midazolam (92%), often in combination with an opioid (64%). Ten physicians (3%) used morphine only. During the administration of continuous sedation, 8% (n=29) of the patients were still receiving artificial fluids or nutrition, predominantly patients who were being sedated in hospitals. Of all 370 patients, 87% were deeply sedated (eyes closed, arousable only by physical stimuli or 'eyes closed, not arousable by physical stimuli'). Of these patients, 7% were receiving artificial fluids; for the mildly sedated patients this was 21%. In 99% of cases, the procedures pertaining to CPS were recorded in writing. For their last patient receiving CPS, 53% of respondents indicated that they had used the national guideline on palliative sedation and 10% mentioned that they had used another guideline.

Table 5 Characteristics regarding procedure of CPS.

	General practitioners, (n = 250) N (%)	Clinical specialists (n = 56) N (%)	Nursing home physicians (n = 64) N (%)	Total (n = 370) N (%)
Presence at the start of sedation; *				
attending physician	207 (84)	45 (80)	44 (69)	296 (81)
nurse	157 (63)	47 (86)	59 (92)	263 (72)
relatives	206 (83)	37 (67)	41 (64)	284 (78)
Missing; n	*3*	*1*	*0*	*4*
Medication as from the start of sedation*†				
midazolam	233 (93)	50 (89)	56 (86)	339 (92)
opioids	147 (59)	45 (80)	45 (70)	237 (64)
levomepromazine	11 (6)	0	3 (6)	14 (5)
other	5 (2)	1 (2)	4 (6)	10 (3)
The patient received artificial fluids and/ or food during CPS	6 (2)	23 (42)	0	29 (8)
Missing; n	*4*	*1*	*2*	*7*
Length of sedation; median (quartiles (25-75%), hours	45 (24–72)	36 (24–59)	48 (23–82)	48 (24–82)
Missing; n	*4*	*4*	*1*	*9*
What depth of continuous sedation was reached?				
drowsy	8 (3)	2 (4)	1 (2)	11 (3)
eyes closed, responding promptly to verbal commands	14 (6)	2 (4)	2 (3)	18 (5)
eyes closed, arousable only by physical stimuli	87 (36)	28 (52)	28 (44)	143 (39)
eyes closed, not arousable by physical stimuli	126 (50)	20 (37)	30 (47)	176 (48)
other	13 (5)	2 (4)	3 (5)	18 (5)
Missing; n	*2*	*2*	*0*	*4*
Did you keep a written document regarding the course of events on CPS?*				
Yes, in medical records	228 (93)	56 (100)	59 (92)	343 (94)
Yes, in nursing records	50 (20)	28 (50)	24 (38)	102 (28)
Yes, in multidisciplinary records	7 (3)	1 (2)	11 (17)	19 (5)
Yes, in home care records	79 (32)	0	0	79 (22)
Other	5 (2)	0	5 (8)	10 (3)
Missing; n	*5*	*0*	*0*	*5*
Used guideline for last patient receiving CPS*				
national guideline	131 (54)	21 (39)	40 (64)	192 (53)
other guideline (e.g. hospital guideline)	22 (9)	12 (22)	2 (3)	36 (10)
none	92 (38)	21 (39)	21 (33)	134 (37)
Missing; n	*5*	*2*	*1*	*8*

* Several alternatives could be ticked off.
† Variable without missings.
CPS, continuous palliative sedation until death.

Table 6 Effects of continuous sedation until death.

	General practitioners, (n = 250); N (%)	Clinical specialists (n = 56); N (%)	Nursing home physicians (n = 64); N (%)	Total (n = 370); N (%)
Symptoms alleviated adequately				
Yes	226 (93)	55 (100)	59 (98)	340 (95)
No	10 (4)	0	1 (2)	11 (3)
Don't know	6 (3)	0	0	6 (2)
Missing; n	*8*	*1*	*4*	*13*
Relatives were satisfied				
Yes	228 (92)	53 (95)	62 (97)	343 (94)
No	16 (6)	3 (5)	1 (2)	20 (5)
Don't know	4 (1)	0	1 (2)	5 (1)
Missing; n	*2*	*0*	*0*	*2*
Quality of dying				
Good - extremely good	201 (82)	48 (81)	50 (88)	299 (83)
Neutral	32 (13)	6 (15)	9 (11)	47 (13)
Bad – extremely bad	11 (5)	1 (5)	3 (2)	15 (5)
Missing; n	*6*	*1*	*2*	*11*

Evaluation

Doctors indicated that continuous sedation had adequately alleviated the symptoms of 95% of patients (table 6). They were of the opinion that relatives were satisfied in 94% of cases. Physicians judged the quality of death of 83% of patients to be good to extremely good.

Experiences with the RDMA guideline

Of all respondents (n=606), 82% mentioned that they knew the content of the RDMA guideline, predominantly the general outline (table 2). From these respondents 29% indicated to have problems with aspects of the guideline regarding the estimation of life expectancy and 13% with establishing whether a symptom is refractory or not. Another 7% indicated that some aspects of the procedure were missing from the guidelines. This included information on the dosage and titration of midazolam and levomepromazine, dealing with family members who are exercising pressure, and sedation for predominantly psychosocial or existential problems.

DISCUSSION

There is a burgeoning international literature on CPS and many initiatives have been taken to review this literature and to develop guidelines to promote careful clinical guidance regarding this far-reaching treatment.[10,17-19,23-27] Some guidelines refer to CPS in general terms and promote guidance on a (inter) national level[10,17] while others refer to a specific context.[26] The bottom line of all guidelines concerns: presence of refractory symptoms, a limited life expectancy, the necessity of communication with the patient and family, the choice of sedatives, and recommendations regarding the use of artificial fluids. The Dutch guideline differs from other guidelines in that it also formulates criteria that facilitate to distinguish palliative sedation from euthanasia, because the latter is a legal procedure in The

Netherlands. In some countries, a guideline on palliative sedation has recently been developed, like Belgium.[18] In other countries, sedation practices have already been evaluated in relation to certain aspects of a sedation guideline;[28] however, sometimes these evaluations are not easily available to nonnative speakers.[29,30]

In this study, the majority of Dutch physicians indicated that they were aware of the RDMA guideline on palliative sedation. More than half of the physicians reporting about their most recent case of continuous sedation had used this guideline in that case. The majority indicated that the patient's symptoms had been adequately relieved, that the relatives were satisfied and that a good quality of dying had been achieved.

Practice reflecting RDMA guideline's recommendations

On several points CPS practice largely reflected the guideline recommendations. In nearly all cases, physicians estimated the life expectancy of the patient to be less than 2 weeks. All patients had one or more refractory symptoms that nearly always had led to unbearable suffering. Physical exhaustion and existential suffering were fairly often reported as being decisive for starting continuous sedation, which confirms earlier research.[28] Since it is also known that the refractory nature of non-physical sources of suffering is difficult to assess,[31] these findings underline the importance of focusing on these symptoms in the updated version of the RDMA guidelines.[2] The physicians discussed the decision to continuously sedate with all patients who were capable of making a conscious decision. This seems in line with findings from others who have concluded that patient involvement in decision-making had been improved after the introduction of the Dutch national guideline.[28] Nevertheless, we found that one out of five patients who were able to make a conscious decision were only informed about the decision to start continuous sedation. From our data, it is unclear whether these patients had given appropriate informed consent. This finding may be explained by the fact that time for discussion is not always available when symptoms are so acute that they require immediate intervention. It is also possible that patients do not always want to be involved in the decision-making process,[32,33] or that physicians try to prevent dying patients who are suffering severely from having to deal with the decision-making process. Our data therefore suggest that there still is room for further improvement of involving competent patients in the decision-making. Compared with the practice of sedation prior to the guideline, the frequency with which a palliative care team was consulted was higher, and more sedations were carried out using the recommended drug, that is, midazolam.[6,28,34] Also, opioids as a stand-alone drug for continuous sedation were used less frequently, which is an improvement in comparison with the situation before the guideline was available.[35] Last, nearly all physicians had indicated that they had kept a written document regarding the course of events on CPS.

Practice not reflecting RDMA guideline's recommendations

We also identified a few areas that did not reflect the recommendations of the RDMA guideline. In January 2009, that is, during our study period, the RDMA guideline committee had already identified some problem areas needing further exploration.[2] Our finding that in a fifth of the cases there was no physician present at the start of continuous sedation was one of them. Possibly, not all physicians felt that it was necessary to be present at this time or did not have the opportunity to be present at the time sedation was initiated. Furthermore, the guideline recommends not administering artificial fluids in cases of continu-

ous deep sedation until the moment of death. Our data show that in a minority of cases this recommendation is not reflected in practice. This may be explained by the fact that such recommendations are not always easily put into practice since practice on this vulnerable issue differs[36] or because other guidelines reflect that the decision to forego artificial fluids should be made separate from a decision for sedation.[27] Other problem areas identified by the RDMA guideline committee related to the evaluation of refractory symptoms, the life expectancy of the patient, the skills of the physician, the limited information on acute and intermittent sedation in the guideline, the medication schedule, and the monitoring of sedation.

Our study uncovered two issues that were not mentioned by the guideline committee. The guideline states that proportionally administered palliative sedation does not lead to hastening of death when used for patients with a limited life expectancy. Despite the fact that we found that sedation was in nearly all cases used for patients with a limited life expectancy, 15% of the physicians used CPS with the (partly) intention to hasten death and 41% of them thought that the administration of sedation had had a minor life-shortening effect. This may be explained by the fact that sedatives may give rise to respiratory depression. Furthermore, evidence suggests that some physicians may be giving larger doses of medications than strictly needed for relief of pain or suffering.[37]

Also, it has been reported that approximately a third of Dutch physicians associate continuous sedation with life-shortening effects from dehydration.[28] On the other hand, it should be noted that physicians commonly have difficulty in estimating life expectancy and are often inclined to overestimate it.[38-40] This also holds true for the life-shortening effects of sedative medication and of withholding of nutrition and fluid in patients with a limited life expectancy.[28] In line with this are reports indicating that the life-shortening effects of opioid administration in the last phase of life are overestimated.[41,42] One final issue that was not mentioned by the guideline committee is that 14% of physicians felt pressured to start sedation. This may be an indication of the fact that the decision-making process concerning continuous sedation does not always run smoothly. Uncertain prognosis, unpredictable disease progression and emotions such as fear and despair all play a role in hampering communication among physicians, patients and their loved ones about the approaching end of life and the (im)possibility of easing suffering.[43] Consultation of a palliative care team, which was found to be rather uncommon, may address these feelings of pressure and other problematic aspects in the guideline, especially when they coincide with limited individual experience with CPS. To study these issues more extensively we suggest performing prospective studies with a qualitative design, which take into account the perspectives of patients and relatives. This would allow for more indepth analysis of experiences and considerations of all those involved.

Limitations

We asked physicians to inform us about their last patient treated with CPS by filling out a questionnaire after the guideline was introduced. Based on the pilot study among 55 general practitioners, we have chosen a sample size that we expected to be large enough to represent palliative sedation practices after the introduction of the national guideline. This approach makes it hard to draw conclusions regarding the importance of the differences found between settings. Furthermore, our approach has limitations compared with an approach in which medical files can be studied directly. As the response rate differed between

settings, and especially was rather low among clinical specialists, our results should be interpreted with some caution, even though a low response rate is not uncommon in comparable studies.[34,44] Since we included physicians in two regions of The Netherlands, it is not clear that our findings can be generalised to others regions. Although our (rather limited) non-response analyses revealed that main reasons for non-response were that the physician had little or no experience with continuous palliative sedation, selection bias cannot fully be ruled out because there is still a possibility that physicians with a specific interest in the research topic or who had read or applied the guideline were more likely to respond. Recall bias might also have been a problem, although most respondents reported a case that had occurred less than a year earlier. Given the fact that physicians are relatively seldom involved in the use of palliative sedation and the fact that it is a far-reaching procedure, it is likely that they might remember such cases relatively clearly.

CONCLUSION

We conclude that the practice of continuous sedation therapy largely reflected the recommendations described in the RDMA guideline. Nevertheless, there is room for improvement in communication among physicians, patients and their families. This should be further studied in future studies. Since one out of seven physicians had felt pressure to start CPS and two out of five physicians estimated that continuous sedation had hastened death to some extent, future studies of CPS should also take these findings into account. Cross-national comparisons could add to the understanding of this practice. For these reasons, research and exchange of knowledge of and experiences with such a delicate and radical intervention as continuous sedation up to the moment of death and the implementation of guidelines should continue, nationally and internationally.

Acknowledgements We received written permission from the deputy editor of the Netherlands Tijdschrift voor Geneeskunde to republish the original Dutch article according to ICJM rules. We thank Wijnanda van Burg-Verhage, Marco Blanker, Wouter Zuurmond and Miel Ribbe for their contribution to the original article. Furthermore, we would like to thank the Comprehensive Cancer Centres of Amsterdam and Rotterdam for their assistance with the data collection and all the respondents for filling out the questionnaires.

References

1. Verkerk M, van Wijlick E, Legemaate J, et al. A national guideline for palliative sedation in the Netherlands. J Pain Symptom Manage 2007;34:666–670.
2. KNMG. KNMG-richtlijn palliatieve sedatie 2009. Available from: http://knmgartsennet-nl/Diensten/knmgpublicaties/KNMGpublicatie/Guideline-forpalliative-sedation-2009htm (accessed 3 May 2011).
3. Miccinesi G, Rietjens JA, Deliens L, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage 2006;31:122–129.
4. Seale C. End-of-life decisions in the UK involving medical practitioners. Palliat Med 2009;23:198–204.
5. Chambaere K, Bilsen J, Cohen J, et al. Continuous deep sedation until death in Belgium: a nationwide survey. Arch Intern Med 2010;170:490–493.
6. Rietjens J, van Delden J, Onwuteaka-Philipsen B, et al. Continuous deep sedation for patients nearing death in the Netherlands: descriptive study. BMJ 2008;336:810–813.
7. van Delden JJ. Terminal sedation: source of a restless ethical debate. J Med Ethics 2007;33:187–188.

8. Materstvedt LJ, Bosshard G. Deep and continuous palliative sedation (terminal sedation): clinical-ethical and philosophical aspects. Lancet Oncol 2009;10:622–627.
9. Quill TE, Lo B, Brock DW, et al. Last-resort options for palliative sedation. Ann Intern Med 2009;151:421–424.
10. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. J Palliat Med 2007;10:67–85.
11. Steinhauser KE, Christakis NA, Clipp EC, et al. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 2000;284:2476–2482.
12. Sykes N, Thorns A. Sedative use in the last week of life and the implications for endof-life decision making. Arch Intern Med 2003; 163:341–344.
13. Maltoni M, Pittureri C, Scarpi E, et al. Palliative sedation therapy does not hasten death: results from a prospective multicenter study. Ann Oncol 2009;20:1163–1169.
14. Hasselaar JG, Verhagen SC, Vissers KC. When cancer symptoms cannot be controlled: the role of palliative sedation. Curr Opin Support Palliat Care 2009;3:14–23.
15. Rietjens JA, van der Heide A, Vrakking AM, et al. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med 2004;141:178–185.
16. Rietjens JA, Buiting HM, Pasman HR, et al. Deciding about continuous deep sedation: physicians' perspectives: a focus group study. Palliat Med 2009;23:410–417.
17. Cherny NI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med 2009;23:581–593.
18. Vogel L. Framework urges physicians to proceed with caution on palliative sedation. Cmaj. 2011 Jan 10.
19. Claessens P, Menten J, Schotsmans P, et al. Palliative sedation: a review of the research literature. J Pain Symptom Manage 2008;36:310–333.
20. Swart SJ, Brinkkemper T, Rietjens JA, et al. Physicians' and nurses' experiences with continuous palliative sedation in the Netherlands. Arch Intern Med 2010;170:1271–1274.
21. Swart SJ, Rietjens JA, van Zuylen L, et al. Continuous palliative sedation for cancer and noncancer patients. J Pain Symptom Manage 2012;43:172–181.
22. Royal Dutch Medical Society. RDMS guideline palliative sedation, 2005. http://knmg.artsennet.nl/actueel/Nieuwsartikel/KNMG-richtlijn-palliatieve-sedatie-herzien-1.htm (last accessed 10 Apr 2010).
23. Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. J Palliat Care 1994;10:31–38.
24. Braun TC, Hagen NA, Clark T. Development of a clinical practice guideline for palliative sedation. J Palliat Med 2003;6:345–350.
25. Morita T, Bito S, Kurihara Y, et al. Development of a clinical guideline for palliative sedation therapy using the Delphi method. J Palliat Med 2005;8:716–729.
26. Hawryluck LA, Harvey WR, Lemieux-Charles L, et al. Consensus guidelines on analgesia and sedation in dying intensive care unit patients. BMC Med Ethics 2002;3:E3.
27. Broeckaert B, Mullie A, Gielen J, et al. Ethics Commission Federation Palliative Care Flanders. Palliative Sedation Guideline, 2010. http://www.pallialine.be/template.asp?f=rl_sedatie.htm#page=page-1 (accessed 30 November 2011).
28. Hasselaar JG, Verhagen SC, Wolff AP, et al. Changed patterns in Dutch palliative sedation practices after the introduction of a national guideline. Arch Intern Med 2009;169:430–437.
29. Materstvedt LJ, Forde R. (Guidelines for palliative sedation should be revised) Retningslinjene for lindrende sedering bor revideres. Tidsskr Nor Laegeforen 2009;129:426–8.
30. Swart SJ, Rietjens JA, Brinkkemper T, et al. (Palliative sedation largely in accordance with Dutch national guideline). Ned Tijdschr Geneeskd 2011;155:A2857.
31. Hales S, Zimmermann C, Rodin G. The quality of dying and death. Arch Intern Med 2008;168:912–918.
32. Levinson W, Kao A, Kuby A, et al. Not all patients want to participate in decision making. A national study of public preferences. J Gen Intern Med 2005;20:531–535.
33. Deber RB, Kraetschmer N, Urowitz S, et al. Do people want to be autonomous patients? Preferred roles in treatment decision-making in several patient populations. Health Expect 2007;10:248–258.

34. Van Deijck RH, Krijnsen PJ, Hasselaar JG, et al. The practice of continuous palliative sedation in elderly patients: a nationwide explorative study among Dutch nursing home physicians. J Am Geriatr Soc 2010;58:1671–1678.
35. Onwuteaka-Philipsen BD, Gevers JK, van der Heide A, et al. Evaluatie Wet toetsing levensbeeindiging op verzoek en hulp bij zelfdoding, 2007.
36. Morita T, Chinone Y, Ikenaga M, et al. Ethical validity of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan. J Pain Symptom Manage 2005; 30:308–319.
37. Sprung CL, Ledoux D, Bulow HH, et al. Relieving suffering or intentionally hastening death: where do you draw the line? Crit Care Med 2008;36:8–13.
38. Brandt HE, Ooms ME, Ribbe MW, et al. Predicted survival vs. actual survival in terminally ill noncancer patients in Dutch nursing homes. J Pain Symptom Manage 2006;32:560–566.
39. Glare P, Virik K, Jones M, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. BMJ 2003; 327:195–198.
40. Clarke MG, Ewings P, Hanna T, et al. How accurate are doctors, nurses and medical students at predicting life expectancy? Eur J Intern Med 2009;20:640–644.
41. Rurup ML, Borgsteede SD, van der Heide A, et al. Trends in the use of opioids at the end of life and the expected effects on hastening death. J Pain Symptom Manage 2009;37:144–155.
42. Bercovitch M, Adunsky A. Patterns of high-dose morphine use in a home-care hospice service: should we be afraid of it? Cancer 2004;101:1473–1477.
43. van Marwijk H, Haverkate I, van Royen P, et al. Impact of euthanasia on primary care physicians in the Netherlands. Palliat Med 2007;21:609–614.
44. Hasselaar JG, Reuzel RP, van den Muijsenbergh ME, et al. Dealing with delicate issues in continuous deep sedation. Varying practices among Dutch medical specialists, general practitioners, and nursing home physicians. Arch Intern Med 2008;168:537–543.

3

Physicians' and nurses' experiences with continuous palliative sedation in the Netherlands

Siebe J. Swart
Tijn Brinkkemper
Judith A.C. Rietjens
Marco H. Blanker
Lia van Zuylen
Miel Ribbe
Wouter W.A. Zuurmond
Agnes van der Heide
Roberto S.G.M. Perez

Arch Int Med. 2010;170:1271-4

ABSTRACT

Background Continuous sedation until death is an intensively debated type of palliative sedation. For this intervention a multidisciplinary approach, including at least the physician and nursing disciplines, is considered important. We investigated how physicians and nurses experienced this practice, focusing on the clinical characteristics, the decision making process and the effect of continuous sedation.
Methods A structured questionnaire regarding their last patient receiving continuous sedation until death was sent to 1580 physicians and 576 nurses working in homecare, nursing homes, hospices or hospitals.
Results 606 Physicians (38%) and 278 nurses (48%) filled out the questionnaire. Of the described patients, 75%-80% had cancer. The most frequently mentioned (>50%) severe symptoms were fatigue, pain and longing for death. Dyspnoea and pain were the most frequently mentioned decisive indications for starting continuous sedation. Patients and relatives were more often involved in the decision-making in nurses' cases (76% and 90%, respectively) than in physicians' cases (66% and 81%, respectively). Physicians more often reported that they had felt pressure to start continuous sedation than nurses (14% and 3%, respectively; $p<0.01$); they reported less often a (co)-intention to hasten the patient's death (15% and 24%, respectively; $p<0.01$).
Conclusions Although the decisive indications for the use of sedation are in most cases severe physical symptoms, non-physical symptoms also contribute to the clinical picture. Physicians' cases differ from nurses' cases with respect to decision-making. End-of-life care can benefit from timely and adequate communication between physicians and nurses about all relevant aspects of the patients' situation.

INTRODUCTION

Continuous palliative sedation is regarded as an indispensable treatment for alleviating intolerable refractory symptoms in dying patients.[1] This far-reaching treatment requires a multidisciplinary approach, at least involving physicians and nurses.[2,3] As this practice has, to our knowledge, not been studied from both these perspectives at the same time, we describe physicians' and nurses' experiences with continuous sedation until death, focusing on patients' characteristics, decision making, and the effects of sedation.

METHODS

In 2008, a structured questionnaire was sent to a random sample of 1580 physicians and a nonrandom sample of 576 nurses working in the northern and western Netherlands in home care, nursing homes, hospices, and hospitals. Nurses who were likely to be involved in the practice of continuous sedation received a questionnaire through contact persons in their setting. The questionnaire contained questions on the patient the respondents had most recently treated with continuous sedation until death. The questionnaire had been pretested among physicians and nurses.[4]

The statistical significance of differences between physicians and nurses was assessed with χ^2 and Kruskal-Wallis tests. Logistic or linear regression analysis was performed to adjust for setting and working experience. For all tests, $P<.05$ was considered statistically significant.

RESULTS

The questionnaire was completed by 606 physicians (response rate, 38%) and 278 nurses (response rate, 48%). Cases were reported by 370 physicians (61%), mainly in general practice, and 185 nurses (67%), mainly hospital nurses. Most patients had cancer (Table). The severe symptoms that were most commonly reported before the start of continuous sedation by physicians and nurses were fatigue, pain, and longing for death. Nurses reported anxiety significantly more often than physicians.

The decisive indications for starting continuous sedation that were most reported by both physicians and nurses were dyspnea and pain (data not shown). Nurses specified pain as the decisive indication more often than physicians, who reported physical exhaustion and delirium more often than nurses. Psychological exhaustion and existential suffering were reported mainly when there was more than 1 decisive indication.

In most cases, life expectancy at the start of continuous sedation was estimated to be less than 2 weeks. In nurses' cases, competent patients and relatives had been involved in the decision making significantly more often.

While physicians reported more often than nurses that they felt they were put under pressure to start continuous sedation, mostly by patients and relatives, they less often reported that continuous sedation had been provided with the full or partial intention of hastening the patient's death. In most cases, respondents reported that symptoms had been properly relieved, that relatives had seemed satisfied with the course of continuous sedation, and that the quality of dying had been good.

Table 1 Respondents, patient characteristics, decision-making and effect of continuous sedation[a]

	Physicians (n=370)	Nurses (n=185)	*P* value, χ^2 test	*P* value adjusted[b]
Respondents				
Age, mean (SD), y	49 (8)	40 (11)	0.001	NA
Work experience, mean (SD), y	19 (9)	17 (11)	0.03	NA
Setting				
Home	250 (68)	50 (27)		
Nursing home/hospice	64 (17)	58 (26)	<0.001	NA
Hospital	56 (15)	87 (47)		
Patients				
Age, mean (SD), y	70 (14)	65 (16)	<0.001	NA
Diagnosis: cancer[c]	265 (75)	144 (80)	0.21	NA
Severe symptoms before start of continuous sedation[d]				
- fatigue	258 (73)	119 (69)	0.66	0.46
- pain	212 (58)	115 (67)[e]	0.07	0.07
- longing for death	207 (58)	90 (54)[e]	0.64	0.11
- loss of dignity	172 (48)	63 (37)[e]	0.11	0.07
- hopelessness	170 (48)	72 (43)[e]	0.66	0.51
- loss of control	143 (40)	67 (40)[e]	0.53	0.85
- dyspnea	138 (38)	82 (47)[e]	0.13	0.84
- motor restlessness	111 (31)	62 (36)[e]	0.16	0.26
- anxiety	111 (31)	74 (42)[e]	0.001	0.03
- delirium	96 (27)	40 (24)[e]	0.49	0.54
- nausea/vomiting	95 (27)[e]	33 (20)[e]	0.11	0.73
- loss of interest	88 (25)[e]	35 (21)[e]	0.77	0.56
- burden to environment	57 (16)	26 (16)[e]	0.67	0.15
- depression	28 (8)[e]	14 (9)[e]	0.52	0.72
Decision making				
Life expectancy at start continuous sedation				
- <2 d	130 (36))	63 (34)		
- 2 d to 2 wk	223 (61)	101 (55)	0.49	NA
- >2 wk	10 (3)	18 (10)		
Decision to use continuous sedation discussed with competent patient	(n=255)	(n=124)		
- yes, patient was informed	46 (18)	9 (7)	<0.001	NA
- yes, patient was involved	208 (81)	110 (88)		

COMMENT

Pain, dyspnea, and delirium are commonly reported indications for palliative sedation.[5,6] Our study confirmed these findings and pointed to physical exhaustion as another decisive indication. This is consistent with fatigue being the most common severe symptom before the start of the sedation, apparently to the extent that it can become refractory to treatment and thus become an indication for continuous sedation until death. Psychological exhaustion and existential suffering were also mentioned as indications, mostly in combination with physical symptoms. The use of continuous sedation until death, therefore, often follows from a clinical picture in which a combination of physical and nonphysical symptoms results in a refractory state.

Table 1 Continued

	Physicians (n=370)	Nurses (n=185)	*P* value, χ^2 test	*P* value adjusted[b]
Decision to use continuous sedation discussed with relatives				
- relatives were informed	68 (19)	17 (10)	0.009	NA
- relatives were involved	296 (81)	160 (90)		
Physicians' intention when using continuous sedation				
- no intention to hasten death	312 (85)	131 (75)		
- partial intention to hasten death	50 (14)	35 (20)	0.002	NA
- explicit intention to hasten death	4 (1)	9 (5)		
Effect of continuous sedation				
Symptoms were properly relieved[f]	340 (95)	162 (90)	0.52	0.36
Relatives were satisfied with the course of continuous sedation[g]	343 (93)	156 (86)	0.44	0.33
Estimated shortening of life[h]				
- no shortening	148 (41)	66 (36)		
- <2 d	82 (25)	34 (19)	0.18[i]	NA
- 2 d to 2 wk	54 (15)	15 (9)		
- >2 wk	5 (1)	0		
Quality of dying[j]	299 (83)	126 (74)	0.03	0.85

NA: not applicable

[a] Data are given as number (percentage) unless otherwise indicated. Missing data per question ranged from 0.6% to 15.1%. Valid percentages are used; variables with more than 5% missing values are indicated.

[b] Corrected for experience and setting using logistic regression analysis.

[c] The most-common other diagnoses were heart failure, chronic obstructive pulmonary disorder, dementia, and neurologic disease.

[d] Number (percentage) of patients who were given a score of 4 or 5 on a Likert scale of 1 to 5.

[e] Percentage missing values was greater than 5%.

[f] Answer "don't know" was given by 2% of the physicians and 6% of the nurses ($P = .01$).

[g] Answer "don't know" was given by 1% of the physicians and 7% of the nurses ($P < .001$).

[h] Answer "don't know" was given by 18% of the physicians and 36% of the nurses ($P < .001$).

[i] Tested as no shortening vs shortening of life.

[j] Number (percentage) of patients who were given a score of 1 or 2 on a Likert scale of 1 to 5.

Nurses more often than physicians reported that patients and relatives were involved in decision making, they less often felt pressure from patients or relatives to start continuous sedation, and they more often thought that the physicians' intention for using sedation was to hasten the patient's death.

Although these physicians and nurses did not report on the same cases, we think we can interpret these differences because the practice on which they reported seems to be comparable. First, virtually all these respondents' cases involved both a physician and a nurse. Second, our respondents were selected in the same regions of the Netherlands and in the same period. Lastly, the patients' characteristics did not differ notably, and physicians and nurses assessed the frequency of severe symptoms similarly.

We therefore think that the differences in decision making, feelings of pressure, and intention might at least be partly related to the different roles of physicians and nurses in continuous sedation practice.

First, nurses usually have more frequent contacts with patients. Such frequent contacts might explain why more nurses indicated that patients and relatives were actively involved

in the decision making. Nurses' greater involvement in patient handling might explain why more nurses mentioned pain as a decisive indication for starting continuous sedation and why they also reported more feelings of anxiety. Both pain and anxiety might be more easily recognized during daily care and nursing activities.
Second, the differences might also reflect the physicians' and nurses' different responsibilities. Because physicians are responsible for the decision making on the use of continuous palliative sedation, patients and relatives might put particular pressure on them to start sedation.[7] In studies of euthanasia, physicians have also reported to feel subjected to pressure.[8] Thus, taking account of the varying perspectives and emotions of all those involved in end-of-life decision making may be complex.
Finally, it has been shown elsewhere that nurses sometimes worry about the potential use of continuous sedation for accelerating death.[9] Taken together with our finding that more nurses than physicians think that continuous sedation was used with the intention to hasten death, this may reflect that physicians are not always clear about their intentions. This stresses the paramount importance of proper communication between physicians and nurses.[10]

In conclusion, while continuous sedation until death is usually provided because of severe and refractory physical symptoms, nonphysical symptoms may also contribute to the clinical picture. At several points, physicians and nurses experience the decision-making process differently. End-of-life care would benefit from fuller communication between physicians and nurses about all relevant aspects of the patients' situation and the care provided.

Acknowledgements We would like to thank Wijnanda van Burg-Verhage for her work on the pilot. We want to thank Prof. dr. Paul van der Maas and Prof. dr. Hans van Delden for their critical comments on earlier versions of this article. Furthermore we would like to thank Anneke Tooten, Claudette Promes, Jaap Talsma and the Comprehensive Cancer Centres of Amsterdam and Rotterdam for their assistance with the data collection and all the respondents for filling out the questionnaires.

References

1. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. J Palliat Med. 2007;10(1):67-85.
2. World Health Organization (WHO).WHOdefinition of Palliative Care. http://www.who.int/cancer/palliative/definition/en/. Accessed November 3, 2009.
3. Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA. 2000;284(19):2476-2482.
4. Perez R, Stoffer-Brink A, Zuurmond W, Deliens L, Klinkenberg A. Current practice of palliative sedation at home: a survey of Dutch nurses involved in the practice of palliative sedation at home [abstract]. Palliat Med. 2008;22(4):471.
5. Mercadante S, Intravaia G, Villari P, Ferrera P, David F, Casuccio A. Controlled sedation for refractory symptoms in dying patients. J Pain Symptom Manage. 2009;37(5):771-779.
6. Hasselaar JGJ, Verhagen CAHHVM, Wolff AP, Engels Y, Crul BJP, Vissers KCP. Changed patterns in Dutch palliative sedation practice after the introduction of a national guideline. Arch Intern Med. 2009;169(5):430-437.
7. van Dooren S, van Veluw HT, van Zuylen L, Rietjens JA, Passchier J, van der Rijt CC. Exploration of concerns of relatives during continuous palliative sedation of their family members with cancer. J Pain Symptom Manage. 2009;38(3):452-459.

8. van Marwijk H, Haverkate I, van Royen P, The A-M. Impact of euthanasia on primary care physicians in the Netherlands. Palliat Med. 2007;21(7):609-614.
9. Rietjens JA, Hauser J, van der Heide A, Emanuel L. Having a difficult time leaving: experiences and attitudes of nurses with palliative sedation. Palliat Med. 2007;21(7):643-649.
10. de Veer AJ, Francke AL, Poortvliet EP. Nurses' involvement in end-of-life decisions. Cancer Nurs. 2008;31(3):222-228.

4

Continuous Palliative Sedation: not only a response to physical suffering

Siebe J. Swart
Agnes van der Heide
Lia van Zuylen
Roberto S.G.M. Perez
Wouter W.A. Zuurmond
Paul J. van der Maas
Johannes J.M. van Delden
Judith A.C. Rietjens

Submitted

5

Considerations of physicians about the depth of palliative sedation at the end of life

Siebe J. Swart
Agnes van der Heide
Lia van Zuylen
Roberto S.G.M. Perez
Wouter W.A. Zuurmond
Paul J. van der Maas
Johannes J.M. van Delden
Judith A.C. Rietjens

CMAJ 2012;184:E360-6

ABSTRACT

Background Although guidelines advise titration of palliative sedation at the end of life, in practice the depth of sedation can range from mild to deep. We investigated physicians' considerations about the depth of continuous sedation.

Methods We performed a qualitative study in which 54 physicians underwent semistructured interviewing about the last patient for whom they had been responsible for providing continuous palliative sedation. We also asked about their practices and general attitudes toward sedation.

Results We found two approaches toward the depth of continuous sedation: starting with mild sedation and only increasing the depth if necessary, and deep sedation right from the start. Physicians described similar determinants for both approaches, including titration of sedatives to the relief of refractory symptoms, patient preferences, wishes of relatives, expert advice and esthetic consequences of the sedation. However, physicians who preferred starting with mild sedation emphasized being guided by the patient's condition and response, and physicians who preferred starting with deep sedation emphasized ensuring that relief of suffering would be maintained. Physicians who preferred each approach also expressed different perspectives about whether patient communication was important and whether waking up after sedation is started was problematic.

Interpretation Physicians who choose either mild or deep sedation appear to be guided by the same objective of delivering sedation in proportion to the relief of refractory symptoms, as well as other needs of patients and their families. This suggests that proportionality should be seen as a multidimensional notion that can result in different approaches toward the depth of sedation.

INTRODUCTION

Palliative sedation is considered to be an appropriate option when other treatments fail to relieve suffering in dying patients.[1,2] There are important questions associated with this intervention, such as how deep the sedation must be to relieve suffering and how important it is for patients and their families for the patient to maintain a certain level of consciousness.[1] In the national guidelines for the Netherlands, palliative sedation is defined as "the intentional lowering of consciousness of a patient in the last phase of life."[3,4] Sedatives can be administered intermittently or continuously, and the depth of palliative sedation can range from mild to deep.[1,5]

Continuous deep sedation until death is considered the most far reaching and controversial type of palliative sedation. Nevertheless, it is used frequently: comparable nationwide studies in Europe show frequencies of 2.5% to 16% of all deaths.[6-8] An important reason for continuous deep sedation being thought of as controversial is the possible association of this practice with the hastening of death,[9-11] although it is also argued that palliative sedation does not shorten life when its use is restricted to the patient's last days of life.[12,13] Guidelines for palliative sedation often advise physicians to titrate sedatives,[2,3,14] which means that the dosages of sedatives are adjusted to the level needed for proper relief of symptoms. To date, research has predominantly focused on the indications and type of medications used for sedation. In this study, we investigated how physicians decide the depth of continuous palliative sedation and how these decisions relate to guidelines.

METHODS

Participants

This study is part of a larger project aimed at studying the practice of palliative sedation in the Netherlands after the introduction of a national guideline on palliative sedation.[15] For the quantitative part of the study, we enrolled by random sampling physicians working in general practice, nursing homes and hospitals (n = 1580); of these, 370 reported about their most recent case of continuous palliative sedation. Frequent indications for sedation were dyspnea, pain and physical exhaustion. Details of this study are described elsewhere.[15-17] Of the 370 respondents, 51 (22 general practitioners, 22 nursing home physicians and 7 clinical specialists) indicated that they were willing to participate in an additional qualitative interview. We also included the pilot interviews with one physician from each of the settings. In total, we interviewed 54 physicians (Table 1).

Procedures

We developed a semistructured interview scheme with open-ended questions. For each question, possible prompts were formulated. Questions related to the depth of sedation are listed in Box 1. The full interview scheme is available in Appendix 1 (www.cmaj.ca /lookup /suppl /doi :10 .1503 /cmaj .110847/-/DC1). To facilitate receiving answers that were as specific as possible, we included several questions pertaining to the case that the respondents had described in the quantitative questionnaire. Additional questions were asked about physicians' general sedation practices and attitudes.

Table 1 Characteristics of interviewed physicians

	Practice location; no. (%) of physicians		
	General practice *n*=23	**Nursing homes *n*=23**	**Hospital *n*=8**
Age			
< 40 yrs	1 (4)	3 (13)	2 (25)
40-49 yrs	9 (39)	7 (30)	4 (50)
50-59 yrs	11 (48)	11 (48)	2 (25)
> 60 yrs	2 (9)	2 (9)	0
Gender			
Male	13 (57)	6 (26)	5 (63)
Female	10 (44)	17 (74)	3 (38)
Working in current specialism			
0-9 yrs	2 (9)	8 (35)	2 (25)
10-19 yrs	9 (39)	7 (30)	4 (50)
20-29 yrs	7 (31)	8 (35)	2 (25)
30-39 yrs	5 (22)	0	0
Working in hospice or palliative care unit	2 (9)	10 (44)	4 (50)
Palliative care consultant	3 (14)	4 (17)	3 (38)

We conducted interviews between October 2008 and April 2009. Participants gave consent for audiotaping, and the interviews lasted between 30 and 65 minutes. Information about the physician's age, sex, work experience and medical specialty was obtained from the original questionnaire (Table 1). We ensured consistency among interviewers through the use of a semistructured interview with fixed prompts, a oneday training session about interview techniques and monthly meetings aimed at discussing findings and interim analyses. During one of the monthly meetings, the interviewers agreed that they had reached a saturation point (i.e., all relevant perspectives had been captured).

Analysis

The recordings were transcribed verbatim. We removed names and privacy-related information. We performed the analyses using the constant comparative method. The themes were independently derived from the interviews by S.J.S. and J.A.C.R. In addition, these authors compared and organized these themes in a coding tree, which was discussed several times with the rest of the authors, who have multiprofessional backgrounds and who had also read large parts of the raw material. The final coding tree, which captured all relevant themes for the purpose of this study, was agreed upon and used by S.J.S. and J.A.C.R. for

Box 1 Interview questions related to the depth of sedation

1. Did this case concern mild or deep sedation?
2. Was the dose of the medication in this case determined by the desired depth of sedation or by the severity of symptoms? Why?
3. To what extent was it important in this case that the patient could communicate as long as possible?
4. Do you think, in general, that when using continuous sedation until death, the patients' consciousness should be preserved as long as possible? Why?

coding all interviews independently. These authors discussed any differences. All authors discussed the coded fragments in depth during several meetings. During all phases of the analyses, alternative explanations of the findings were proposed and discussed to avoid potential preconceived notions. Quotes were selected by S.J.S. and J.A.C.R. to illustrate the arguments; the quotes were translated into English by a professional translator. Half of the quotes are case-specific and half are general.

RESULTS

Approaches for choosing the depth of sedation

Independent of any specific approach, physicians considered it important that the effect of continuous palliative sedation be reflected in the appearance of the patient. (Box 2, quote 1). Within this context, there were two approaches described for choosing the depth of continuous sedation. Physicians either started with mild sedation and, when considered necessary, deepened it gradually (n = 22; Box 2, quote 2) or they aimed for deep sedation right from the start (n = 32; Box 2, quote 3).

Box 2 Approaches to the depth of continuous sedation

In general, the effect of continuous palliative sedation therapy has to be reflected in the appearance of the patient

- Quote 1: You're looking for them to be peaceful. … If someone is short of breath, that's when you really want to see that the fight is over – that they're not twisting and turning, or breathing heavily, or sweating a lot. So you tend to base the dosage on the outwardly visible signs of suffering. — Clinical specialist A602

First approach: mild sedation and, when considered necessary, deepen it gradually

- Quote 2: It is usually a gradual process. When the sedation is light, the patient dozes off easily, but can still be woken. But if that's not really desirable, if you feel that the patient is still really suffering, that is when you give deeper sedation. … But I don't think I ever opt for deep sedation right from the start. — Clinical specialist R566

Second approach: deep sedation right from the start

- Quote 3: Sedation with the aim that there was no longer any visible suffering, that the patient would no longer respond when you spoke to them. … Deep sedation. — Clinical specialist A602

Box 3 Arguments for starting with mild sedation

Alleviation of symptoms

- Quote 1: Yes, on the basis of … it was constantly being adjusted on the basis of symptoms. You start out on a treatment, you see its effect, see whether it is enough. If it isn't, then we adjust it. — Nursing home physician A367
- Quote 2: I always begin with light sedation to see if it is sufficient. And I then see what the patient needs, what he indicates, which depth of sedation he wants. If light sedation is enough — which is often the case, I find – it is fine with me. — General practitioner A165

Enabling communication

- Quote 3: Tailor it carefully, I'd say. So if I see that someone is very peaceful, but opens their eyes from time to time, or is able to say something if necessary, and also experiences it as pleasant, then I see no reason to say that the sedation should be deeper. — General practitioner R182
- Quote 4: Yes, it is always possible that they will wake up, you do tell them that. But many people find that very unpleasant – they tell you beforehand that they don't want it. But you can't guarantee that beforehand. — Clinical specialist P003

Arguments for choosing the depth of sedation

Mild sedation

There were two arguments for the alleviation of symptoms by starting with mild sedation and increasing the depth if necessary. Physicians who aimed for mild sedation considered a gradual approach toward the relief of refractory symptoms to be sufficient and most appropriate. These physicians generally referred to sedation as a process in which the depth of sedation is guided by the clinical condition of the patient and the patient's response to the sedatives (Box 3, quote 1 and 2).

Physicians who aimed for mild sedation also considered communication of the patient with relatives and professional caregivers before and during sedation to be important. When adjusting the depth of sedation, they took into account the wishes of the patient and relatives about communication.

Physicians also referred to the unpredictable course of continuous sedation, implying that waking up should always be taken into account. They did not consider waking up during sedation to be problematic if patients and relatives had been informed and prepared for this possibility (Box 3, quote 3 and 4).

Deep sedation

Physicians who aimed for deep sedation from the start also voiced alleviation of symptoms as their guiding principle. But they argued that, if there is an indication for continuous sedation, the symptoms causing suffering require the use of deep sedation right from the start (Box 4, quote 1 and 2). They stated that patients and relatives need to be reassured that the suffering will continue to be relieved once continuous sedation has been started. Refractory symptoms such as breathlessness, seizures and symptoms related to delirium were specifically mentioned as indications for deep sedation. Only physicians who practised in nursing homes mentioned deep continuous sedation as being appropriate for patients with end-stage dementia (e.g., to relieve refractory restlessness) (Box 4, quote 3).

In some cases, possible awakening of the patient during sedation was considered to be problematic. To reduce the chance of this happening, physicians aimed for deep sedation right from the start. A patient who wakes from continuous sedation could, according to the respondents, be suffering from the underlying disease and refractory symptoms, which should be prevented. Physicians also felt that waking up was problematic because unexpected awakening could give rise to agitation of the patient and distress of the relatives (Box 4, quote 4).

Physicians in general practice mostly considered waking up to be something that had to be prevented. However, those who practised in hospitals and nursing homes generally regarded it as something that could be remedied if necessary (Box 4, quote 5). Physicians sometimes made explicit agreements with or promises to the patient and relatives about the prevention of waking up during the course of continuous sedation. Whereas in all settings, the perspectives of the patient and relatives about waking up were considered, general practitioners, compared with the other physicians, more explicitly referred to the wishes of, agreements with and promises to patients and relatives (Box 4, quotes 6 and 7).

Most physicians who aimed for deep sedation considered that, once sedation was started, communication with the patient was no longer important. Instead, they stressed the im-

Box 4 Arguments for deep continuous sedation from the start

Alleviation of symptoms

- Quote 1: Yes, it's what I just said – semi-sedation isn't really an option. Someone who's so delirious [that it cannot be treated otherwise] has nothing to gain from mild sedation. — General practitioner A232
- Quote 2: Of course, the purpose of sedation is to show you that the patient no longer needs to have a hard time, no longer has to suffer unbearably. And in this particular case the patient needed so much sedation before she'd no longer respond to your voice. … Of course, it's different each time …, but I usually find that once you've decided on continuous sedation … that you need so much, that the patient no longer responds to your voice. — Clinical specialist R521
- Quote 3: In this case it was deep sedation in a person with end-stage dementia. Which doesn't happen often, I have to say. But sometimes the situation's like the one with this patient, when you say to yourself, look, neither patient nor family have anything to gain when the patient is restless and short of breath. You can try out all kinds of medicines in the hope that they'll help, but you'd need such a mass of medication, while deep sedation was really all we needed to solve the problem. — Nursing home physician R320

Prevention of awakening

- Quote 4: At a certain moment it was more that the family felt that something had to be done – out of a fear that he would wake up … that was the most important argument, I think – the family's fear. — General practitioner R59
- Quote 5: Recently we had a situation with someone … well, we were still establishing the dose … that after a time someone woke up again. So we adjusted the dose to get the sedation so deep that there were no more reactions to pain stimuli. — Nursing home physician R367
- Quote 6: Someone might say, "No, I want to sleep more deeply," and that's fine. And the patient can indicate beforehand what they want. Which is what we act on. If they say "Just let me keep on sleeping," that's fine. — General practitioner A165
- Quote 7: Yes, because it gives the family quite a shock, doesn't it, especially if you'd promised them that, no, he won't wake up again – people have accepted that he'll just fall asleep and won't wake up; that things will quietly come to an end. So if someone does wake up, the first thing they'll think is "He's in so much pain that it woke him up." They then start to panic, as that's exactly what they didn't want. Q: And that's what you want to avoid? A: Yes. — General practitioner R218
- Quote 8: It is important that you don't leave it too late to talk things through with the patient and the family. Otherwise, of course, it will all go wrong. You'll have problems, either in the family or … well, things will go badly. But if you bring it up on time … Q: So it is especially the preparations …? A: Yes. If you've done them properly, carrying it all out isn't the problem – if you're good at providing support … well, then it's not really a problem. — General practitioner A165

portance of careful communication before the start of continuous sedation, both with the patient and family (Box 4, quote 8).

Expert advice

Both physicians who started with mild sedation and those who started with deep sedation mentioned the use of expert advice when choosing the depth of continuous sedation. This included instructions from palliative care teams, experienced colleagues or teams of specialized nurses; or medication schemes in guidelines and protocols (Box 5, quote 1). Expert advice was not always followed nor did it result in one preferred approach (Box 5, quotes 2–4).

Box 5 Expert advice

- Quote 1: I rang the palliative care team, … discussed it with them, and asked what the options were. And they said, "Well, all things considered, in this case this is a good option." And we talked about it with the family, and that's what I adopted. — General practitioner R117
- Quote 2: But I wasn't very happy with the pharmacist's advice, which pretty much came down to what the palliative care team advise[d]: you know, put up the infusion and then wait until deep sleep begins. But if that's the method you use, the patient essentially lies there waiting to fall asleep. It can take an hour, which is very hard on them – it can be a very stressful hour. … in fact, I think that's unethical. — General practitioner R100
- Quote 3: We've got a protocol for it. And while I have to say that I don't know the protocol by heart, the "TT nurse"* I call in for the infusion pump – or pumps – she does know it by heart. So we discuss it – you know, things like "She's very restless: shall we take it a bit deeper?" and then we do. And once someone is sleeping very peacefully, we just let things go according to plan. So I think … erhm … I don't do it as often as the TT nurse … — General practitioner A018
- Quote 4: So with the last patient, we thought the dose proposed by the anesthetist was too high. But because the man was so cachectic we thought that if we gave that, it would be … but in retrospect, it's probably what we should have done, as he woke up twice. Q: Why do you think that was? A: Well, according to the anesthetist, due to the initial dose … that we should just have given the proposed bolus, which would eventually have achieved a better blood level. And because we didn't dare to do it, as it really isn't very nice if someone dies during the injection. — Clinical specialist P003

*A TT (technical team) nurse is a nurse working in home care, who has been trained to provide technical assistance to physicians.

INTERPRETATION

We found that physicians have different approaches about the depth of continuous palliative sedation. Physicians either aim for deep sedation right from the start or begin with mild sedation and deepen it gradually if needed. The arguments that the interviewed physicians used for a specific approach related to alleviation of symptoms, communication, the possibility of awakening and expert advice. The patient's clinical situation was taken into account, as were physicians' and patients' personal preferences.

The notion of proportionality is often mentioned in guidelines and debates about palliative sedation. Proportional sedation is typically thought to be sedation in which the dose is individually titrated to the relief of distress caused by refractory symptoms;[1] in this case, consciousness is reduced no more than necessary to adequately relieve suffering.[18,19] Although most interviewed physicians did not use the term "proportionality," their statements suggest that proportionality is a major factor in their decisionmaking process. However, proportionality seems to be understood as being more than strictly titrating drugs to the relief of refractory symptoms.

We found that physicians use a multidimensional concept of proportionality, in which other factors also play a role.

Factors that contribute to proportionality

First, the preferences of the patient contribute to proportional sedation. Patients' fear of awakening and their conviction that "it has been enough" codetermine the required dosage of sedatives. These preferences not only reflect the wishes of the patient, but they may also relate to inherent convictions of both patients and physicians on how the dying process under continuous sedation should evolve. The fact that waking up during continuous seda-

tion was less often considered problematic by physicians practising in hospitals and nursing homes in our study may reflect that the quick availability and continuity of care may influence these preferences.

Second, preservation of communication is often considered important as it allows for the assessment of the indication for and the efficacy of palliative sedation.[1] Our results, however, indicate that the preservation of communication is sometimes also considered to be a goal in itself. Physicians who stated that the preservation of communication was important, considered mild sedation, in general, to be proportionate sedation. In cases in which preservation of communication was not considered important anymore, the threshold for applying deeper sedation was lower. In such cases, physicians used phrases such as "everything had been said" and the patient was "ready to die." Although guidelines do not reflect the preservation of communication as an inherent point of consideration, physicians do take this into account when deciding the required depth of sedation.

Third, relatives' wishes are considered important. We have reported elsewhere that physicians and nurses sometimes feel pressure to start continuous sedation.[15,16] The results of our study indicate that relatives' fears about the patient waking up contribute to physicians' decisionmaking. Finally, physicians often reflect upon esthetic aspects related to depth of sedation. The appearance of the patient is expected to be peaceful after the start of continuous palliative sedation. In some cases, this leads to the goal of deep sedation from the start. In other cases, this leads to a more gradual approach that reflects "a more natural way of dying."[20]

Comparison with other studies

Recent publications describing guidelines for the use of sedation for patients nearing death acknowledge that repeated doses of sedatives, titrated to ease an individual's distress, are the mark of proportionate sedation.[1,2] In addition, they suggest that clinicians' considerations for using sedation must be within accepted medical guidelines of beneficence, nonmaleficence and informed consent. Differences in the frequency of the application of continuous deep sedation[6-8] potentially reflect differences in attitudes toward the use and depth of sedation. Our study contributes to discussions about the proportionality of palliative sedation[9,21] by adding practice-based information to theoretical and moral reasoning. Quill and colleagues proposed that there are three types of palliative sedation: ordinary sedation, proportionate sedation and palliative sedation to unconsciousness.[9] However, based on our results, we support the suggestion that all palliative sedation should be classified as proportionate sedation,[21] because our results suggest that, from a multidimensional perspective on proportionality, palliative sedation to unconsciousness can be regarded as proportionate sedation in specific circumstances. The proportionality of continuous palliative sedation is determined within a context in which patients, relatives and caregivers interact and interpret clinical signs and symptoms and their consequences. This supports the notion that clinical decision-making at the end of life should be a shared deliberative process involving physicians and patients.[22]

Because the use of both mild and deep sedation was based on expert advice (i.e., from guidelines or palliative care experts) in our study, expert advice becomes part of this context. Apparently, its meaning and practical consequences are open to interpretation. If one interprets expert advice (e.g., a guideline) as suggesting that gradual deepening of sedation is the preferred approach in all cases, one could conclude that this guideline is not

always followed. If, however, one accepts a multidimensional concept of proportionality as a cornerstone for decision-making about continuous sedation, then one can conclude that proportionality is indeed used for determining the depth of sedation, but in a broader sense. Others have suggested that the "proportionality principle" should be distinguished from the "principle of therapeutic responsiveness"[23] in order to differentiate physical (neurocognitive) suffering from existential agent-narrative suffering. Such an approach fits well in the multidimensional concept of proportionality which we suggest, because the principle of therapeutic responsiveness supports physicians in distinguishing between therapeutic options that are within their realm (e.g., prescribing opioids) and therapeutic options for which others have to be involved (e.g., spiritual needs).

Because it has been proposed that the main objective of advance-care planning is to prepare patients and relatives to participate in making the best possible in-the-moment decision,[24] it is important that the writers of guidelines pay attention to the management of expectations about the course of continuous palliative sedation from the perspective of patients, families and clinicians.

Strengths and limitations

A major strength of a qualitative study is that it allows for an in-depth analysis of arguments involved in medical decision-making. Although we did not pursue a design of purposive sampling, the large number of interviews held with respondents who had experience with continuous sedation and who were working in different settings allowed for a broad practice-based description of continuous sedation. Moreover, using each physician's most recent case as a starting point for the interviews facilitated the collection of specific information. Because this may not always be a reflection of physicians' usual practices or approaches, the most recent case served as a reference for more general reflections during the interview, which we also included in the analyses. Physicians sometimes mentioned difficulties in recollecting the details of their "most recent" patient, especially when they had been involved in the care of other patients as a consultant in palliative care. Whereas physicians were randomly selected for the original questionnaire study, the present study included physicians who volunteered to participate, which could imply that only physicians with a specific interest in the research topic responded, leading to possible selection bias.

Conclusions

When providing continuous palliative sedation, physicians may aim for deep sedation from the start or choose for a more gradual approach. In both situations, proportionality refers not only to the titration of sedatives for the relief of refractory symptoms but also to titration to patients' preferences, communication needs, wishes of relatives and esthetic consequences. This suggests that proportionality should be seen as a multidimensional notion, taking into account guidelines and external advice. For further improvement of medical care at the end of life, we recommend that the arguments that physicians use about the depth of sedation should be studied in relation to the expectations of patients and families.

Acknowledgements The authors thank Anneke Tooten, Tijn Brinkkemper and Gwendolyn Salvelder for interviewing respondents.

References

1. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. J Palliat Med 2007;10:67-85.
2. Cherny NI, Radbruch L. Board of the European Association for Palliative C. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med 2009;23:581-93.
3. Royal Dutch Medical Association. Guideline for palliative sedation. Utrecht (Netherlands); The Association; 2009. Available: http://knmg.artsennet.nl/Diensten/knmgpublicaties/KNMG publicatie/Guideline-for-palliative-sedation-2009.htm (accessed 2011 Apr. 12).
4. Verkerk M, van Wijlick E, Legemaate J, et al. A national guideline for palliative sedation in the Netherlands. J Pain Symptom Manage 2007;34:666-70.
5. Morita T, Tsuneto S, Shima Y. Definition of sedation for symptom relief: a systematic literature review and a proposal of operational criteria. J Pain Symptom Manage 2002;24:447-53.
6. Miccinesi G, Rietjens JA, Deliens L, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage 2006;31:122-9.
7. Seale C. End-of-life decisions in the UK involving medical practitioners. Palliat Med 2009;23:198-204.
8. Anquinet L, Rietjens JA, Van den Block L, et al. General practitioners' report of continuous deep sedation until death for patients dying at home: a descriptive study from Belgium. Eur J Gen Pract 2011;17:5-13.
9. Quill TE, Lo B, Brock DW, et al. Last-resort options for palliative sedation. Ann Intern Med 2009;151:421-4.
10. Hasselaar JG, Verhagen SC, Vissers KC. When cancer symptoms cannot be controlled: the role of palliative sedation. Curr Opin Support Palliat Care 2009;3:14-23.
11. Rietjens JA, Buiting HM, Pasman HR, et al. Deciding about continuous deep sedation: physicians' perspectives: a focus group study. Palliat Med 2009;23:410-7.
12. Sykes N, Thorns A. Sedative use in the last week of life and the implications for end-of-life decision making. Arch Intern Med 2003;163:341-4.
13. Maltoni M, Pittureri C, Scarpi E, et al. Palliative sedation therapy does not hasten death: results from a prospective multicenter study. Ann Oncol 2009;20:1163-9.
14. Hasselaar JG, Reuzel RP, Verhagen SC, et al. Improving prescription in palliative sedation: compliance with dutch guidelines. Arch Intern Med 2007;167:1166-71.
15. Swart SJ, Brinkkemper T, Rietjens JA, et al. Physicians' and nurses' experiences with continuous palliative sedation in the Netherlands. Arch Intern Med 2010;170:1271-4.
16. Swart SJ, Rietjens JA, Brinkkemper T, et al. Palliative sedation largely in accordance with Dutch national guideline [article in Dutch]. Ned Tijdschr Geneeskd 2011;155:A2857.
17. Swart SJ, Rietjens JA, van Zuylen L et al. Continuous Palliative Sedation for Cancer and Noncancer Patients. J Pain Symptom Manage 2012;43:172-81.
18. Claessens P, Menten J, Schotsmans P, et al. Palliative sedation: a review of the research literature. J Pain Symptom Manage 2008; 36: 310-33.
19. Henry B, Dean M, Cellarius V, et al. To "sleep until death." Hastings Cent Rep 2011;41:4; author reply 4-5.
20. Raus K, Sterckx S, Mortier F. Continuous deep sedation at the end of life and the 'natural death' hypothesis. Bioethics 2011 Jan. 17 [epub ahead of print].
21. Cellarius V, Henry B. Justifying different levels of palliative sedation. Ann Intern Med 2010;152:332; author reply 333.
22. Jansen LA. Deliberative decision making and the treatment of pain. J Palliat Med 2001;4:23-30.
23. Jansen LA, Sulmasy DP. Proportionality, terminal suffering and the restorative goals of medicine. Theor Med Bioeth 2002;23:321-37.
24. Sudore RL, Fried TR. Redefining the "planning" in advance care planning: preparing for end-of-life decision making. Ann Intern Med 2010;153:256-61.

6

Continuous palliative sedation for cancer and non-cancer patients

Siebe J. Swart
Judith A.C. Rietjens
Lia van Zuylen
Wouter W.A. Zuurmond
Roberto S.G.M. Perez
Paul J. van der Maas
Johannes J.M. van Delden
Agnes van der Heide

J Pain Symptom Manage 2012;43:172-81

ABSTRACT

Context Palliative care is often focused on cancer patients. Palliative sedation at the end of life is an intervention to address severe suffering in the last stage of life.
Objectives To study the practice of continuous palliative sedation for both cancer and noncancer patients.
Methods In 2008, a structured questionnaire was sent to 1580 physicians regarding their last patient receiving continuous sedation until death.
Results A total of 606 physicians (38%) filled out the questionnaire, of whom 370 (61%) reported on their last case of continuous sedation (cancer patients: *n* = 282 [76%] and noncancer patients: *n* = 88 [24%]). More often, noncancer patients were older, female, and not fully competent. Dyspnea (odds ratio [OR] = 2.13; 95% confidence interval [CI]: 1.22, 3.72) and psychological exhaustion (OR = 2.64; 95% CI: 1.26, 5.55) were more often a decisive indication for continuous sedation for these patients. A palliative care team was consulted less often for noncancer patients (OR = 0.45; 95% CI: 0.21, 0.96). Also, preceding sedation, euthanasia was discussed less often with noncancer patients (OR = 0.42; 95% CI: 0.24, 0.73), whereas their relatives more often initiated discussion about euthanasia than relatives of cancer patients (OR = 3.75; 95% CI: 1.26, 11.20).
Conclusion The practice of continuous palliative sedation in patients dying of cancer differs from patients dying of other diseases. These differences seem to be related to the less predictable course of noncancer diseases, which may reduce physicians' awareness of the imminence of death. Increased attention to noncancer diseases in palliative care practice and research is, therefore, crucial as is more attention to the potential benefits of palliative care consultation.

INTRODUCTION

Palliative care originated in care for cancer patients but is generally recognized to be equally important for patients with other incurable diseases.[1-4] This also is reflected in the World Health Organization's definition of palliative care, which refers to all patients and their families facing problems associated with life-threatening illness.[1] However, noncancer patients have less access to palliative care services,[2-4] and they seem less likely to receive effective symptom control at the end of life.[2]

To alleviate intolerable refractory symptoms, palliative sedation is considered to be an indispensable treatment, the application of which requires due caution and good clinical practice.[5,6] In the Dutch national guideline, launched in 2005, palliative sedation is defined as "the intentional lowering of consciousness of a patient in the last phase of life."[6,7] It refers to all subtypes of sedation – intermittent and continuous sedation as well as deep and superficial sedation. Continuous sedation until death is the most far-reaching subtype of palliative sedation, and its benefits and drawbacks are frequently debated.[8,9] The estimated frequency of the use of palliative sedation varies considerably in the scientific literature, partly because of differences in definition and research settings. Comparable nationwide studies show frequencies of continuous deep sedation in Europe of 2.5% up to 16% of all deaths.[10-12] In The Netherlands, this frequency was estimated at 8.2% of all deaths.[13] Guidelines distinguish palliative sedation from euthanasia by stating that these are two distinct practices that should be used in different clinical contexts; palliative sedation is meant to reduce the conscious experience of symptoms that cannot otherwise be palliated, whereas euthanasia is aimed at the termination of life at the explicit request of a competent patient.[7] The guidelines state that continuous sedation does not shorten life when its use is restricted to the patient's last one to two weeks of life. However, in practice, physicians sometimes use sedation with the intention of hastening death.[10,14-16]

Our knowledge about the practice of palliative sedation is predominantly based on research with cancer patients.[17] However, in a nationwide Dutch study, continuous deep sedation was used in 53% of noncancer patients, and in a study in six European countries, the probability of receiving continuous deep sedation was only 15% greater for cancer patients than for noncancer patients.[11,13] As little information is available about palliative sedation for nonmalignant disease and the importance of palliative care for nonmalignant disease is increasingly acknowledged,[2,4] we wanted to investigate the practice of continuous sedation for noncancer patients to assess possible differences compared with cancer patients.

METHODS

Study design and data collection

A study using a structured anonymous questionnaire was performed among physicians from February to September 2008. A paper version of the questionnaire was sent to a random sample of 1580 physicians: 1128 in the northwestern and southwestern regions of The Netherlands (general practice, n = 466; nursing home, n = 195; and hospital, n = 467) and 452 general practitioners in the northeastern region. The sample of clinical specialists (internal medicine, cardiology, pulmonology, neurology, and geriatrics) was stratified into clinicians working in university hospitals and those working in nonuniversity hospitals.

Nonresponding physicians received a paper reminder after two months and an e-mail reminder after four months. Finally, in the southwestern region, all nonresponding clinical specialists (n = 109) were asked by e-mail and 20% of the nonresponding general practitioners and nursing home physicians (n = 39) were asked by telephone for their reasons for nonresponse.

Questionnaire

A draft version of the questionnaire was tested in a pilot study among general practitioners. After this, the questionnaire was revised and then filled out by 12 physicians working in palliative care. Using their comments, we finalized the questionnaire. Physicians were asked to report on the last patient for whom they had been responsible for providing continuous sedation until death. They were asked to have the clinical notes at hand. Continuous sedation refers to the use of sedatives in patients at the end of life, intended specifically for lowering consciousness continuously from a certain point in time until the patient dies.[18] The questions addressed patient characteristics (gender, age, competence, most important diagnosis, symptoms during the decision-making process [on a 5-point Likert scale], decisive indication for starting sedation, decision making [communication with patients and relatives, consultation with a palliative care team before continuous sedation, and use of a guideline], and aspects of continuous sedation related to the possibility of hastening death [life expectancy, physician's intention when administering continuous sedation, time until death, estimated hastening of death, and discussion of euthanasia]), as well as general respondent characteristics. The questionnaire was mailed together with a letter of recommendation from the Royal Dutch Medical Association. Under Dutch regulations, the study did not require review by an ethics committee or written informed consent from the patients' relatives because the data collection was anonymous with respect to the deceased patient.

Analysis

We analyzed cases that had occurred after the introduction of the national guideline on palliative sedation in December 2005. For each case, the most important diagnosis was recoded as "cancer" or "non-cancer." Patients having both cancer and noncancer diagnoses (n = 11) were excluded from the analysis. The Likert scales for symptoms were recoded into "severe" (scores 4-5) and "not severe" (scores 1-3). The statistical significance of univariate differences between cancer and noncancer patients was calculated with t-tests, Mann-Whitney U tests, or Chi-squared tests, where appropriate. To adjust for the possible influence of the reporting physician's specialty, multivariate logistic regression analyses were performed.[19] For all tests, a P-value lower than 0.05 was considered statistically significant. Missing data varied per question and ranged from 0% to 8%. Valid percentages are used throughout the text. Variables with more than 5% missing values are indicated in the tables. Data were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL).

RESULTS

Respondents and patients: general characteristics

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. The main reasons for nonresponse (clinical specialists [n = 32] and general practitioners/

Table 1 Characteristics of respondents presenting a case and of the patients[a]

	Cancer (*n*=271), %	**Noncancer[b] (*n*=88), %**	***P*-value[c]**
Respondents presenting a case			
Gender male	64	64	0.99
Age (years), mean (SD)	49 (8)	49 (10)	0.89
Type of physician			
- general practitioner	76	42	<0.01
- nursing home physician	11	39	
- medical specialist[d]	13	19	
Experience (years), mean (SD)	19 (9)	17 (10)	0.08
Working in palliative care	10	9	0.76
Number of dying people cared for in 2007, median (SD)	10 (16)[e]	15 (13)	<0.01
Patients			
Gender male	57	38	<0.01
Age (years), mean (SD)	66 (13)	80 (11)	<0.01
Competence[f]			
- fully competent	76	52	<0.01
- not fully competent	16	13	
- incompetent	8	35	

[a] Patients (*n*=11) with both a cancer and a non-cancer diagnosis were excluded from our analysis
[b] Most common non-cancer diagnoses were heart failure (*n*=18; 20%), COPD (*n*=8; 9%), dementia (*n*=15;17%), neurological disease (*n*=16;18%), other (*n*=17;19%). 14 respondents reported two non-cancer diagnosis (16%)
[c] *P*-value: Chi-Square tests, Mann-Whitney *U* tests and *t*-tests.
[d] Internal medicine, cardiology, pulmonology, neurology, geriatrics
[e] Missing 6%
[f] Competence was defined as that at the moment the decision to start continuous sedation was made, the patient was able to judge and decide carefully about his/her situation.

nursing home physicians [*n* = 39]) were: too busy with patient care (17%), no experience with continuous palliative sedation (14%), practiced continuous sedation too long ago (11%), receives too many requests for participation in research (11%), and never participates in research (11%). Of the responding physicians, 370 (61%) had recently provided continuous sedation until death and reported about their last case. Of 370 cases, 68% were reported by general practitioners, 17% by nursing home physicians, and 15% by clinical specialists. Cancer was the main diagnosis in 85%, 47%, and 70% of all cases for general practitioners, nursing home physicians, and clinical specialists, respectively. Main non-cancer diagnoses were heart failure, neurological diseases, chronic obstructive pulmonary disease, and dementia (Table 1). On average, noncancer patients were older than cancer patients (mean age: 80 years vs. 67 years), more often female, and more often mentally incompetent during the decision-making process.

Continuous sedation: symptoms, signs, and decisive indications

Noncancer patients were significantly more often reported to have had the following severe symptoms and signs before the start of continuous sedation: dyspnea (50% vs. 34%, odds ratio [OR] = 1.92; 95% confidence interval [CI]: 1.11, 3.32), motoric discomfort (45% vs. 27%; OR = 1.78; 95%CI: 1.03, 3.08), confusion (42% vs. 22%; OR = 1.88; 95% CI: 1.05, 3.34), and depression (16% vs. 6%; OR = 3.23; 95% CI: 1.37, 7.64) (Table 2). Nausea and vomiting were reported significantly less often for noncancer patients (11% vs. 31%; OR =

Table 2 Continuous sedation: symptoms and decisive indications

	Cancer (n=271), %	Noncancer (n=88), %	OR (95%CI)[a]
Severe[b] symptoms and complaints before the start of continuous sedation			
- fatigue	76	66	0.63 (0.36-1.12)
- longing for death	59	55	1.26 (0.72-2.19)
- loss of dignity	45	54	1.20 (0.71-2.01)
- loss of control	37	51	1.38 (0.81-2.34)
- dyspnoea	34	50	1.92 (1.11-3.32)
- pain	62	49	0.68 (0.38-1.09)
- motoric discomfort	27	45	1.78 (1.03-3.08)
- anxiety	28[c]	44	1.50 (0.86-2.59)
- hopelessness	49	43[d]	0.98 (0.57-1.67)
- confusion	22[c]	42	1.88 (1.05-3.34)
- loss of interest	22[d]	33	1.69 (0.95-3.01)
- depression	6[e]	16[f]	3.23 (1.37-7.64)
- burden to environment	17	14	1.28 (0.61-2.70)
- nausea/vomiting	32	11[g]	0.32 (0.15-0.69)
Decisive indication for continuous sedation[h]			
- dyspnoea	24	41	2.13 (1.22-3.72)
- pain	33	22	0.57 (0.31-1.04)
- physical exhaustion	33	21	0.57 (0.31-1.05)
- psychological exhaustion	10	17	2.64 (1.26-5.55)
- existential suffering	13	15	1.38 (0.67-2.88)
- delirium	13	11	0.72 (0.32-1.63)
- anxiety (fear)	5	9	1.53 (0.57-4.15)
- cachexia	7	7	1.27 (0.46-3.51)
- motoric discomfort	6	5	0.59 (0.18-1.99)
- nausea/vomiting	12	4	0.30 (0.09-1.16)
- depression	0	3	n.a.
- bleeding	2	1	0.69 (0.07-6.84)
- other	10	8	0.72 (0.29-1.83)

n.a = not applicable
[a] Multivariate logistic regression analyses, adjustment for setting
[b] Number (percentage) of patients who were given a score of 4 or 5 on a 1-5 Likert scale
[c] Missing values 5.2%
[d] Missing values 5.5%
[e] Missing values 5.9%
[f] Missing values 5.7%
[g] Missing values 8%
[h] 37% of the respondents mentioned more than one decisive indication, although the questionnaire asked for only one decisive indication

0.32; 95% CI: 0.15, 0.69). The most common decisive indications for starting continuous sedation in both groups were: pain, physical exhaustion, dyspnea, delirium, existential suffering, and psychological exhaustion.

Decisive indications reported more often for noncancer patients were dyspnea (41% vs. 24%; OR= 2.13; 95% CI: 1.22, 3.72) and psychological exhaustion (17% vs. 10%; OR = 2.64; 95% CI: 1.26, 5.55). In most cases where psychological exhaustion was a decisive indication, other decisive indications were reported as well. The most frequent drug used for continuous sedation was midazolam. For noncancer patients, this was used significantly less often than for cancer patients (84% vs. 93%; OR = 0.44; CI: 0.20, 0.98).

Table 3 Decision-making on continuous sedation

		Cancer (%)	Noncancer (%)	OR (95% CI)[a]
Discussion of continuous sedation				
1. Competent patient		*n*=206[b]	*n*=46	
- Patient	was informed	17	18	0.81 (0.34-1.94)[c]
	was involved	83	82	
	decision was not discussed with patient	0	0	
- Relatives	were informed	20	13	1.61 (0.63-4.15)[c]
	were involved	80	87	
	decision was not discussed with relatives	0	0	
2. Not fully competent or incompetent patient		*n*=64	*n*=42	
- Patient	was informed	29	17	0.30 (0.08-1.08)[c]
	was involved	40	12	
	decision was not discussed with patient	32	71	
- Relatives	were informed	17	18	0.84 (0.26-2.71)[c]
	were involved	83	83	
	decision was not discussed with relatives	0	0	
		n=271	*n*=88	
Consultation of palliative care team before continuous sedation?		27	10	0.45 (0.21-0.96)
		n=75	*n*=9	
Consultation palliative care team before start continuous sedation helpful		89	89	1.00
		n=271	*n*=88	
Use of guideline in case	- national guideline	55	52	0.82 (0.48-1.40)[d]
	- local guideline	9	9	
	- no	36	38	

[a] Multivariate logistic regression analyses, adjustment for setting
[b] Missing n=1
[c] Involved vs informed or not discussed
[d] Guideline versus no guideline

Decision making

For competent patients, the decision to start continuous palliative sedation was always discussed with the patient and their relatives (Table 3). Approximately four of five patients and their relatives were actively involved in the decision making; the remaining patients and relatives were only informed. For competent patients, there were no differences between patients with or without cancer. For incompetent patients, the decision to use sedation was not discussed with 71% of noncancer patients and 32% of cancer patients. However, in these cases there always was discussion with their relatives, who were in approximately four of five cases actively involved in making the decision to use sedation, rather than being merely informed.

Consultation with a palliative care team before the start of sedation occurred significantly less often for noncancer patients than for cancer patients (10% vs. 27%; OR = 0.45). This consultation was considered helpful in 89% of the cases, for both cancer and noncancer patients. The use of a guideline for continuous sedation did not differ significantly between noncancer (61%) and cancer (64%) patients.

Table 4 Continuous sedation and hastening of death

	Cancer (%)	Noncancer (%)	OR(95%CI)[a]
Life expectancy at start of continuous sedation	*n*=271	*n*=88	
- Less than a day	4	5	1.67[b] (0.93-3.01)
- Between 1-2 days	33	30	
- Between 3-6 days	39	38	
- Between 1-2 weeks	22	23	
- Between 2-4 weeks	2	5	
- More than a month	0	1	
Duration of the sedation			
- Less than a day	33	30	1.32 (0.77-2.26)[c]
- Between 1-2 days	33	30	
- Between 3-6 days	31	33	
- Between 1-2 weeks	3	7	
Estimated hastening of death due to continuous sedation			
- None	46	25	2.97 (1.60-5.52)[d]
- Less than a day	11	10	
- Between 1-2 days	14	16	
- Between 3-6 days	6	15	
- Between 1-2 weeks	7	3	
- Between 2-4 weeks	0	5	
- Don't know	15	25	
Talked about euthanasia before continuous sedation			
- Yes	72	42	0.42 (0.24-0.73)[e]
- No	27	55	
-Don't know	1	3	
Who initiated talking about euthanasia[f]	*n*=194	*n*=37	
- Patient	36	36	0.95 (0.45-2.03)
- Responding physician or other physician	53	42	0.63 (0.30-1.33)
- Relatives	5	19	3.75 (1.26-11.20)
- Other	1	0	n.a.
Request for euthanasia?			
- Yes	28	35	1.47 (0.68-3.19)
Reason for not complying with euthanasia request[g]	*n*=53	*n*=13	
- Patient withdraw request	14	8	0.54 (0.05-6.08)
- Patient preferred continuous sedation	43	23	0.39 (0.95-1.60)
- Physician preferred sedation	16	15	0.98 (0.18-5.31)
- To avoid legal euthanasia procedure	4	15	4.12 (0.51-33.40)
- Immediate intervention was necessary	33	15	0.36 (0.70-1.83)
- Request did not meet legal criteria	20	46	3.80 (1.01-14.19)
- Principal objections physician	4	15	4.11 (0.51-33.40)
- Other	22	0	n.a.

n.a. = not applicable
[a] Multivariate logistic regression analyses, adjustment for setting
[b] Less than one week versus more than one week
[c] Less than two days versus more than two days
[d] No shortening and less than one day versus more than one day; "don't know" excluded
[e] "Don't know" excluded
[f] More than one answer was possible: eight respondents mentioned patient and relatives and four respondents mentioned patient and physician
[g] More than one answer was possible

Continuous sedation and hastening of death

At the start of continuous sedation, most of the noncancer (94%) and cancer (98%) patients had an estimated life expectancy of less than two weeks (Table 4). Two-thirds of the patients died within two days after the start of the sedation (noncancer, 60% and cancer, 66%). An estimated hastening of death of more than one day was reported more often for noncancer patients (39%) than for cancer patients (27%) (OR = 2.97; 95% CI: 1.60, 5.52).

Preceding continuous sedation, physicians talked less often about euthanasia with noncancer patients (42%) than with cancer patients (72%) (OR= 0.42; 95% CI: 0.24, 0.73). Talking about euthanasia was initiated by the patient in 36% of the cases in both groups. Physicians initiated talking about euthanasia less often for noncancer patients (42%) than for cancer patients (53%). Relatives initiated talking about euthanasia significantly more often for noncancer patients (19%) than for cancer patients (5%) (OR= 3.75; 95% CI: 1.26, 11.20). An actual request for euthanasia followed discussion about euthanasia in 35% of the cases for noncancer patients and in 28% for cancer patients. Reasons most often reported for not having complied with the request for euthanasia for both patient groups (*n*= 68) were: the patient preferred continuous sedation (38%), immediate intervention was necessary (29%), and the case did not meet legal criteria for euthanasia (24%). The latter reason was significantly more often reported for noncancer patients (*n*= 6; 46%) than for cancer patients (*n*= 9; 20%) (OR= 3.80; 95% CI: 1.01, 14.19).

DISCUSSION

Data on palliative sedation for noncancer patients are scarce. Our results suggest that there are several ways in which the practice of continuous palliative sedation differs in noncancer and cancer patients. First, noncancer patients receiving sedation were older than cancer patients, more of them were female, and more were mentally incompetent. Second, dyspnea and psychological exhaustion were more often reported as a decisive indication to start continuous sedation. Third, in noncancer patients, a palliative care team had been consulted less often before the start of sedation, continuous sedation also had more often been provided with the intention of hastening death, and life more often was estimated to have been shortened as a consequence of sedation. Finally, physicians discussed euthanasia with fewer noncancer patients than cancer patients. But if it was discussed, more of these patients requested euthanasia.

Clinical aspects

Nursing home care originated from care for elderly patients with chronic diseases like dementia, neurologic disease, and heart failure. Hence, the population in nursing homes predominantly consists of elderly patients with noncancer diseases. This explains why nursing home physicians predominantly report about noncancer patients.

Dyspnea has a prevalence of 35% in the last two weeks of life.[20] It has been identified as a factor that predicts a high symptom burden as well as dying in hospitalized cancer patients.[21,22] Our findings suggest that this may hold even more for noncancer patients, for whom dyspnea is more often a decisive indication for continuous sedation. Patients with chronic lung disease experience dyspnea as very distressing in the last year and last week of life.[23] Recently, it was found that despite optimal conventional pharmacological and non-

pharmacological therapies, some patients with advanced chronic obstructive pulmonary disease still suffer from dyspnea at the end of life and that they need an approach in which their psychosocial needs, as well as those of their relatives, are met.[24,25] Although it has been questioned whether palliative sedation is appropriate for nonphysical symptoms,[26] existential pain and exhaustion have been described as indications for continuous sedation.[27] These findings are confirmed by our data, which indicated that psychological exhaustion in particular contributes to the indication for continuous palliative sedation in noncancer patients. Taken together with our finding that palliative care teams are consulted less often for noncancer patients, this suggests that palliative care should be incorporated more in advance care planning for noncancer patients and their relatives. In this way, the physical, psychosocial, and spiritual aspects of – for example, dyspnea – can be addressed in a timely and proper manner.[5]

Decision making

The involvement of patients and relatives in decision making about continuous sedation did not differ significantly between noncancer and cancer patients. Although the decision to start continuous sedation was discussed with all competent patients, almost one in five of them were not actually involved in the decisionmaking process. This may be explained by the fact that patients do not always wish to be involved in end-of-life decision making.[28,29] It is also possible that the clinical condition of terminal patients suffering from refractory symptoms deteriorated so suddenly or unexpectedly that immediate intervention was required, leaving no time to involve them in the decision making. Timely discussion of the option of palliative sedation, therefore, seems important.

Nearly two of three physicians had used a guideline in their last case of continuous sedation, with cancer and noncancer patients alike. The Dutch national guideline on palliative sedation recommends but does not oblige physicians to consult a palliative care team if they lack experience or expertise with palliative sedation. Although the importance of consultation for noncancer is acknowledged in the national guideline,[18] our data indicate that a palliative care team is consulted less often for continuous palliative sedation in noncancer patients, which is in line with other data.[30] This finding may be explained by two factors. First, in The Netherlands, palliative care consultation is embedded in the organizational structure of comprehensive cancer centers, probably resulting in a lower inclination to use this service for noncancer patients. Second, in noncancer patients, end-of-life disease trajectories often involve a rather long-term fluctuating process of gradual decline punctuated by episodes of acute deterioration and eventually a seemingly unexpected death.[4] Such trajectories may make it more difficult to decide when a palliative care approach, including consultation with a palliative care team, would be appropriate.

Hastening death

The Dutch national guideline states that palliative sedation, if administered proportionally, does not hasten death.[18] Nevertheless, in our study, continuous sedation was reported to have hastened death in some cases, more often in noncancer patients than in cancer patients. On the other hand, euthanasia – an act explicitly intended to hasten death – was discussed with noncancer patients less often, although such discussions were followed relatively more often by an actual patient's request for euthanasia. The content of these discussions is not

known, but probably often related to explaining and clarifying differences between euthanasia and palliative sedation.

These findings suggest that, especially in noncancer patients, physicians may feel uncertain about the possibility of hastening death. Physicians commonly have difficulties in estimating and tend to overestimate patients' life expectancies.[31,32] Physicians also may overestimate the life-shortening effects of sedative medication in patients with a limited life expectancy.[27] Noncancer diseases often involve a fluctuating and less predictable disease trajectory, which may reduce awareness of the imminence of death and increase physicians' inclination to consider hastening of death as a potential consequence of continuous sedation. The greater tendency of relatives of noncancer patients to ask for euthanasia also may be the result of uncertainty among relatives about the unpredictable disease course and suffering of their loved one. Physicians should thus very carefully consider and discuss treatment alternatives to address severe suffering at the end of life.

Strengths and limitations

To our knowledge, this is the first study to compare the practice of continuous sedation for patients with cancer to that of patients with other diseases. Despite great effort, the response rates in our study were only moderate, albeit comparable with other studies in this area.[19] Our results, therefore, may not be representative for all physicians, especially clinical specialists, whose response rate was the lowest. Our nonresponse analyses, however, showed that an important reason for nonresponse was that physicians had no experience with continuous sedation until death. Hence, we think that selection bias is rather limited. Recall bias also might have been a problem, although most respondents reported a case that had occurred less than a year earlier. Given the facts that physicians are relatively seldom involved in the use of palliative sedation and that it is a far-reaching procedure, it is likely that they might remember such cases quite clearly. Nevertheless, studies investigating the practice of palliative sedation with a prospective design are recommended.

Because we studied three regions, it may not be possible to extrapolate our results to The Netherlands as a whole. Because other studies in this field predominantly report about patients with cancer, a major strength of our study is that it included and separately reported about noncancer patients.[11,14,15] Furthermore, to minimize possible differences in the perception of what sedation entails across the respondents, we provided them with a descriptive definition of the practice (continuous sedation until death). Most other studies use terms such as palliative or terminal sedation, which can have varying connotations and implications for clinical practice. Furthermore, in our study, we not only report about indications for palliative sedation but also on the clinical picture before the start of sedation.

CONCLUSIONS AND RECOMMENDATIONS

The practice of continuous palliative sedation to alleviate suffering in the last stage of life in patients dying of cancer differs from patients dying of other diseases. These differences seem to be related to the less predictable course of noncancer diseases, which may diminish physicians' awareness of the imminence of death. Advance care planning and end-of-life decision making are challenging aspects of palliative care, and may be even more challenging when dealing with patients having noncancer diseases. Increased attention for noncancer

diseases in palliative care practice and research is, therefore, crucial as is more attention for the potential benefits of palliative care consultation. Last, whether and how continuous palliative sedation contributes to a dignified death deserves further study, not only from the perspective of physicians but also from the perspective of patients, relatives, and other professional carers.

Acknowledgements
The authors would like to thank Wijnanda van Burg-Verhage for her work on the pilot, the Comprehensive Cancer Centers of Amsterdam and Rotterdam for their assistance with the data collection, and all the respondents for filling out the questionnaires.

References

1. World Health Organization (WHO). WHO definition of Palliative Care. [cited 2009 10 June]; Available from: http://www.who.int/cancer/palliative/definition/en/.
2. Burt J, Shipman C, Richardson A, Ream E, Addington-Hall J. The experiences of older adults in the community dying from cancer and non-cancer causes: a national survey of bereaved relatives. Age Ageing. 2010 Jan;39(1):86-91.
3. Van den Block L, Deschepper R, Bossuyt N, Drieskens K, Bauwens S, Van Casteren V, et al. Care for patients in the last months of life: the Belgian Sentinel Network Monitoring End-of-Life Care study. Arch Intern Med. 2008 Sep 8;168(16):1747-54.
4. Gielen B, Remacle A, Mertens R. Patterns of health care use and expenditure during the last 6 months of life in Belgium: Differences between age categories in cancer and non-cancer patients. Health Policy. 2010 Mar 30.
5. Cherny NI, Radbruch L, Board of the European Association for Palliative C. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med. 2009 Oct;23(7):581-93.
6. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. J Palliat Med. 2007 Feb;10(1):67-85.
7. Verkerk M, van Wijlick E, Legemaate J, de Graeff A. A national guideline for palliative sedation in the Netherlands. J Pain Symptom Manage. 2007 Dec;34(6):666-70.
8. van Delden JJ. Terminal sedation: source of a restless ethical debate. J Med Ethics. 2007 Apr;33(4):187-8.
9. Materstvedt LJ, Bosshard G. Deep and continuous palliative sedation (terminal sedation): clinical-ethical and philosophical aspects. Lancet Oncol. 2009 Jun;10(6):622-7.
10. Seale C. End-of-life decisions in the UK involving medical practitioners. Palliat Med. 2009 Apr;23(3):198-204.
11. Miccinesi G, Rietjens JA, Deliens L, Paci E, Bosshard G, Nilstun T, et al. Continuous deep sedation: physicians' experiences in six European countries. J Pain Symptom Manage. 2006 Feb;31(2):122-9.
12. Chambaere K, Bilsen J, Cohen J, Rietjens JA, Onwuteaka-Philipsen BD, Mortier F, et al. Continuous deep sedation until death in Belgium: a nationwide survey. Arch Intern Med. 2010 Mar 8;170(5):490-3.
13. Rietjens J, van Delden J, Onwuteaka-Philipsen B, Buiting H, van der Maas P, van der Heide A. Continuous deep sedation for patients nearing death in the Netherlands: descriptive study. BMJ. 2008 Apr 12;336(7648):810-3.
14. Maltoni M, Pittureri C, Scarpi E, Piccinini L, Martini F, Turci P, et al. Palliative sedation therapy does not hasten death: results from a prospective multicenter study. Ann Oncol. 2009 Jul;20(7):1163-9.
15. Rietjens JA, van der Heide A, Vrakking AM, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wal G. Physician reports of terminal sedation without hydration or nutrition for patients nearing death in the Netherlands. Ann Intern Med. 2004 Aug 3;141(3):178-85.
16. Rietjens J, Buiting H, Pasman H, van der Maas P, van Delden J, van der Heide A. Deciding about continuous deep sedation: physicians' perspectives. Palliat Med. 2009 Apr 7.
17. Hasselaar JG, Verhagen SC, Vissers KC. When cancer symptoms cannot be controlled: the role of palliative sedation. Curr Opin Support Palliat Care. 2009 Mar;3(1):14-23.

18. KNMG. KNMG-richtlijn palliatieve sedatie 2009. http://knmgartsennetnl/Diensten/knmgpublicaties/KNMGpublicatie/Guideline-for-palliative-sedation-2009htm. 2009.
19. Hasselaar JG, Reuzel RP, van den Muijsenbergh ME, Koopmans RT, Leget CJ, Crul BJ, et al. Dealing with delicate issues in continuous deep sedation. Varying practices among Dutch medical specialists, general practitioners, and nursing home physicians. Arch Intern Med. 2008 Mar 10;168(5):537-43.
20. Teunissen SC, Wesker W, Kruitwagen C, de Haes HC, Voest EE, de Graeff A. Symptom prevalence in patients with incurable cancer: a systematic review. J Pain Symptom Manage. 2007 Jul;34(1):94-104.
21. Stäritz A, Alt-Epping B, Altfelder N, Simon ST, Lindena G, Nauck F. Disease specific symptom prevalences in patients with lung cancer and pulmonary metastases. Abstracts of EAPC (European Association for Palliative Care) 2010. June 10-12, 2010. Palliat Med. 2010 Jun;24(4 Suppl):S5-229.
22. Teunissen SC, de Graeff A, de Haes HC, Voest EE. Prognostic significance of symptoms of hospitalised advanced cancer patients. Eur J Cancer. 2006 Oct;42(15):2510-6.
23. Edmonds P, Karlsen S, Khan S, Addington-Hall J. A comparison of the palliative care needs of patients dying from chronic respiratory diseases and lung cancer. Palliat Med. 2001 Jul;15(4):287-95.
24. Rocker G, Horton R, Currow D, Goodridge D, Young J, Booth S. Palliation of dyspnoea in advanced COPD: revisiting a role for opioids. Thorax. 2009 Oct;64(10):910-5.
25. Horton R, Rocker G. Contemporary issues in refractory dyspnoea in advanced chronic obstructive pulmonary disease. Curr Opin Support Palliat Care. 2010 Jun;4(2):56-62.
26. National Ethics Committee VHA. The ethics of palliative sedation as a therapy of last resort. Am J Hosp Palliat Care. 2006 Dec-2007 Jan;23(6):483-91.
27. Hasselaar JG, Verhagen SC, Wolff AP, Engels Y, Crul BJ, Vissers KC. Changed patterns in Dutch palliative sedation practices after the introduction of a national guideline. Arch Intern Med. 2009 Mar 9;169(5):430-7.
28. Levinson W, Kao A, Kuby A, Thisted RA. Not all patients want to participate in decision making. A national study of public preferences. J Gen Intern Med. 2005 Jun;20(6):531-5.
29. Deber RB, Kraetschmer N, Urowitz S, Sharpe N. Do people want to be autonomous patients? Preferred roles in treatment decision-making in several patient populations. Health Expect. 2007 Sep;10(3):248-58.
30. Kuin A, Courtens AM, Deliens L, Vernooij-Dassen MJ, van Zuylen L, van der Linden B, et al. Palliative care consultation in The Netherlands: a nationwide evaluation study. J Pain Symptom Manage. 2004 Jan;27(1):53-60.
31. Brandt HE, Ooms ME, Ribbe MW, van der Wal G, Deliens L. Predicted survival vs. actual survival in terminally ill noncancer patients in Dutch nursing homes. J Pain Symptom Manage. 2006 Dec;32(6):560-6.
32. Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. Bmj. 2003 Jul 26;327(7408):195-8.

7

General discussion

In this thesis, we studied the practice of continuous palliative sedation (CPS) after the introduction of the Dutch national palliative sedation guideline in 2005, using a mixed methods design. This chapter presents the main findings of the studies, followed by an interpretation of these findings and a reflection on strengths and weaknesses of the studies. Finally some implications and recommendations for clinical practice and further research will be given.

MAIN FINDINGS

Findings from quantitative studies

The practice of CPS and guideline recommendations

We found that 82 % of the responding physicians knew the content of the national guideline, mostly in general terms. According to their reports, CPS-practices largely reflect the recommendations in the guideline regarding the two most important aspects (Chapter1): nearly all physicians stated that their last patient who had received CPS had experienced one or more refractory symptoms and nearly always such symptoms had led to unbearable suffering while physicians had estimated the life expectancy of the patient to be less than two weeks. Nevertheless, 13% of the respondents indicated to have problems with establishing whether a symptom is refractory and 29% had problems with the estimation of life expectancy.

We also identified several other discrepancies between guideline recommendations and CPS-practice: 3% of the patients were estimated to have had a life expectancy between 2 and 4 weeks at the start of CPS and 41% of the physicians thought that CPS might have had a life shortening effect (Chapter 2). Further, 7% of the patients had received artificial fluids during continuous deep sedation, and 19% of the physicians were not present at the start of sedation. In 22% of all cases, physicians had consulted a palliative care team prior to initiation of CPS. An additional finding from our studies, not referred to in the national guideline, was that one out of seven physicians felt pressured by patients or relatives to start CPS.

Physicians' and nurses' perspectives

We found that nurses more often than physicians report that patients suffer from anxiety preceding the start of continuous sedation and that pain is the decisive indication to start CPS. Nurses also more often than physicians thought that the physicians' intention for using sedation was to hasten the patient's death, but they less often felt pressure from patients or relatives to start CPS (Chapter 3).

CPS for non-cancer patients.

We found differences in palliative sedation practices between cancer patients and non-cancer patients. Firstly, dyspnoea and psychological exhaustion were more often reported as a decisive indication to start continuous sedation in non-cancer patients. Furthermore, for non-cancer patients, a palliative care team had been consulted less often prior to the initiation of sedation, sedation had more often been provided with the intention of hastening

death, and life more often was estimated to have been shortened as a consequence of sedation. (chapter 6).

Findings from qualitative studies

Findings from the qualitative studies offered more in-depth insights in palliative sedation practice.

Indications for CPS

Whereas the national guideline states that the indication for CPS is based on one or more refractory symptoms, we found that CPS may also be used to address an accumulation of physical and non-physical symptoms leading to a 'refractory state'.[1] Another finding was that opinions about the importance of the life expectancy criterion diverged. Some physicians consider imminence of death important (e.g. to avoid hastening of death), while others consider life expectancy to be less important when it is outweighed by the necessity to relieve refractory symptoms. Additionally, we found that the decision to use CPS may be influenced by preferences and values concerning a dignified and good death of patients and their relatives as well as caregivers (Chapter 4).

Depth of sedation

Physicians had two different approaches towards the depth of CPS. They either aim at deep sedation right from the start, or they start with mild sedation and only deepen it gradually if needed. In the guideline, proportional sedation is understood as sedation in which the dose of sedatives is individually titrated to the relief of distress caused by refractory symptoms.[1] We found that preferences of patients and relatives, the importance that patients and caregivers attach to preservation of communication, and the appearance of the patient, also contributed to physicians' approaches towards the depth of continuous sedation. We have denoted this approach as reasoning from a multidimensional concept of proportionality (Chapter 5).

INTERPRETATION

In the Netherlands, in 2001, continuous deep sedation was used in 5.6 % of dying patients. Since then, this figure rose from 8.2 % in 2005 to 12.3 % in 2010.[2,3] These frequencies reflect that palliative sedation has become a substantial practice in Dutch end of life care.

Whereas the Dutch guideline considers palliative sedation as a normal medical procedure of last resort, it is remarkable that the frequency of palliative sedation has doubled during the last decade. Has normal medical practice changed within this decade? Do physicians more often label specific interventions as palliative sedation? Do physicians, after the launch of the national guideline, feel more comfortable to use palliative sedation? Do these figures reflect a change of attitudes in patients, relatives or physicians towards dealing with severe suffering at the end of life?

Although these questions cannot be answered based on the studies presented in this thesis, they are relevant in view of the portrayal of palliative sedation in the Dutch national guideline. In this guideline palliative sedation is defined as the intentional lowering of con-

sciousness of a patient in the last phase of life.[4] If practiced properly, the national guideline considers palliative sedation as a normal medical procedure, "meaning that indications and procedures for its use are determined by current standards within the medical profession, and that it is the right of patients to receive palliative sedation (like other normal medical procedures), if the accepted indications and preconditions are present".[4] The guideline describes euthanasia as an exceptional medical procedure that is based on a well-considered request of a patient. Other differences between palliative sedation and euthanasia that are mentioned in the guideline are: CPS relieves suffering by lowering consciousness while euthanasia does so by terminating life; deep CPS does not in itself shorten life, while euthanasia certainly does; and deep CPS is in principle reversible, while euthanasia is not.

This thesis shows that the practice of CPS largely, but not in all cases, reflects the recommendations of the national guideline. Therefore, it can be questioned to what extent CPS can be regarded as a *normal* medical procedure in *all* cases. This can be illustrated by looking more closely at the two most important preconditions for CPS (refractory symptoms and a limited life expectancy) and the use of consultation of expert palliative care services.

Refractory symptoms and depth of sedation

Although guidelines on palliative sedation take into account psychosocial and existential dimensions[4-6], some stress the importance of the physical aspects of suffering.[7] In chapter 2 we show that in case a combination of symptoms was considered decisive for the indication for CPS, psychosocial and existential factors more frequently contributed.

While specific refractory symptoms are often an important indication to use CPS, this thesis also shows that CPS may also be used to relieve the general state the patient is in (chapter 4). Guidelines stress that CPS should be applied proportionately. CPS is then recommended to involve administration of the minimal titrated dosage of sedatives needed to achieve proper relief of refractory symptoms. This thesis describes that psychosocial and existential dimensions of suffering may contribute to refractoriness[8], illustrating the importance of proper and timely assessment of these dimensions to facilitate a good quality of death and dying.[9]

The indication for which CPS is used also impacts the desired depth of sedation. We found two different approaches: mild sedation that is gradually increased if needed and deep sedation from the start. The severity of symptoms, but also preferences of patients and relatives, the importance that is attached to communication and the appearance of the patient contribute to deciding upon the dosages of sedating drugs administered. This illustrates, that in clinical practice, proportionality is a multidimensional concept. Thus, CPS may not in all cases be a strictly medical response to a strictly medical problem. This may not per se be considered problematic if one accepts the multidimensional nature of medical care at the end of life. However, our finding that physicians not infrequently feel pressured by patients and relatives to initiate CPS, suggests that the decision making process regarding continuous palliative sedation does not always run smoothly and that physicians sometimes struggle with how to weigh preferences of patients and relatives in the decision making process. The multidimensional nature of medical care at the end of life involves that there is often no one-size-fits-all approach to address patients' needs. Careful and clear information and communication about the use of CPS are thus very important and preferably started in an early phase.

Life expectancy

A characteristic feature of patients who are approaching the point at which death is inevitable is that they virtually cease to eat and drink. To prevent that eating and drinking cease because of the start of continuous sedation, i.e. to prevent that the start of sedation may lead to hastening death by dehydration, the guideline includes a life expectancy criterion: the sedation is not considered to be a causal factor in the dying process, when at the start of CPS the patient's life expectancy is less than two weeks. The guideline assumes that within this timeframe the patient does not benefit from artificial administration of fluids, so these should not be initiated or continued during CPS. Adherence to this criterion is a prerequisite for considering CPS as a normal medical procedure, i.e. a procedure that does not hasten death. A small minority of the cases (3%) in our study did not meet this criterion.

Ample literature demonstrates the uncertainties regarding prognostication and estimating life-expectancy.[10-13] Since valid predictions of patients' life expectancy apparently are so difficult to make, one should question the applicability of the guidelines' life expectancy criterion in clinical practice. For instance, should on the basis of this criterion CPS not be initiated when a patient is suffering from refractory symptoms while having an estimated life expectancy of three weeks or not be started in case the physician is unsure about whether the life expectancy criterion applies? Our studies suggest that some physicians would use CPS for unbearably suffering patients in whom death is not imminent, with the argument that they feel a duty to relieve the patient's suffering.
So, apparently, when ends meet physicians may interpret the criterion of life expectancy in view of the circumstances. Thus the question arises how to deal with uncertainties around non-adherence to the guidelines' life expectancy criterion. One way of addressing this issue is to try to make the life expectancy criterion concrete in such a way that it can be more easily applied in clinical practice. Another way is to accept that estimating life expectancy will always be surrounded by uncertainties.

Making the life expectancy criterion applicable more concretely, may be possible for instance by using clinical characteristics of dying.[12] In a recent study decreased blood pressure and low oxygen saturation were identified as factors that reliably predict death.[14] The authors of this study point out that because these factors may vary during the course of illness, awareness of the clinical trajectory that preceded the terminal phase is very important to recognize a patient is dying. This is also highlighted in the Liverpool Care Pathway for the dying patient (LCP).[15] The LCP acknowledges that clinical signs associated with approaching death may vary according to the underlying diagnosis and must be interpreted in light of the overall clinical picture of the patient. Clinical signs that may be observed in dying patients include somnolence, anuria, 'livid spots', death rattle, cyanosed extremities, pulseless radial artery, reduced oral intake and difficulty with oral medications.[16-18] In the most recent version of the LCP, it is stated that, to prevent a mistaken diagnosis of dying, the LCP should only be started if the team of caregivers confirms the statement 'the team believes the patient is dying', which statement should be reassessed at least every 3 days.[15] The fact that even a care pathway for the dying states that diagnosing dying should be reassessed every three days, may be interpreted as a reflection of what is described elsewhere as an 'inherent uncertainty' in predicting dying.[19] Thus diagnosing dying is not simply checking symptoms and signs, but also interpreting them within the context of a disease trajectory,

which requires clinical experience and expertise.[12] Despite the aforementioned inherent uncertainty, in clinical practice, diagnosing the imminence of death becomes less difficult the nearer death is. Adding clinical and laboratory signs to the life expectancy criterion may increase the applicability of this criterion. Others have suggested that decision making on when to start CPS may be facilitated by emphasizing the importance of clinical signs of approaching death in the national guideline.[20]

However, making the life expectancy criterion more concrete does not solve the issue of patients who are suffering unbearably from refractory symptoms while not meeting the life expectancy criterion, or for whom it remains uncertain or unlikely that this criterion applies. The question remains: how to deal with patients suffering from refractory symptoms with a life expectancy that (possibly or probably) exceeds two weeks. This brings us back to the inevitable consequence of accepting that prognostication will continue to be surrounded by uncertainties. This is not to say that it is impossible to make worthwhile statements about life expectancy. Rather, the uncertainties or difficulties relating to estimating patients' life expectancy in end of life care can offer an opportunity for physicians to discuss the meaning of clinical signs and symptoms with patients and their relatives. Prognostication has been described to involve two components: formulating the prediction and its uncertainty (i.e. foreseeing) as well as communicating the prediction (i.e. foretelling).[21] Foretelling involves communication, not only with the patient and relatives, but also with other health care professionals. Proper communication about prognostication amongst health care professionals may facilitate and/or prepare the act of informing patients and relatives about impending death. When a team has agreed that certain clinical signs within a specific disease trajectory suggest that the patients' death is imminent, caregivers can share this information with the patient and relatives. After this information has been communicated, a change in focus of care can be marked and care can be adapted accordingly.

Although it is impossible to foresee in all cases how disease trajectories will develop, timely discussion of possible routes and patients' preferences regarding the last phase of their lives may preclude preventable suffering and facilitate decision making. Shared decision making, advance care planning and preference based medicine should therefore emphatically be supported,[22-24] especially in view of recent findings that perspectives of physicians on decision making and treatment at the end of life not necessarily coincide with those of the general public.[25,26] In this respect adequate transfer of medical information is crucial, especially during out of hours services.[27,28]

Consultation

This thesis demonstrates that physicians' reasons for seeking advice from a palliative care team prior to the initiation of CPS predominantly concern the assessment of refractoriness, advice on medication and anticipation of what may come (Chapter 2). Furthermore, although physicians consider it helpful in cases of both cancer and non-cancer patients, consultation was sought less often for non-cancer patients.[29] In its 2009-update, the guideline committee reflected upon whether consultation before initiating CPS should be made compulsory. Recently, important reasons for Dutch physicians to consult a palliative consultation team prior to the use of CPS were described: lack of expertise, and general and emotional support when decision making is complicated.[30] In this study also objections

against mandatory consultation were formulated. Practical objections were found to relate to a lack of time and a possible inhibitory effect of obligation. Theoretical objections related to the argument that obligating consultation might collide with the professional responsibility of physicians and the argument that this would change the status of palliative sedation as normal medical practice. Others have argued that objections against mandatory consultation might well be related to the fact that the guideline presents palliative sedation as a normal medical procedure in sharp contrast with euthanasia, which is a 'non-normal' or exceptional medical procedure for which consultation of an independent physician is legally required.[31,32] The approach of the guideline may thus blur the fact that consultation and normal medical treatment are not at all mutually exclusive.[31]

Both timely discussion of patients' preferences regarding the last phase of their lives and timely expert consultation in difficult cases are important elements of high quality medical care at the end of life. In view of these considerations, expert consultation should be considered as an important element of CPS as a practice that touches upon the borders of normal medical practice. It is at the same time important to acknowledge that timely consultation may not always be possible e.g. because of unforeseeable or rapidly evolving clinical emergencies. Nevertheless, a starting point of all normal medical practice should be: whenever there is lack of expertise, consultation of exert services is an essential part of such practice. This is not to say that lack of experience is the only reason for consulting such services. Also physicians who are experts in CPS come across complicated cases or difficult issues. In such cases, inter-subjectivity may be the (only) basis for proper decision-making. Therefore, it should be part of normal medical practice to seek for advice in complex cases, both for experienced and less experienced physicians. If the assessment of refractoriness or estimating life expectancy is difficult, such consultation may involve seeking a second opinion of a physician. If the complexity relates to hampering communication, clergy, social workers or psychologists can be consulted. Normal medical practice is not a given. The normality of CPS as a normal medical procedure can be shown in the way it is practised, taking into account legal, medical and ethical regulations, guidelines or principles. Organising, facilitating and using expert consultation services is part of normal medical practice

STRENGTHS AND WEAKNESSES

Since the terminology regarding palliative sedation greatly varies, for the purpose of this thesis we studied this practice from a well-defined perspective: continuous palliative sedation. To minimise possible differences in the perception of what CPS entails across the respondents we provided them with a description of the practice that we used in both the original quantitative questionnaire and the subsequent qualitative interviews: continuous sedation until death. This description refers to the use of sedatives in patients, at the end of life, intended specifically for lowering consciousness continuously from a certain point in time until the patient dies. In addition to research only focusing on continuous deep sedation,[2,33-35] we also included continuous mild sedation in our studies. A major strength of the mixed methods design is that it adds an in-depth analysis of considerations on CPS to a general description of the frequency of this practice and its characteristics. Inclusion of both physicians and nurses from different settings allowed for a broad practice- based

description. To our knowledge this is the first time this method is used in studying the practice of CPS.

Quantitative studies

Recall bias might have influenced our findings. Difficulties in recollecting the details of the patient were sometimes mentioned by physicians who were consultant in palliative care and who after filling out the questionnaire had been involved in other cases, or by nurses who could not get access to the medical files. Despite great efforts the response rates for the quantitative studies were moderate, although comparable with other studies in this area.[8] Physicians were selected randomly, but it was not possible to select nurses randomly, because for them a complete data base does not exist. Selection bias might have been a problem since especially physicians and nurses with a specific interest in the research topic may have responded.

Qualitative studies

In addition to the strengths and weaknesses mentioned above some issues hold especially for the qualitative interviews. We used semi-structured interviews with prompts. All interviewers received an interview training during which interview-techniques were taught and which was concluded with a pilot interview. To ensure that all interviewers asked the same questions, interviewers were instructed to read the questions literally. During the interview period, the interviewers met in monthly sessions aimed at discussing the findings and interim analyses, with special attention to consistency in interviewing practices among the interviewers. We aimed at including physicians and nurses from different settings where CPS occurs, as well as different cases with respect to the depth of sedation. With the conclusion of all prescheduled interviews, the interviewers agreed that they had captured all relevant perspectives for our studies. Physicians and nurses were asked in the original quantitative questionnaire if they would be willing to participate in an additional qualitative interview study. Since all participants in these qualitative interviews volunteered, this may have resulted in further selection bias.

IMPLICATIONS AND RECOMMENDATIONS

This thesis reveals that in clinical practice the application of recommendations from the national palliative sedation guideline varies. Does this mean that the guideline should be adjusted? Or does this mean that practices should be adjusted? Prior to thinking in terms of possible adjustments, whether in the guideline or in practice, it should be first noticed that apparently some kind of tension exists between 'what the guideline recommends' and 'how this may work out in practice'.

The national palliative sedation guideline emphasizes that proper communication with patients and relatives is paramount and that their wishes and preferences should be taken into account. Our studies however show that careful communication apparently not only forms the basis of the decision making on CPS, but that in turn such communication also influences decision making: preferences of patients and relatives contribute to the indications for and the depth of CPS. An uncertain prognosis, an unpredictable disease trajectory and emotions such as fear and despair may impede communication between health care

professionals, patients and their relatives about how to respond to severe suffering of dying patients.

Ultimately, the response to a difficult clinical situation is born in practice, taking into account legal, medical and ethical regulations, guidelines or principles. By providing a practical and legal framework, guidelines not only offer a starting point for such responses, they also facilitate asking relevant questions in complex clinical situations and their evaluation. The tension between guideline recommendations and their application in practice must be understood as an opportunity for moral and clinical reflection on a specific case. For example with respect to our finding that in practice there sometimes may be a tendency to let 'relief of suffering' prevail above 'always strictly following guideline recommendations on life expectancy'. Health care professionals should regard this as a starting point for and an opportunity to account for possible deviations from the guideline. Timely consultation of experienced colleagues or expert services is helpful. The objections against (mandatory) consultation[30,32] may be reconsidered in view of our finding that CPS can involve decision making in complex situations and the fact that the practice of CPS touches upon the borders of normal medical practice.

Transparency on and awareness of deviations from the guideline should be part of normal practice. Such a practice of continuous palliative sedation in turn is an important source of information for development of the guideline. Practice based information may give rise to adjustments, as already has been shown by the 2009-update of the guideline. Bearing in mind that there always will be more questions than can be answered, this thesis demonstrates how Dutch physicians and nurses deal with clinical situations in which CPS is practised. It would be worthwhile to initiate comparable studies in other countries. Not only to compare practices, but also to learn from each other how to deal with complexities at the end of life and to be able to evaluate how cultural and spiritual issues may influence end-of-life practices. Taking into account the perspective of patients and relatives more explicitly than we were able to do would further enrich such studies.

References

1. Swart SJ, Brinkkemper T, Rietjens JA, Blanker MH, van Zuylen L, Ribbe M, et al. Physicians' and nurses' experiences with continuous palliative sedation in the Netherlands. Arch Intern Med. 2010 Jul 26;170(14):1271-4.
2. Rietjens J, van Delden J, Onwuteaka-Philipsen B, Buiting H, van der Maas P, van der Heide A. Continuous deep sedation for patients nearing death in the Netherlands: descriptive study. BMJ. 2008 Apr 12;336(7648):810-3.
3. Onwuteaka-Philipsen BD, Brinkman-Stoppelenburg A, Penning C, de Jong-Krul GJ, van Delden JJ, van der Heide A. Trends in end-of-life practices before and after the enactment of the euthanasia law in the Netherlands from 1990 to 2010: a repeated cross-sectional survey. Lancet. 2012 Sep 8;380(9845):908-15.
4. KNMG. KNMG-richtlijn palliatieve sedatie 2009. http://knmgartsennetnl/Diensten/knmgpublicaties/KNMGpublicatie/Guideline-for-palliative-sedation-2009htm. 2009.
5. Broeckaert B, Mullie A, Gielen J, Desmet M, Vanden Berghe P. Ethics Commission Federation Palliative Care Flanders. Palliative Sedation Guideline. 2010 [30 novembre 2011]; Available from: http://www.pallialine.be/template.asp?f=rl_sedatie.htm#page=page-1.
6. Cherny NI, Radbruch L, Board of the European Association for Palliative C. European Association for Palliative Care (EAPC)

recommended framework for the use of sedation in palliative care. Palliat Med. 2009 Oct;23(7):581-93.
7. AMA. Sedation to Unconsciousness in End-of-Life Care. 2008 [cited 2012 March 9]; Available from: http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2201.page.
8. Hasselaar JG, Verhagen SC, Wolff AP, Engels Y, Crul BJ, Vissers KC. Changed patterns in Dutch palliative sedation practices after the introduction of a national guideline. Arch Intern Med. 2009 Mar 9;169(5):430-7.
9. Hales S, Zimmermann C, Rodin G. The quality of dying and death. Arch Intern Med. 2008 May 12;168(9):912-8.
10. Brandt HE, Ooms ME, Ribbe MW, van der Wal G, Deliens L. Predicted survival vs. actual survival in terminally ill noncancer patients in Dutch nursing homes. J Pain Symptom Manage. 2006 Dec;32(6):560-6.
11. Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. Bmj. 2003 Jul 26;327(7408):195-8.
12. Glare PA, Sinclair CT. Palliative medicine review: prognostication. J Palliat Med. 2008 Jan-Feb;11(1):84-103.
13. Clarke MG, Ewings P, Hanna T, Dunn L, Girling T, Widdison AL. How accurate are doctors, nurses and medical students at predicting life expectancy? Eur J Intern Med. 2009 Oct;20(6):640-4.
14. Hwang IC, Ahn HY, Park SM, Shim JY, Kim KK. Clinical changes in terminally ill cancer patients and death within 48 h: when should we refer patients to a separate room? Support Care Cancer. 2012 Sep 7.
15. J E. Liverpool Care Pathway for the Dying Patient (LCP). 2009 [cited 2012 06 Decembre]; Available from: http://www.liv.ac.uk/mcpcil/liverpool-care-pathway/.
16. Morita T, Ichiki T, Tsunoda J, Inoue S, Chihara S. A prospective study on the dying process in terminally ill cancer patients. Am J Hosp Palliat Care. 1998 Jul-Aug;15(4):217-22.
17. Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK. Oxford Textbook of Palliative Medicine (ed). 2011.
18. van Zuylen C, van Veluw H, van Esch J. Richtlijn Zorg in de stervensfase. 2009 [cited 2012 06 Decembre]; Available from: http://www.pallialine.nl/stervensfase.
19. Taylor PM, Johnson M. Recognizing dying in terminal illness. Br J Hosp Med (Lond). 2011 Aug;72(8):446-50.
20. van Wijlick E, de Graeff A, Verkerk M, Legemaate J. [Meer houvast voor arts. Medisch Contact. 2009 22 januari 2009(5):194-7.
21. Glare P, Sinclair C, Downing M, Stone P, Maltoni M, Vigano A. Predicting survival in patients with advanced disease. Eur J Cancer. 2008 May;44(8):1146-56.
22. Detering KM, Hancock AD, Reade MC, Silvester W. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. BMJ. 2010;340:c1345.
23. Quill TE, Holloway RG. Evidence, preferences, recommendations–finding the right balance in patient care. N Engl J Med. 2012 May 3;366(18):1653-5.
24. Bakitas M, Kryworuchko J, Matlock DD, Volandes AE. Palliative medicine and decision science: the critical need for a shared agenda to foster informed patient choice in serious illness. J Palliat Med. 2011 Oct;14(10):1109-16.
25. van Delden JJM, van der Heide A, van de Vathorst S, Weyers H, van Tol DG. Kennis en opovattingen van publiek en professionals over medische besluitvorming en behandeling rond het einde van het leven. Het KOPPEL-onderzoek. Den Haag, ZonMw. 2011.
26. Rietjens JA, Raijmakers NJ, Kouwenhoven PS, Seale C, van Thiel GJ, Trappenburg M, et al. News media coverage of euthanasia: a content analysis of Dutch national newspapers. BMC Med Ethics. 2013;14:11.
27. Schweitzer BP, Blankenstein N, Deliens L, van der Horst H. Out-of-hours palliative care provided by GP co-operatives: availability, content and effect of transferred information. BMC Palliat Care. 2009;8:17.
28. Slort W, Schweitzer BP, Blankenstein AH, Abarshi EA, Riphagen, II, Echteld MA, et al. Perceived barriers and facilitators for general practitioner-patient communication in palliative care: a systematic review. Palliat Med. 2011 Sep;25(6):613-29.
29. Swart SJ, Rietjens JA, van Zuylen L, Zuurmond WW, Perez RS, van der Maas PJ, et al. Continuous Palliative Sedation for Cancer and Noncancer Patients. J Pain Symptom Manage. 2011 Sep 17.
30. Koper I, van der Heide A, Janssens R, Swart SJ, Perez RS, Rietjens JA. Consultation with

specialist palliative care services in palliative sedation. Considerations of Dutch Physicians. (submitted)
31. Janssens R, van Delden JJ, Widdershoven GA. Palliative sedation: not just normal medical practice. Ethical reflections on the Royal Dutch Medical Association's guideline on palliative sedation. J Med Ethics. 2012 Nov;38(11):664-8.
32. Keizer AA, Swart SJ. [Palliative sedation, the sympathetic alternative for euthanasia?] Palliatieve sedatie, het sympathieke alternatiefvoor euthanasie? Ned Tijdschr Geneeskd. 2005 Feb 26;149(9):449-51.
33. Chambaere K, Bilsen J, Cohen J, Rietjens JA, Onwuteaka-Philipsen BD, Mortier F, et al. Continuous deep sedation until death in Belgium: a nationwide survey. Arch Intern Med. 2010 Mar 8;170(5):490-3.
34. Carvalho TB, Rady MY, Verheijde JL, Robert JS. Continuous deep sedation in end-of-life care: disentangling palliation from physician-assisted death. Am J Bioeth. 2011 Jun;11(6):60-2.
35. Raus K, Sterckx S, Mortier F. Continuous Deep Sedation at the End of Life and the 'Natural Death' Hypothesis. Bioethics. 2011 Jan 17.

8

Summary
Samenvatting

SUMMARY

Palliative sedation is a medical intervention aimed at relieving intractable suffering at the end of life. Palliative sedation can be initiated for severe, intractable (= refractory) symptoms when patients have a life expectancy less than two weeks. Then, to establish symptom relief drugs are administered to lower the consciousness of the patient. In 2005 the Royal Dutch Medical Association (RDMA) launched a national guideline. In this guideline palliative sedation is defined as 'the intentional lowering of consciousness of a patient in the last phase of life'. The guideline further explicates that palliative sedation should be administered proportionally: it is the degree of symptom control rather than the degree to which consciousness must be reduced that determines the dose, combinations, and duration of the drugs administered. Palliative sedation practised in such a way is considered a normal medical procedure, meaning –according to the guideline- 'that the indications for it and its use in medical practice are determined by current standards within the medical profession, and that it is the right of patients to receive palliative sedation (like other normal medical procedures), provided the accepted indications and preconditions are present.'
Palliative sedation refers to several subtypes of sedation: intermittent or continuous sedation and deep or mild sedation. In the national guideline recommendations are formulated regarding the decision making and the procedure of palliative sedation. The most important recommendations in the guideline in view of our research are listed in box 1.

Box 1 Most important criteria and recommendations regarding the use of continuous palliative sedation until death (CPS) in the Dutch national guideline.

Decision making
- Indication: one or more refractory symptoms, leading to unbearable suffering for the patient.
- 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 his 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.

Procedure
- 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 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, no artificial administration of fluids should be provided.
- Accurate records must be kept about the decision-making process, the way medication for palliative sedation is being administered as well as the effect of this intervention

We studied the practice of continuous palliative sedation (including both deep and mild sedation) after the launch of the national guideline in 2005 and formulated the following research questions:
1. Is physicians' practice of Continuous Palliative Sedation (CPS) in accordance with the main recommendations of the Dutch national guideline on palliative sedation?

2. Do the perspectives of nurses regarding the practice of palliative sedation differ from those of physicians?
3. What considerations do physicians and nurses have regarding the indications for CPS and what factors influence these considerations?
4. What arguments do physicians use for choosing the depth of CPS?
5. Does the practice of CPS differ between cancer and non-cancer patients?

The practice of CPS and guideline recommendations

In ***chapter 2*** we present a study investigating whether the practice of CPS is in accordance with the main recommendations of the Dutch national guideline on palliative sedation.
A total of 606 out of 1580 physicians (response rate 38%) working in general practice, nursing homes or hospitals filled out a questionnaire inquiring about the last patient for whom they had used CPS. We found that CPS-practice largely reflected the guideline recommendations. All patients had one or more refractory symptoms that nearly always had led to unbearable suffering. We found that -next to dyspnoea, pain and delirium-, physical exhaustion and existential suffering were fairly often reported as being decisive for starting continuous sedation.
Accordance with guideline recommendations was also found with respect to the life expectancy criterion: in nearly all cases physicians estimated the life expectancy of the patient to be less than two weeks. Taking into account that physicians commonly have difficulties with estimating life expectancy, and are often inclined to overestimate, this suggests that this precondition for the application of continuous sedation, i.e. the expectation that death will ensue in the reasonably near future, is mostly adhered to.
We also identified a few topics that did not reflect the recommendations of the RDMA guideline. Although the guideline states that proportionally administered palliative sedation does not lead to hastening of death, some physicians use continuous palliative sedation with a (partly) intention to hasten death or think that the administration of sedation had a (minor) life-shortening effect. Furthermore, while the guideline recommends not administering artificial fluids in cases of continuous deep sedation until death, artificial fluids were provided in a minority of cases. Finally, in one-fifth of the cases, there was no physician present at the start of continuous sedation.

Physicians' and nurses' perspectives

Next to physicians, 278 out of 576 nurses (response rate 48%) working in homecare, nursing homes, hospices or hospitals filled out a questionnaire inquiring about their last patient for whom CPS had been used. In ***chapter 3*** we present a study investigating whether the perspectives of nurses regarding the practice of palliative sedation differ from those of physicians. We found that nurses more often than physicians indicated that patients were anxious prior to the start of continuous sedation and they more often mentioned pain as the decisive indication for starting CPS. Nurses also more often thought that the physicians' intention for using sedation was to hasten the patient's death, but they less often felt pressure from patients or relatives to start CPS. These differences may be a reflection of the different roles of physicians and nurses in clinical practice. First of all, nurses usually have more frequent contacts with patients, so both anxiety and pain might be more easily recognized. Secondly, the differences might reflect physicians' and nurses' different responsibilities. Because physicians decide on the use of continuous palliative sedation, patients and

relatives might in particular put pressure on them to start sedation. Our finding that more nurses than physicians think that continuous sedation was used (partly) with an intention to hasten death, may reflect that physicians not always communicate clearly about their intentions. This stresses the importance of careful communication between physicians and nurses regarding the indications for and the procedure of CPS.

Indications for CPS

We asked both physicians and nurses who filled out the questionnaire if they were willing to participate in an additional qualitative interview. In chapter 4 we present an interview study investigating physicians' (n=54) and nurses' (n=36) considerations concerning the two most important conditions for initiating CPS: refractory symptoms and a life expectancy less than two weeks. Health care providers not only provided CPS in situations in which one symptom was decisive. CPS was also used to address an accumulation of physical and non-physical symptoms leading to a 'refractory state'. In these situations suffering is not so much refractory because of the absence of treatment options for a specific symptom, but due to the impossibility of relieving the overall state the patient is in.

In ***chapter 4*** we also describe that considerations regarding the importance of the life expectancy criterion for CPS diverged. Some physicians consider it important that CPS is only initiated when death is imminent to avoid possible associations with hastening of death, while other physicians consider the precondition of life expectancy to be less important when this is outweighed by an urge or a necessity to relieve refractory symptoms. In literature, initiating CPS in patients with a longer life expectancy has been described as 'early terminal sedation'. Furthermore, we describe in ***chapter 4*** that the indication for CPS may also be influenced by preferences and values of patients and relatives concerning notions regarding how sedation can contribute to a dignified and good death. When the preferences and wishes of the patient and the relatives are known, this may facilitate the decision to start CPS. However, it may sometimes also complicate decision making, especially when health care providers feel that they are put under pressure to start CPS.

Depth of sedation

In ***chapter 5,*** we present an interview study investigating the considerations of physicians (n=54) regarding the depth of continuous sedation. We found two different approaches towards the depth of CPS. Physicians either aim at deep sedation right from the start, or they aim at mild sedation and only deepen it gradually if needed. Preferences of patients and relatives not only influence *the indications* for CPS (chapter 4), but also contribute to the choice for *the depth* of continuous sedation. Patients' and relatives' fear of awaking from sedation or the patients' conviction that 'it has been enough', may affect the dosage of sedatives administered. The importance that physicians attach to communication also influences the depth of sedation. Whereas preservation of communication is often considered important as it allows for (re)assessment of the indication and efficacy of palliative sedation, we found that preservation of communication can also considered to be a goal in itself. Physicians who consider preservation of communication important, in general opted for mild sedation instead of deep sedation. Also, the search for peacefulness and comfort plays a role in choosing the depth of sedation. In some cases this leads to an approach aiming for deep sedation from the start. In other cases this leads to a more gradual approach that reflects 'a more natural way of dying'. In guidelines, proportional sedation is typically understood as

sedation in which the dose of sedatives is individually titrated to the relief of distress caused by refractory symptoms, implying that consciousness is reduced no more than necessary to properly relieve suffering. Our study shows that in actual medical practice proportionality seems to be understood as more than strictly titrating drugs to the severity of refractory symptoms. Preferences of patients and relatives, preservation of communication as well as appearance and comfort of the patient also contribute. On the basis of our findings we conclude that the notion of proportionality should be understood as a multidimensional notion.

CPS for non cancer patients.

In ***chapter 6,*** we present a questionnaire study comparing the practice of CPS for non-cancer patients (e.g heart failure) with the practice for cancer patients. Dyspnoea and psychological exhaustion were more often reported as a decisive indication to start continuous sedation in non-cancer patients than in cancer patients. For non-cancer patients, a palliative care team had been consulted less often before the start of sedation and life more often was estimated to have been shortened more than a day as a consequence of sedation. We suggest that the different nature of disease trajectories may account for the differences in CPS practices between cancer patients and non-cancer patients. End-of-life disease trajectories in non-cancer patients often involve a rather long-term fluctuating process of gradual decline punctuated by episodes of acute deterioration and eventually a seemingly unexpected death. Such trajectories may make it more difficult to decide when a palliative care approach, including consultation of a palliative care team, would be appropriate. We therefore recommend timely incorporation of palliative care services in advance care planning for non-cancer patients. This may facilitate the proper and timely recognition, support and treatment of physical, psychosocial as well as spiritual aspects of symptoms.

Interpretation

In ***chapter 7*** the main findings of this thesis are summarized and interpreted. Strengths and weaknesses of the studies are addressed, and implications and recommendations for clinical practice and future research are formulated.

This thesis shows that both psychosocial and existential dimensions of suffering may have great impact on the decision to use CPS. Further, although specific refractory symptoms are often an important indication to use CPS, we found that CPS is also used to relieve the general state the patient is in. Next to the severity of symptoms, also preferences of patients and relatives, the importance that is attached to communication and the appearance of the patient contribute to deciding upon the dosages of sedating drugs administered. This reflects that in the practice of CPS proportionality can be interpreted as a multidimensional notion. This notion may elicit two responses towards the depth of CPS: physicians initiate deep sedation right from the start or start mild sedation and deepen it if needed.

Opinions about the importance of the life expectancy criterion for CPS diverged. Some physicians consider it important that patients are in de dying phase before CPS is initiated, while others weigh the life expectancy criterion against the necessity to relieve refractory symptoms. Ample literature is available demonstrating the uncertainties related to prognostication and estimating life-expectancy. Although the life expectancy criterion can be made more concrete by incorporating clinical characteristics, these uncertainties can never be entirely taken away. Communication about clinical characteristics in the last phase of life

and their meaning may facilitate a timely change in focus of care contributing to a proper end of life care.
Not only timely discussion of patients' preferences regarding the last phase of their lives is an important element of high quality medical care at the end of life: the same holds for expert consultation. Since CPS touches upon the borders of normal medical practice, expert consultation should be considered as an important means for considering continuous palliative sedation normal medical practice.

Finally

And then the final chapter, which I think in fact should be considered as the first chapter: words of thanks. In this chapter I have tried to say thanks, to all the people who have contributed somehow to this thesis. Not only the people who learned me 'how to do research', but also the patients who taught me how to be a doctor and the people who taught me how to love, to work together and to teach. Since it took me quite some time to find my own way in research, these words of thanks refer to a period of many years. This may risk that not all names that should have been mentioned in the final chapter, in fact are mentioned there. Therefore, I want to say to all the people who were not in my head during the writing of my words of thanks: you are in my heart.

SAMENVATTING

Palliatieve sedatie is een medische handeling die gericht is op het verlichten van ernstig lijden aan het einde van het leven. Palliatieve sedatie kan worden toegepast als er ernstige, onbehandelbare (= refractaire) symptomen bestaan en de levensverwachting van de patiënt minder is dan twee weken. Om dan toch symptoomverlichting te bereiken worden medicamenten gebruikt die het bewustzijn van de patiënt verlagen. In 2005 bracht de Koninklijke Nederlandsche Maatschappij tot bevordering der Geneeskunst (KNMG) een landelijke richtlijn uit. Hierin wordt palliatieve sedatie gedefinieerd als het opzettelijk verlagen van het bewustzijn van een patiënt in de laatste levensfase. Verder geeft de richtlijn aan dat palliatieve sedatie proportioneel dient te worden toegepast: niet de mate van bewustzijnsverlaging, maar de mate van symptoomcontrole bepaalt de dosering, de combinaties en de duur van de inzet van medicamenten die gebruikt worden. Op deze wijze toegepaste palliatieve sedatie beschouwt de richtlijn als normaal medisch handelen. Dit houdt in "dat de geldende medisch-professionele standaard de indicatiestelling en de toepassing van palliatieve sedatie bepaalt en dat palliatieve sedatie (net als alle andere vormen van normaal medisch handelen) een recht is van de patiënt, mits aan de binnen de beroepsgroep geaccepteerde indicatie en voorwaarden is voldaan." Palliatieve sedatie kan continu, tijdelijk of met tussenpozen (intermitterend) worden toegepast en diep of oppervlakkig. In de KNMG-richtlijn worden aanbevelingen gedaan voor besluitvorming over en uitvoering van palliatieve sedatie. De voor ons onderzoek belangrijkste aanbevelingen uit de richtlijn zijn weergegeven in kader 1.

Kader 1 Belangrijkste criteria en aanbevelingen met betrekking tot Continue Palliatieve Sedatie (CPS) in de KNMG-richtlijn palliatieve sedatie.

Besluitvorming

- De indicatie voor palliatieve sedatie wordt gevormd door het bestaan van één of meer onbehandelbare ziekteverschijnselen (refractaire symptomen), welke leiden tot ondraaglijk lijden van de patiënt.
- Bij continu en diep sederen tot het moment van overlijden is een levensverwachting van hooguit één tot twee weken een voorwaarde.
- Palliatieve sedatie wordt toegepast na een zorgvuldige exploratie van de situatie van de patiënt. Hierbij is informatie afkomstig van de patiënt, diens vertegenwoordiger(s) en de betrokken hulpverleners essentieel. Alleen in acute situaties waarin het niet mogelijk is voorafgaand aan het besluit tot sedatie te overleggen, heeft de behandelend arts de ruimte om zonder uitgebreid overleg op geleide van de toestand van de patiënt tot palliatieve sedatie te besluiten.
- Het consulteren van een deskundig arts is een voorwaarde als de arts onvoldoende deskundigheid heeft en/of als twijfel bestaat over kernpunten (de indicatie, de levensverwachting).

Uitvoering

- De sedatie is gericht op het verlichten van lijden en niet op het bespoedigen of uitstellen van de dood.
- De behandelend arts dient aanwezig te zijn bij de start van continue palliatieve sedatie.
- Midazolam is het medicament van keuze: het gebruik van morfine als sedativum wordt beschouwd als onjuiste praktijk. Morfine dient alleen toegediend of gecontinueerd te worden (naast sedativa) om pijn en/of benauwdheid te verlichten.
- Bij continue en diepe sedatie tot het moment van overlijden wordt geen kunstmatig vocht toegediend.
- Goede verslaglegging ten aanzien van het besluitvormingsproces, de uitvoering en het effect van palliatieve sedatie is een vereiste.

Wij bestudeerden de praktijk van continue palliatieve sedatie tot aan het overlijden (zowel diepe als oppervlakkige sedatie) na het verschijnen van de KNMG-richtlijn in 2005. Hiervoor formuleerden wij de onderstaande onderzoeksvragen:

1. Is de wijze waarop Continue Palliatieve Sedatie (CPS) door artsen in de praktijk wordt toegepast in overeenstemming met de belangrijkste aanbevelingen van de KNMG-richtlijn palliatieve sedatie?
2. Verschillen de ervaringen van verpleegkundigen rond de praktijk van CPS met die van artsen?
3. Wat zijn de overwegingen van artsen en verpleegkundigen met betrekking tot de indicaties voor CPS en welke factoren hebben invloed op deze overwegingen?
4. Welke argumenten gebruiken artsen bij het kiezen van de diepte van CPS?
5. Bestaan er verschillen tussen de praktijk van CPS voor patiënten met kanker en patiënten met niet-oncologische aandoeningen?

De praktijk van CPS en aanbevelingen van de KNMG-richtlijn

In ***hoofdstuk 2*** wordt beschreven in hoeverre de praktijk van CPS in overeenstemming is met de belangrijkste aanbevelingen van de KNMG-richtlijn palliatieve sedatie.
In totaal vulden 606 van de 1580 benaderde artsen (respons 38%) werkzaam in de eerste lijn, verpleeghuizen of ziekenhuizen een vragenlijst in over de laatste patiënt bij wie zij CPS hadden toegepast. Wij vonden dat de praktijk van CPS in grote lijnen aansluit bij de aanbevelingen van de richtlijn. Alle patiënten hadden één of meer refractaire symptomen die in bijna alle gevallen hadden geleid tot ondraaglijk lijden. Naast kortademigheid pijn en delier werden lichamelijke uitputting, existentieel lijden en geestelijke uitputting ook genoemd als doorslaggevende symptomen voor het starten van CPS. Met betrekking tot de voorwaarde betreffende de levensverwachting was de praktijk ook grotendeels in overeenstemming met de aanbeveling uit de richtlijn: bijna alle responderende artsen schatten de levensverwachting van de patiënt bij de start van CPS op minder dan twee weken. Rekening houdend met het gegeven dat artsen in het algemeen moeite hebben met het inschatten van de levensverwachting en vaak neigen tot overschatting, betekent dit dat meestal voldaan lijkt te worden aan de voorwaarde dat de dood zich op korte termijn aandient.
We vonden ook punten die niet overeenkwamen met de aanbevelingen uit de KNMG-richtlijn. Alhoewel de richtlijn stelt dat proportioneel toegepaste palliatieve sedatie niet leidt tot levensbekorting, gebruiken sommige artsen CPS (mede) met het doel om het levenseinde te bespoedigen, of denken ze dat toepassen van sedatie een levensbekortend effect heeft. Verder beveelt de richtlijn aan om niet kunstmatig vocht toe te dienen tijdens continue diepe sedatie tot aan het overlijden. Toch werd dat bij een minderheid van de patiënten wèl gedaan. Hoewel de richtlijn aangeeft dat als regel geldt dat de arts bij de aanvang van continue sedatie zelf aanwezig moet zijn, was bij één op de vijf gevallen de arts niet aanwezig bij de start van continue sedatie.

Perspectieven van artsen en verpleegkundigen

Naast bovengenoemde artsen vulden ook 278 van de 576 door ons benaderde verpleegkundigen (response 48%), een vragenlijst in over de laatste door hen verzorgde patiënt bij wie CPS was toegepast. Zij werkten in de thuiszorg, verpleeghuizen, hospices of ziekenhuizen.
In ***hoofdstuk 3*** wordt beschreven in hoeverre de perspectieven van verpleegkundigen met betrekking tot de praktijk van CPS verschilden van die van artsen. In vergelijking met art-

sen waren verpleegkundigen vaker van mening dat patiënten voorafgaande aan de start van CPS angstig waren. Daarnaast benoemden zij vaker pijn als de doorslaggevende indicatie voor het starten met CPS. Ook dachten verpleegkundigen vaker dat artsen sedatie toepasten (mede) met het doel om het levenseinde te bespoedigen, maar gaven zij minder vaak dan artsen aan dat zij zich onder druk gezet voelden door patiënten of naasten om te starten met CPS. Deze verschillen kunnen samenhangen met de verschillende rollen van artsen en verpleegkundigen in de klinische praktijk. Zo hebben verpleegkundigen in het algemeen vaker contact met patiënten, waardoor angst en pijn gemakkelijker herkend kunnen worden. Ook kunnen de verschillen voortkomen uit verschillende verantwoordelijkheden van artsen en verpleegkundigen. Patiënten en naasten zouden met name druk op artsen kunnen uitoefenen om te starten met sedatie omdat zij eindverantwoordelijk zijn voor een besluit tot CPS. Onze bevinding dat verpleegkundigen vaker dan artsen denken dat CPS werd toegepast (mede) met het doel het levenseinde te bespoedigen kan er op wijzen dat artsen niet altijd duidelijk communiceren over hun intenties. Dit onderstreept het grote belang van zorgvuldige communicatie tussen artsen en verpleegkundigen over de aanleiding tot en de uitvoering van CPS.

Indicaties voor CPS

Aan iedere arts en verpleegkundige die aan het vragenlijstonderzoek deelnam, werd gevraagd of ze ook bereid waren tot een aanvullend kwalitatief interview. In ***hoofdstuk 4*** wordt het deel van de interviewstudie beschreven, waarin we de overwegingen van artsen (n=54) en verpleegkundigen (n=36) onderzochten die betrekking hebben op de twee belangrijkste voorwaarden voor palliatieve sedatie: refractaire symptomen en een levensverwachting van minder dan twee weken. We laten zien dat zorgverleners CPS niet alleen toepassen in situaties waarin één symptoom doorslaggevend is. CPS wordt ook toegepast om een cumulatie van lichamelijke en niet-lichamelijke symptomen die leidt tot een refractair toestandsbeeld te verlichten. In dergelijke situaties is het lijden niet zozeer refractair vanwege de afwezigheid van behandelingsmogelijkheden voor een specifiek symptoom, maar vanwege de onmogelijkheid om de algehele toestand waarin de patiënt zich bevindt te verlichten. In ***hoofdstuk 4*** beschrijven we daarnaast dat over de voorwaarde dat sprake dient te zijn van een levensverwachting van minder dan twee weken, verschillend wordt gedacht. Sommige artsen hechten er grote waarde aan dat CPS alleen wordt toegepast als de dood nadert, om associaties met eventuele levensbekorting te vermijden. Andere artsen kennen hieraan minder gewicht toe omdat zij de noodzaak om refractaire symptomen te verlichten belangrijker vinden dan het voldoen aan de voorwaarde van een levensverwachting van minder dan twee weken. In de literatuur wordt CPS bij een wat langere levensverwachting ook wel beschreven als 'vroege terminale sedatie'. Verder beschrijven we in ***hoofdstuk 4*** dat de indicatie voor CPS ook beïnvloed wordt door voorkeuren van patiënten en naasten met betrekking tot een waardige en goede dood. Als de voorkeuren en wensen van patiënten bekend zijn kan dat de besluitvorming rond CPS soms vergemakkelijken. Het kan de besluitvorming echter ook bemoeilijken, in het bijzonder wanneer zorgverleners zich onder druk gezet voelen om te starten met CPS.

Diepte van sedatie

In ***hoofdstuk 5*** beschrijven wij het deel van de interviewstudie betreffende de overwegingen van artsen (n=54) met betrekking tot de keuze voor de diepte van continue sedatie. Artsen

gebruikten twee verschillende benaderingen aangaande de diepte van de sedatie: zij streven ofwel diepe sedatie na, direct vanaf de start, ofwel zij beginnen met oppervlakkige sedatie en verdiepen deze geleidelijk wanneer dit noodzakelijk blijkt te zijn. Voorkeuren van patiënten en naasten hebben niet alleen invloed op *de indicatiestelling* voor CPS (hoofdstuk 4), maar blijken ook bij te dragen aan de keuze voor *de diepte* van de sedatie. De angst van patiënten en naasten om wakker te worden tijdens continue sedatie, of de overtuiging van patiënten bij de start van de sedatie dat 'het genoeg is geweest', kunnen invloed hebben op de medicatie die wordt toegediend. Ook het belang dat door artsen wordt gehecht aan communiceren heeft invloed op de diepte van de sedatie. Terwijl behoud van communicatie veelal van belang wordt geacht vanwege de mogelijkheid om zowel de indicatie als de effectiviteit van de palliatieve sedatie te kunnen (her)beoordelen, vonden wij dat (behoud van) communicatie ook beschouwd wordt als een doel op zichzelf. Artsen die behoud van communicatie belangrijk vinden kiezen in het algemeen voor oppervlakkige sedatie in plaats van diepe sedatie. Daarnaast speelt het streven naar rust en comfort een rol bij de voorkeur voor de diepte van sedatie. In sommige gevallen leidt dit tot een benadering waarbij vanaf de start wordt gestreefd naar diepe sedatie. In andere gevallen leidt dit tot een geleidelijke benadering die 'een meer natuurlijke manier van sterven' weerspiegelt. In de KNMG-richtlijn wordt proportionele sedatie omschreven als sedatie waarbij de keuze en de dosering van de medicamenten wordt bepaald door de ernst van de symptomen. Dit houdt in dat het bewustzijn niet meer verlaagd dient te worden dan noodzakelijk is om het lijden adequaat te verlichten. Onze studie laat zien dat in de praktijk proportionaliteit breder opgevat wordt dan het strikt titreren van medicamenten op de ernst van de symptomen. Voorkeuren van patiënten en naasten, behoud van communicatie en het comfort van de patiënt spelen hierbij ook een rol. Op basis van deze bevindingen kan worden geconcludeerd dat het concept proportionaliteit kan worden opgevat als een multidimensioneel concept.

CPS bij patiënten met niet-oncologische aandoeningen

In ***hoofdstuk 6*** vergelijken wij op basis van het vragenlijstonderzoek de praktijk van CPS voor patiënten met niet-oncologische aandoeningen (bijvoorbeeld hartfalen) met de praktijk voor patiënten met kanker. Kortademigheid en psychische uitputting werden bij patiënten met een niet-oncologische aandoening vaker genoemd als een doorslaggevende indicatie om te starten met CPS dan bij patiënten met kanker. Daarnaast werd bij patiënten met een niet-oncologische aandoening minder vaak een consultatieteam palliatieve zorg geraadpleegd voorafgaande aan de start van de sedatie en werd vaker ingeschat dat het leven meer dan een dag was bekort door de sedatie. Een verschillend beloop van ziektetrajecten kan deze verschillen tussen patiënten met kanker en patiënten met niet-oncologische aandoeningen deels verklaren. De laatste fase van de ziektetrajecten van mensen met een niet-oncologische aandoening kenmerkt zich veelal door een langdurig, fluctuerend proces van langzame achteruitgang, onderbroken door perioden van acute verslechtering en uiteindelijk een schijnbaar onverwacht sterven. Bij dergelijke ziektetrajecten is het moeilijk om vast te stellen wanneer de palliatieve fase van de ziekte is ingegaan en wanneer raadplegen van een consultatieteam palliatieve zorg opportuun is. Het verdient aanbeveling om (consultatieve) diensten op het gebied van palliatieve zorg eerder in te zetten bij advance care planning voor patiënten met niet-oncologische aandoeningen. Hierdoor kunnen zowel de fysieke als de psychosociale dimensies van symptomen tijdig en adequaat besproken, begeleid en behandeld worden.

Interpretatie

In ***hoofdstuk 7*** worden de belangrijkste bevindingen in dit proefschrift besproken. Tevens wordt ingegaan op sterke en zwakke punten van de studies en worden suggesties en aanbevelingen gedaan voor de klinische praktijk en toekomstig wetenschappelijk onderzoek. Dit proefschrift laat zien dat psychosociaal en existentieel lijden een grote impact kunnen hebben op het besluit om CPS toe te passen. Hoewel specifieke refractaire symptomen vaak een belangrijke indicatie blijken te zijn voor het toepassen van CPS, wordt CPS ook toegepast om de algehele toestand waarin de patiënt verkeert te verlichten. Ook blijkt de dosering van de toegediende sedativa bij CPS niet alleen bepaald te worden door de ernst van de symptomen, maar spelen ook de voorkeuren van patiënt en naasten een rol, alsmede het belang dat wordt toegekend aan communicatie en comfort van de patiënt. Dit geeft aan dat proportionaliteit in de praktijk een multidimensioneel concept is. Dit weerspiegelt zich in de manier waarop artsen de diepte van sedatie benaderen: ofwel zij sederen diep vanaf de start, ofwel zij beginnen oppervlakkig en verdiepen de sedatie wanneer dat nodig is.
De opvattingen over het belang van dat wordt toegekend aan de voorwaarde betreffende levensverwachting verschilden. Sommige artsen vinden het belangrijk dat de stervensfase is ingetreden alvorens zij CPS toepassen, terwijl andere artsen het levensverwachtingscriterium afwegen ten opzichte van de noodzaak tot het verlichten van refractaire symptomen. Er is een ruime hoeveelheid literatuur over de onzekerheid van het stellen van prognoses en het schatten van levensverwachting. Hoewel de voorwaarde betreffende levensverwachting concreter gemaakt kan worden door hieraan klinische kenmerken te verbinden (hoofdstuk 7), zijn deze onzekerheden nooit geheel weg te nemen. Zorgvuldige communicatie over de waarneming van symptomen in de laatste levensfase en de betekenis daarvan, bevordert het tijdig markeren van het moment waarop de zorg zich specifiek gaat richten op symptoomverlichting en comfort. Niet alleen het tijdig bespreken van de wensen en voorkeuren van de patiënt met betrekking tot de laatste levensfase is een belangrijk onderdeel van goede kwaliteit van de medische zorg rond het levenseinde: hetzelfde geldt voor tijdige consultatie van deskundigen op het gebied van palliatieve zorg. Juist omdat continue palliatieve sedatie raakt aan de grenzen van het normale in de medische praktijk, dient consultatie van deskundigen gezien te worden als een belangrijk middel om continue palliatieve sedatie als normaal medisch handelen te kunnen beschouwen.

Tot slot

Dan het laatste hoofdstuk, dat nu ik er over nadenk eigenlijk het eerste hoofdstuk is: het dankwoord. In dat hoofdstuk wil ik mijn dank uitspreken aan alle mensen die op een of andere wijze hebben bijgedragen aan dit proefschrift. Niet alleen de mensen die me hebben geleerd hoe je onderzoek doet, maar ook de patiënten die me geleerd hebben hoe je dokter kunt zijn en de mensen die me geleerd hebben lief te hebben, samen te werken en op te leiden. Omdat het me enige tijd gekost heeft om mijn weg in het onderzoek te vinden, bestrijken deze woorden van dank vele jaren. Dat maakt dat mogelijk niet alle namen die hier nu genoemd worden, de namen zijn die hier genoemd zouden moeten worden. Daarom zeg ik tegen een ieder wiens naam niet naar boven kwam tijdens het schrijven van mijn dankwoord: je zit in me!

DANKWOORD

Het laatste hoofdstuk. Nu ik er goed over nadenk, is dit eigenlijk het eerste hoofdstuk. Hier wil ik mijn dank uitspreken aan alle mensen die op een of andere wijze hebben bijgedragen aan dit proefschrift. Niet alleen de mensen die me hebben geleerd hoe je onderzoek doet, maar ook de patiënten die me geleerd hebben hoe je arts kunt zijn en de mensen die me geleerd hebben lief te hebben, samen te werken en op te leiden. Omdat het me enige tijd gekost heeft om mijn weg te vinden binnen het onderzoek, bestrijken deze woorden van dank vele jaren. Dat maakt dat mogelijk niet alle namen die hier nu genoemd worden, de namen zijn die hier genoemd moeten worden. Daarom zeg ik tegen een ieder wiens naam niet naar boven kwam tijdens het schrijven van mijn dankwoord: je zit in me.

Om te kunnen oogsten moet onderzoek kunnen rijpen. Toen ik in aansluiting op mijn studie geneeskunde begon aan een promotie-onderzoek op de afdeling celbiologie van de Faculteit Geneeskunde aan de Vrije Universiteit te Amsterdam, bleken omstandigheden en ikzelf nog onvoldoende rijp om zo'n traject af te ronden. Toch heb ik toen al veel geleerd: niet alleen het belang van doorzettingsvermogen (Jeike) en het anderen tijdig deelgenoot maken van je overwegingen (Bert), maar bovenal het ervaren van ruimte om keuzes te maken (Taede). Taede, met name jouw enthousiasme voor onderzoek (en onderwijs!) en onze gesprekken over keuzemomenten hebben bij mij het idee levend gehouden dat je soms wat geduld moet hebben voor de tijd ergens rijp voor is. Hoe belangrijk het is om in een stimulerende onderzoeksgroep te werken, hebben Dona, Josien, Emmelien, Christien, Joke, Paula, Harry en Ingeborg mij destijds al duidelijk gemaakt. Dank daarvoor!

Ook in Amsterdam, in verpleeghuis Vreugdehof ("Ja, tranendal zal je bedoelen, dokter!") werd vanaf 1990 de basis voor dit proefschrift gelegd. Daar heb ik multidisciplinair leren samenwerken. Bert, Alien, Paul, Dineke, Barend, Marlies en Monique jullie waren mijn collegae-verpleeghuisartsen van het eerste uur. Dat schept een bijzondere band: het blijft en blijkt bij iedere ontmoeting stimulerend om met elkaar van gedachten te wisselen over 'ons' vak en onszelf. Jolanda, Ria, Loes, Bep en Atie stonden ons in administratief, röntgenologisch en farmacologisch opzicht bij. Van de verpleging en verzorging kan ik niet iedereen noemen, maar in het bijzonder van Ronald, Piet, Jolanda, Mart en ……..Els,- en dan vooral tijdens de decubitusronde- heb ik veel geleerd over samenwerken. Met fysiotherapeuten (Erwin, Jos, Wim) en maatschappelijk werker (Bert) is veelvuldig naar een antwoord gezocht op de vraag hoe het verder moest met mensen na hun revalidatie in het verpleeghuis. Maar bovenal ben ik in Vreugdehof gaan beseffen hoe belangrijk het is dat mensen goed kunnen sterven en dat degenen die achter blijven daarop goed terug kunnen kijken. Bert, dankzij jouw begeleiding tijdens mijn opleiding kon ik groeien in het bijstaan van mensen die lijden. De vele gesprekken die we voerden als ons weer eens gevraagd werd: "Waar zijn jullie nou toch eigenlijk de hele dag mee bezig als je zo weinig mensen echt beter kunt maken?", hebben de basis voor dit proefschrift gelegd. Het doet me deugd dat ik nu eens een keer in een boek iets over jou kan schrijven! Zoals een kookboek geen kok maakt en een richtlijn geen arts, zo maakt een universitair protocol geen paranimf. Dat je als paranimf naast me staat, is dan ook vooral een weerspiegeling van onze vriendschap en onze voortgaande gedachtewisselingen over de aard en de kern van ons vak.

Niet alleen de basis voor dit proefschrift werd in Vreugdehof gelegd: ook Els ontmoette ik daar. Het begon tijdens een toneelspel, en, zoals dat kan gaan in de liefde: van het één kwam het ander en na een aantal jaren Jolijn en Jurjen. *Vreugde*hof, ik zei het al!

Na mijn opleiding tot (toen nog) verpleeghuisarts ging ik in Amersfoort werken. Met plezier denk ik terug aan de samenwerking met mijn collega-artsen Jan, Janny en Suzanne en natuurlijk met onze doktersassistente Willeke. Samenwerking met geestelijk verzorger Elsbeth, psycholoog Coby en maatschappelijk werkenden Nanning en Jitske werd intensiever. Met de avondhoofden Corrie en Thea heb ik menig bijzondere situatie tijdens de dienst beleefd. Ook aan de fysiotherapeuten Ole, Arjen, Huub, Jeanette, Magda en Hans, bewaar ik goede herinneringen. In Amersfoort ontmoette ik ook Piet, eerst als begeleider van de intercollegiale toetsingsgroep, later –en belangrijker- als wandelaar en nog later – en nog belangrijker - als schaatser en vriend . Wie had toen kunnen vermoeden dat jij het nog eens tot mijn paranimf zou schoppen? Dat ik jou een plezier kon doen door je te vragen het feest te helpen organiseren, voelt voor mij als een feestje!

Onderwijs ging steeds meer boeien. Op aanraden van Huub solliciteerde ik naar een functie bij de verpleeghuisartsenopleiding van de VU in Amsterdam. Daar werd ik samen met Anne Margriet groepsbegeleider. In het bijzonder van haar en van Coby , Marlies, de beide Jossen en Henk heb ik toen veel geleerd. Gevoed tijdens retraitedagen heb ik gemerkt hoe inspirerend het is om bij te dragen aan de ontwikkeling van je vak. Frank ben ik dankbaar voor zijn luisterend oor en adviezen rond keuzemomenten. Zeker het afgelopen jaar heb ik vaak moeten denken aan je uitspraak dat je naast je privé-leven slechts tijd hebt om twee dingen echt goed te kunnen doen…… Het is daarom goed dat mijn promotietraject tot een einde komt.

Verdieping in palliatieve zorg volgde. Frans vroeg me om in Rotterdam te komen werken. Het werd me sindsdien steeds duidelijker dat palliatieve zorg niet 'iets is wat (verpleeghuis) artsen altijd al deden'. Werken in een palliatieve setting verdiept zorgverlening door middel van multidisciplinaire samenwerking tot multidimensionele zorgverlening. Hierbij is er niet alleen aandacht voor de lichamelijke, psychische en sociale aspecten van ernstig ziek zijn, maar ook voor de ruimte om de betekenis hiervan te verkennen. Ook is toen duidelijker voor mij geworden dat om aandacht te kunnen geven aan de zingevingsdimensie van ziek(t) en, deze ruimte niet alleen nodig is voor zieken, maar ook voor hun naasten en zorgverleners. Marij, Anja, Marinus, Mirjam, Elisabeth, Monique, Ellen en Hannie, jullie hebben me op de unit geleerd vorm te geven aan vier-dimensionele zorg in een drie-dimensionele wereld. Marinus, ons gezamenlijk onderwijs aan studenten geneeskunde heeft me geholpen om de palliatieve dimensie van zorg te verwoorden en te verbeelden. Riekje, jouw stimulans en luisterend oor rond de afwegingen voorafgaande aan mijn keuze om onderzoek te gaan doen, zal ik niet snel vergeten. Gesprekken met Anne Mei en Henk droegen bij aan mijn rijpingsproces tot onderzoeker. Dank daarvoor! Carlo ontmoette ik toen hij een praktijkstage palliatieve zorg volgde op de unit. Hoewel de samenloop van omstandigheden ons beiden heeft verrast, voelt het heel vanzelfsprekend om jouw oratie en mijn promotie gezamenlijk te vieren.

Vanuit Rotterdam volgde na enige jaren een stap terug, naar Amsterdam, maar ook verder, namelijk in het onderwijs. Henk vroeg me om samen met Bernardina de Kaderopleiding Palliatieve Zorg verder te ontwikkelen. Deze tweejarige opleiding voor artsen zal dit najaar al weer voor de zevende keer starten. Ik beleef veel plezier aan de samenwerking met Marijke en Gerda, Dick en Henk, alsmede de mentoren Marijanne, Marjo, Maaike en Pieter, en voorheen Fons en Wiljo. Aafke, Dick, Carola, Cora, Ellen en Anne-Marie: het vraagt geduld, maar het gaat lukken: het realiseren van een kader voor kaderartsen.

In Rotterdam ontstond vanuit Laurens een intensievere samenwerking rond palliatieve zorg met het Erasmus MC en IKR (nu IKNL-Rotterdam). Dit zowel op het gebied van consultatie (Lia, Karin, Marjolein, Paul, Rob, Erica, Helen, Erna, Angelique, Elsbeth (†), Hetty) als rond het Zorgpad Stervensfase (Hetty, Anneke, John). Voor mijn onderzoek heb ik veel gehad aan het bespreken van consulten binnen het consultatieteam palliatieve zorg Rotterdam (Cees, Frans, Ino, Hannie, Jet, Atef, Hermien, Anne, Mathilde, Pascalle, Renske en Wilma). Door onderzoek met het Zorgpad Stervensfase kwam ik in contact met Agnes en Judith. Vanuit de daaropvolgende samenwerking rond het proefschrift van Laetitia over het Zorgpad Stervensfase ontstond het idee voor wat 3 jaar later het AMROSE-onderzoek (AMsterdamROtterdamSEdatie) zou worden. Mede dankzij een impuls van Jan Jansen, apotheker bij Laurens, de ondersteuning van het Sint Laurensfonds (dank, Hans, Mark en Ids) en de Stichting Palliatieve Zorg Calando (dank, Paul en Janneke) werd de basis gelegd voor een door ZonMw gehonoreerd onderzoeksproject waarin Rotterdam ging samenwerken met Amsterdam.

Het resultaat van mijn bijdrage aan het AMROSE-project ligt voor U. Dit proefschrift was er niet gekomen zonder de stimulerende inspiratie van mijn (bege)leiders. Mede door hun kritische inbreng lukte het om een overgang te maken van 'deel uitmaken van een praktijk' naar 'onderzoeken van die praktijk'. Judith, met jou heb ik binnen AMROSE het meest intensief samengewerkt. Als mijn gedachten weer eens vele kanten opgingen, hielp jij me om koers te houden en om te focussen. We hebben vele en pittige gesprekken gevoerd over de accenten die in artikelen aangebracht konden worden: "Choose your battles and kill your darlings". Hoewel ik dat natuurlijk wel was, een junior-onderzoeker, heb jij me nooit dat gevoel gegeven. Agnes, als iemand de kunst verstaat om met minder woorden meer te zeggen dan ben jij dat wel. Dat is heel handig bij schrijven van artikelen. Het zal nooit mijn voorkeursaanpak worden, maar jij hebt me laten inzien dat het schrijven van een artikel heel goed kan beginnen met het schrijven van een samenvatting: dan kom je namelijk direct tot de kern. Hoewel je (wat mij betreft: eindelijk) hoogleraar bent, ben je dat voor mij niet alleen vanwege je vakkennis. Je hebt een gave om mensen ruimte te geven en toch zelf touwtjes in handen te blijven houden. Dat heb ik als zeer stimulerend ervaren. Agnes en Judith, ik kijk er naar uit om onze vruchtbare samenwerking voort te zetten, te beginnen met het onderzoek binnen Laurens naar advance care planning in verzorgingshuizen. Hans, hoewel we beiden specialist ouderengeneeskunde zijn, hebben we elkaar eerst tijdens mijn promotie onderzoek beter leren kennen. Je weet inmiddels dat het niet zo in mijn aard zit, toch waardeer ik de wijze waarop jij me uitdaagt om meer stelling te nemen zeer. Door jou ben ik beter gaan snappen dat scherpe kritiek helemaal niet vervelend is, zolang deze maar to the point is. Ik bewaar een dierbare herinnering aan de eerste keer dat we samen op jouw kamer thee dronken. Paul, gaande mijn promotie kwam je, mede doordat Agnes meer op

de voorgrond kwam, meer op de achtergrond. Maar toch, jouw taalsuggesties ('krabbels') en vooral je vragen ter verduidelijking zal ik niet snel vergeten: constructief en to the point. Lia, we kenden elkaar al langer en verwachtten dat toen onze werkplekken dichter bij elkaar kwamen te liggen, onze contacten frequenter zouden worden. Dat bleek niet zo te zijn. Maar gelukkig weten we beiden maar al te goed dat ook waar het onderlinge contacten betreft, kwalitatieve aspecten een toegevoegde waarde hebben.

Karin, Patrick en Dick, grote dank voor jullie bereidheid zitting te willen nemen in de kleine commissie. Alexander en Wouter: het doet me plezier dat jullie beiden zitting wilden nemen in de grote commissie.

Dit proefschrift was er zeker niet gekomen als 606 artsen en 278 verpleegkundigen niet de moeite hadden genomen om een vragenlijst in te vullen. Hartelijk dank daarvoor. In het bijzonder ben ik dank verschuldigd aan de 54 artsen en 36 verpleegkundigen die geïnterviewd wilden worden. Jacqueline en Anneke (IKR) wil ik bedanken voor de logistieke ondersteuning bij het verzenden van de vragenlijsten. De hulp van mijn onderzoeksassistente Anneke was van onschatbare waarde bij het organiseren, uitvoeren en transcriberen van de interviews.

Tijn, dank voor je hulp bij tabellen en statistiek. Zonder jouw inzet en die van Roberto, Miel, Wouter, Marco, Wijnanda en Gwendolyn, waren de artikelen niet in deze vorm verschenen, dank!

Mijn aanstelling bij de afdeling Maatschappelijke Gezondheidszorg werd geformaliseerd in een gastvrijheidsovereenkomst. Ik heb me zeer welkom gevoeld op deze afdeling, maar dat kwam natuurlijk niet door die overeenkomst, dat komt door de enthousiaste mensen die op deze afdeling werken. Allereerst onze sectie: besluitvorming en zorg rond het levenseinde. Agnes, Judith, Hilde, Erica, Natasja, Sophie, Ineke, Arianne en Eric, 'what a team we are!'. Dat die academische jaarprijs er net niet gekomen is, lag zeker niet aan ons of aan ons idee. En dan natuurlijk mijn kamergenoot, Sake ("Al is Fryslân plat, it hat syn hichtepunten"). Jij denkt volgens mij nog steeds dat er vaker voor mij telefoon is dan voor jou. Toch heb ik sterk de indruk dat jij vaker gezocht wordt dan ik… Hester, Ed, Suzie, Alice, Arry, Marian, Mona, Paul, Eva, Mirjam, Marielle, Vivian, Esther, Marieke, Ineke, Mirjam, Gerard, Caspar, Luc, Jesse, Gladys, Koos, Rianne, Farsia, Marieke, Vicki, Lenneke, Rick, Suzan, Ton, Cees, Alwin, Gianni, Frank, Ida, Suzanne, Britt, Wilma, Anja, Sanne, Yvonne, Lex, Jan Hendrik, Jan Willem, Johan, Ewout, Hein, Harry, ik hoop de komende jaren met jullie te kunnen blijven samenwerken.

En dan mijn collega's in Laurens Zuid-Oost: als ik verdiept was in wetenschappelijk onderzoek, waren jullie bereid om als dat nodig bleek op de afdelingen waar ik werkzaam ben, lichamelijk onderzoek te verrichten. Halima, Feriyal, Jeroen, Moheb, Hielke, Jan, Jet, Esther, Kamran, Marjon, Riekje dank voor jullie ondersteuning. Ben, jouw enthousiasme heeft me overgehaald om mede vorm te geven aan een Leerhuis Niet Aangeboren Hersenaandoeningen (NAH) binnen Laurens. Je had goed ingeschat dat een nieuwe samenwerking tussen Rotterdam en Amsterdam (lees: Gideon) opnieuw vruchten kan gaan afwerpen. Ik wil op deze plek niet onbenoemd laten dat we mede dankzij jouw inzet en die van Johan, als spinn

off van het AMROSE-onderzoek kunnen starten met het al eerder genoemde onderzoek rond advance care planning. Annemarie, Astrid, Thea, Monique, Maaike, Margot en Elize en natuurlijk Gideon: we gaan verder op het NAH-pad. En, Judith, Sandra, Eline, Yvonne en Chantal, ik vind het inspirerend om binnen dat kader met jullie onderwijs te ontwikkelen. Pascalle, Elja, Marleen, Fons, Romke, Ben, Frans en Ronald: ik heb goede hoop dat we de Wetenschappelijk Onderzoek Commissie een herkenbare plek binnen Laurens gaan geven.

Rob, Saskia, Harry, Ben en Dick: mijn eerste schreden op het gebied van de 'palliatieve schrijverij' heb ik samen met jullie gezet toen we Pallium startten. Hieraan en aan de latere samenwerking binnen de redactie met Jolanda, Nel, Piet, Hugo en Mathilde bewaar ik goede herinneringen. Inmiddels kent dit tijdschrift een vijftiende jaargang. Samen met Marjo, Anke, Anne Mieke, Rob, Mieke, Karin en (ook vanaf het begin) Rob hoop ik in Pallium nog lang te kunnen verhalen over palliatieve zorg.

Jeu de Boules-ers Cor, Jan, Remko, Cees, Jan, Sander, KeesJan, Sjoerd, Jaap, Tom, Job, Ronald, Dick, Jan Willem, Peter, Lennart, Louis, Roland en JaapJan: "Jongens waren we - maar aardige jongens. Al zeg ik 't zelf..." VGSB-ers Ron, Maarten, Dieter, Henk, Dick, Cor, Jan en Ewald: de bal blijft rond, ook al rolt hij de laatste jaren minder vaak.
Jet, Pascalle, Piet, Elsbeth: dat we nog maar vele etentjes tegemoet kunnen zien onder het motto: inspireren bij dineren! Een goede buur beter dan een verre vriend? Ivo en Marjelle, Marco en Els, Ben en Marjan, Sibout en Nelleke: ik hoop nog lang van ons contact te genieten.
Bart, 'the English say: an apple a day keeps the doctor away'. In jouw geval pakte dat anders uit: ik kwam de afgelopen jaren steeds terug! Het was heerlijk om me te ontspannen in je boomgaard en op markten tussen appels en peren in de periode dat ik werkte aan mijn promotie onderzoek. Wat mij betreft worden de komende jaren opnieuw goede fruitjaren.

Tot slot, mijn naaste familie. Fijn dat jullie er bij zijn vandaag. Jullie die 'er bij gekomen' zijn: Bob, Jeroen, Paula, Michiel, Marion, Kari, Peter, Peggy, neven, nichten en Robin. Rineke en Thea, eigenlijk geldt dat 'erbij gekomen zijn' ook voor jullie: ik ben nu eenmaal de oudste! Mama, dat geldt niet voor u. U was er al voor me, toen ik er nog niet was. En dat is nog steeds zo. Maar, wie had 'onderweg naar Apeldoorn' kunnen denken dat we een dag als deze zouden beleven? Papa zou trots geweest zijn! Helaas maakt hij dit niet meer mee.
Het AMROSE-project waarvan dit proefschrift onderdeel is, is afgerond. Dat geldt gelukkig niet voor ons AMROSA -'project', ooit in AMsterdam begonnen en via een tussenstop in Leusden in de omgeving van ROtterdam SAmen voortgezet: Els, Jolijn en Jurjen, ik hoop dat dat nog heel lang zo zal blijven.

Siebe Swart
Barendrecht, april 2013

ABOUT THE AUTHOR

Siebe Swart werd op 7 januari 1962 geboren in Apeldoorn. Hij behaalde zijn Atheneum-B diploma aan het Christelijk College Groevenbeek te Ermelo. In 1988 slaagde hij in Amsterdam aan de Vrije Universiteit voor zijn artsexamen. Aan dezelfde universiteit werd in 1994 de opleiding tot (toen nog) verpleeghuisarts met succes afgerond. Het leren in de praktijk vond in deze periode plaats in verpleeghuis Vreugdehof ("Ja, tranendal zal je bedoelen, dokter") te Amsterdam. Van 1995 tot 1999 werkte hij als verpleeghuisarts in zorgcentrum de Lichtenberg te Amersfoort. Aan de Radboud Universiteit in Nijmegen rondde hij in 1996 met goed gevolg de opleiding Ethiek in de Zorgsector af. Van 1997 tot 2000 was hij tevens parttime in dienst bij de opleiding verpleeghuisgeneeskunde van de Vrije Universiteit als verpleeghuisartsbegeleider en schrijver van onderwijsprogramma's voor het blok (toen nog) terminale zorg. Vanaf de start in 1998 is hij als redacteur verbonden aan het multidisciplinaire tijdschrift voor palliatieve zorg, Pallium.
Sinds 1999 werkt hij, eerst als verpleeghuisarts en later als specialist ouderengeneeskunde, bij Laurens Rotterdam (regio Zuid Oost, locatie Antonius IJsselmonde). Hier verdiepte hij zich in de praktijk van de palliatieve zorg. In 2002 behaalde hij aan de universiteit van Cardiff (Coleg Meddygaeth Prifysgol Cymru) het Postgraduate Diploma in Palliative Medicine. Sinds 2004 is hij wederom tevens werkzaam voor het VU medisch centrum (afdeling huisartsgeneeskunde en ouderengeneeskunde, onderafdeling Gerion) als stafdocent voor de kaderopleiding palliatieve zorg. In 2007 startte hij binnen het AMROSE-project zijn promotie onderzoek bij de afdeling Maatschappelijke Gezondheidszorg van het Erasmus Medisch Centrum te Rotterdam. Van dit onderzoek wordt verslag gedaan in het proefschrift dat voor u ligt. Hij hoopt na afronding van zijn promotie de vruchtbare samenwerking die ontstaan is tussen zorg (Laurens) en onderzoek (Erasmus MC) voort te zetten en te verdiepen.

OVERVIEW OF PUBLICATIONS AND MANUSCRIPTS

English

2013

Bruinsma SM, Rietjens JAC, Swart SJ, Perez RSGM, van Delden, JJM, van der Heide A. Estimating the potential life-shortening effect of continuous sedation until death: A comparison between two approaches. Under review

Koper I, van der Heide A, Janssens R, Swart SJ, Perez RSGM, Rietjens JAC. Consultation with specialist palliative care services in palliative sedation. Considerations of Dutch physicians. Submitted

Swart SJ, Van der Heide A, Van Zuylen L, Perez RSGM. Zuurmond WWA, Van der Maas PJ, Van Delden JJM, Rietjens JAC Continuous Palliative Sedation: not only a response to physical suffering. Under review

Brinkkemper T, Rietjens JAC, Swart SJ, Ribbe MW, Deliens L, Loer SA, Zuurmond WWA, Perez RSGM. Determining sedation depth during continuous palliative sedation: associated factors as viewed by Dutch nurses. In: Palliative Sedation in the Netherlands. Thesis, Tijn Brinkkemper 17 april 2013 Vrije Universiteit Amsterdam

Brinkkemper T, Rietjens JAC, Deliens L, Ribbe MW, Swart SJ, Loer SA, Zuurmond WWA, Perez RSGM. A favourable course of palliative sedation – searching for indicators using caregivers' perspectives. In: Palliative Sedation in the Netherlands. Thesis, Tijn Brinkkemper 17 april 2013 Vrije Universiteit Amsterdam

2012

Arevalo J, Rietjens J, Swart SJ, Perez RSGM, Van der Heide A. Day-to-day Caring in Palliative Sedation: Survey of nurses' experiences with decision-making and performance. Int J Nurs Stud. 2012 Oct 25. doi:pii: S0020-7489(12)00335-5. 10.1016/j.ijnurstu.2012.10.004. [Epub ahead of print] http://dx.doi.org/10.1016/j.bbr.2011.03.031

Rietjens JAC, Swart SJ, van Delden JJM, van der Heide A. Pre-emptive Use of Palliative Sedation and Amyotrophic Lateral Sclerosis. J Pain Symptom Manage. 2012 Sep;44(3):e5-7. doi: 10.1016/j.jpainsymman.2012.05.003.

Blanker MH, Koerhuis-Roessink M, Swart SJ, Zuurmond WWA,van der Heide A, Perez RSG Rietjens JAC. Pressure during decision making of continuous sedation in Dutch general Practice. BMC Fam Pract. 2012 Jul 3;13:68. doi: 10.1186/1471-2296-13-68.

Swart SJ, Rietjens JAC, Brinkkemper T, van Zuylen C, Perez RSG, van der Heide A. Continuous Palliative Sedation until death: Practice after introduction of the Dutch national guideline. BMJ Pal & Supp Care 2012; BMJ Supportive & Palliative Care (2012). doi:10.1136/bmjspcare-2011-000063

Swart SJ, Van der Heide A, Van Zuylen L, Perez RSGM. Zuurmond WWA, Van der Maas PJ, Van Delden JJM, Rietjens JAC. Considerations of physicians about the depth of palliative sedation at the end of life. CMAJ. 2012 Apr 17;184(7):E360-6. Epub 2012 Feb 13.

Swart SJ, Rietjens JAC, van Zuylen L, Zuurmond WWA, Perez RSGM, van der Maas PJ, van Delden JJM, van der Heide A. Contninous palliative sedation for cancer and non-cancer patients J Pain Symptom Managem 2012;43:172-81

Swart SJ, Rietjens JA, van Zuylen L, Perez RS Zuurmond WW, van Delden JJ, van der Heide A. Health care professionals' considerations regarding indications for continuous palliative sedation until death (CPS). Palliative Medicine 2012(26):501(abstract)

Huisman BAA, Brinkkemper T, Gootjes JRG, Swart SJ, Rietjens JAC, Deliens L, Ribbe MW, Zuurmond WWA Perez RSGM. The reliability of the PAINAD in patients receiving palliative sedations for intractable pain. Palliative Medicine 2012(26):589 (abstract)

2010

Swart SJ, Brinkkemper T, Rietjens JAC, Blanker MH, Zuylen van L, Ribbe M, Zuurmond WWA, Heide van der A, Perez RSGM. Physicians' and nurses experiences with continuous palliative sedation in the Netherlands. Arch Int Med. 2010;170:1271-4

Heide van der A, Veerbeek L, , Swart SJ, van der Rijt CC, Van der Maas PJ, Zuylen L van. End-of-life decision making for cancer patients in different clinical settings and the impact of the LCP. JPSM 2010;39(1):33-43

2008

Veerbeek L, Zuylen L van, Swart SJ, Jongeneneel G, Van der Maas PJ, van der Heide A. Does recognition of the dying phase have an effect on the usse of medical interventions? J Palliat Care. 2008 Summer; 24:94-9.

Veerbeek L, Heide van der A,Vogel de-Voogt E, Bakker de B, Rijt van der CCD, Swart SJ, Maas van der PJ, Zuylen van L. Using the LCP: bereaved relatives'assessments of communication and bereavement. Am J Hosp Palliat Care. 2008 Jun-Jul;25(3):207-14. doi: 10.1177/1049909108315515. Epub 2008 Apr 10.

Veerbeek L, Zuylen L van, Swart SJ, Van der Maas PJ, de Vogel-Voogt E, van der Rijt CC, van der Heide A. The effect of the Liverpool Care Pathway for the dying: a multi-centre study. Palliat Med. 2008 Mar;22(2):145-51.

2007

Veerbeek L, Zuylen L van, Swart SJ, Van der Maas PJ, van der Heide A. The last 3 days of life in three different care settings in The Netherlands. Support Care Cancer. Support Care Cancer. 2007 Oct;15(10):1117-23. Epub 2007 Mar 15.

2006

Swart SJ, Veluw van H, Zuylen van L, Gambles M, Ellershaw J.. Dutch experiences with the Liverpool Care Pathway. Eur J Pal Care 2006;13:156-9

Veerbeek L, Zuylen L van, Gambles M, Swart SJ, Heide A van der, Rijt CCD van der, Ellershaw JE. Audit of the Liverpool Care Pathway for the dying patient in a dutch cancer hospital. J Pal Care 2006;22:305-8

Nederlands

2013

Natasja Raijmakers, Agnes van der Heide, Judith Rietjens, Siebe Swart & Lia van Zuylen
De resultaten van OPCARE9.Richtinggevend voor onderzoek en zorg in de laatste levensfase. Ned-Vlaams Tijdsch Pal Zorg 2012;3/4:51-6

Carlo Leget, Marijke van Daelen, Siebe Swart. Spirituele zorg in de Kaderopleiding Palliatieve Zorg. Tijdschrift voor Ouderengeneeskunde 2013;3:x-xx

2012

Swart SJ, van der Heide A, van Zuylen C, Perez RSG, Zuurmond WWA, van der Maas PJ, van Delden JJM, Rietjens JAC. Palliatieve sedatie: hoe diep? Huisarts en Wetenschap 2012; 55:434-8

2011

Swart SJ, Rietjens JAC, Brinkkemper T, van Zuylen L, van Burg-Verhage WA, Zuurmond WWA, Ribbe MW, Blanker MH, Perez RSGM, van der Heide A. Palliatieve sedatie na introductie van de KNMG-richtlijn. Ned Tijdschr Geneesk 2011;155:A2857

Raijmakers N, van der Heide A, Rietjens JAC, Swart SJ, van Zuylen L. OPCARE9: Samenwerken in Europa aan betere zorg in de stervevensfase. Ned-Vlaams Tijdsch Pal Zorg 2011;1:6-10

Van der Heide A, Brinkman-Stoppelenburg, Swart SJ, Rietjens JAC. Vroege inzet van palliatieve zorg in het ziekenhuis. Ned-Vlaams Tijdsch Pal Zorg 2011;1:27-30

Swart SJ, Rietjens JAC, van Zuylen L, van der Heide A. Continue palliatieve sedatie bij patiënten met kanker en patiënten met andere ziekten Ned-Vlaams Tijdsch Pal Zorg 2011;1:56 (abstract)

2010

Deijck RHPD, Swart SJ, van Heugten P. Een stervende patiënt. In: Palliatieve zorg in de dagelijkse praktijk. Red. Wanrooij BS, de Graeff A et al. Houten 2010 blz 269-283

2009

Swart SJ, Leeuwen van PW, Zoest van H, Bruntink R. EAPC-congres in Wenen: waar was Nederland? Pallium 2009;3:14-5

Swart SJ, Thewissen M. Afscheid nemen doet pijn. Bijdrage aan lustrumbundel ter gelegenheid van het 20-jarige bestaan van de opleiding verpleeghuisgeneeskunde aan de Vrije Universiteit te Amsterdam. 1 oktober 2009

2008

van Zuylen L, Vos PJ, Veerbeek L, Swart SJ. , Dekkers AGWM, van der Rijt CCD, van der Heide A. Een goed einde. Medisch Contact 2008;50:2098-2101

Swart SJ. Palliatieve sedatie. Bijdrage in congresbundel 'Ontwikkelingen in de Geneeskunde' Erasmus MC 30 oktober 2008

Swart SJ. Als palliatieve zorg uitmondt in sedatie… Pro Vita Humana 2008;15:64-6

Swart SJ. Mens en pijn. Problemen en perspectieven. Ned Tijdschr Palliatieve zorg 2008;8:13 (boekbespreking)

2007

Boerlage A, van Herk R, Swart SJ, Baar FPM. Pijnmeting bij mensen met een uitingsbeperking. Pallium 2007;9:10-3

Swart SJ. Palliatieve zorg: richtlijnen voor de praktijk Ned Tijdschr Geneesk: 2007;151:159 (boekbespreking)

2005

Keizer A.A. en Swart SJ. Palliatieve sedatie, het sympathieke alternatief voor euthanasie? Ned Tijdschr Geneesk 2005;149:449-52

Swart SJ. Cicely Saunders, founder of the hospice movement. Selected letters 1959-1999 Ned Tijdschr Geneesk 2005;149:2946 (boekbespreking)

2004

H. Van Veluw, Y. Schrofer, S.J.Swart en L. van Zuylen: Een zorgpad voor de stervensfase. Tijdschrift voor verpleegkundigen 2004;(114):45-8

2003

Siebe Swart, Lia van Zuylen, Paul J Lieverse, Karin van der Rijt, Alexander de Graeff en Sicco Verhagen. Sterven kost tijd: sedatie in de laatste levensfase is geen alternatief voor euthanasie. Medisch Contact 2003;(58):910-11

S.J. Swart, H. van Veluw, J. Koningswoud, F.P.M. Baar, C.C.D van der Rijt en L. van Zuylen. Van 'Liverpool integrated Care Pathway for the dying phase' naar 'Zorgpad voor de Stervensfase-Rotterdam' Nederlands Tijdschrift voor Palliatieve Zorg 2003;12-6

Siebe Swart en Hetty van Veluw. Sedatie in de laatste levensfase. Oncologica 2003(3):119-121

2002

M. Thewissen en S.J. Swart: Nazorg door Voorzorg: begeleiding van familie van stervenden. Pallium 2002;3:15-8

R.J.J. van Boxtel, H de Graaf-Waar, Dr C. van Zuylen, S.J. Swart, H. Schreuder, E. de Mooy, M van Veen-'t Mannetje, Dr C.C.D. van der Rijt: COPZ-Rotterdam Voortgang Palliatieve Consultatieteams Oncologica 2002;2:37-40

Swart SJ. Evidence-based palliative care across the life span; Ned Tijdschr Geneesk 2002;146:590-1 (boekbespreking)

Swart SJ. Handboek palliatieve zorg. Ned Tijdschr Geneesk 2002;146:2324 (boekbespreking)

2001

S. Teunissen, S.J. Swart: "Artsen en verpleegkundigen vragen om ondersteuning": consultatie met betrekking tot de zorg voor patiënten in de palliatieve fase van hun ziekte. Pallium 2001;2:10-4

2000

S.J. Swart, M. Thewissen: "Afscheid nemen doet pijn": een multidimensionele benadering van pijn. Pallium 2000;3:16-9

PhD Portfolio Summary

Summary of PhD training and teaching activities

Name PhD student: SJ Swart
Erasmus MC Department: MGZ
Research School: NIHES

PhD period: oktober 2007-juni 2013
Promotor(s): A van der Heide en JJM van Delden
Supervisor: A van der Heide en JAC Rietjens

	Year	Workload (Hours)	ECTS
1. PhD training			
General academic skills			
- Qualitative research in healthcare, Antwerpen	2009	40	
- Biomedical English Writing and Communication	2010		4
- Integrity in Medical Research	2010		2
Research skills			
- SPSS, 2 days, Gorinchem	2008	16	
In-depth courses (e.g. Research school, Medical Training)			
- NIHES Principles of Research in Medicine	2008		0,7
- NIHES Introduction to Data-analysis	2008		0,9
- NIHES Clinical Decision Analysis	2010		0,7
- NIHES Methods of Public Health Research	2010		0,7
- NIHES Conceptual foundation of Epidemiologic Study Design	2010		0,7
- NIHES Methods of Clinical Research	2011		0,7
- NIHES History of Epidemiologic Ideas	2011		0,9
Presentations			
- De praktijk van palliatieve sedatie. Voordracht voor Reformatorisch Maatschappelijke Unie 29-11-2007	2007		1
- Petra Deprès-Brummer lezing; Bergen op Zoom, 6-12-2007 De verwarrende praktijk rond palliatieve sedatie	2007		1
- Palliatieve Sedatie. Lezing op opleiding voor verpleegkundigen Hogeschool Rotterdam 15-01-2008	2008		1
- Workshop palliatieve sedatie en euthanasie. Scholing voor consulenten palliatieve zorg IKR-regio, Oostvoorne 3-4-2008	2008		1
- Lustrumsymposium Pro vita, Eindhoven +bijdrage congresbundel; 17-05-2008	2008		2
- Palliatieve sedatie. Voordracht voor regionale huisartsenvereniging. Goes 26-5-2008	2008		1
- Lustrumsymposium Nieuwe Waterweg Noord, Vlaardingen, 3 oktober, Zorgen voor of zorgen om een goede dood	2008		1
- Lustrumsymposium Netwerk Oost Veluwe, Apeldoorn, 9 oktober 2008, Verdieping in sedatie	2008		1
- Erasmus Nascholing huisartsen; Rotterdam, de Doelen, 30-10-2008 +bijdrage congresbundel	2008		2
- Praktijk en besluitvorming rond palliatieve sedatie: Utrecht, Julius Centrum UMCU 20-01-2009	2009		1

-	KNMG nascholing palliatieve sedatie; Utrecht Domus Medica, 20-02-2009	2009		1
-	Ervaringen van artsen en verpleegkundigen met palliatieve sedatie na introductie van de KNMG-richtlijn; Den Haag ZonMw, 11-3-2010	2010		1
-	AMROSE-onderzoek palliatieve sedatie; Amsterdam, Netwerk Palliatieve Zorg, 30-3-2010	2010		1
-	KNMG-symposium 'Geneeskunde: beletsel voor een waardige dood?'; Amsterdam 21-10-2010	2010		1
-	Continue palliatieve sedatie bij patiënten met kanker en patiënten met andere ziekten; Antwerpen, Vlaams-Nederlands onderzoeksforum palliatieve zorg, 26-11-2010	2010		1
-	Palliatieve zorg en Palliatieve Sedatie; Utrecht, post-HBO opleiding Palliatieve Zorg UMCU 14-07-2011	2011		1
-	Palliatieve sedatie na introductie KNMG-richtlijn; Rotterdam, Kenniscentrum Palliatieve Zorg Rotterdam, 24-10-2011	2011		1
-	Palliatieve sedatie in de praktijk van artsen en verpleegkundigen; Oncologiedagen, Ede, 27-10-2011	2011		1
-	Ketenzorg; Symposium NA Hersenletsel, Rotterdam, 30-10-2012	2012		1
-	Workshop Palliatieve Sedatie en Euthanasie 1-2-2013 Netwerk gynaecologie/IKNL Rotterdam	2013		1
-	Palliatieve zorg bij niet-oncologische aandoeningen. Rotterdam, 11-2-2013	2013		1
-	Palliatieve sedatie in de praktijk. Congres voor artsen in opleiding tot specialist ouderengeneeskunde, 18-4-2013, Domus Medica, Utrecht	2013		1
(Inter)national conferences				
-	European association of Palliative Care; Wenen 7-10 May	2009	30	
-	Seminar on ethical perspectives of sedation at the end of life Queen Mary University of London, 19th February	2010	10	
-	Resarch congres EAPC, Glasgow 10 – 12 June	2010	24	
-	Nederlands-Vlaams onderzoeksplatform palliatieve zorg (2 abstracts, 1 praatje)	2010	10	
-	Nationaal congress Palliatieve zorg, Lunteren (1 abstract, voorzitter sessie)	2010	10	
-	Congres: continuous sedation at the end of life: ethical perspectives; 11 en 12 maart Gent	2011	24	
-	European Association of Palliative Care, Lissabon, 20-23 May (3 abstracts)	2011	45	
-	Research congress EAPC, Trondheim 7-9 June (1 abstract)	2012	24	
-	Nationaal Congres Palliatieve Zorg, Lunteren, 15-17 november 2012 (voorzitter sessie)	2012	20	
-	17th ECCO - 38th ESMO - 32nd ESTRO European Cancer Congress (ECC2013), Amsterdam, invited speaker, chairing session 'Palliative care in 2014' (scheduled)	2013	?	
Seminars and workshops				
-	MGZ seminars 2008-2009-2010-2011			4

Didactic skills

-	Workshop didactische vaardigheden Erasmus MC	2009	12

Other

-	Country Representative Opcare 9 2008-2011	2008-2011	60/jr
-	Opcare conference Weggis 2-6 March	2009	30
-	Opcare conference Cologne 22-24 September	2009	20
-	Opcare conference Rotterdam 21-24 september	2010	30
-	Opcare Conference Liverpool 28 feb-2 maart	2011	20
-	Uitwerking communicatie-schets voor Academische Jaarprijs 2012 (met collega-onderzoekers afd MGZ): De dood in beeld.	2012	30
-	Projectadviseur bij door ZonMW gehonoreerd onderzoeksvoorstel 'Cost and effects of advance care planning in Dutch care homes'.	2012	25

2. Teaching activities

Supervising practicals and excursions

-	Blok populatie als patiënt (begeleiding scriptie (3x) + excursie	2007	16
-	Blok populatie als patiënt (begeleiding scriptie (3x) + inleiding +excursie	2008	20
-	Blok populatie als patiënt (begeleiding scriptie (3x) + inleiding	2009	16
-	Blok populatie als patiënt (begeleiding scriptie (3x) + inleiding + excursie	2010	20
-	Voorbereiding community projecten afdeling MGZ	2011-2013	20

Supervising Master's theses

-	Niet-reanimeer beleid in Erasmus MC, jan-jul 2011	2011	75

Other

-	Redactielid Pallium, tijdschrift voor palliatieve zorg	2007-heden	?
-	Stafdocent kaderopleiding palliatieve zorg	2007-heden	?
-	Lid visitatiecommissie consulentendiensten Vereniging Integrale KankerCentra okt 2008-september 2009	2008-2009	60
-	Voorbereidingscommissie Nationaal Congres Palliatieve Zorg, Lunteren september 2010	2010	30
-	Advisory board member International Multidisciplinary Forum on Palliative Care, Budapest November 2010	2010	10
-	Voorzitter sectie Zorg en Deskundigheid van Palliactief, vereniging voor professionals in de palliatieve zorg	2010-2012	?
-	Gastredacteur van het themanummer over palliatieve zorg van het Tijdschrift voor Ouderengeneeskunde, nummer 3	2013	?

AMROSA