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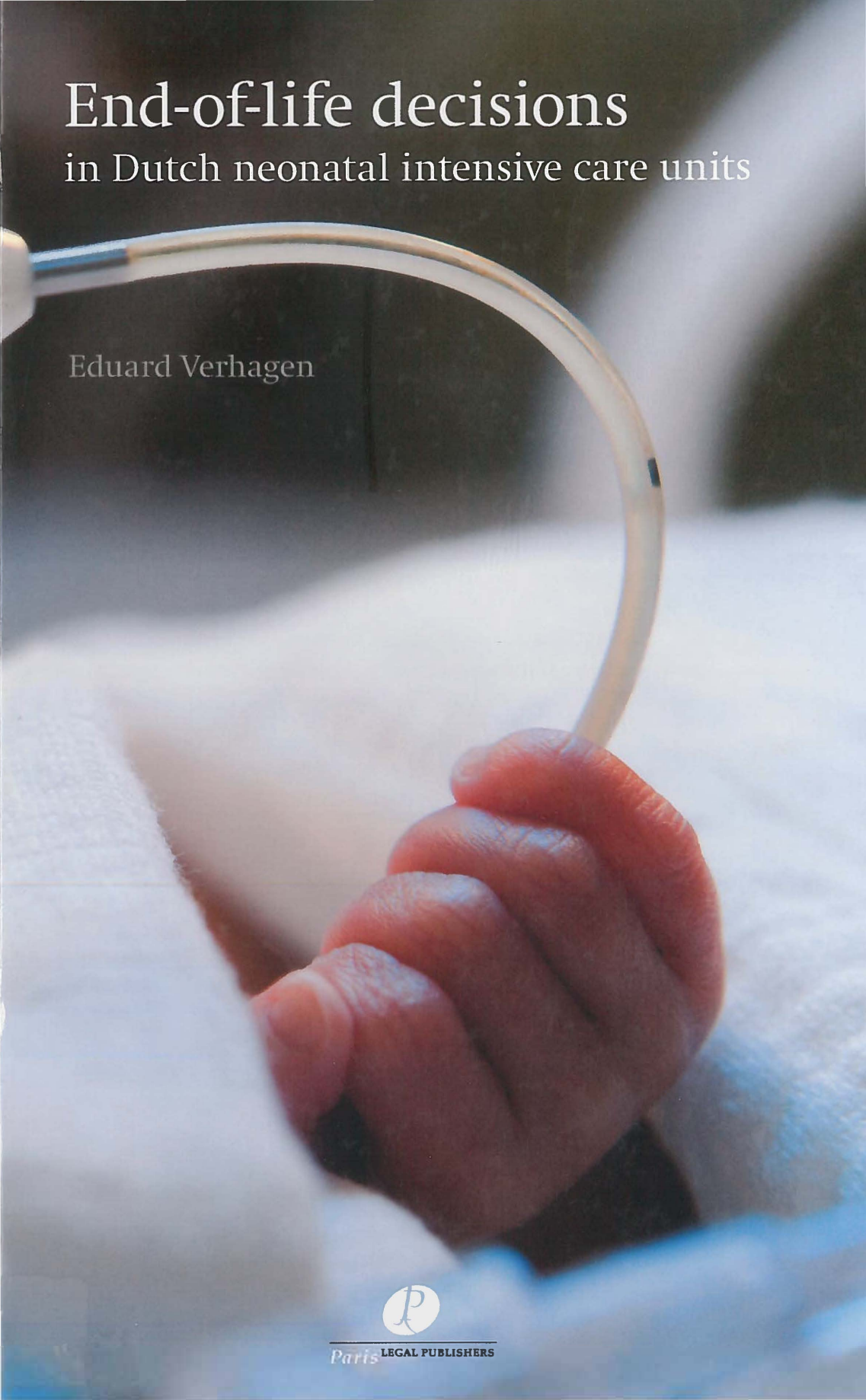
End-of-life decisions
in Dutch neonatal intensive care units

Eduard Verhagen



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Despite the rapid technical innovations in neonatology, a considerable proportion of newborns still die shortly after birth. The death of many of these infants is often preceded by an end-of-life decision. End-of-life decisions are medical decisions with the effect or the probable effect that death is caused or hastened. They include the decision to withhold or withdraw life-sustaining treatment, as well as the decision to deliberately end a newborn's life with lethal drugs.

Neonatal end-of-life decision-making is one of the most controversial areas of medicine as it raises all kinds of medical, ethical and legal questions regarding clinical management of severely ill newborns. *End-of-life decisions in Dutch neonatal intensive care units* examines these questions and provides a description of end-of-life decision-making practice in the Netherlands based on empirical studies by the author and his colleagues.

The first part of the book covers physician's end-of-life decision-making considerations, including those leading to deliberate termination of life, the role of the parents and the use of medication as a part of end-of-life decisions. The last section covers a comparison of end-of-life decision-making in four NICU's in the USA, Canada and the Netherlands followed by a reflection on the key aspects of Dutch neonatal end-of-life decision-making.

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Stellingen behorend bij het proefschrift: 'End-of-life decisions in Dutch neonatal intensive care units'

1. De meeste pasgeborenen overlijden in de Nederlandse neonatale intensive care afdelingen nadat het besluit is genomen om de kunstmatige beademing te stoppen. (Dit proefschrift)

2. De beslissingen om de levensverlengende behandeling bij een zieke pasgeborene te stoppen, worden in Nederland even vaak op de overlevingskans als op de inschatting van de toekomstige kwaliteit van leven van het kind gebaseerd. (Dit proefschrift)

3. Actieve levensbeëindiging bij stabiele, ernstig lijdende pasgeborenen komt waarschijnlijk veel minder vaak voor dan voorheen werd aangenomen. (Dit proefschrift)

4. Het 'Gronings Protocol' voor actieve levensbeëindiging bij pasgeborenen is ontwikkeld om meer duidelijkheid te geven over de vereiste zorgvuldigheid bij de besluitvorming en om de meldingsdrempel te verlagen. (Dit proefschrift)

5. Beslissingen over het levenseinde worden door de behandelteams van de NICU's zeer zorgvuldig genomen. De ouders zijn er altijd bij betrokken en bij meningsverschillen wordt de beslissing uitgesteld tot er consensus is bereikt. (Dit proefschrift)

6. Na de beslissing om een levensverlengende behandeling te stoppen, geeft de arts extra medicatie om onnodige pijn en lijden te bestrijden. In bijzondere gevallen wordt daaraan een spierverslappend middel toegevoegd als het stervensproces erg lang duurt en daardoor heel belastend voor de ouders is. (Dit proefschrift)

7. Door toegenomen kennis van de omstandigheden waaronder de besluitvorming over het levenseinde plaatsvindt, wordt het grensvlak tussen gangbaar medisch handelen en actieve levensbeëindiging verder verduidelijkt. Het is echter nog onduidelijk hoe palliatief gebruik van medicatie bij stervende pasgeborenen in dat kader moet worden geduid. (Dit proefschrift)

8. Vergelijking van beslissingen over het einde van het leven tussen neonatale intensive care afdelingen in Nederland, Canada en de Verenigde Staten is goed mogelijk en laat meer overeenkomsten dan verschillen zien. (Dit proefschrift)

9. "Anyone considering having a child while in the Netherlands, or traveling there with someone whom the Dutch authorities might consider disabled, should think again." (Barr B. Euthanasia, or the Dutch treat. *The Washington Times 2004 December 26;Sect. B07*)

10. Het negatieve imago van Curaçaose jongeren in Nederland is door Churandy Martina in 19.82 seconden omgebogen in diep respect.

11. Het is merkwaardig dat binnen het Koninkrijk der Nederlanden op de Antillen euthanasie vrijwel nooit, en in Nederland voortdurend een onderwerp van discussie is. (Alex Roose, huisarts te Curaçao)

12. Er zijn twee domeinen waarbij je de woorden 'nooit' en 'altijd' met een korrel zout moet nemen: de geneeskunde en de liefde.

Groningen, 21 januari 2008
Eduard Verhagen

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RIJKSUNIVERSITEIT GRONINGEN

END-OF-LIFE DECISIONS IN DUTCH NEONATAL INTENSIVE CARE UNITS

Proefschrift

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Chapter 1

General introduction and outline of the thesis

Background

Despite the rapid technical innovations in neonatology, a considerable proportion of newborns still die shortly after birth. The death of many of these infants is often preceded by an end-of-life decision. End-of-life decisions are medical decisions with the effect or the probable effect that death is caused or hastened. They include the decision to withhold or withdraw life-sustaining treatment, the decision to administer medication with potentially life-shortening effect to alleviate pain and suffering, and the decision to deliberately end a newborn's life with lethal drugs.

End-of-life decision-making in newborns raises all kinds of medical, ethical and legal dilemmas. Medical and ethical dilemmas occur when an infant is born with a very low gestational age and birth weight, alive but at the margin of viability (1-3). Although the mortality of such infants is generally high, initiating intensive care treatment may result in a small number of them surviving (4-8). Intensive care treatment, however, also induces pain, suffering and severe morbidity even if the infant were to survive the intensive care period. Prognostications about survival or morbidity for individual infants is often difficult despite the availability of many advanced tests and diagnostic tools (9-14). The physician is faced with the obligation to relieve suffering and the obligation to save the infant's life but he cannot always do both at the same time. Another example is the situation of the severely asphyxiated infant on the ventilator whose neurological prognosis is uncertain because it is difficult to accurately predict the likelihood of significant impairments (15-19). Physicians and parents may have different opinions about the impact impairments might have on the quality of the infant's life and about the purpose of continued intensive care therapy. Parents and physicians may also hold different views on the levels of cognitive or neurological functions that make life worth living.

Legal dilemmas may occur when analgesics, sedatives or neuromuscular blocking agents are used to relieve pain and suffering at the time of withdrawing life support (20). Potentially, analgesics and sedatives have life-shortening effects and the use of high doses may be regarded as intentionally hastening death. Neuromuscular blocking agents cause paralysis and respiratory arrest and are therefore considered by many authors as a form of illegal 'life-ending' (21-26). Many physicians are uncertain about where the demarcation line lies between administering medication with life-shortening effect as a part of normal palliative care on the one hand and pharmacological life-shortening that constitutes a criminal offence (murder), on the other hand.

Most of the information on the practice of end-of-life decision-making and how physicians and parents deal with these dilemmas stems from descriptive studies of neonatal end-of-life care. In the Netherlands, reports from the medical profession about the acceptability of end-of-life decisions and three court cases have also contributed to insight into medical practice at the end of newborns' lives. The most important findings are summarized below.

In this overview, rather than speaking of 'newborn euthanasia' we use the phrase 'deliberate termination of life'. The reason being that the word 'euthanasia' may cause confusion. In the Netherlands 'euthanasia' is reserved for terminating the life of a mentally competent patient at the patient's considered request. Since infants are not mentally competent they cannot make any such request. Deliberate termi-

nation of life is defined here as administering lethal drugs with the express purpose of ending or shortening the life of a newborn who is otherwise stable.

The Situation in the Netherlands

— The acceptability of neonatal end-of-life decisions

In the Netherlands, end-of-life decision-making has been a topic of debate for several decades (27-31). Between 1990 and 1997, influential reports by the Royal Dutch Medical Association (KNMG) and by the Dutch Pediatric Association (NVK) on the medical and ethical acceptability of end-of-life decisions were published and reflect the views of the medical profession on the subject (32, 33). Two reasons for withholding or withdrawing life-sustaining treatment are recognized: either treatment stands no chance of success, or treatment would be futile. In the first case the physician should withhold and withdraw life-sustaining treatment. With regards to the latter, the position is taken that not only the survival of the infant per se is important but the child's the quality of life, if it were to survive, is also very important. The reports share the view that both the life-ending decisions (withholding and withdrawal of care) and the life-prolonging decisions should be legitimized. According to these reports, prolonging intensive care treatment in situations were prognosis is very grim might not always be in the infant's best interest. The quality-of-life considerations, as operationalized in the reports, should be bound strictly to medical criteria (34). In 1989 the much-debated case of the Dutch infant 'Baby Ross', who had trisomy 21 and duodenal atresia, illustrated that physicians sometimes interpret these criteria differently (35-38). Baby Ross died after the pediatric surgeon decided not to perform a life-saving operation. In order to determine whether the surgeon's considerations enjoyed wide support by the medical profession the court sought two medical expert opinions. The one expert supported the surgeon's decision by declaring that the operation was difficult and that in many ways the infant's post-operative prospects would have been very grim. The other expert contended the complete opposite: the operation was relatively easy and the infant would have led a medically uneventful life thereafter. The court followed the first expert's reasoning.

The KNMG and NVK reports also addressed the disagreement that exists among physicians about the acceptability of deliberately ending the life of a newborn. In the Netherlands deliberate termination of a newborn's life is a criminal offence. Based on two court cases held in the mid-nineteen nineties, known as the Prins and Kadijk cases, it is now accepted that under certain circumstances the physician can claim impunity, i.e. the defense of necessity (39, 40). In such circumstances the patient's suffering should be extreme, thus compelling the physician to choose between the duty to save lives on the one hand, and to do everything possible to prevent unbearable suffering, on the other hand. If the physician exercises due care, deliberate termination of life may be justified. The requirements of due medical care were formulated for the first time in the Prins and Kadijk cases.

Based on the review procedure implemented in 1994, it was a physician's statutory duty to report a case of deliberate termination of life of a newborn to the Public Prosecuting Service. Here the case was reviewed and the decision made whether or not to institute criminal proceedings against the physician in question (41). However, not al cases are reported to the authorities (42). Fear of criminal prosecution and uncertainty about the consequences of reporting such cases is the most

important barrier (43). In 1996, the Dutch Minister of Health, Welfare and Sport and the Minister of Justice jointly appointed a consultative committee to investigate the possibilities of implementing a more adequate review procedure. Among other things, the group recommended that a multidisciplinary committee of experts (consisting of physicians, a lawyer and a medical ethicist) be appointed to review the cases of medical procedures that had resulted in deliberate termination of life of newborns and to advise the officers of the Public Prosecution Service (44). This recommendation is supported by NVK (45). In the meantime, a guideline on deliberate termination of life has been drawn up and endorsed by the Dutch pediatricians (46). In 2006 a multidisciplinary committee of experts was finally installed (47). Currently, this committee of experts reviews all cases of deliberate termination of life.

— *Medical Practice in the Netherlands*

At the time the KNMG and NVK reports were issued, no systematic data were available on the circumstances and frequency of neonatal end-of-life decisions in the Netherlands. The first nation-wide surveys were held in 1995 and 2001. These showed that the death of two-thirds (65%) of infants younger than 12 months of age is preceded by an end-of-life decision (48, 49). In 18% to 23% of cases the decision is based on the poor prognosis of the infant. Palliative care medication (analgesics and sedatives) with potentially life-shortening effect were used in approximately 50% of newborns in the neonatal intensive care units (NICUs) (50). Administering medication with the intention to hasten death in newborns without a preceding decision to withhold or withdraw life-sustaining treatment occurs in 1% of deaths (48, 49, 51). Based on the data of the 1995 and 2001 surveys, it is estimated that at least 15 to 20 cases of deliberate termination of life take place annually (46, 48). No national guidelines on the administration of analgesics, sedatives and neuromuscular blockers as part of end-of-life care have been issued in the Netherlands.

— *Medical practice in Europe and the USA*

Studies about end-of-life practice in other European countries confirmed that withholding and withdrawing treatment are a common mode of death in most European NICUs (52-60). The proportion of newborns that died following a decision to withhold or withdraw life support increased to at least 60% during the past ten years in most European centers (55, 57, 58). Neonatologists reported that in a substantial proportion (20%—50%) of deaths these decisions are based on considerations regarding quality-of-life (56-58). Only a few authors reported details on the contents of the considerations. Provoost et al. reported that no hope for a 'bearable future' is the most frequently used quality-of-life consideration used by physicians in Flanders, the Flemish region of Belgium (62). More recently, Hentschel et al. reported that considerations such as severe disabilities and long-term, far-reaching therapy are used by neonatologists in Freiburg, Germany (61).

A European survey held in 1996 to 1997 showed that the proportion of neonatologists who ever decided to administer medication to hasten death varies considerably between countries (53). In the Netherlands and France large proportions of physicians have done so (75% and 43% respectively), while in Italy and Spain the proportions are much smaller (2% and 4% respectively). The only data on the practice of

administering medication with potentially life-shortening effects at the end of life in newborns stem from Flanders (62). These data showed that in 7% of newborn deaths drugs are administered with the intention to hasten death. In 11% of cases the administration of drugs clearly result in hastening the infants' deaths without the physicians intending to do so. Opinions on the acceptability of deliberate termination of life vary widely among physicians in Europe (25). Deliberate termination of life is reported to occur in exceptional situations in Flanders and France (53, 56).

Most studies reporting on neonatal end-of-life practices in the USA described the situation in individual units. The decision to withhold or withdraw treatment precede death in 14% to 30% in the early publications on neonatal end-of-life care (63, 64). More recent reports described rates between 25% and 72% (65-70). The proportion of end-of-life decisions based on quality-of-life considerations is reported in only a few publications and varies between 40% to 83% of deaths (65, 66, 68). Only two reports provided a more detailed description of these considerations. Wall and Partridge reported the prognosis for severe disabilities and the predicted suffering of the infants as the main quality-of-life concerns (65). Sing et al. stated that treatment is limited if the burden of continuing interventions outweigh the benefits of prolonging life (66). The most recent guidelines on non-initiation or withdrawal of care in the high risk newborn issued by the American Academy of Pediatrics (AAP) recommends that intensive care is not indicated if early death is highly probable and if survival would be accompanied by a high risk of unacceptable severe morbidity (71). According to AAP, in cases where the prognosis is uncertain but likely to be very poor and if survival is likely to be associated with diminished quality-of-life for the child, parental desires should determine the treatment approach. No data have been reported on physicians' adherence to these guidelines. Empirical data on the use of drugs as part of neonatal end-of-life care practice in the USA are not available. Guidelines on palliative or comfort care recommend physicians to increase analgesics and sedatives at the end of life to ensure that the patient is comfortable, even if possible side-effects of these drugs could hasten death (72-74). Using neuromuscular blockers as part of end-of-life decision-making is not accepted in end-of-life practice in the USA (22, 23, 75). In a neonatal palliative care protocol published recently, Catlin et al. reported that if at all possible neuromuscular blockers should be weaned from an infant's system prior to any form of treatment withdrawal (76). The main concerns against the use of neuromuscular blockers are: (a) paralysis precludes the possibility of survival (b) paralysis may hinder the clinician's assessment of the patient's comfort and (c) the opportunities for interaction between dying patients and their families are diminished (22). The issue of deliberately terminating a newborn's life is highly controversial in the USA and no cases have been published to date (77-86).

More Insight into End-of-Life Decision-Making

A limitation of most domestic and foreign studies on neonatal end-of-life decision-making is that they describe the physician's attitude towards end-of-life decisions and not the actual practice (87-92).Withholding or withdrawing care are rarely explicitly described in publications on NICU deaths. Even when withdrawal of care is described, the distinction between infants that would have died despite intensive interventions (moribund infants extubated to spend their last moments in their

parents' arms) and infants that were extubated to die for quality-of-life reasons, is rarely made (48, 55, 93-95). Moreover, it is often difficult to compare studies because the authors use different definitions of patient groups and interventions. A final limitation is that most studies provide only crude data on the physicians' reasons for administering potentially life-shortening medication, and data on the dosages used is incomplete (50, 62).
Insight into the considerations that lead to end-of-life decisions would facilitate the review of these decisions and may promote debate about end-of-life decision-making. It may also help the decision-making process of other physicians about what procedures to follow at the bed-side when faced with the medical, ethical and legal dilemmas described above.

Objective and Research Questions
The objectives of this thesis were to describe in detail the practice of end-of-life decision-making in severely ill newborns in the Netherlands and to describe how the end-of-life decisions were implemented, and when.
The following research questions were addressed:

1. How often were end-of-life decisions made in case of severely ill newborns and how could these decisions be typified (Chapters 3 and 4)
2. What were the considerations that led to the end-of-life decisions? (Chapters 3 and 4)
3. How were the end-of-life decisions implemented in these severely ill newborns, and when? (Chapters 3, 4 and 6)
4. What was the role of the parents in end-of-life decision-making? (Chapter 5)
5. How often did neonatologists decide to administer medication with a potentially life-shortening effect (analgesics, sedatives) and neuromuscular blockers as a part of their end-of-life practices? (Chapter 6)
6. What were the considerations that led to the decision to administer analgesics, sedatives and neuromuscular blockers? (Chapter 6)
7. Was the end-of-life decision sufficiently documented for internal and external review? (Chapters 3, 4 and 6)
8. How did end-of-life decisions made by neonatologists in the Netherlands compare to decisions made by neonatologists in other countries, and were they different? (Chapter 7)

Contents
In **Chapter 2** we present the background, the production-process and the contents of the 'Groningen Protocol' for deliberate termination of life of newborns. In **Chapter 3** we describe a pilot-study that investigated end-of-life decision-making and implementation in two Dutch centers. In **Chapter 4** we present the nation-wide frequencies of end-of-life decisions in severely ill newborns, the characteristics of the decisions and the considerations of the physicians that led to these decisions. In **Chapter 5** We describe the role of the parents in the end-of-life decision-making process concerning their infants and the frequency and nature of the differences of opinion between the medical team and the parents, and within the medical team itself. In **Chapter 6** our aim was to analyze the use of analgesics, sedatives and neuromuscular blockers as part of end-of-life decisions in Dutch NICUs. In **Chapter 7 we** compare the end-of-life decisions in severely ill newborns in centers

in the Netherlands (Groningen), Canada and the United States. Finally, in **Chapter 8** we summarize and discuss the main findings of the thesis, and put forward some suggestions for future research in end-of-life decision-making.

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Chapter 2

The Groningen protocol Euthanasia in severely ill newborns

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Of the 200,000 children born in the Netherlands every year, about 1000 die during the first year of life. For approximately 600 of these infants, death is preceded by a medical decision regarding the end of life. Discussions about the initiation and continuation of treatment in newborns with serious medical conditions are one of the most difficult aspects of pediatric practice. Although technological developments have provided tools for dealing with many consequences of congenital anomalies and premature birth, decisions regarding when to start and when to withhold treatment in individual cases re-main very difficult to make. Even more difficult are the decisions regarding newborns who have serious disorders or deformities associated with suffering that cannot be alleviated and for whom there is no hope of improvement. Suffering is a subjective feeling that cannot be measured objectively, whether in adults or in infants. But we accept that adults can indicate when their suffering is unbearable. Infants cannot express their feelings through speech, but they do so through different types of crying, movements, and reactions to feeding. Pain scales for newborns, based on changes in vital signs (blood pressure, heart rate, and breathing pattern) and observed behavior, may be used to determine the degree of discomfort and pain. Experienced caregivers and parents are able to evaluate the degree of suffering in a newborn, as well as the degree of relief afforded by medication or other measures. In the Netherlands, euthanasia for competent persons older than 16 years of age has been legally accepted since 1985. The question under consideration now is whether deliberate life-ending procedures are also acceptable for newborns and infants, despite the fact that these patients cannot express their own will. Or must infants with disorders associated with severe and sustained suffering be kept alive when their suffering cannot be adequately reduced? In the Netherlands, as in all other countries, ending someone's life, except in extreme conditions, is considered murder. A life of suffering that cannot be alleviated by any means might be considered one of these extreme conditions. Legal control over euthanasia in newborns is based on physicians' own reports, followed by assessment by criminal prosecutors. To provide all the information needed for assessment and to prevent interrogations by police officers, we developed a protocol, known as the Groningen protocol, for cases in which a decision is made to actively end the life of a newborn. During the past few months, the international press has been full of blood chilling accounts and misunderstandings concerning this protocol.

Infants and newborns for whom such end-of-life decisions might be made can be divided into three categories (1). First, there are infants with no chance of survival. This group consists of infants who will die soon after birth, despite optimal care with the most current methods available locally. These infants have severe underlying disease, such as lung and kidney hypoplasia.

Infants in the second group have a very poor prognosis and are dependent on intensive care. These patients may survive after a period of intensive treatment, but expectations regarding their future condition are very grim. They are infants with severe brain abnormalities or extensive organ damage caused by extreme hypoxemia. When these infants can survive beyond the period of intensive care, they have an extremely poor prognosis and a poor quality of life.

Finally, there are infants with a hopeless prognosis who experience what parents and medical expert deem to be unbearable suffering. Although it is difficult to define in the abstract, this group includes patients who are not dependent on in-

tensive medical treatment but for whom a very poor quality of life, associated with sustained suffering, is predicted. For example, a child with the most serious form of spina bifida will have an extremely poor quality of life, even after many operations. This group also includes infants who have survived thanks to intensive care but for whom it becomes clear after intensive treatment has been completed that the quality of life will be very poor and for whom there is no hope of improvement. Deciding not to initiate or to withdraw life-prolonging treatment in newborns with no chance of survival is considered good practice for physicians in Europe and is acceptable for physicians in the United States. Most such infants die immediately after treatment has been discontinued.

Neonatologists in the Netherlands and the majority of neonatologists in Europe are convinced that intensive care treatment is not a goal in itself. Its aim is not only survival of the infant, but also an acceptable quality of life. Forgoing or not initiating life-sustaining treatment in children in the second group is acceptable to these neonatologists if both the medical team and the parents are convinced that treatment is not in the best interest of the child because the outlook is extremely poor.

Confronted with a patient in the third category, it is vital for the medical team to have as accurate a prognosis as possible and to discuss it with the parents. All possible measures must be taken to alleviate severe pain and discomfort. There are, however, circumstances in which, despite all measures taken, suffering cannot be relieved and no improvement can be expected. When both the parents and the physicians are convinced that there is an extremely poor prognosis, they may concur that death would be more humane than continued life. Under similar conditions, a person in the Netherlands who is older than 16 years of age can ask for euthanasia. Newborns, however, cannot ask for euthanasia, and such a request by parents, acting as the representatives of their child, is invalid under Dutch law. Does this mean that euthanasia in a newborn is always prohibited? We are convinced that life-ending measures can be acceptable in these cases under very strict conditions: the parents must agree fully, on the basis of a thorough explanation of the condition and prognosis; a team of physicians, including at least one who is not directly involved in the care of the patient, must agree; and the condition and prognosis must be very well defined. After the decision has been made and the child has died, an outside legal body should determine whether the decision was justified and all necessary procedures have been followed.

A national survey of neonatologists in the Netherlands has shown that each year there are 15 to 20 cases of euthanasia in newborn infants who would be categorized in the third group (2). According to Dutch law, it is a doctor's duty to file a death certificate when a patient has died from natural causes. If a death is due to euthanasia, it cannot be certified as "natural." The doctor must inform the coroner, who inspects the body and, in turn, informs the district attorney, whose office reviews each case in light of the applicable laws or jurisprudence. The district attorney presents the case, together with his or her own opinion, to the College of Attorneys General, whose four members manage the national public prosecution department and provisionally decide whether or not to prosecute. The final decision is made by the minister of justice.

Two court cases, decided in the mid-1990s, regarding euthanasia in infants in the Netherlands provide some guidance for both judges and physicians. In the first

case, a physician ended the life of a newborn who had an extreme form of spina bifida. In the second case, a physician ended the life of a newborn who had trisomy 13. Both cases involved a very limited life expectancy and extreme suffering that could not be alleviated. In their verdicts, the courts approved the procedures as meeting the requirements for good medical practice. Although these rulings have given some guidance, many organizations have repeatedly pleaded for clearer guidelines, arguing that a committee with multidisciplinary (medical, legal, and ethical) expertise would be more capable than judges of assessing such cases. Physicians would be expected to be much more willing to report procedures to such a committee than they are to report to a district attorney. The Dutch government, however, has neither created a committee nor offered other guidance, despite having promised repeatedly, since 1997, to do so.

Twenty-two cases of euthanasia in newborns have been reported to district attorneys' offices in the Netherlands during the past seven years. Recently, we were allowed to review these cases (3). They all involved infants with very severe forms of spina bifida. In most cases (17 of the 22), a multidisciplinary spina bifida team was consulted. In the remaining five cases, at least two other independent medical experts were consulted. The physicians based their decisions on the presence of severe suffering without hope of improvement (see Table 1). The decisions were always made in collaboration with, and were fully approved by, both parents. The prosecutor used four criteria to assess each case: the presence of hopeless and unbearable suffering and a very poor quality of life, parental consent, consultation with an independent physician and his or her agreement with the treating physicians, and the carrying out of the procedure in accordance with the accepted medical standard. The conclusion in all 22 cases was that the requirements of careful practice were fulfilled. None of the physicians were prosecuted.

Given that the national survey indicated that such procedures are performed in 15 to 20 newborns per year, the fact that an average of three cases were reported annually suggests that most cases are simply not being reported. We believe that all cases must be reported if the country is to prevent uncontrolled and unjustified euthanasia and if we are to discuss the issue publicly and thus further develop norms regarding euthanasia in newborns. With that aim, we developed a protocol in 2002, in close collaboration with a district attorney. The protocol contains general guidelines and specific requirements related to the decision about euthanasia and its implementation. Five medical requirements must be fulfilled; other criteria are supportive, designed to clarify the decision and facilitate assessment (see Table 2). Following the protocol does not guarantee that the physician will not be prosecuted. Since implementing this protocol, our group has reported four cases in which we performed a deliberate life-ending procedure in a newborn. None have resulted in prosecution.

Dilemmas regarding end-of-life decisions for newborns with a very poor quality of life and presumably unbearable suffering and no hope of improvement are shared by physicians throughout the world. In the Netherlands, obligatory reporting with the aid of a protocol and subsequent assessment of euthanasia in newborns help us to clarify the decision-making process. This approach suits our legal and social culture, but it is unclear to what extent it would be transferable to other countries.

Table 1. Considerations Used to Support the Decision to End the Life of a Newborn (22 Cases).*

Consideration	Number of Cases (%)
Extremely poor quality of life (suffering) in terms of functional disability, pain, discomfort, poor prognosis, and hopelessness	22 (100)
Predicted lack of self-sufficiency	22 (100)
Predicted inability to communicate	18 (82)
Expected hospital dependency	17 (77)
Long life expectancy[Φ]	13 (59)

* Data are from Verhagen et al.(3)

[Φ] The burden of other considerations is greater when the life expectancy is long in a patient who is suffering.

Table 2. The Groningen Protocol for Euthanasia in Newborns

Requirements that must be fulfilled
The diagnosis and prognosis must be certain Hopeless and unbearable suffering must be present The diagnosis, prognosis, and unbearable suffering must be confirmed by at least one independent doctor Both parents must give informed consent The procedure must be performed in accordance with the accepted medical standard
Information needed to support and clarify the decision about euthanasia
-Diagnosis and prognosis Describe all relevant medical data and the results of diagnostic investigations used to establish the diagnosis List all the participants in the decision-making process, all opinions expressed, and the final consensus Describe how the prognosis regarding long-term health was assessed Describe how the degree of suffering and life expectancy were assessed Describe the availability of alternative treatments, alternative means of alleviating suffering, or both Describe treatments and the results of treatment preceding the decision about euthanasia -Euthanasia decision Describe who initiated the discussion about possible euthanasia and at what moment List the considerations that prompted the decision List all the participants in the decision-making process, all opinions expressed, and the final consensus Describe the way in which the parents were informed and their opinions -Consultation Describe the physician or physicians who gave a second opinion (name and qualifications) List the results of the examinations and the recommendations made by the consulting physician or physicians -Implementation Describe the actual euthanasia procedure (time, place, participants, and administration of drugs) Describe the reasons for the chosen method of euthanasia -Steps taken after death Describe the findings of the coroner Describe how the euthanasia was reported to the prosecuting authority Describe how the parents are being supported and counseled Describe planned follow-up, including case review, postmortem examination, and genetic counseling

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Chapter 3

Physician medical decision-making at the end of life in newborns: insight into implementation at 2 Dutch centers

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Abstract

Objective. Decisions regarding end-of-life care in critically ill newborns in the Netherlands have received considerable criticism from the media and from the public. This might be because of a lack of proper information and knowledge. Our purpose was to provide detailed information about how and when the implementation of end-of-life decisions, which are based on quality-of-life considerations, takes place.

Methods. We reviewed the charts of all infants who died within the first 2 months of life at 2 university hospitals in the Netherlands from January to July 2005 and EoL—end-of-life extracted all relevant information about the end-of-life decisions. We interviewed the responsible neonatologists about the end-of-life decision and the underlying quality-of-life considerations and about the process of implementation.

Results. Of a total of 30 deaths, 28 were attributable to withholding or withdrawing life-sustaining treatment. life-sustaining treatment. In 18 of 28 cases, the infant had no chance to survive; in 10 cases, the final decision was based on the poor prognosis of the infant. In 6 patients, 2 successive different end- of-life decisions were made. The arguments that most frequently were used to conclude that quality of life was deemed poor were predicted suffering and predicted inability of verbal and nonverbal communication. Implementation consisted of discontinuation of ventilatory support and alleviation of pain and symptoms. Neuromuscular blockers were added shortly before death in 5 cases to prevent gasping, mostly on parental request.

Conclusions. The majority of deaths were attributable to withholding or withdrawing treatment. In most cases, the newborn had no chance to survive and prolonging of treatment could not be justified. In the remaining cases, withholding or withdrawing treatment was based on quality-of-life considerations, mostly the predicted suffering and predicted inability of verbal and nonverbal communication. Potentially life-shortening medication played a minor role as a cause of death.

Introduction

In the past 2 years, the foreign press (especially in Italy, the United Kingdom, and the United States) has paid extensive attention to a supposedly outrageous practice in the Netherlands of physicians' terminating the life of severely defective newborn infants (1-7). It was suggested that all end-of-life (EoL) decisions in the Netherlands were in fact acts of euthanasia based on quality-of-life considerations, with reference to the medical practice in Germany during the Second World War. These accounts were based on the (mis)interpretation of publications regarding EoL decisions and the use of potentially life-shortening drugs in newborns in the Netherlands (8-13). Decisions on when to start, withhold, or withdraw treatment in very sick newborns are among the most difficult decisions in pediatric practice. The difficulty lies to a large extent in the dilemma that is presented by 2 views: the value of life and the quality of life. The advances in technology and pharmacology have created new possibilities to save and prolong the life of newborns, but extension of life can also result in endless and severe suffering, which might not be in the interest of the infant. Studies from the United States and Europe have reported that the proportion of sick newborns in whom the decisions to withhold or withdraw life support preceded death increased substantially during the past 10 years (14-16). Quality-of-life concerns have been reported by neonatologists as reasons for these decisions in a substantial proportion (20%—50%) of deaths (8, 9, 14, 17-20). Despite the frequency of these decisions, not much is known about what these quality-of-life concerns really are or about how the implementation of the decision takes place in practice. With respect to the latter, the role of potentially life-shortening drugs that alleviate pain and other symptoms at the end of life of newborns is of special interest. The legal difference between letting die and active ending of life is in principle based on the administration of these drugs.

The quality of EoL decisions, including the decisions regarding palliation of pain and symptoms, can be evaluated and compared between various countries only when sufficient insight is provided about medical practice at the end of life. With the purpose to gain more insight into what the medical practice in the Netherlands actually is, we conducted a retrospective descriptive study in 2 large university-based tertiary NICUs to determine the reasons that motivate physicians to make EoL decisions and how those are implemented in practice.

Methods

— *Demographics*

We reviewed the charts of all newborn infants who died in 2 university hospitals (A and B) with tertiary NICUs within the first 2 months of life between January and July 2005. We abstracted information from the attending physicians' and nurses' notes to determine demographics: birth weight, gestational age, day of death and diagnoses (using both clinical data and autopsy materials when available), and details about the decision-making process. According to Dutch law, no approval for this study from the ethical committee is required because it is a retrospective study using anonymous data.

The total number of NICUs in the Netherlands is limited to 10 by law to promote efficient use of expertise, manpower, and resources. All deliveries before 32 weeks'

gestation take place in a hospital with a NICU. Older newborn infants who require intensive care treatment are referred to these NICUs. Extracorporeal membrane oxygenation is not available in the study hospitals, and heart surgery is not available in NICU B. Patients who require these facilities are transferred to another NICU. In both NICUs, all medical decisions are made by a multidisciplinary team that is led by the attending neonatologist, who is ultimately responsible. The attending neonatologist also informs the parents of their infant's status and proposed treatment plans during regular discussions with the parents. Discussions regarding limiting treatment options are initiated by both the parents and the physicians. Consensus among all team members and the parents in EoL decisions is always sought. During the study period, 423 patients were admitted (280 in NICU A and 143 in NICU B), and the average daily census of critically ill patients was 19 in NICU A and 13 in NICU B.

— *Classification of Newborns*

The attending neonatologist's daily notes and death summaries were used to determine whether death had occurred with or without a preceding medical EoL decision. Medical EoL decisions were defined as medical decisions with the effect or the probable effect that death was hastened. These decisions include the decisions to withhold or withdraw life-prolonging treatment and the decision to end deliberately the life of a newborn. On the basis of the notes, we categorized the newborns at the time of each EoL decision into 1 of the following groups from the literature (10, 21): group 1, no chance to survive (NCTS); group 2, theoretical chance to survive, very poor prognosis (PP); or group 3, stable, hopeless prognoses with severe suffering, not depending on intensive care. During the study period, in neither center was a patient found to belong in group 3.

— *Decision-making and Implementation*

Physicians' notes were also reviewed to determine the physician's reasons to withhold or withdraw life-prolonging treatment in all deaths. We also ascertained which individuals were involved in the decision-making process. The treatment orders that were given by the physician on the basis of the EoL decision were collected from the files to describe the practice of implementation of these decisions. We used the medical charts and pharmacy notes to identify potentially life-shortening medication, comparing medication before and after the EoL decision. Medication before the decision was defined as the highest dosage of medication with potentially life-shortening effect as administered in the 12 hours before the EoL decision. We interviewed all neonatologists who were involved in each EoL decision with quality-of-life arguments face to face. We crosschecked all data that were extracted from the medical charts and asked them to explain in detail why they took the decision to withhold or withdraw treatment and how the decision was implemented. In cases in which potentially life-shortening drugs were used, we asked for the purpose. The reasons to limit treatment were grouped into categories that were derived from publications in the Dutch medico legal literature (22, 23).

— *Definitions*

Withholding treatment was defined as withholding potentially life-saving treatment, which included not only withholding cardiopulmonary resuscitation but also not providing additional intensive care treatment (eg, not making additional ventilator changes despite hypoxemia, not providing additional catecholamines despite hypotension) in accordance with definitions in the 1992 report by the Dutch Pediatric Association (22). Withdrawing treatment was taken to be equivalent to withdrawing life-sustaining treatment (eg, withdrawing the ventilator). Deliberate ending of life was defined as administering lethal drugs with the purpose to end the life or shorten the life of a newborn who is otherwise stable. We do not use the term "euthanasia" because in the Netherlands, this can be used only when a physician ends the life of a patient on the patient's explicit request, in accordance with the Dutch euthanasia law. In this legal framework, life shortening as an inevitable adverse effect of appropriate pain and/or symptom alleviation is considered acceptable clinical practice. The legal and moral status of administering lethal drugs with the purpose to shorten life in an unstable newborn in the dying phase, as part of careful EoL management, is still uncertain and subject to ongoing debate.

Results

— *Demographics*

A total of 30 newborns died within the first 2 months of life in the 2 hospitals during the 6-month study period: 21 died in hospital A, and 9 died in hospital B. Twenty-nine infants died in a NICU, and 1 patient died on a PICU. Table 1 shows the main characteristics of all deaths and the categories in which all newborns were classified. Overall, 24 (83%) deaths were attributable to withdrawal of treatment, 4 (10%) were by withholding treatment, and 2 (7%) occurred despite maximum treatment. The diagnoses that led to death varied, the largest group being term newborns with hypoxic-ischemic encephalopathy (23%).

— *Classification of Newborns*

The data from the medical charts were sufficient to classify all patients in categories. Of all 28 deaths that were preceded by an EoL decision, 18 (64%) were classified as NCTS and 10 (36%) as PP at the time of the final decision. The proportion of deaths in the PP category was the same in both hospitals: 6 (35%) of 17 in hospital A and 4 (36%) of 11 in hospital B. In 9 (32%) of cases, 2 EoL decisions were made, with a median of 24 hours (range: 6-210 hours) between the first and the second decision. Six of these patients were initially classified as PP and moved to NCTS at the time of the second EoL decision. The proportion of deaths that were preceded by an EoL decision and classified as PP was the same in both hospitals: 6 (35%) of 17 in hospital A and 4 (36%) of 11 in hospital B.

— *Decision-making and Implementation*

In all deaths in the NCTS group, it was apparent from the physicians' notes that treatment was withdrawn because there was no chance of survival. Both the parents and the medical team consented to the decision in all documented cases (Table 2). The median time between the final decision and implementation of the decision was 2 hours (range: 0—24 hours). In 1 case, the time course was undocumented.

The implementation consisted of discontinuation of artificial ventilation and removal of the endotracheal tube in all cases except 1. In 1 case, the patient was gradually weaned from the ventilator in 24 hours on parental request. Intravenous medication and fluids were continued until death in all cases. The median time between implementation and death was 30 minutes (range: 1—105 minutes).
In all cases of PP, treatment was withheld or withdrawn because the prognosis was considered very poor. The considerations that led to this conclusion were documented in the medical charts but without much detail (eg, treatment stopped because quality of life is deemed low). Table 3 shows more detailed information from the interviews indicating that in all cases, >1 consideration was present. The predicted very low quality of life was most frequently based on the predicted suffering and predicted inability to communicate. With inability to communicate, the neonatologists meant inability to be engaged in any kind of communication with other people, verbally or nonverbally (eg, because of deafness and blindness combined with predicted severe mental retardation or predicted vegetative state).
The median time between the decision and implementation of the decision in cases of PP was 1 hour (range: 0—24 hours). The implementation consisted of discontinuation of artificial ventilation and extubation in all cases except 1. In 1 case, the ventilatory support was weaned stepwise in 24 hours on the parents' request. The median time between implementation and death in this group was 60 minutes (range: 15—360 minutes).
Each of the documented decisions was preceded by at least 1 or more decision-making meetings of the medical team followed by 1 or more with the parents. In these meetings, provision of sedation and analgesia as potentially life-shortening medication was also discussed. Table 4 presents the use and dosing of this medication before and after the final EoL decision. Before the final EoL decision was made, the majority of cases in NCTS (n=15; 83%) and in PP (n=9; 90%) received opioids and benzodiazepines. In all cases, the dosage was within the normal dosing range. Two newborns with pulmonary hypertension were treated with neuromuscular blockers (NMBs) as part of the hospital's standard treatment of this disease. Additional medication after the final EoL decision was administered in 7 (39%) cases in NCTS and 8 (80%) cases in PP. It was given as an increased dosage of the existing continuous medication or as a bolus infusion. The dosages remained within normal dosing range. The reasons to provide additional medication were treatment of presenting symptoms (eg, pain, dyspnea, discomfort) and prevention of suffering from these symptoms in the process of dying. None of the physicians interviewed considered hastening death as the aim of additional medication, but all declared that they would consider it an acceptable adverse effect. NMBs were added in 5 newborns in PP. Four of them had a diagnosis of hypoxic-ischemic encephalopathy, 1 with sepsis/meningitis. In 4 of 5 cases, NMBs were prescribed to prevent gasping. In 3 of these cases, this was done on explicit parental request, and in 1 case, it was the physician's decision to do so because it was expected that gasping would scare the parents away from their dying child. In the remaining case, the dosage of previously prescribed NMB was increased to ensure optimal effect, whereas discontinuation was expected to impose unnecessary suffering. All cases were classified as deaths from natural cause by the attending neonatologists.

Discussion

The attitude of neonatologists in the Netherlands regarding EoL issues has been reported extensively in several publications (8-11, 24-26). This study is the first to report in detail to which practices this attitude really leads. We acknowledge several limitations of this study. First, our data may not be representative of the medical practice regarding sick newborns nationwide, because we evaluated data from 2 of 10 hospitals with NICUs. However, these 10 NICUs have regular meetings, and they use the same practice guidelines including those regarding EoL decision-making. Second, no information is provided on other potentially important factors in the decision-making, such as the parents' experience and their perception of the management of symptoms around the time of death. Third, our retrospective analysis of decision-making may have been influenced by inaccuracy in recall of arguments by the neonatologists who were interviewed.

We found that 28 (93%) of a total of 30 deaths were attributable to the decision to withhold or withdraw life-sustaining treatment. Withdrawal of life-sustaining treatment was much more common than withholding treatment (86% vs 14%). The proportion of deaths that resulted from withholding or withdrawal of treatment in our study is substantially higher than that described in the early articles on neonatal EoL care (14%—30%) (27, 28).

Most more recent reports from centers in the United States, the United Kingdom, Australia, and Europe have reported rates between 58% and 75% (15-18, 29). Only 2 studies have described similar proportions as our study. Barton and Hodgman (30)reported that 124 (86%) of 146 deaths had treatment withheld or withdrawn in their unit between 1998 and 2002. Arlettaz et al (19) reported that in 93% of 199 deaths, treatment was withheld or withdrawn. The relatively high proportion in our study is likely to reflect the prevailing approach of the Dutch neonatologists that in sick newborns, it is not only the life-ending decision but also the life-prolonging decision that must be justified (10, 22). In their opinion, if treatment is medically futile, then it should be stopped to prevent unnecessary suffering of the infant. Considering that this is a nationwide approach, it can be assumed that the high proportion reported by us is representative of the whole country. It may also reflect the philosophy of Dutch physicians that when a newborn is clearly dying or going to die despite treatment, all efforts must be made to let the child die in the arms of the parents, disconnected from the ventilator. In our study, the decision to withhold treatment under these circumstances was taken as an EoL decision, whereas in other studies, these cases were classified as deaths despite maximal support (16) or classification remained unclear (15, 30). This observation illustrates that comparison of the contribution of withholding or withdrawing treatment between studies is difficult because definitions vary between studies. Singh et al (14) took withholding treatment to be equivalent to withholding cardiopulmonary resuscitation and withdrawing as withdrawing of mechanical ventilation. A much broader definition, as used by Wall and Partridge(18)and by us, is likely to result in a higher rate of deaths after withholding or withdrawing of treatment.

Decisions that were based on quality-of-life arguments (PP) preceded death in 16 (57%) of 28 deaths in our study. Comparison of this finding with other studies is hampered by the fact that all other studies focused on the final decision that led to death. We included all EoL decisions that preceded death in our analysis and observed that in a substantial number of cases (9 [32%] of 28), 1 type of EoL decision

was made. Our results show that in most cases, the first decision was the decision to withhold treatment because of the patient's PP. Several hours to days later, it was determined that the patient had NCTS and the second decision to stop treatment was made. The newborn had shifted from PP to NCTS. One explanation for this shift could be that the first decision to withhold treatment was made to gain time without imposing additional burden, hoping that the restricted treatment would still lead to improvement. Instead of improving, the clinical situation of the child worsened over time, as a result of the underlying disease, resulting in absence of a chance of survival. Another explanation could be that the decision to withhold treatment was initially more acceptable for the parents. A third possibility could be that by withholding life-saving treatment, the physician created a situation in which survival was simply not possible. By evoking this situation, the physician prevented the more difficult discussion about quality of life. We think that our observation suggests that classification of EoL decisions in newborns can not be based on the final decision only. Evaluation and comparison of the decision-making process in NICUs and, specifically, the quality-of-life arguments at the end of life in newborns must include all previous decisions because of the possible causality between these decisions.

The neonatologists in our study used general and specific quality-of-life considerations to justify why the predicted quality of life was deemed very low. The general considerations relate to the moral principle of proportionality of treatment, suggesting that the "costs" in terms of additional burden for the patient versus the foreseeable "effects" in terms of improvement of the patient's medical condition must be balanced. The most frequently used specific considerations were predicted suffering and the predicted inability to be engaged in any kind of verbal and nonverbal communication. These considerations seem to legitimize limitation of treatment for neonatologists in the Netherlands. Only a few authors have reported similar details regarding quality-of-life arguments. Wall and Partridge (18) reported the prognosis for severe disabilities and the infant's predicted suffering as the main quality-of-life concerns. Sing et al. (14) described that treatment was limited if the burden of continuing interventions outweighed the benefits of prolonging life. Recently, Hentschel et al. (31)reported PP; severe disabilities; and long-term, far-reaching therapy as considerations.

The infants in this study died relatively fast after the last decision to withhold or withdraw life-saving treatment. Death occurred after a median time of 30 and 60 minutes in NCTS and PP groups, respectively. We were interested in the role of medication with potential life shortening effect around the time of death. We found that provision of sedation and analgesia was discussed at each decision-making meeting. The medication was administered before and after most EoL decisions to treat symptoms around the time of death (pain, dyspnea, and discomfort). Dosages have consistently remained within normal dosage levels in all cases. This finding suggests a limited role of the potentially life-shortening medication as the cause of death, although lethal adverse effects of the medication cannot be ruled out completely. Earlier studies about the use of potentially life-shortening drugs in the Netherlands focused on the intentions of the physician to differentiate between active ending of life and letting die (8, 9, 32). The problem with intentions is that they are very subjective, ambiguous, and sometimes unclear even to the physician himself or herself (33, 34). We have tried to find the medical reasons for

the decision to administer medication. Neonatologists in our study consistently pointed out that the purpose was alleviation of symptoms in all cases. At the same time, they confirmed in the interviews that hastening death as a possible adverse effect of adequate palliative care would be acceptable. This is in line with other reports from neonatologists (12, 35, 36). The underlying "double effect" principle, suggesting that an action that causes a serious harm (death) can be permissible as an adverse effect of promoting some good end (relief of pain and suffering), is accepted in common medical practice of critical care and EoL care (34).

Pain and symptom management at the end of life is known to be of great concern to parents (37). A remarkable finding in this respect was that NMBs were administered shortly before death in 5 patients in the PP group. In 4 of these cases, the purpose was to prevent gasping of the infant. In 3 of 4 cases, administration took place on explicit request of the parents. In the discussions with the medical team, the parents made it clear that they would not accept suffering and agony. The role of NMBs in symptom management at the end of life is controversial. Several studies have reported a practice in the use of these agents at the end of life in children (12, 38-40). Most commentary on this issue has concluded that the initiation of these agents as the ventilator is being withdrawn is morally indefensible (40-42). Some have argued that the desire to comfort the patient's family is an important consideration and that initiating neuromuscular blockade can be acceptable when the patient's death after the withdrawal of mechanical ventilation is certain (43-45). However, others believe that the patient's well-being is always more important than family interests. They argue that neuromuscular blockade potentially masks symptoms of pain and suffering and makes proper assessment and adequate treatment impossible (46). Our study is the second to report that parents sometimes explicitly request the use of lethal drugs for their child (47). We think that a request from parents shortly before a certain death is completely understandable because the sight of a gasping child is a potent source of stress and discomfort to all people who witness the dying newborn. Neonatologists in our study were prepared to grant the parental request. This suggests that they accepted the parents' distress as their responsibility. It is uncertain whether the use of medication with a certain lethal effect can be legitimized by referring to this responsibility. We are convinced that robust palliative care is indicated in all EoL situations, providing parental education and support about the EoL physical signs in the dying child, supportive staff, anticipatory grief work, and bereavement service follow-up. If the parental request to administer NMBs to the dying newborn consistently persists despite all of theses measures, then we think that the requests should be granted in the presence of skilled and experienced clinicians.

The results of this study also confirm that deliberate ending of life in newborns remains a rare event, also in the Netherlands, where it is considered to be legally acceptable (48-50). In 6 months, no cases were registered in the study hospitals.

Conclusions

We report that the vast majority of deaths in 2 Dutch units were attributable to withholding or withdrawing of treatment. In most cases, the newborns had NCTS and prolonging of treatment could not be justified. In the remaining cases, the decision was based on a combination of quality-of-life considerations, mostly the predicted suffering and predicted inability of verbal and nonverbal communication. Potentially life-shortening medication played a minor role as a cause of death in the implementation. No case of deliberately ending the life of a newborn occurred.

Table 1. Patient characteristics, EOL-decision characteristics of all deaths in 2 NICU's from January to July 2005

patient, hospital	GA, wk	weight g	age at death, d	diagnosis that lead to death	decisions and patient-classification		time between decisions, h
					preceding decision	final decision	
1, A	31	2210	1	hydrops foetalis		continue treatment	
2, A	29	990	1	lunghypoplasia		continue treatment	
3, A	40	2800	29	hypoplastic heart syndrome		withdraw, NCTS	
4, A	34	1900	1	congenital malformations		withdraw, NCTS	
5, A	28	630	33	extremely low birth weight, sepsis		withdraw, NCTS	
6, A	40	4100	2	meconium ileus, perforation, sepsis		withdraw, NCTS	
7, A	41	3530	1	diaphragmatic hernia		withdraw, NCTS	
8, A	32	2150	1	lunghypoplasia		withdraw, NCTS	
9, A	27	1100	8	sepsis		withdraw, NCTS	
10, B	27	760	10	extremely low birth weight, sepsis		withdraw, NCTS	
11, B	28	1005	7	sepsis, IVH		withdraw, NCTS	
12, B	31	680	1	circulatory failure, hyperkaliemia		withdraw, NCTS	
13, B	33	1560	1	diaphragmatic hernia, cong malformations		withdraw, NCTS	
14, B	37	2675	1	Potter's Syndrome		withhold, NCTS	
15, A	31	1128	2	trisomy 18	withhold, PP	withdraw, NCTS	6
16, A	36	2950	1	dysplastic kidney, lunghypoplasia	withhold, PP	withdraw, NCTS	12
17, A	39	3850	50	cong heart disease	withhold, PP	withdraw, NCTS	144
18, A	30	1370	20	cong heart disease, cerebral malformation, NEC	withhold, PP	withdraw, NCTS	72
19, B	29	970	2	HIE, convulsions	withhold, PP	withdraw, NCTS	20
20, B	31	515	81	NEC, MOF	withhold, PP	withdraw, NCTS	216
21, A	36	3500	3	hydrops foetalis, HIE	withhold, PP	withdraw, PP	24
22, A	40	3445	3	HIE	withhold, PP	withdraw, PP	43

23, A	34	2600	10	sepsis/meningitis, sinus thrombosis	withhold, PP	withdraw, PP	24
24, A	27	915	1	PPHN		withhold, PP	
25, A	39	3400	1	HIE		withhold, PP	
26, B	37	2760	1	HIE, convulsions		withhold, PP	
27, A	39	2750	11	HIE, cong.malformations		withdraw, PP	
28, B	37	2645	6	chondrodysplasia punctata, sepsis, PPHN		withdraw, PP	
29, B	39	3940	4	HIE, MOF		withdraw, PP	
30, B	37	3100	10	HIE, MOF, NEC		withdraw, PP	

GA indicxates gestational age; IVH, intraventricular hemorrhage, HIE, hypoxic ischemic encephalopathy, NEC, necrotizing enterocolitis, MOF, multiorgan failure, PPHN, persistent pulmonary hypertension of the neonate

Table 2. Decision making and implementation in 30 deaths

patient	Parental consent	Team decision	Time between last EOL decision and Implementation, h:min	Time between implementation and death, h:min
1	-	-	-	-
2	-	-	-	-
3	+	+	3:15	0:05
4	+	+	5:30	0:45
5	+	ND	4:30	0:30
6	+	+	1:45	0:30
7	ND	+	ND	ND
8	+	+	0:00	0:15
9	+	+	0:00	0:10
10	+	ND	0:00	ND
11	+	+	0:15	0:10
12	+	+	0:00	0:05
13	+	+	0:00	0:01
14	+	+	0:00	0:30
15	+	+	17:30	1:00
16	+	+	0:10	1:15
17	+	+	17:00	0:15
18	+	+	3:35	0:45
19	+	+	2:00	0:30[a]
20	+	+	24:00	0:30
21	+	+	21:00	3:0
22	+	+	0:00	1:15
23	+	+	5:00	0:30
24	+	+	0:00	1:45[a]
25	+	+	0:00	6:0
26	+	+	0:00	1:0
27	+	+	16:30	0:15
28	ND	ND	0:00	1:50
29	+	+	2:00	0:30
30	+	+	7:30	0:25

Data are derived from the medical files. ND indicates not documented.

[a] no extubation on parental request

Table 3. Considerations to decide to withhold or withdraw treatment because of a PP in all newborns in group 2 (n=16)

Considerations	Hospital A (n=11) Frequency (Patient)	Hospital B (n=5) Frequency (Patient)
Treatment does not contribute to medical condition	3 (17,23,28)	4 (19,20,29,30)
Treatment is disproportionate	6 (15-18,22,28)	1 (30)
Predicted very low quality of life:	6 (15,16,21,22,25,27)	5 (19,20,25,29,30)
Predicted inability to communicate	3 (22,24,27)	2 (26,30)
Predicted lack of self-sufficiency	1 (24)	1 (26)
Expected hospital dependency	1 (16)	1 (26)
Long life expectancy	-	-
Predicted suffering:	5 (15,16,22,25,27)	4 (18,19,29,30)
from pain (now and future)	-	1 (30)
from discomfort	-	-
from functional disability	1 (25)	1 (29)
from poor prognosis	2 (15,16)	5 (19,20,26,29,30)
from hopelessness	3 (15,16,22)	2 (19,29)
Other: patient not aware of own existence	1 (21)	

Data are derived from interviews with the responsible neonatologists

Table 4. Use of potentially life-shortening medication, before and after the last EOL-decision, in NCTS and PP groups

Patient	classification [a]	Mediation before the last EOL-decision (dosage)[b]	Additional medication after last EOL-decision (dosage)	motivation for additional medication[c]
1	-	-	-	-
2	-	-	-	-
3	NCTS	Fentanyl (5) , lorazepam (B 100)		
4	NCTS	Morphine (20)		
5	NCTS	Morphine (10)	Morphine (20)	pain
6	NCTS	Morphine (20)		
7	NCTS	Morphine (15), midazolam (0,05)	Morphine (20)	ND
8	NCTS	Morphine (15)		
9	NCTS	-	Morphine (20)	pain, dyspea
10	NCTS	Morphine (10)		
11	NCTS	Fentanyl (3), midazolam (0,02)	Fentanyl (B: 4)	pain, discomfort
12	NCTS	Fetanyl (3)		
13	NCTS	-		
14	NCTS	-		
15	NCTS	Morphine (5) midazolam (0,05)	Morphine (15), midazolam (B: 0,1)	discomfort, dyspnea
16	NCTS	Morphine (15)		
17	NCTS	Morphine (15), midazolam (0,02), lorazepam (B: 0,1)	Morphine (20), midazolam (0,04)	discomfort
18	NCTS	Morphine (20)	Morphine (50)	discomfort, gasping
19	NCTS	Fentanyl (2)	Fentanyl (B: 5 + 5)	Pain, discomfort
20	NCTS	Fentanyl (2), midazolam (0,02)		

21	PP	Morphine (20), midazolam (0,02)	Midazolam (I: 0,15)	
22	PP	Midazolam (I: 0,15)	Vecuronium (B: 50)	prevention of parental discomfort (gasping)
23	PP	Midazolam (I: 0.15)	Morphine (20), vecuronium (40)	discomfort, parental request (gasping)
24	PP	Morphine (10), vecuronium (40)	Morphine (10), midazolam (0,02), vecuronium (B: 50)	discomfort, prevent gasping
25	PP	Morphine (15), midazolam (I: 0.1)	Morphine (B: 10), midazolam (I: 0,1), vecuronium (B: 50)	discomfort, parental request (gasping)
26	PP	Fentanyl (2)		
27	PP		Midazolam (0,02), morphine (10)	pain, discomfort
28	PP	Morphine (15) vecuronium (40)		
29	PP	Fentanyl (2)	Vecuronium (B: 50)	gasping, parental request
30	PP	Fentanyl (3), midazolam, (0,02)	Fentanyl (B: 3+3)	discomfort

Dataare as stated in the medical charts. B: indicates bolus infusion, I, intermittend dose

[a] at the time of the last EOL-decision

[b] highest dose in 12 hours before final EOL-decision, continuous IV unless indicated differently, in units as used in normal dosing. Normal dosing: morphine 25-50 ugr/kg/h, fentanyl 0,5-5 ugr/kg/h, midazolam 0,01-0,06 mg/kg/h, intermittent (I) 0,05-0,15 mg/kg/dose, lorazepam 0,1-0,4 mg/kg/dose, vecuronium 30-150 ug/kg/h, intermittent 100 ug/kg/dose.(51)

[c] motivation in PP group was taken from the interviews

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Chapter 4

End-of-life decisions in severely ill newborns in the Dutch NICU

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Abstract

Background. Many deaths in newborns are preceded by the decision to withhold or withdraw life-sustaining treatment. We performed a nationwide study in the Netherlands of the practise of end-of-life decision-making in severely ill newborns.

Methods. We reviewed the files of 359 deaths over a 12 months period in all 10 NICU's and interviewed the physicians attending 147 out of 150 deaths preceded by an end-of-life decision based on quality of life.

Results. End-of-life decisions preceded death in 95% of cases and in 5%, treatment was continued until death. Of all deaths, 58% were classified as no chance to survive and 42% were stabilised newborns with a poor prognosis. Withdrawal of life-sustaining therapy was the main mode of death in both groups. One case of deliberate ending of life was found. In 92% of deaths in the poor prognosis group, end-of-life decisions were based on the patient's future quality of life and concerned mainly future suffering. In 44% of deaths, these considerations were used in conjunction with considerations regarding the present quality of life. Parents were always involved in the decision making process. Consultation of colleagues within the medical team occurred in 99% of cases.

Conclusion. Virtually all deaths in the Dutch NICU's are preceded by the decision to withdraw life-sustaining treatment and many decisions are based on the future quality of life. The decision to deliberate end the life of newborn may occur less frequently as was previously assumed.

Introduction

The increasing technical possibilities to save and extend the lives of newborns have also created discussions about the role of physicians in decisions regarding the timing and modes of death and dying of newborns. Many deaths of neonates in the developed countries are not merely the result of a natural course, these are frequently preceded by the medical decision to withhold or withdraw potentially life-sustaining treatment.(1-6) Most studies describing end-of-life practice, however, do not make the important distinction between withholding or withdrawing treatment in situations where death is imminent or the newborn is moribund, and the situation where this takes place in stabilised newborns for quality of life reasons. Recent data from the USA and Europe suggest that the future quality of life is the main reason for the decision to withdraw life-sustaining treatment in 16-50% of newborn deaths.(1, 2, 4, 7-11) Despite the considerable frequency, only few studies have reported details about what the considerations leading to end-of-life decisions are and how they are used. As a consequence, real insight in medical end-of-life practice has remained limited and comparison of outcomes between units is problematic. After repeated requests by the Dutch medical profession for more transparency and clarity about the review procedure of deliberate termination of life of newborns, the criteria and requirements of due care (12, 13), the Dutch government appointed a committee of experts in 2006 and as a result the procedures for reporting such cases were changed (14, 15). One of the important reasons for having a notification and external review procedure in place in cases of deliberate termination of life of newborns is to supervise that the physician's conduct meets the criteria of due care (16). Based on these new regulations, physicians are required to report all cases of deliberate termination of a newborn's life to the public prosecutor who in turn submits the report to the committee of experts (17). The committee (consisting of a lawyer-chairman, an ethicist and three physicians specialized in the field of neonatology) reviews the case in order to establish whether or not the physician has met the criteria of due care (18). The committee's recommendations are taken into account by the prosecuting authorities who decide whether prosecution will be instituted against the physician.

With the purpose of clarifying end-of-life practice in seriously ill newborns in the Netherlands, we performed a nationwide retrospective study to determine when and how physicians take end-of-life decisions.

Methods

We performed a retrospective descriptive study of the Dutch end-of-life practice in seriously ill newborns. In the Netherlands, clinical care for these newborns is centralised in 8 university hospitals and 2 large general hospitals with level III NICU's. The total number of NICU's is limited to 10 by law in order to promote efficient use of resources. All deliveries before 32 weeks gestation should take place in a hospital with a NICU. Transportation teams operated by these hospitals provide transportation services for ill newborn infants admitted in other hospitals.

Demographics

We reviewed the files of 367 newborns that died in the first 2 months of life in the 10 NICU's in the Netherlands between October 2005 and September 2006. Identification took place through the national perinatal registry and these data were crosschecked with the hospital's admission and discharge register. Infants who died immediately after birth in the delivery room were not included. The patients were eligible for the study when a medical file was available for review. We found 359 deaths with complete documentation and abstracted information from the attending physicians' and nurses' notes to determine demographics: birth weight, gestational age, day of death and diagnoses (using both clinical data and autopsy materials when available). The attending physicians' daily notes and death summaries were used to determine whether or not death had occurred with a preceding end-of-life decision. End-of-life decisions were defined as medical decisions with the effect or the probable effect that death was hastened. These decisions include the decision to withhold or withdraw life-sustaining treatment and the decision to deliberately end the life of a newborn. Deliberate ending-of-life was defined as administering lethal drugs to end the life, or shorten the life of a newborn. With respect to deliberate ending of life, we focused on newborn infants who were physiologically stabile.

Classification of deaths

We used the physician's motives for withholding or withdrawing life-sustaining treatment to categorise the newborns as group I, II or III in accordance with a two-dimensional classification from the literature.(19, 20) The classification is based on the infant's prognosis and its dependency on intensive care for physiologic stability. Group I encompasses infants whose death is imminent. Newborns who are actually dying (heart rate falling, blood pressure dropping, oxygen saturation dropping) are included but also those with inoperable life-threatening congenital defects or with diseases that are considered untreatable by the medical team. Group II consist of physiologically stabilized intensive care dependent newborns with a very poor prognosis. Newborns in this group stand a theoretical chance of survival, but the predicted quality of life is very poor. Many newborn infants with severe hypoxic ischemic encephalopathy are included in this group, together with babies with chromosomal or neurological disease and extreme premature infants with grade IV intracranial bleedings with clinical symptoms. Group III encompasses stable newborns with a very poor prognoses and severe suffering, not dependent on intensive care.

We first identified from the medical charts patients belonging to group I. The infants who could not be categorized due to unclear or absent descriptions, and those with end-of-life decisions based on the patients' prognosis (groups II and III) were evaluated in a face-to-face interview with the physician who was responsible for the end-of-life decision. The interviews were used to categorise the unassigned infants, to crosscheck the assigned category and to discuss the physicians' arguments for each decision. The physicians were asked to consult medical charts during the interview. The arguments were grouped into categories derived from the literature and crosschecked again for accuracy with the physician.(21, 22) All interviews were conducted by an experienced paediatrician (AV) and lasted between 30-45 minutes per patient. Several interviews took place in the presence of a qualified legal scholar

(JD). Here, the physicians were asked whether or not their motives for an end-of life decision were related to legal considerations and if so, to which. These outcomes will be published separately.
In the Netherlands, previous studies on end-of-life practice were done with the guarantee of legal immunity for the data collection.(7, 23) For this study this additional protection was lacking, and therefore, we tested the study design and feasibility in two pilot studies. (11, 24) According to Dutch law, no approval for this study from the Ethical Review Board is required as it is a retrospective study using anonymous data.

Statistical analysis
We compared the causes of death by using chi-squared test for categorical variables. P values of less then 0.05 were considered to indicate statistical significance

Results
Of the 367 newborns that died during 12 months in the 10 Dutch NICU's, complete documentation was available for 359 deaths. (98%) The main demographic data and patient characteristics are shown in table 1. The main causes of death in term patients were asphyxia (47%) leading to severe brain dysfunction and multi-organ failure (MOF) together with congenital malformations (37%) predominately from the heart (table 2). Below 30 weeks of gestational age, the main causes of death were MOF caused by sepsis/necrotising enterocolitis (NEC) (41%) or complications of extreme prematurity (31%). The distribution of causes of death was similar in all 10 units.
Of 359 deths, 340 (95%) were preceded by an end-of-life decision and 19 (5%) died while receiving cardiopulmonary resuscutation (CPR). The most frequent end-of-life decision was to withdraw life-sustaining treatment (294 cases). Death attributable to withholding treatment occurred in 46 cases, deliberate ending of life was found in 1 case.
A total number of 208 of 359 deaths (58%) were classified as no chance of survival (group I) and 150 (42%) as poor prognosis (group II) (figure 1.) There was no difference in the percentage of patients in group I and II between the 10 centres. One newborn with type II osteogenesis imperfecta was classified as: not intensive care dependent but with a poor prognosis and severe suffering (group III). The attending physician intentionally increased the morphine medication until death occurred, after it became evident that the patient's intolerable suffering could not be relieved otherwise. After several weeks, the medical team reviewed the case and concluded that in retrospect, their practice could best be described as deliberate ending of life.
Congenital malformation and respiratory insufficiency caused death significantly more often in group I than in group II. Asphyxia caused death significantly more frequent in group II patients as compared to those in group 1(table 3).
In 56 out of 359 patients (16%), two end-of-life decisions were made. The first decision not to intensify treatment by adding more life support was followed by the final decision to withdraw treatment after a median interval of 24 hours (range 0,4-425 hours) between both decisions. Ten of these patients were initially classified as group II but changed to group I at the time of the final end-of-life decision.
We interviewed 80 physicians, responsible for the decision to withhold or withdraw life-sustaining treatment in 147 out of 150 group II deaths. Data of 3 deaths were

missing because we were unable to locate 2 physicians. Table 3 shows the quality of life considerations used by the physicians in end-of-life decision-making. In most cases (119 out of 147), more than one consideration was used. Considerations regarding the patient's expected future quality of life were used in 135 of 147 patients (92%) and concerned mostly predicted suffering (76%). Considerations regarding the present quality of life were used in 71 patients. In 64 patients, both types of considerations were considered important.
According to the medical files, the parents of newborns in group I consented with the end-of-life decision in 194 out of 208 cases and no documentation of parental involvement was found in 14 out 208 cases. In group II, the parents were always involved in the decision making process and the end-of-life decision was never against the parent's wishes. This was stated in the medical files and confirmed in the interviews. Consultation of colleagues within the medical team occurred in 99% of group II cases. In 22 cases, independent physicians from another NICU were consulted

Discussion
This retrospective descriptive study investigated end-of-life decisions in newborns in the Dutch NICU's over a period of 1 year. The study has yielded three important findings. First, this study showed that in 95% of all deaths below 2 months of age, any form of physician end-of-life decision took place. This indicates that physicians play a prominent role in the timing and modes of death and dying in the Dutch NICU. Second, we report that infants who had no chance of survival made up the largest proportion of deaths (58%). In the remaining group of infants, treatment was withdrawn or withheld because of the very poor prognosis for later life, mostly based on the patient's predicted suffering (76%). Third, we found only one case of deliberate ending of a newborn's life. This suggests that deliberate ending of life in severely ill newborns occurs less frequently than was previously assumed.

More than 95% of deaths in the neonatal intensive care units in our study occurred after withdrawal or withholding of potentially life saving treatment. This proportion is substantially higher than that described in the early papers on neonatal end of life care (14—30%). (25, 26)
It is also slightly higher than the rates reported more recently in studies from other units in the USA, Europe and Australia (58-93%).(1-4, 6, 8, 10, 11, 27-29)
The relatively high proportion of deaths that followed an end-of-life decision may reflect the referral base of the NICUs. In the Netherlands high-risk neonatal care is centralized in the ten NICUs and referral of severely ill newborns takes place at least partly to ensure careful end-of-life decision-making. It is also likely to reflect the prevailing cultural approach of Dutch neonatologists. In the Netherlands, physician end-of-life decision-making has been a topic of debate for several decades.(20, 30, 31) Between 1990 and 1997, influential reports by the Royal Dutch Medical Association (KNMG) and by the Dutch Pediatric Association (NVK) on the medical and ethical acceptability of end-of-life decisions were published and reflect the views of the medical profession on the subject.(21, 32) Two reasons for withholding or withdrawing life-sustaining treatment are recognized: either treatment stands no chance of success and death is imminent (comparable with group I in our study) or treatment would be futile (group II). In particular in the group of

newborns whose death is imminent (group I), it is regarded as less than ideal to die on the ventilator so artificial ventilation is withdrawn preferably before the actual dying process (with bradycardia etc.) has started.(20) This is done to give the parents enough time and opportunity to say good-bye and to let the child die in what they perceive as a dignified way, in the arms of the parents and disconnected from the ventilator. With regards to the latter (group II), the position is held that not only survival of the infant per se is important but the child's quality of life, if it were to survive, is also very important. The intensive care treatment is used to overcome a life-threatening period in life and it should only be initiated and continued when there is a reasonable prognosis for the infant after this period.(21)Both reports share the view that both the life-ending decisions (withholding and withdrawal of care) and the life-prolonging decisions should be legitimized. According to these reports, prolongation of intensive care treatment in situations were the prognosis is very grim might not always be in the infant's best interest. The quality-of-life considerations, as operationalized in the reports, should be bound strictly to medical criteria (22).

Although this prominent role of the physician is considered appropriate is the Netherlands, it can be challenged. First because some parents of newborns whose death is imminent may not share the definition of dignity as dying in the arms of a parent. They may, for example, sincerely believe that the most dignified way for their newborn to die is with the care providers actively attempting to save their child's life. Second, this prioritization of the decision-making authority in patients with a poor prognosis may allow the physicians to control the information and make decisions in situations where their perspective may be problematic. Several studies have suggested that intensivists routinely overestimate bad outcomes and conflate acute critical illness with long-term prognosis. (33-38) Third, the question remains how the best interest of the child should be defined, and whether or not he physician is the best person to make that judgement.

We have examined the physician's use of quality-of-life considerations in group II deaths and found that the considerations described in the reports are still used, except 'life expectancy' and no new considerations were added. Two distinct types of considerations are distinguishable: those concerning the infant's present quality of life, used in 48% of group II decisions, and those concerning expected future quality of life, used in 92%. Our findings confirm that Dutch physicians consider future quality of life of critical importance. They are prepared to withhold or withdraw life-sustaining treatment exclusively based on the predicted quality of life. In virtually all end-of-life decisions in group II, consultation took place with other physicians and parents were always involved. The high rate of involvement of other physicians and parents may reflect the awareness of physicians that decisions based on quality of life considerations can never be based on a single opinion. Some questions, however, about the decision-making in these patients can be asked. For example, if there exists a pervasive bias or anti-disability sentiment among the Dutch, will the consultations and the involvement of the parents be sufficient safeguards to protect the interests of the child? Moreover, is there enough acknowledgment among the counselling physicians that they may exert considerable influence over the forecasting of outcomes such that the ultimate consent is an ex-

pected product of the way the predicted outcomes are framed? This way, the outcome of the decision-making process would become dependent on the physician's opinion about what is in the infant's best interest. An intriguing question is whether these different outcomes as such are compatible with the intant's right to equal treatment in equal cases and protection against discrimination under international human rights law. This question needs to be investigated in more detail.

In one patient, diagnosed with type II osteogenesis imperfecta, the end-of-life decision was retrospectively categorized as deliberate ending of life (group III). In the Netherlands, the decision to deliberately end a newborn's life is regarded legally as well as morally very different from the decision to withhold or withdraw life-sustaining therapy. The first is in principle a criminal offence (murder or homicide) whereas the latter is regarded as a medical decision without legal consequences. The KNMG and NVK reports also addresses the disagreement that exists among physicians about the acceptability of deliberate ending of the life of a newborn. Based on two court cases held in the mid nineteen nineties, known as the Prins and Kadijk cases, it is now accepted that under certain circumstances, the physician can claim impunity, i.e. the defense of necessity (39, 40). In such circumstances, the patient's suffering should be extreme, thus compelling the physician to choose between the duty to save lives on the one hand and to do everything possible to prevent unbearable suffering, on the other hand. If the physician exercises due care, deliberate ending of life may be justified. The requirements of due medical care were formulated for the first time in the Prins and Kadijk cases. These requirements also constitute the fundaments of the 'Groningen Protocol' for deliberate ending of life in severely ill newborns. The Protocol was accepted as a national guideline by Dutch pediatricians in 2005.(41)Based on the data from surveys in 1995 and 2001, it is estimated that at least 15 to 20 cases of deliberate termination of life take place annually.(7, 8) Our study suggests that the frequency of deliberate ending of life may have dropped considerably. The incidence reported by us could however have been underestimated, because we could not exclude that incidentally a group III newborn may have been referred from the NICU to a local hospital (without a NICU) where deliberate ending of life took place. In group III we also did not include cases where death might have been caused by the use of palliative care-medication with potentially life-shortening effect around the time of withdrawal of life-sustaining therapy. Another relevant consideration could be that our study was limited to newborns that died in the first 2 months of life where the survey-based estimations regarded newborns below 12 months of age.

Neonatal end-of-life decision-making in the Netherlands has received considerable criticism from the media and from the public.(42-47) The ongoing debate focuses on the acceptability of quality of life motives in decision-making (group II) and on the acceptability of deliberate ending of life (group III).(16, 47-50) Our study contributed to the discussion about quality of life motives by, for the first time, providing qualitative and quantitative data about the considerations leading to those decisions. Furthermore, we believe that detailed knowledge of the medical practice is an essential requirement for further debate about end-of-life decisions and for comparison of outcomes between units and countries.

Contrary to the situation in the Netherlands, the possibility of deliberate ending of life in newborns in group III is rejected in the USA and in may other countries, even when life is intolerable.(51, 52) One of the reasons is that active ending of life as a therapeutic option is seen as a 'slippery slope' towards its wider use in situations that are now considered undesirable.(51) Other arguments against this practice are (1) the fear that active killing may have a negative impact on the psychology of professional staff, and that (2) parents may feel pressured to accept the option of deliberate life-ending so that they do not become a burden on medical and social services (53), (3) the conviction that physicians do not have the right and the capability to determine what unbearable suffering is and to practise deliberate ending of life on that basis (45, 54) and (4) that palliative care is always an alternative to deliberate ending of life (55). Most other objections that have been raised against the 'Groningen Protocol' for deliberate ending are based on serious misconceptions.(43, 47) The dilemma of discussing the arguments that lead to rejection of deliberate ending of life is that hard evidence for these fears and convictions (and for the denial) is not available. The case of osteogenesis imperfecta described in our study has illustrated however, that physicians cannot always alleviate pain and suffering with palliative medication.

Does the finding concerning the frequency of deliberate ending of life help allay some of the concerns about Dutch practice? Maybe it does help partly. The very low frequency may be seen another example showing that regulation of complex end-of-life decision making may lead to control of medical practice and does not necessarily result in sliding on the slippery slope.(56) The remaining concerns regarding for example the parent's role in the decision-making process and the use of potentially life-shortening medication at the end of life could probably be best addressed by combining our results with more comparative studies in the near future that would include comparison of quality of life considerations used in different units in different countries. We expect that the appointed advisory committee, mentioned in the introduction, can help to clarify what cases qualify as deliberate termination of life and need to be reported to the authorities for this reason. This would help physicians to decide on this matter. The process of review by this multidisciplinary committee of experts is more transparent than the procedure that the prosecuting office used in order to review such cases in the past. As soon as the first cases are reported, the reviews by the multidisciplinary committee of experts will contribute to the ongoing development and clarification of the standards regarding deliberate termination of life of newborns. This will encourage attending physicians to notify the authorities, which in turn will enhance transparency of medical practice and increase debate about what is going on at ground level. This procedure can also help to clarify if hopeless and unbearable suffering is present, another important criterion for the legal acceptance of deliberate termination of life of newborns. This requirements is drawn from the standards of due care for euthanasia and needs to be 'translated' to newborns. For this translation of hopelessness (being without prospects) the multidisciplinary input of epidemiologists, pediatricians, neonatologists, pain specialists and others will be necessary. Reporting cases of deliberate termination of life and analyzing the committee of expert's review will contribute to clarify, at least partly, what constitutes 'unbearable suffering' in newborns.

A potential limitation of our study is its retrospective nature. However, the availability of the medical files during each interview will have limited potential inaccuracy in the physician's recall of the circumstances surrounding death. Another limitation is the fact that findings are based on the perception of the physician, and not on other care providers or the parents. A strength of our study is that all NICU's have participated.

In conclusion, we have found that virtually all deaths in the Dutch NICU's are preceded by the decision to withdraw life-sustaining treatment and many decisions are based on the predicted future quality of life. Deliberate ending of life in severely ill newborns may occur less frequently as was previously assumed.

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Table 1. Demographics and clinical characteristics of newborns who died in 10 neonatal intensive care units in the Netherlands over a 12 months period

	All deaths (n=359)
Gestational age, weeks	
<30	123 (34%)
31-36	92 (26%)
≥37	144 (40%)
Birth weight, gram	
<800	43 (12%)
800-1500	99 (27%)
1501-2500	63 (18%)
>2500	154 (43%)
Sex	
male	210 (58%)
female	149 (42%)
Age at death	
early neonatal death (<7 days)	215 (60%)
late neonatal death (7-27 days)	107 (30%)
post neonatal death (>27 days)	37 (10%)

Data on birth weight were missing in 2 cases

Table 2. Cause of death per gestational age

	Primary organ dysfunction				
	Brain	heart/circulation	Lungs	MOF**	
GA*(n) Cause of death					Total (%)
<30 wks (n=123)					
asphyxia	1	0	0	9	10 (8)
congenital anomalies	0	1	4	3	8 (7)
sepsis/nec[γ]	1	2	2	37	42 (34)
extreme prematurity[Ψ]	1	0	5	32	38 (31)
respiratory insufficiency	0	0	11	4	15 (12)
intracranial bleeding	4	0	0	6	10 (8)
31-36 wks (n=92)					
asphyxia	7	1	2	10	20 (22)
congenital anomalies	1	6	7	20	34 (37)
sepsis/nec	1	3	1	16	21 (23)
extreme prematurity	0	0	0	0	0 (0)
respiratory insufficiency	0	0	11	1	12 (13)
intracranial bleeding	0	2	0	3	5 (5)
≥37 wks (n=144)					
asphyxia	33	2	1	32	68 (47)
congenital anomalies	4	30	5	14	53 (37)
sepsis/nec	0	0	0	13	13 (9)
extreme prematurity	0	0	0	0	0 (0)
respiratory insufficiency	1	0	5	1	7 (5)
intracranial bleeding	3	0	0	0	3 (2)

* GA: gestational age;

**MOF: multi organ failure, if dysfunction of 2 or more organs leads to death.

γ nec: necrotising enterocolitis;

Ψ extreme prematurity: gestational age <27 weeks

Figure 1. Flowchart of the categorisation process.

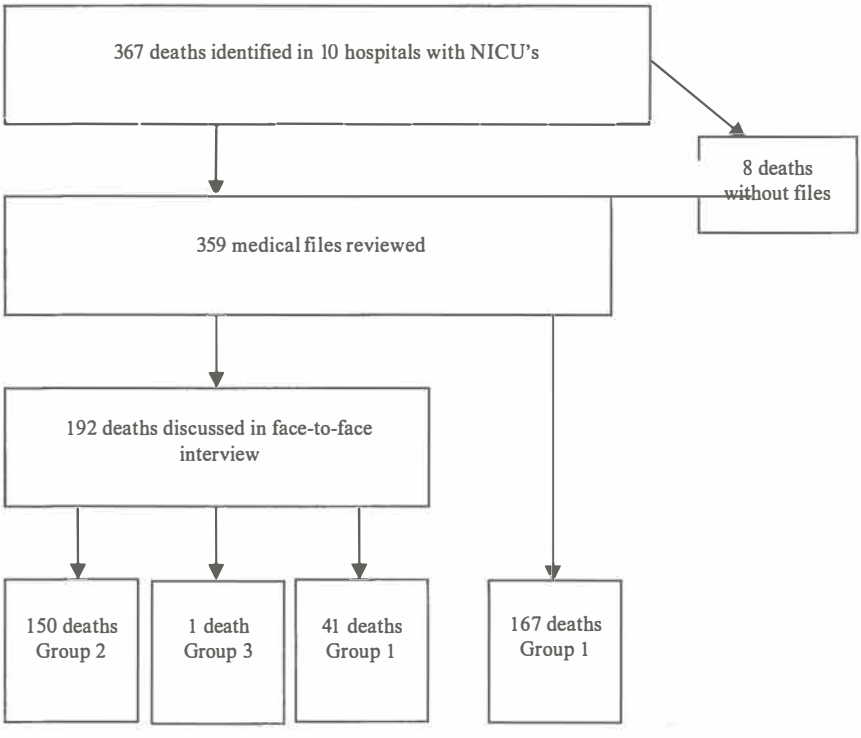

Table 3. Comparison of cause of death in groups I and II

Diagnosis	Group I n=208	Group II N=150	p-value
asphyxia	20% (41/208)	38% (57/150)	<0,001
congenital anomalies	33% (69/208)	17% (25/150)	<0,001
sepsis/nec[γ]	24% (50/208)	17% (26/150)	0,059
extreme prematurity[ψ]	7% (14/208)	16% (24/150)	0,0049
respiratory insufficiency	12% (25/208)	6% (9/150)	0,055
intracranial bleeding	4% (9/208)	6% (9/150)	0,47

group 1: no chance to survive, group 2: poor prognoses.

[ψ] extreme prematurity: gestational age <27 weeks;

[γ] nec: necrotising enterocolitis

Table 4. Quality of life considerations used for end-of-life decisions in patients with a very poor prognosis (n=147)*

	Frequency
Considerations regarding the child's present quality of life (n=71)	
Treatment does not contribute to medical condition	48
Treatment is disproportionate	33
Considerations regarding to the future quality of life (n=135)	
Predicted inability to communicate	18
Predicted lack of self-sufficiency	2
Expected hospital dependency	2
Predicted suffering:	112
from pain	4
from discomfort	8
from functional disability	53
from poor prognosis	46
other	1

* from interviews with the responsible physician, 3 interviews were missing

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Chapter 5

Differences of opinion regarding end-of-life decisions in severely ill newborns in the NICU; results of a nationwide study in the Netherlands

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Abstract

Objectives. To determine the frequency and background of differences of opinion in neonatal end-of-life decision-making.

Patient and Methods. We reviewed the medical files of 367 newborns who died during 12 months in the 10 Dutch NICU's and identified 150 deaths preceded by an EOL-decision based on the child's poor prognosis. The neonatologists in charge of 147 of 150 newborns were interviewed in order to obtain details about the decision-making process.

Results. Parents were involved in all EOL-decisions and consensus was always reached. Differences of opinion between parents and the medical team occurred in 18/147 cases and mostly concerned the child's poor neurological prognosis. Disagreement within the team occurred in 6/147 cases and concerned the uncertainty of the prognosis. Differences of opinion resulted in postponement of an end-of-life decision. Consensus was reached by allowing time for more meetings, diagnostics or second opinion. Physicians considered religion and unclear communication between parents and the team the main risk factors for disagreement.

Conclusion. Parents were involved in all end-of-life decisions and consensus was reached in all cases. Differences of opinion occurred within the team (4%) and between the team and the parents (12%) and they were resolved by postponing the EOL-decision.

Introduction

Reports describing end-of-life practice in severely ill newborns have shown that death in the Neonatal Intensive Care Unit (NICU) is often preceded by the decision to withhold or withdraw life-sustaining treatment (1-4). In the Netherlands, as in many countries, the neonatologist is responsible for this decision. Parents are usually involved in the decision-making process as they are well informed, their views are heard and that they are asked for their agreement of the proposed decision. Differences of opinion between families and the medical team about stopping or continuing life support for severely ill newborns may however occur (2, 5). These differences of opinion most likely arise in situations where the prognosis for the child is considered to be very poor and continued treatment involves therapies that may cause discomfort or suffering. The physicians and the parents may have different perceptions of which decision is in the best interest of the child. Given the irreversibility of the decision to withhold or withdraw life-sustaining therapy, and the enormous impact on all parties involved, resolving and preventing differences of opinion can be regarded as a priority in end-of-life situations.

Several theoretical discussions, guidelines and case-reports have been published about how the chances of unresolved disagreement regarding end-of-life decisions can be minimized (6-14). However, empirical data about differences of opinion preceding end-of-life decisions in the NICU are scarce and often lack detailed descriptions the role of physicians and parents parent's in the decision-making process (15-17).

The aim of this study was to determine the frequency and background of differences of opinion within the medical team and between the parents and the team in end-of-life decision-making regarding severely ill newborns

Patients and methods

We performed a retrospective descriptive study of the Dutch end-of-life practice regarding severely ill newborns. In the Netherlands, clinical care for these newborns is centralized in 10 level III NICU's. In all NICU's medical decisions are taken by a multidisciplinary team led by the attending neonatologist, who is ultimately responsible. Both the parents and the physicians can initiate discussions regarding withholding or withdrawing treatment.

There are no shortages of resources relevant to decision-making in neonatology in the Netherlands. End-of-life decisions in newborns are made irrespective of the financial status of the parents, physician, hospital or any third-party payer, as all costs (clinical care and post-discharge care) are covered by health insurances. All inhabitants of the Netherlands are fully insured. The ethical review board indicated that no approval is required because it concerns a retrospective study using anonymous data. The study-design complied with the national regulations for medical privacy and medical research.

Data collection

The background of the study population and the study design has been described elsewhere (ref). We identified 150 out of all 359 newborns who died in the first 2 months of life in the 10 Dutch NICU's between October 2005 and September 2006,

with a preceding decision to withhold or withdraw life-sustaining treatment based on the child's poor prognosis. The physician's and nurse's notes were used to determine demographics (birthweight, sex, gestational age, day of death, diagnosis) and to obtain details about the decision making process. We approached the neonatologists who were responsible for the end-of-life decisions for a semi-structured interview. The interview was used to ascertain general characteristics of the physicians (age, sex, years in the NICU and religion) and to crosscheck the data retrieved from the files. The interviews were also used to obtain details regarding the decision-making process with special attention to potential differences of opinion, their causes and resolutions. At the end of the interview, we asked the physicians to score the degree of satisfaction with the decision-making process and to which extend the parents had influenced the final end-of-life decision. Both items were scored with a 5 point likert-scale for both items (1: strongly disagree; 5: strongly agree). We also asked each physician: 'to mention all factors that he/she perceives as risk factors for differences of opinion in decision-making between parents and the medical staff, based on their own NICU-experiences'. The physicians were requested to consult medical charts during the interview. All interviews were conducted by an experienced pediatrician (AV) and lasted between 30-45 minutes per patient. Several interviews took place in the presence of a qualified legal scholar (JD). Here, the physicians were asked — among other things — whether or not legal considerations influenced their way of dealing with a conflict within the team or with the parents. The findings in these matters are discussed elsewhere.

Definitions

End-of-life decisions were defined as medical decisions with the effect or the probable effect that death was hastened. These decisions include the decision to withhold or withdraw life-sustaining treatment and the decision to deliberately end the life of a newborn. Withholding treatment was defined as withholding potentially life saving treatment including not only withholding CPR but also not providing additional intensive care treatment (e.g. no catecholamines despite hypotension). Withdrawing treatment was considered to be equivalent to withdrawing life-sustaining treatment. Deliberate ending-of-life (newborn euthanasia) was defined as administering lethal drugs to end the life, or shorten the life of a newborn. With respect to newborn euthanasia, we focused on newborn infants who were physiologically stabile. This type of end-of-life decision s subject to specific requirements regarding decision-making, reporting and review.(18) No cases of newborn euthanasia were identified at the time of decision-making in the NICU.

Results

The diagnosis in the majority of the 150 cases with a preceding EOL-decision involved asphyxia (38%), followed by congenital anomalies (17%) and sepsis/nec (17%). The distribution of diseases leading to death was similar in all 10 units. Of all deaths, the most frequent end-of-life decision was to withdraw life-sustaining treatment (88%), withholding of therapy took place in 12% of cases.

Interviews were held with the physicians of 147 of the 150 patients. Table 1 shows the baseline characteristics of the physicians who were interviewed. Data of 3 deaths were missing because we were unable to locate 2 of the 82 responsible physicians (2%).

In all 147 cases, parents were involved in the decision making process and agreement with the parents was reached in all cases.
In 6 out of 147 cases (4%), the decision to withdraw life-sustaining treatment was postponed because differences of opinion occurred within the multidisciplinary team. Three of these cases also caused a difference of opinion between the team and the parents. Details are shown in table 2. In 5 out of 6 cases, the difference of opinion concerned the neurological prognosis of the child, which was very poor but not sufficiently certain for all team members. In 2 of these cases, additional team-meetings were held. In these meetings, the exchange of thoughts about the future medical and neurodevelopmental sequelae resulted in consensus to withdraw treatment. In the three remaining cases, clinical deterioration resulted in consensus among the team members to withdraw treatment. In one patient with severe BPD, continued treatment was no longer in the patient's best interest according to the team, but only part of the team was prepared to act against the parent's opinion that treatment should continue. Deterioration of the clinical condition of this child also led to team consensus about withdrawal in this case. The differences of opinion within the team were resolved in a median time-interval of 24 hours (range 8-96 hour).
In 18 cases (12%), the end-of-life decision was postponed because differences of opinion occurred between the medical team and the parents (table 3).
In 14 out of 18 cases, the medical team suggested withdrawal of life-sustaining therapy mainly because of the infant's very poor neurological prognosis, while according to the parents, the patient's treatment should continue. In 5 of these 14 cases, the parents refused withdrawal of artificial ventilation because according to their religion, withdrawal of care was not allowed. Here, the team members adjusted their opinion after additional meetings with the parents were held, and the team agreed not to withdraw artificial ventilation and to refrain from increasing or adding intensive care. In all cases, the team-members adjusted their opinion because the benefits of taking an end-of-life decision in agreement with the parents outweighed the potential additional suffering for the child. All 5 infants died, connected to the ventilator. In 2 out of the14 cases, clinical deterioration changed the parent's opinion. In the other 7 out of 14 cases, additional meetings and 2nd or 3rd opinions by independent medical teams resulted in consensus to withdraw artificial ventilation. The meetings were held to overcome language problems (2 cases) or to provide the parents with more medical information (2 cases). The 2nd opinions (3 cases) were requested by the parents because they were not convinced that the medical diagnosis and prognosis as provided by the treating physicians were correct. All 2nd opinions corresponded with the team's opinion.
In 4 out of 18 cases, the parents requested withdrawal of life-sustaining therapy while the team suggested continuing treatment. In 2 of these cases, the team postponed the end-of-life decision to acquire more data (ultrasound, MRI) to be better informed about the infant's neurological status. The results were discussed in additional team meetings and led to withdrawal of therapy. In the remaining 2 cases, consensus was reached within 12 hours after the infant's clinical situation deteriorated and all agreed that in the new situation withdrawal of life-sustaining therapy was appropriate.
In all 18 cases, the responsible neonatologist expressed that solving the differences of opinion was regarded as a priority by the team-members because in they were

convinced that unresolved disagreements would hamper the grieving process. The disagreement between team members and the parents was resolved within a median time-interval of 24 hours (range 4-336 hours).
The mean score for the physician's general satisfaction with the decision-making process was 4,8 on a 5 point Likert-scale. No apparent connection was seen between overall satisfaction and reported differences of opinion between the team and the parent. In 16 out of 147 cases, physicians reported that parents had substantially influenced the final end-of-life decision. Five of these cases concerned difference of opinion between the team and the parents. In the remaining 11 cases, parental influence involved the timing of the decision to withdraw life-sustaining therapy. Withdrawal was postponed in 5 of these 11 cases to allow the parents time and opportunity to say goodbye. In the other 6 cases, parents requested a prompt decision to end the child's suffering. This resulted in a team-meeting several hours earlier than originally planned.
Table 4 shows the physician's reported risk factors for differences of opinion between parents and physicians. The risk factors are divided into 4 categories: risk factors related to the parents, the patient, the medical team or other factors. The majority of physicians (63%) indicated that they consider religious convictions that forbid withdrawal of life-sustaining therapy as an important risk factor. Unclear communication by the medical team was the second most frequently reported risk factor.

Discussion
This retrospective descriptive study investigated differences of opinion regarding end-of-life decisions in the Dutch NICU's over a period of 1 year. We focused on differences of opinion in situations where end-of-life decisions were based on the infant's poor prognosis. In the Netherlands, physicians should stop intensive care treatment when death is imminent (19).
The strength of our study is the unrestricted cooperation of all Dutch NICU's and the willingness of all physicians to cooperate in the interviews. A first limitation is the study's retrospective nature, although the availability of well documented medical files during each interview has limited potential inaccuracy in the physician's recall. A second limitation is that the findings are based on the physician's perception and not on other care providers or the parents. A third limitation is the small number of differences of opinion found, which limits the generalizability of our findings. Our study was limited to the NICU-population and did not include decision-making in severely ill newborns admitted in, or transferred to smaller local hospitals.

In our study, parents were involved in all end-of-life decisions and physicians considered the parent's opinion very important. No end-of-life decision was made without consensus between the parents and the medical team. Differences of opinion initially occurred between the parents and the medical team in 12% of cases and within the medical team in 4% of cases and resulted in temporary postponement of an end-of-life decision in all cases.
International and national guidelines prescribe that the medical team should always make decisions about withholding or withdrawing treatment in close consultation with the parents. Furthermore, the decisions must be based solely on the best in-

terest of the infant (14, 19, 20). The 100% rate of parental involvement in end-of-life decisions found in our study is in accordance with these guidelines. Previous studies in the Netherlands have reported comparable high rates of 93-97% (1-3). Other studies from Europe and the USA have reported rates between 48-100 % for parental involvement (16, 21-23). The cultural background of both caregivers and parents were reported to be the most important factor influencing parental involvement (24, 25).

Differences in opinion between the members of the medical team occurred mainly in relation to the uncertainty of the neurological prognosis. In the NICU, end-of-life decisions are often based on a prediction of neurodevelopmental impairment (1, 3). In an attempt to reliably predict impairments, all kinds of clinical scores, algorithms and prognostic findings on ultrasound and MRI have been developed, but these tools have not been able to eliminate uncertainty in individual cases (26). Moreover, no clear cut-off levels exist for the amount of certainty, or for the level of severity of impairment that are required to justify an end-of-life decision. Surprisingly, the large majority of end-of-life decisions based on the infant's poor neurological prognosis did not lead to differences of opinion in the team.

From our study, it can be concluded that no end-of-life decisions are made if team members have different opinions. If the patient's condition allows it, consensus is sought in additional team meetings. We could not determine whether the consensus represented a mere practical compromise or whether it was based on in-depth discussion about the existing uncertainty that was finally accepted as sufficient for an end-of-life decision. This would require interviewing all team members.

Furthermore, our results clearly show that no end-of-life decision is taken if the parents disagree with the opinion of the medical team. The differences of opinion were solved by providing more information to the parents and by giving them more time. This finding confirms the critical importance of allowing parents enough time to understand the situation and to let them assimilate to what is happening. This is in accordance with studies that focused on the parental perspective (27-29).

Occasionally, parental refusal to withdraw ventilation for religious reasons resulted in an adjusted end-of-life decision because the team wanted to make a decision that the parents could agree with. One other study from Great Britain and one from a Muslim community in Oman have reported similar responses by the medical team to parental refusal to withdraw treatment (17, 24). Agreement between the team and the parents regarding end-of-life decisions has been shown to be an important aid for the grieving process of bereaved parents. (27, 30). The importance of agreement was also mentioned in the interviews by the physicians of all 18 cases with disagreement between the team and the parents. The team's adjusted decision not to withdraw artificial ventilation may, however, also have prolonged the child's suffering. The neonatologists were well aware of this potential consequence and were prepared to accept it. Here the question is raised whether acting in the child's best interest may depend, at least partly, on the views and convictions of the parents. Recently this dilemma was also described by Kopelman et al. They proposed as a possible solution that in difficult practical situations the best interests standard does not necessarily require to do what is 'the best', but rather what is good enough and reasonable (31).At the same time this adjustment may point to the fact that children who are in similar bad health can end up differently, that is to say: continue to live or rather die depending on what parents interpret as being in their

child's best interest. Such different outcomes of the decision-making process can also result from differences of opinion among physicians about what is in the child's best interest: withholding or continuing artificial ventilation? A question that intrigues is whether or not these different outcomes as such are compatible with the child's right to equal treatment in equal cases and protection against discrimination under international human rights law.In a separate publication this issue will be discussed further.

In the experience of the physicians interviewed, parental religious convictions and unclear communication by the medical team are the most important risk factors for differences in opinion between the team and the parents. Differences in cultural background of the parents and the medical team and a poor understanding of the medical facts by parents were also mentioned. A remarkable finding is that conflict within the team was also seen as a risk factor for a difference of opinion with the parents. We were not able to confirm that in our study nor could we determine how team conflicts would result in disagreement with the parents. Awareness of the reported risk factors may be useful, because it might enable physicians to anticipate to differences of opinion.

In conclusion, our study results also shows that differences of opinion between team and parents can virtually always be resolved by postponing the end-of-life decision and this way allowing more time for additional meetings, for additional diagnostics and for a 2nd opinion. This has a dual effect. It gives a further foundation of the end-of-life decision and it gives parents time to accept a very difficult decision in the best interest of their child.

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Table 1. Characteristics of 80 physicians responsible for prognoses based end-of-life decision making in 150 deaths

	All physicians (n=80)
Age (years)	
<35	12 (15%)
35-40	17 (21%)
41-50	31 (39%)
>50	16 (20%)
Sex	
male	39 (39%)
female	41 (51%)
NICU-experience (years)	
<4	22 (28%)
4-10	31 (40%)
11-20	13 (17%)
>20	12 (15%)
Self-reported degree of religiousness	
1: not religious	36 (46%)
2: a little bit religious	25 (32%)
3: religious	13 (17%)
4: very religious	3 (4%)

Table 2. Characteristics of 6 cases with differences in opinion within in the medical team preceding the decision to withdraw life-sustaining treatment

	GA (wk)	Bweight (gr)	Cause of death	Age (days)	Subject of difference of opinion in team	Parental opinion regarding treatment	Intervention leading to consensus	Time interval[β] (hours)
1	41,4	3666	Asphyxia	2	Neurological prognosis	continuation	Repeated meetings	8
2	30,7	1600	Sepsis/nec	3	Neurological prognosis	withdrawal	Clinical deterioration,	12
3	41,7	3525	Asphyxia	4	neurological prognosis	withdrawal	Clinical deterioration	24
4	25,6	820	Extreme prematurity	3	Neurological prognosis	withdrawal	Clinical deterioration,	24
5	25	800	Extreme prematurity	22	Neurological+pulmonary prognosis	withdrawal	Repeated meetings	96
6	29,9	640	Resp insufficiency	21	Pulmonary prognosis	continuation	Clinical deterioration	52

Cases 1,2,6 also involved differences of opinion between the team and the parents and correspond with cases 17, 3 and 9 in table 3

GA: gestational age

Bweight: birthweight

[β] Time interval`; interval between team's suggested end-of-life decision and the final decision with parental consent.

nec: necrotising enterocolitis

Table 3. Characteristics of 18 cases with difference of opinion in the medical team preceding the decision to withhold or withdraw life-sustaining treatment

Nr	GA (wk)	Bweight (gr)	Cause of death	Age (days)	Team's opinion regarding treatment	Team's medical concern	Parental opinion regarding treatment	Intervention leading to consensus	Time interval[β] (hours)
1	26,3	975	Extreme prematurity	3	continuation	neurological prognosis	withdrawal	more tests (US), meeting	24
2	26,3	980	Extreme prematurity	11	continuation	neurological prognosis	withdrawal	clinical deterioration	12
3	30,7	1600	Sepsis/nec	3	continuation	neurological prognosis	withdrawal	clinical deterioration	12
4	41	3250	asphyxia	7	continuation	neurological prognosis	withdrawal	more tests (MRI), meetings	72
5	25	780	Sepsis/nec	10	withdrawal	neurological prognosis	continuation	more meetings, DNR	24
6	25,2	730	Extreme prematurity	8	withdrawal	Neuro+pulm prognosis	continuation	more meetings	24
7	26,6	1080	Sepsis/nec	8	withdrawal	neurological prognosis	continuation	more meetings	4
8	29	730	Sepsis/nec	25	withdrawal	neurological prognosis	continuation	more meetings, 2nd opinion	72
9	29,9	640	Resp. insufficiency	21	withdrawal	pulmonary prognosis	continuation	clinical deterioration	52
10	31,7	1400	Resp.	13	withdrawal	neurological	continuation	more meetings, DNR	168

			insufficiency			prognosis			
11	32,4	1800	Congenital anomalies	39	withdrawal	neurological prognosis	continuation	more meetings, 2nd opinion	336
12	37,4	3300	asphyxia	16	withdrawal	neurological prognosis	continuation	2nd and 3rd opinion	133
13	37,4	2980	Resp. insufficiency	25	withdrawal	neurological prognosis	continuation	more meetings, 2nd opinion, DNR	240
14	37,9	2760	asphyxia	2	withdrawal	neurological prognosis	continuation	more meetings, DNR	8
15	39,7	2200	asphyxia	3	withdrawal	neurological prognosis	continuation	clinical deterioration	12
16	41	2800	Resp. insufficiency	19	withdrawal	neurological prognosis	continuation	more meetings	24
17	41,4	3666	asphyxia	2	withdrawal	neurological prognosis	continuation	more meetings, DNR	6
18	41,7	3850	Congenital anomalies	8	withdrawal	neurological prognosis	continuation	more meetings	24

Cases 3,9,17 also involved differences of opinion within the medical team and correspond with cases 2,6,1 in table 2

GA: gestational age

Bweight: birthweight

β Time interval'; interval between team's proposed end-of-life decision and the final decision with parental consent.

nec: necrotising enterocolitis

Table 4. Risk factors for conflicts between parents and the medical team reported in a face-to-face interview by 80 neonatologists

	frequency[γ]
Parents-related factors	
strong religious convictions	50 (63%)
cultural background	18 (23%)
low intellectual capacities, poor medical knowledge	14 (18%)
unclear communication	7 (9%)
language problems	3 (4%)
negative previous medical experiences	3 (4%)
disagreement between parents	2 (3%)
Patient-related factors	
unclear diagnosis and or prognosis	12 (15%)
absent physical signs of illness	7 (9%)
Team-related factors	
unclear communication with parents	28 (35%)
conflict within the team	16 (20%)
decision-making too fast for parents	4 (5%)
many different attending physicians per infant	4 (5%)
low respect for parental opinion	2 (3%)
strong religious convictions (team member)	2 (3%)
Other factors	
duration of NICU-admission	3 (4%)

[γ] factors reported by ≥2 physicians are reported

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Chapter 6

Analgesics, sedatives and neuromuscular blockers as part of end-of-life decisions in Dutch NICU's

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Abstract

Background. Clinicians frequently administer analgesics and sedatives at the time of withholding or withdrawal of life-sustaining treatment in severely ill newborns. This practice might be regarded as intentionally hastening of death.

Objective. to describe type, doses and reasons for administering medications as part of end-of-life decision-making in the Dutch NICU's.

Design and Setting. Data from the medical files and from interviews of 359 NICU-deaths over a 12 months period were used to describe administration of analgesics, sedatives and and/or neuromuscular blockers before and after the end-of-life decision. We compared data from newborns whose death was imminent with those of newborns with a poor prognosis.

Results. Analgesics and sedatives were administered to 224 of 340 newborns before the end-of-life decision and to 292 newborns after the decision. The medication was increased in 94 of 189 newborns whose death was imminent and in 110 of 150 newborns with a poor prognosis. Reasons for the increase were treatment of symptoms, prevention of suffering and in 4% of cases hastening of death. Reasons were undocumented in 55% of deaths. Neuromuscular blockers were administered in 16% of patients because they already received these agents or to stop or prevent gasping.

Conclusions. Analgesics and sedatives are generally increased after the end-of-life decision to treat symptoms, to prevent suffering and rarely to hasten death. Neuromuscular blockers were administered in 16% of deaths, mostly to stop gasping of moribund newborns. Medical files provide insufficient documentation of considerations leading to the increase of medication, which hinders (external) review.

Introduction

Neonatologists frequently administer analgesics and sedatives and sometimes also neuromuscular blockers to manage pain and suffering at the time of withdrawing or withholding life-sustaining treatment in severely ill newborns. Administration of medication for that purpose is estimated to occur in 20-45% of newborns (1-5). Analgesics and sedatives may have the effect that life is shortened. Neuromuscular blocking agents shorten life by causing paralysis. In many countries in the industrialized world, administering medication around the time of death to alleviate symptoms is considered good medical practice, regardless the fact that this medication may have life shortening side effects. In these countries, death caused by the unintended side effects of medication is regarded as permissible under the widely adopted 'double effect doctrine' (6-8). In contrast, the administration of medication with the sole purpose of ending the newborn's life is a criminal offence. The distinction between providing appropriate relieve of symptoms and intentionally ending a life may not always be obvious from the type or dosage of the medication used. The underlying considerations and explanations are essential to be able to qualify the physician's acts. This is especially important in situations where withdrawal of treatment took place for quality of life reasons in infants that might survive, as opposed to situations where treatment was withdrawn in moribund infants.

Four previous studies have reported that paediatricians occasionally administer medication with the explicit intention to hasten death (4, 9-11). These studies were all based on self-report questionnaires and two studies concerned physician's attitude and not medical practice. Moreover, two studies provide only crude data on the physician's considerations to administer medication and report incomplete data on the dosages. We report a nationwide study to describe type, doses and reasons for administering medications as part of end-of-life decision-making in the Dutch NICU's based on chart reviews and face-to-face interviews.

Patients and methods

We conducted a retrospective descriptive study on medications administered to severely ill newborns as a part of end-of-life decision-making in the Dutch NICU's. The study-design complied with the national regulations for medical privacy and medical research.

— Classification of patients

We identified 359 newborns who died in the first 2 months of life in 10 NICU's between October 2005 and September 2006. Details about the background of the study population and the study design are described elsewhere (ref). Based on the medical charts, we determined whether or not death had occurred with a preceding end-of-life decision. End-of-life decisions were defined as decision with the effect or the probable effect that death was hastened. We used the physician's arguments for this decision to classify the newborns in groups I, II or III in accordance with the literature (12, 13). This classification enables us to make the important distinction between decision-making in moribund infants and decision-making in stabile children based on the infant's poor prognosis. Group I encompasses infants whose

death is imminent. Group II consist of physiologically stabile newborns who are intensive care dependent with a very poor prognosis. Group III encompasses stable newborns with a very poor prognoses and severe suffering but not dependent on intensive care. Face-to-face interviews were held with all physicians responsible for newborns in group II

— *Data collection*
We abstracted demographic data from the files: birth weight, gestational age, time and day of death and diagnoses. We used the medical charts and pharmacy notes to identify analgesic and sedative medication and neuromuscular blockers (NMB's), comparing medication before and after the end-of-life decision. Medication before the decision was defined as the highest dosage of any of the medication administered in the 12 hours before the end-of-life decision. Medication after the decision was defined as the highest dosage of medication administered between the end-of-life decisions and death. We took the following values as normal dosages for continuous intravenous infusion of analgesics and sedatives: morphine: 5-50mgr/kg/hr, fentanyl: 0,5-5mg/kg/hr, midazolam: 0,1-0,5 mg/kg/hr, vecuronium: 30-150 mgr/kg/hr. Normal values for intermittent infusion were: morphine: 50-200 mg/kg, fentanyl: 1-4 mgr/kg, midazolam: 0,05-0,15mg/kg (14). The reasons for increasing medication were collected from the files together with data concerning the presence or absence of painful procedures (operation, CPR, chest tubes, ventilation etc.) in the last 48 hours before death. Initiation of analgesic or sedative medication following the end-of-life decisions was taken to be equivalent to the increase of the existing medication.

— *Interviews*
We interviewed 80 neonatologists who attended 147 of the 151 deaths with a preceding end-of-life decision based on the infant's poor prognosis (groups II and III). The semi-structured interview was used to crosscheck details about the medication. The physicians were asked to give an explanation for their decision to increase medication and to provide details about symptoms around the time of death. We asked the physicians to score their satisfaction with the medication strategy using a 5 point likert-like scale (1: strongly disagree; 5: strongly agree). The physicians were asked to consult medical charts during the interview. All interviews were conducted by an experienced paediatrician (AV) and lasted between 30-45 minutes per patient. During some of these interviews a qualified legal scholar (JD) was present as well. An in-depth analysis of the legal aspects of the use of NMB's especially in group II will be published elsewhere.

— *Statistical analysis*
We compared the use of comfort medication in group I and groups II/III by using chi-squared test for categorical variables. P values of less then 0.05 were considered to indicate statistical significance

Results
— *Data from the medical files*
Of a total of 359 deaths, 340 (95%) were preceded by an end-of-life decision and 19 (5%) died while receiving CPR. In 314 deaths (93%), the end-of-life decision was to withdraw artificial ventilation; in 7% of deaths the decision involved not increasing

ventilatory or circulatory support. Overall, 208 (61%) newborn deaths were classified as group I, 150 as group II (44%) and one as group III.
Analgesics and sedatives were administered to 244 newborns (72%) before the end-of-life decision and to 292 (86%) newborns after the decision ($p<0,001$) (table 1). In 204 newborns (60%), medication was increased following the decision. Of all 19 newborns that died during CPR, 16 patients received no analgesics or sedatives although they had many painful interventions and 3 patients received medication before CPR. No association was found between the increase of medication and painful procedures in the 48 hours before death.

In group I, analgesics and/or sedatives were increased after the end-of-life decision in 94 of 187 patients (50%) (table 1). The reasons for the increase, shown in table 2, were documented in 43 out of 94 cases (46%). The dosages of opioids were above normal values in 6 out of 189 patients before the decision and in 9 patients after the decision. Administration of benzodiazepines remained within the normal dosing range. Neuromuscular blockers were administered in 24 patients (13%) before the end-of-life decision as a part of the treatment regimen. The reasons for administration were to prevent asynchronous respiratory efforts in newborns with severe respiratory problems or PPHN in 16 patients and to facilitate endotracheal intubation in 4 patients. In 4 cases, the reasons were undocumented. After the decision, NMB's were continued in 19 newborns and initiated in 10 without documented reasons in 7 of 10 cases (table 3).

Patients in group II were more likely to have medication increased after the end-of-life decision than infants in group I ($p<0,01$)(table 1). The reasons for the increase were documented in 50 out of 110 patients (45%). Opioids were administered above normal dosage levels in 7 out of 97 patients (7%) before the decision and in 25 out of 133 cases (19%) after the decisions. Benzodiazepines were administered above the normal range in18 patients after the decision, without documented reasons. No explanation was documented. Patients in group II were less likely to receive NMB before the end-of-life decisions than patients in group I ($p<0.01$). The reasons for administration were to prevent asynchronous respiratory efforts in newborns with severe respiratory problems in 3 cases and in 3 other cases the reasons were not documented. After the end-of life decision, NMB's were administered to 26 newborns. In 19 of 26 cases, no explanation was documented.

— *Data from the interviews (group II and III)*
Prevention of suffering, hastening of death and parental request were reported more frequently as reasons for the increase of analgesics and sedatives in the interviews than in the files ($p<0,05$).
Opioids and sedatives were administered above the normal dosage levels to treat symptoms, to prevent dyspnoea following extubation and to stop gasping. Increase of these agents with the intention to hasten death occurred in 11 cases and was documented in only 1 case (table 2). In 5 of 11 cases, medication was increased stepwise to stop gasping, convulsions or restlessness and later to hasten death. In 6 of 11 cases, NMB were added to the existing medications to stop the gasping. The reasons to initiate NMB in 21 cases are shown in table 3. NMB's were continued in 5 of 26 cases because discontinuation was expected to invoke unnecessary suffering.

The interviewed physician's agreed or strongly agreed that they were satisfied with the effects of the increased medication in 82% of cases. In 6 cases the effects were unsatisfactory because the medication did not stop the infant's gasping.

Discussion

This study yields four mayor findings. First, analgesics and sedatives are generally increased following end-of-life decisions, especially in newborns whose treatment is withheld because of the poor prognosis. Second, explanations for the increase are documented in less than 50% of cases, which hinders internal quality control and external review procedures. However, data from the interviews indicate that increase of medication is virtually always aimed at prevention and treatment of symptom, mostly restlessness, discomfort and gasping. Third, the increase of analgesics and sedatives with the intention to hasten death occurs in up to 10% of deaths, to stop gasping in moribund newborns. Fourth, 16% of patients receive NMB's after the end-of-life decision. The reasons for administration are mostly not documented. This way of documenting the motives for the use of NMB is clearly insufficient, as it is only through the interviews that part of the physician's actual intentions could be reproduced. Explanations for the administration given during the interviews are: discontinuation in patients who already receive NMB's would invoke additional suffering, to stop gasping and parental request.

A potential limitation of our study is its retrospective nature, although the availability of medical files during each interview has limited potential inaccuracy in the physician's recall. The strength of our study is that all NICU's have participated.

In many NICU's, analgesics and sedatives are routinely administered to patients to alleviate the symptoms of painful procedures associated with intensive care treatment (15-18). The proportion of newborns who died without this medication was 14% in our study, which is comparable to most reports from the USA, Europe and Australia (2, 3, 7, 18-21).

This study is the first to describe a general increase of analgesics and sedatives as a part of neonatal end-of-life decision-making in detail. This increase might be explained by, first, the finding that almost all end-of-life decisions resulted in withdrawal of the ventilator. Guidelines on paediatric palliative care advise physicians to increase analgesics and sedatives well before extubation to make sure that the patient is comfortable (15, 22). The medication adequate for a patient receiving ventilation is considered inadequate to treat the dyspnoea experienced by dying patients as controlled ventilation is removed. Therefore, doses are often increased with no real maximum (19, 23). A second explanation could be that the decision to increase medication reflects the new treatment goals aimed at providing comfort and no longer at curing the patient. Potential adverse effects that interfered with earlier treatment goals (e.g. hypotension and respiratory depression) are no longer a priority (24-26).

Our study confirms earlier reports indicating that NMB are administered in up to 16% of Dutch NICU-deaths (3, 27).

Three clinical situations involving NMB-administration after the end-of-life decision appear to represent almost all identified cases. In the first situation, the physician administers NMB's to a moribund newborn to stop the infant's gasping after having

increased opioids and sedatives. In the second, the physician continues the administration of NMB's to a newborn who already received these agents as part of the treatment regimen. Restoration of neuromuscular function is expected to delay the dying process and invoke unnecessary suffering. In the third situation, the parents express the whish to let their child die without gasping and the physician administers NMB's before extubation after having increased opioids and sedatives. The pro's and con's of the use of NMB at the end of life have been discussed extensively in the literature (28-32). Those against NMB-use argue that paralysis prevents monitoring of symptoms of the dying newborn. Others argue that there is no normative difference between letting the newborn die and shortening its life with several minutes or hours using NMB's to prevent unnecessary suffering. The latter opinion appears to be shared by most of the interviewed physicians.

A remarkable finding is that none of the deaths involving administration of NMB's were reported as cases of deliberate ending of life, although paralysis clearly causes death. As of March 2007 the Dutch government has established a multidisciplinary expert committee. Cases of deliberate ending of the life of a newborn infant must be reported to this committee, which reviews these cases and advises the Public Prosecution if the physician has acted in accordance with specific requirements of careful practice (33). Although this committee was not yet operational during the period of our study, the legal obligation to report cases of deliberate ending of the life to the juridical authorities was valid then as well (34). Given the absence of documented reasons in the medical files one cannot really judge if the cases where NMB's were administered legally qualify as deliberate ending of life ('neonatal euthanasia') or must be regarded as cases where treatment decisions were predominantly based on careful professional and clinical consideration. The lack of adequate documentation hinders important progress in the debate as to what extent intentional hastening of death by administering NMB's coincides with deliberate killing of an incompetent person and which intentions actually count in this regard: those articulated by the physician or those derived from his actions? These and other legal questions related to this study, such as whether or not the parental request not to be exposed to their child's gasping can justify administration of NMB to their newborn resulting in the child's death, are discussed elsewhere.

We conclude from this study, that analgesics and sedatives are generally increased at the time of death to treat symptoms and to prevent suffering and occasionally to hasten death. Medical files provide insufficient documentation of considerations leading to the increase of medication, which hinders (external) review.

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Competing interests
All authors declare that the answer to the questions on the BMJ competing interest form ((BMJ 1998;317:291 - 2) are all No and therefore have nothing to declare.

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Table 1. Administration of analgesics, sedatives and neuromuscular blockers before and after the end-of-life decision

	Distribution of patients per group (%)*		Total nr of patients (%)
	Group I *(n=189)*	Group II *(n=150)*	(n=340)
Before the EOL-decision:			
Total nr of patients with medication	127 (57%)	117 (57%)	244 (72%)
-opioids	108(69%)	86 (64%)	227 (67%)
-benzodiazepines	54 (57%)	75 (50%)	129 (38%)
-neuromuscular blockers	24 (13%)	6 (4%)	31 (9%)
Increased after the EOL-decision	94 (50%)	110 (73%)ϕ	204 (60%)
After the EOL-decision:			
Total nr of patients with medication	151 (80%)	141 (93%)	292 (86%)
-opioids	149 (79%)	133 (89%)	282 (83%)
-benzodiazepines	79 (42%)	106 (70%)ϕ	185 (54%)
-neuromuscular blockers	29 (15%)	26 (17%)	55 (16%)

*Group I: death is imminent; group II: intensive care, very poor prognosis.

EOL: end-of-life

ϕ $p<0,05$, comparison between groups I and II

Table 2: Reasons to increase analgesics and sedatives after the end-of-life decision from the medical files and the interviews.

Reasons:	From the medical files		From the interviews
	Group I *(n=94)*	Group II *(n=110)*	Group II *(n=105)*[•]
Prevention of suffering/providing comfort	34 (36%)	16[#] (15%)	61[∞] (58%)
Hastening death	0	1 (1%)	11[∞] (10%)
Parental request	2 (2%)	2 (2%)	10 (10%)
Symptoms:	32 (34%)	31 (28%)	51 (49%)
pain	4	2	1
convulsions	6	4	6
gasping	0	6	11
dyspnea	5	2	5
restlessness, discomfort	12	14	23
unspecific	5	3	5
No reasons provided	51 (54%)	60 (55%)	3 (3%)

[•] In 9 patients, administration of medication after the EOL-decision was ordered but did not take place; in 4 patients, medication was administered without documentation in the files

[#] Comparison of data from files between group 1 and group II: $P<0,05$

[∞] Comparison of group II data between the files and the interviews: $P<0,05$

Table 3. Reasons to administer neuromuscular blockers after the end-of-life decision (n=55).

Reasons:	Group I (n=29)[•]	Group II (n=26)[#]
Continuation in patients who already received NMB's	19 (66%)	5 (19%)
To prevent gasping, parental request	-	5 (19%)
To prevent gasping, medical team's request	-	2 (8%)
To stop long lasting gasping	3 (10%)	11 (42%)
To end life	-	1 (4%)
Unknown	7 (24%)	2 (8%)

[•] Group 1-data are from the medical files

[#] Group 2 data are from interviews

What is already known on this topic

1. Medications with potentially life-shortening effects are frequently used to manage pain and suffering in the NICU.
2. Previous studies have reported that paediatricians occasionally administer medication with the explicit intention to hasten death.

What this study adds

1. Analgesics and sedatives are generally increased after the decision to withhold or withdraw life-sustaining treatment to treat symptoms, to prevent suffering and rarely to hasten death.
2. Neuromuscular blocking agents are occasionally administered after the end-of-life decision to stop gasping of moribund newborns.
3. Medical files provide insufficient documentation of considerations leading to the increase of medication, which hinders (external) review.

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Chapter 7

Categorizing neonatal deaths; a cross-cultural study in the USA, Canada and the Netherlands

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Abstract

Background. Most studies on end-of-life practice do not make the important distinction between withdrawing life-sustaining treatment from moribund babies dying in their mothers arms, compared with withdrawing treatment from physiologically stable infants who are electively extubated for quality-of-life reasons. This makes comparison of decision-making and neonatal outcome between units difficult

Objective. We wanted to clarify the process of end-of-life decision-making in culturally different NICUs, using uniform definitions of withholding (WH) or withdrawing (WD) mechanical ventilation correlated with the physiological situation of the patient. Specifically, we determined whether ventilation was either withdrawn or withheld for children who were either moribund and actively dying, or physiologically stable on the ventilator but neurologically devastated.

Design/Methods. We reviewed the medical files of all newborns of greater than 22 weeks gestation that either died in the delivery room (DR) or the NICU between October 2005 and September 2006 in 4 NICUs (Chicago, USA, Wisconsin, USA, Montreal, Canada and Groningen, the Netherlands). In each nursery, we categorized deaths according to withdrawing and/or withholding ventilation, as a function of the child's physiologic stability and neurologic prognosis.For DR deaths, we excluded termination of pregnancies.

Results. The majority of unstable patients in all units died in their parent's arms after artificial ventilation was withdrawn. The decision to electively extubate patients for quality of life reasons was made in 19-35% of deaths in 3 out of 4 units and never occurred in the fourth unit. The proportion of patients who died while receiving cardiopulmonary resuscitation (CPR) varied between 4-12% in Wisconsin, Montreal and Groningen and was higher in Chicago (31%). The proportion of DR deaths in Wisconsin, Montreal, and Groningen was 16-22%. There were no DR deaths in Chicago.

Conclusions. Death in the NICU occurred differently within and between countries. Distinctive end-of-life decisions can be categorized separately using a two-dimensional model. Cross-cultural comparison of end-of-life practice is feasible and important when comparing outcomes between NICUs, both within and across cultures.

Introduction

Rapid technological progress in neonatology has enabled many newborns to survive. At the same time, the risks and burden of a hospitalization and future life may be at times perceived as inferior to the anticipated benefits of intensive care. As a consequence, resuscitation and active treatment of very sick neonates with potential serious neurologic sequelae has become an issue fraught with controversy leading to complex decision-making involving withholding or withdrawal of care (1-11). In modern bioethics, withholding and withdrawing interventions for dying patients are generally seen as morally equivalent, although this does not mean that both actions are legally equivalent (12, 13). However, withdrawing mechanical ventilation in a physiologically stable infant is seen as different by many physicians in comparison to withdrawing, not instituting or escalating care in a moribund infant. This distinction extends to the issue of how outcomes are calculated and described in the literature. Indeed, withholding and withdrawing care are rarely explicitly described in publications describing NICU outcomes. The survival rate of babies with extreme prematurity has been described, but simple calculation of the frequency of survival does not clarify how the babies die, or what is really done at bedside. Consequently, the discussions on what "ought to be done" are difficult to have when what is done is not accurately known. Also, comparing outcomes is difficult. For example, a higher survival rate, and possibly a higher disability rate, may be seen if most extremely premature babies are aggressively resuscitated and withdrawing care is less frequently offered in a particular unit (14).

Most studies of newborn end-of-life care describe the physician's attitude regarding end-of-life decisions and not the practice (15-20). Even when withdrawal of care is described, the distinction is rarely made between the babies who would have died despite intensive interventions (moribund babies extubated to spend their last moments in their parent's arms), and those who were extubated to die for quality of life reasons (21-25). Moreover, studies are often very difficult to compare because the authors used different definitions of patients groups and interventions.

We conducted a cross-cultural study using uniform definitions of interventions and physiological condition of the patients with the aim of describing and comparing the circumstances of dying in NICU's in different parts of the world.

Patients and methods

— *Patient population*

Ethics review:

University Medical Center Groningen. The study-design complied with the national law on medical privacy and medical scientific research. No authorization is legally required for confidential cohort chart review.

MUHC (McGill University Health Center). In order to do a retrospective chart review in Canada, DPS (Director of Professional Services) is necessary. This was obtained before reviewing patient's charts.

Comer Children's Hospital, Chicago. This study was approved by the institutional review board of the University of Chicago

Children's Hospital of Wisconsin. This study was approved by the institutional review board of Children's Hospital of Wisconsin, and the Medical College of Wisconsin.

We reviewed the medical files of all newborns of >22 weeks that died in the delivery room (DR) and the NICU between October 2005 and September 2006 in 4 NICUs; two in the USA (Chicago, IL, and Milwaukee, WI), one in Canada (McGill University Health Center (Royal Victoria and Montreal Childrens' Hospitals) and one in the Netherlands (Groningen). All participating NICU's are (equally sized) tertiary care units that admit between 555 and 800 newborns yearly.
We abstracted information from the medical records to determine all relevant demographics: birth weight, gestational age, day and time of death and diagnoses leading to death (using both clinical data and autopsy materials when available), and details about the decision-making process. For DR deaths, we excluded termination of pregnancies.

— *Classification of newborn deaths*
We categorized all deaths according to a two-by-two model, along the dimensions of physiology and intervention. We first classified all newborns as stable or unstable, based on their physiology. To be classified as unstable babies needed 2 of the following criteria: desaturation in 100% oxygen on a respirator, hypotensive on inotropes, bradycardic for a prolonged period, or anuric for more than 24 hours. They were classified as stable when they were stable with or without artificial ventilation. A second classification took place based on the intervention offered or withdrawn, divided into one of the following categories: (a) babies who died in the delivery room, either having received full treatment or having had treatments withheld and/or withdrawn. (b) babies who died while getting active cardiopulmonary resuscitation (CPR) (no withdrawing nor withholding), (c) babies who died while on the ventilator, without active CPR (no withdrawing, but CPR is being withheld), (d) babies who died after being extubated from a ventilator (withdrawing) to die in the arms of their parents, (e) babies who were electively extubated for quality of life reasons. Newborns in the latter group were subdivided by organ insult (brain, kidney, intestine, heart). Quality of life reasons were defined as reasons based on the poor prognosis of the infant as determined by the physician. Babies on CPAP, BiPAP, and nasal IMV were all counted a being on a ventilator. All data necessary for classification of the newborn deaths were collected in one shared anonymous database and discussed between the investigators from all participating units to ensure similarity in the classification process. Consensus about the classification was reached in all cases.

— *Decision-making process*
From the medical record we ascertained which persons were involved in the decision-making process resulting in the last intervention and what the documented reasons were for the decisions regarding the end of life.

— *Definitions*
Withholding an intervention was defined as withholding potentially lifesaving treatment, which included not only withholding CPR but also not providing addi-

tional intensive care treatment (e.g. not making additional ventilator changes despite hypoxemia, not providing additional inotropes despite hypotension, withholding feeds). Withdrawing treatment was taken to be equivalent to withdrawing the respirator. The NICU's positions on the resuscitation of the very preterm infants in were those issued by their national pediatric societies. The Canadian Paediatric Society suggests a selective approach below 25 weeks gestation, where resuscitation should only be instituted after informed parental consent (26). The American Academy of Pediatrics strategies suggest that resuscitation may be considered in infants between 23-25 weeks in individual cases (10) The suggested strategy in the Netherlands is that intensive neonatal treatment should start at 25 weeks; below 25 weeks, care is aimed at comfort for the child and the family unless intensive treatment is warranted (27).

— *Statistical analysis*

We compared demographics, the causes of deaths and the classification of deaths between the four NICUs by using chi-squared test for multiple variables. P values of less then 0.05 were considered to indicate statistical significance.

— *Results*

A total of 183 patients of above 22 weeks died in the 4 institutions during the 12 months study period. Table 1 presents patient demographic data for these patients. Of 183 newborns, 32 died in the delivery room. Some number of these died despite resuscitative efforts, while others died there because intensive care was not offered by the physician, or because parents agreed to providing palliative care in lieu of intensive care. Six of these infants had congenital anomalies with extremely poor outcomes diagnosed prenatally, and the parents and physicians agreed to comfort care immediately after birth. Three premature infants were offered an attempt at resuscitation. This ranged from an attempt to ventilate via endotracheal tube to assess a response, to a full medical code including chest compressions and medications. Even if a full code was attempted, the infant was placed back in the parent's arms after declaration of death. Twenty-five extreme preterms were not intubated at birth and given comfort care because parents agreed to comfort care.

A total of 151 children were admitted to the NICU and subsequently died there. Table 2 shows the distribution of deaths by gestational age. In three NICUs, the majority of deaths were newborns between 27-36 weeks of gestational age and the minority was below 27 weeks. In Chicago, most deaths were extreme preterms of < 27 weeks (45%).

The majority of babies dying from a congenital anomaly were term infants. Proportionally more babies died from respiratory insufficiency in Chicago than in other units and these infants were all 27 weeks of gestational age and below. The primary causes of death were the following: asphyxia, congenital anomalies, respiratory insufficiency, sepsis/necrotizing enterocolitis (NEC) and intracranial bleeding (see table 3). It is apparent that the causes of death were largely similar in all units and that the majority of deaths were caused by congenital anomalies.

— *Classification of newborn deaths*

Table 4 reveals that infants die under different circumstances in different units. In 3 institutions, between 16-24% of newborn deaths occurred in the DR whereas

in Chicago all deaths occurred in the NICU and no DR-deaths were reported. The proportion of babies who died while receiving CPR varied between 31% (Chicago) and 4% (Groningen). The proportion of infants that died while they were still connected to the ventilator was very low (<2%) in Groningen, Montreal and Wisconsin and considerably higher in Chicago (17%).
Withdrawal of ventilation was the most common intervention associated with the infant's death in all units and CPR was withheld in all these cases for obvious reasons. The classification by physiology and intervention provides us with detailed information about the circumstances of dying of these newborns per unit. Between 30% and 52% of extubations were performed in unstable patients who were in the state of dying, in order to let them die in the arms of the parents without tubes and tapes. In Chicago, all extubations followed this scenario. In Groningen, Montreal and in Wisconsin, a substantial proportion of extubations (19-35%) took place in physiologically stable infants for quality of life reasons. The most common reasons for the extubation in these infants was neurologic injury (43-73%), mostly due to asphyxia or intracranial bleeding, followed by cardiac and gastro-intestinal insults.

— *Decision-making in the DR and in the NICU*
In all three units with DR deaths (there were no DR deaths in Chicago), the decision not to initiate resuscitation was made jointly with the parents. In the NICU, the parents were involved in the decision-making process in all patients where withdrawal of the respirator took place. In 15 instances, with a similar occurrence in all 4 centers, the parents did not participate in the decision-making because an emergency situation did not give healthcare providers enough time to do so. Most of these infants died during surgery or while receiving CPR.

Discussion
We conducted a retrospective study on end-of-life decision making in culturally different NICU's in the Netherlands, Canada and the Unites States, using a two-dimensional classification model to involve the newborn's physiology (stable-unstable) and NICU-interventions (withholding-withdrawing). This format allowed us to make a distinction between withholding or withdrawing treatment in moribund infants, and the situation where this takes place in stable newborns for quality of life reasons.
We compared end-of-life practice between the 4 NICU's and found that decisions regarding the end-of-life were made differently within and between countries. We purposefully chose these units because of their cultural differences.
Our study yielded three important findings. First, this study confirms that withholding and withdrawing of artificial ventilation is the primary mode of death in the NICU internationally. We found that 69-93% of all deaths were preceded by a decision to withhold or withdraw ventilation. Most recent reports from centers in America, the United Kingdom, Australia, and Europe have reported rates between 58% and 75% (21, 25, 28-31). Only three studies from the Netherlands, California, and Switzerland have reported higher rates of 86-93% (32-34). The rates found in the present study are also higher than those from earlier studies involving two of the units that also participated in the current study (34, 35).

Second, the proportion of deaths occurring in the DR varies considerably between different units. This may be a reflection of the differences in approach to resuscitation at the "limits of viability" as described in the position statements in different countries (36). However there were differences between the two US NICUs. These differences could be because of physician interpretation of these policies. Or perhaps there are differences in the parent population (e.g. income, social class, level of education) that are at least partially responsible for these differences (37-40).
Finally, comparison of end-of-life decision-making between culturally different units is feasible and important with respect to comparing treatment outcomes. The use of a two-dimensional classification model, as used by us, quantifies a unit's end-of-life approach. Our study shows that the Chicago NICU was least likely to withdraw ventilation based on quality of life considerations. The importance of involving a unit's approach to decision-making in situations with prognostic uncertainty was demonstrated in a study by Lorenz et al (14). They compared outcomes of premature infants in New Jersey and the Netherlands. In this study, they used Rhodens characterization of different approaches to care and described the NICU care in the American unit as the "wait until certain" strategy: resuscitating almost all infants and withdrawing care if they deteriorate (41). The Dutch unit's approach was described as one where treatment was offered to infants who have or are likely to have reasonably good long-term outcomes (statistical prognostic). These two units had different survival rates and long term outcomes, mainly due to this variation. The current guidelines on active treatment at the "limits of viability" from the Netherlands are still somewhat more 'restrictive' than those from the USA and Canada (36). This explains the relative high number of DR deaths with a higher mean gestational age in Groningen in comparison to the other 3 units. We might have expected a higher proportion of deaths following withdrawal of ventilation in stabile newborns in Groningen (and possibly in Canada) due to the neonatologists pro-quality-of-life attitude (42). We found, however, that physicians in Groningen appear to be less likely to withdraw the ventilator in physiologically stable newborn for quality of life reasons.
A potential limitation of our study is the study's retrospective nature and the concerns inherent to the dependency on medical charts for the accurateness of the data. Another limitation could be fact that this study involved only four units and a relatively small number of patients, which puts question marks to the generalizability of the conclusions regarding the use of the classification model. We compared the number of decisions based on quality of life considerations in the four NICU's but we did not examine what the quality of life considerations were. These concerns could probably be best addressed by combining our results with a prospective multicenter study in the near future that would include comparison of quality of life considerations used in the four NICUs. We are currently embarking on precisely this project.

Table 1. Demographics of all deaths in the Delivery Room and in the NICU in 4 institutions (n=183)

	Groningen	Montreal	Wisconsin	Chicago
Delivery Room deaths				
Nr of patients	16	9	7	0
Female	6 (38%)	5 (55%)	4 (57%)	-
Gestational age (mean)	26,2	23,4	26	-
Birthweight (mean)	965	582	902	-
Minutes alive (mean)	61	65	28	-
NICU Admissions	555	700	654	800
NICU deaths	52 (9%)	34 (5%)	36 (5,5%)	29 (4%)
Female	22 (42%)	13 (30%)	16 (44%)	12 (41%)
Gestational age (mean)	34,5	32,9	33,2	30
Birthweight (mean)	2231	2163	2003[#]	1362
Days alive (mean)	22,5	32,7	15,8	31,5
Days alive (median)	5	7,5	7	7

[#] No birthweight documented in 6 cases

Table 2. Distribution of 151 deaths in 4 NICU's according to gestational age

GA	Groningen	Montreal	Wisconsin	Chicago	total
<27 wks	6 (12%)	8 (24%)	9 (25%)	13 (45%)	36 (24%)[#]
27-36 wks	25 (48%)	14 (41%)	15 (42%)	12 (41%)	66 (44%)
>36 wks	21 (40%)	12 (35%)	12 (33%)	4 (14%)	49 (32%)
Total	52	34	36	29	151

GA: gestational age

[#]P<0.05

Table 3. Causes of death and classification according to physiology in 151 NICU deaths

		Groningen (n=52)	Montreal (n=34)	Wisconsin (n=36)	Chicago (n=29)	P
Asphyxia		9 (17%)	7 (20%)	2 (6%)	3 (10%)	0,2
	unstable	5	3	0	3	
	stable	4	4	2	0	
Congenital anomalies		26 (50%)	11 (32%)	20 (56%)	11 (38%)	0,2
	unstable	22	5	12	11	
	stable	4	6	8	0	
Sepsis/nec[γ]		12 (23%)	8 (24%)	8 (22%)	5 (17%)	0,9
	unstable	10	7	8	5	
	stable	2	1	0	0	
Respiratory insufficiency		1 (2%)	1 (3%)	3 (8%)	8 (28%)	-
	unstable	1	1	0	8	
	stable	0	0	3	0	
Intracranial bleeding		4 (8%)	7 (21%)	3 (8%)	2 (7%)	-
	unstable	1	3	1	2	
	stable	3	4	2	0	

[γ]nec: necrotising enterocolitis

Unstable: 2 of the following criteria are present: desaturation in 100% oxygen on a respirator, hypotensive on inotropes, bradycardic for a prolonged period, or anuric for more than 24 hours.

Stable: stable with or without artificial ventilation

Table 4. Circumstances of dying and classification of 183 deaths in the delivery rooms and in the NICUs of 4 institutions.

Intervention	physiology	Groningen (n=68)	Montreal (n=43)	Wisconsin (n=43)	Chicago (n=29)	p
WH+WD (died in DR)	unstable	16 (24%)	9 (21%)	7 (16%)	0	0,04
Not WH, not WD (died while receiving CPR)	unstable	3 (4%)	5 (12%)	4 (9%)	9 (31%)	-
WH CPR, not WD (died on a respirator)	unstable	1 (1%)	1 (2%)	0	5 (17%)	-
WH+WD (extubation to let the child die in parents arms)	unstable	35 (52%)	13 (30%)	17 (40%)	15 (52%)	0,11
WH+WD (electively extubated for qol-reasons)	stable	13 (19%)	15 (35%)	15 (35%)	0	0,001

WH: withholding life-sustaining treatment; WD: withdrawing life-sustaining treatment

Unstable: 2 of the following criteria are present: desaturation in 100% oxygen on a respirator, hypotensive on inotropes, bradycardic for a prolonged period, or anuric for more than 24 hours.

Stable: stable with or without artificial ventilation.

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Chapter 8

Summary and general discussion

The objective of this thesis was twofold: to provide a detailed description of end-of-life decision-making practice in severely ill newborns in the Netherlands, followed by a description of how these decisions were implemented, and when. In this chapter I summarize and discuss the main findings and put forward suggestions for future research.

In **Chapter 2** we described how newborns in whom an end-of-life decision was under consideration, could be categorized into three groups on the basis of their physiology and the physicians' interventions. We focused on Group III, the smallest but probably the most controversial category. It encompasses stabile newborns with intractable suffering. In the Netherlands, deliberate termination of life of such infants is considered an option open to the attending physician. We disclosed the considerations of physicians in support of their decisions to end the lives of 22 newborns between 1997 and 2004. In this chapter, we also describe 'the Groningen Protocol' for deliberate termination of the life of a severely ill newborn. The Protocol was published to prevent uncontrolled and unjustified termination of life of newborns and to bring the issue into the public domain with a view to stimulating discussion. It includes five key requirements of due care that need to be fulfilled and additional issues that require explicit clarification to enable the authorities to review the case properly.

We conducted a pilot-study in two large university-based NICUs to investigate how often newborn deaths were preceded by end-of-life decisions and to determine whether it was possible, retrospectively, to obtain accurate information about the decision-making process. In **Chapter 3** wereported that over a period of six months 93% of 30 newborn deaths were preceded by end-of-life decisions at the centers studied. Twenty-four deaths (83%) could be attributed to the withdrawal of treatment, four (10%) to withholding treatment and two deaths (7%) occurred despite maximum treatment. In approximately two thirds of the cases (64%) the newborns stood no chance of survival and prolonging treatment was considered unjustified. In the remaining cases (36%) withholding or withdrawing treatment was based on quality-of-life considerations, mostly pertaining to predicted suffering and predicted inability to communicate either verbally or nonverbally. Potentially life-shortening medication appeared to play a minor role as the cause of death.

In **Chapter 4** We presented the results of a nation-wide study to determine when and how physicians in the Netherlands took end-of-life decisions in case of severely ill newborns. We reviewed the files of 359 deaths over a period of twelve months in the ten NICUs in the Netherlands. We found that end-of-life decisions were made in 95% of all deaths. In the remaining 5% no decision to terminate the lives of the infants had been made and treatment was continued until they died. Of all the newborns that died 58% had been classified as standing no chance of survival while 42% were stabilized newborns with a poor prognosis. Withdrawal of life-sustaining treatment was the main mode of death in both groups. We found one case of deliberate termination of life. In addition to reviewing the medical files, we interviewed the attending physicians of 147 out of 150 deaths preceded by an end-of-life decision based on quality-of-life considerations. In 92% of deaths in the poor prognosis group, end-of-life decisions were based on the newborns' future quality-of-life and mainly concerned future suffering. In 44% of deaths these considerations were made in conjunction with considerations regarding the present

quality-of-life. Parents were always involved in the decision-making process. Consultation with colleagues on the medical team occurred in 99% of cases.

In **Chapter 5** we reported on the characteristics of the decision-making process in newborns that had died after an end-of-life decision based on their poor prognosis. We found that parents had been involved in all the end-of-life decisions and that in all cases consensus had been reached between the parents and the team. Initial differences of opinion between parents and the medical team occurred in 18 out of 147 cases and mostly concerned the infant's poor neurological prognosis. Initial differences of opinion within the team occurred in 6 out of 147 cases and concerned uncertainty about the prognosis. Differences of opinion resulted in postponing the end-of-life decisions. In some of these cases time was taken to provide the parents with additional information and to strive for consensus between the team and the parents in additional meetings. In other cases additional diagnostic tests (e.g. MRI, or EEG) were ordered to increasing prognostic accuracy or other NICUs were asked to give a second opinion. In all cases consensus was reached eventually. We asked the attending neonatologists what they considered to be the most important factors that had contributed to differences of opinion with parents. According to them these were parents' religious convictions that forbade withdrawal of life-sustaining treatment and miscommunication between the parents and the medical team.

In **Chapter 6** we presented the types and dosages of the analgesics and sedatives administered, the use of neuromuscular blockers (NMBs) and the reasons for administering these drugs at the time of death in severely ill newborns in the ten NICUs. Analgesic and sedative medication was administered to 224 out of 340 newborns before the end-of-life decision and to 292 newborns after the decision had been made. Medication was increased in 94 out of 189 newborns whose deaths were imminent and in 110 out of 150 newborns whose prognoses were poor. Reasons for these increases were the treatment of symptoms, prevention of suffering and to hasten death in 4% of cases. The underlying considerations were documented in 45% of deaths. In 55 (16 %) of the newborns NMBs were administered after the end-of-life decisions had been made. In most cases the reasons for administering these drugs were not documented in the medical files, but during the interviews I was able to partly reproduce the physicians' actual intentions. Explanations given during the interviews were: discontinuing the drug in newborns already on NMBs would invoke additional suffering, to stop the infant from gasping for breath, and on parental request. In general, palliative care medication was increased after the end-of-life decision had been made to treat symptoms or to prevent suffering and, rarely, to hasten death. The considerations leading up to the increase of medication were insufficiently documented in the medical files. This hindered the internal and external review of the cases.

In **Chapter 7** we reported on the results of a comparative study on end-of-life decision-making in four NICUs in three different countries: two in the USA (Chicago, Illinois and Milwaukee, Wisconsin), one in Canada (McGill University Health Centre including the Royal Victoria and the Montreal Children's Hospital) and one in the Netherlands (University Medical Center Groningen). We reviewed the medical files of all newborns of older than 22 weeks of gestation that had died either in the delivery rooms or in the NICUs over a 12 month period. In each unit the deaths were categorized according to withdrawing or withholding ventilation or both as a function of the newborn's physiologic stability, and its neurological prognosis.

In all four the units most of the unstable newborns died in their parents' arms after artificial ventilation was withdrawn. The decision to electively extubate newborns for quality-of-life reasons was made in 19% to 35% of deaths in three units. It never occurred in the fourth unit (Chicago). The proportion of newborns that died while receiving cardiopulmonary resuscitation varied between 4% to 12% in Wisconsin, Montreal and Groningen and was highest in Chicago (31%). The proportion of delivery room deaths in Wisconsin, Montreal and Groningen was 16% to 22%. No delivery room deaths occurred in Chicago. We concluded that the deaths had occurred under different conditions in the four NICUs and that distinctive end-of-life decisions could be categorized separately using a two-dimensional model. Cross-cultural and intra-cultural comparisons of end-of-life practices are feasible and important when comparing outcomes between NICUs.

General Discussion

— Strengths and Weaknesses

A substantial part of this thesis addressed end-of-life decision-making in severely ill newborns and the implementation of these decisions in the NICUs in the Netherlands. To this end we studied all newborn deaths that had occurred in theseNICUs during a period of 12 months. One of the strengths of this study is that all NICUs in the Netherlands participated. Excluded from the study were end-of-life decisions concerning newborns born in a hospital without a NICU and that had died there, as well as newborns that died after they had been transferred from the NICU to another hospital to die there. In the Netherlands, transporting and centralizing high-risk pregnancies and newborns between specialized centers is both well-structured and well-funded. Non-referral of severely ill newborns is probably very rare (1). This was illustrated in the pilot study carried out in two university hospitals with a NICU. The number of newborns transferred to other hospitals to let them die there was small and the pediatricians in the receiving hospital kept close contact with the referring neonatologists to ensure continuity of end-of-life care (2). We think therefore that the results of this study of end-of-life practices in the ten NICUs is representative of the nation-wide approach to end-of-life decision-making in severely ill newborns in the Netherlands.

A limitation of our study was its retrospective nature. This was partly remedied by the medical files that contained good descriptions of the decision-making process regarding withholding or withdrawal of life-sustaining treatment. Medication orders and notes from the pharmacy were also well-documented. Documentation of the considerations for administering neuromuscular blockers, however, was poor and proved insufficient for internal and external review. During the interviews with the neonatologists the medical files were consulted which limited potential inaccuracy of the physicians' recall.

— Some Important Findings and Implications of the Study

In 95% of all infants that had died before the age of two months, death was preceded by an end-of-life decision. In most cases it was decided to withdraw life-sustaining treatment. Infants that stood no chance of survival made up the largest proportion of deaths (58%). In the remaining group treatment was withdrawn or withheld because of the very poor prognosis for later life. End-of-life decisions in this group were based mostly on the infant's expected future quality-of-life. A remarkable

result was that the proportion of the decisions based on quality-of-life considerations was similar in all ten NICUs in the Netherlands. The considerations leading to the decisions were also similar. We also found a similar proportion of end-of-life decisions based on quality-of-life considerations in the NICUs in Groningen, Montreal and Wisconsin. The number of decisions based on quality-of-life considerations between the American NICUs in Chicago and Wisconsin varied considerably. The consistency found in the Netherlands could be explained by the fact that as early as 1992 the Dutch Pediatric Association had published guidelines on end-of-life decision-making (3). This publication also contains a description of the criteria that are helpful to determine what constitutes quality-of-life in this context. The criteria are: (a) the possibility to communicate (b) self-sufficient with regard to everyday activities like sitting, walking and personal care (c) non-dependence on continuing medical care (d) absence of suffering (e) capacities for personal development and (f) life expectancy. The results showed that criteria (a) to (d) were still used as quality-of-life criteria. Criteria (e) and (f) were not mentioned nor were new criteria introduced by the neonatologists although during each interview we offered them the possibility to do so.

In contrast to the situation in the Netherlands, the guidelines on end-of-life decision-making issued by the American Academy of Pediatrics (AAP) and the Canadian Paediatric Society (CPS) do allow quality-of-life considerations but fail to give guidance on what quality-of-life is, or how it can be determined (4, 5). This also holds for the guidelines of most other countries. The differences between Chicago and Wisconsin could be due to differences in the attending physicians' interpretations of the guidelines. Possibly, differences in the parental population with regard to e.g. income, social class and level of education are at least partially responsible for these differences (6-9). The aim of our comparison of NICUs in different countries was not to explore the contents of quality-of-life criteria used by physicians in Montreal, Wisconsin or Chicago. We do, however, acknowledge the importance of involving a unit's approach to decision-making in situations with prognostic uncertainty in comparative studies of NICUs. Lorenz et al. illustrated this point in a study comparing outcomes of premature infants in New Jersey, USA and the Netherlands (10). In this study, based on data from 1983, the NICU care in the American unit is described as a 'wait until certain' strategy: resuscitating almost all infants and withdrawing care if they deteriorate. In the Netherlands the 'statistical prognosis strategy' is used: intervene only in those infants that have a good predicted outcome. As a result, no infants of less than 25 weeks of gestation are resuscitated in the Netherlands and consequently none survive because care is withheld. In New Jersey the survival rate is 30% during the same period. The results of newborns of 25 and 26 weeks of gestation are also affected. In New Jersey less than 10% of hospital deaths is caused by withholding care, whereas on average it is 38% in the Netherlands. As a result, the survival of newborns of 26 weeks of gestation and less is 40% in New Jersey with 8% of them developing cerebral palsy. In the Netherlands survival is 20%, with a 2% rate of cerebral palsy.

A similar difference in approach appeared from our comparative study. The Chicago NICU reported no delivery room deaths. This meant that all newborns older than 22 weeks of gestation were resuscitated, intubated and admitted to the NICU. In the other three NICUs a substantial proportion of deaths did occur in the delivery

rooms - mainly extreme premature newborns with congenital anomalies that were withheld resuscitation or intensive care or both.

Our study demonstrated that the end-of-life decisions were implemented after consensus about the decision had been reached between the medical team and the parents. If differences of opinion occurred, which did happen occasionally, the decision was postponed. From a medical and technical point of view, implementing the end-of-life decision practically always meant discontinuing artificial ventilation and choosing a medication regimen that ensured the comfort of the newborn. Although no Dutch guidelines existed that prescribe the type, dose or timing of analgesics and sedatives adequate to provide comfort to the dying newborn, the medical management of symptoms and suffering proved to be largely similar in all units. Pharmacological end-of-life practices in the Dutch NICUs appeared to be in line with most recommendations in international textbooks and other publications on palliative care (11-13). Two aspects of end-of-life practice in the Netherlands might, however, be regarded as exceptions: increasing analgesics and sedatives with the intention to terminate the life or to hasten the death of an infant, and the use of neuromuscular blockers. Both items are discussed below.

Administering potentially life-shortening medication to treat symptoms and to alleviate suffering at the end of an infant's life is generally regarded as good medical practice, irrespective of the doses needed (11-13). Administering these agents with the intention to cause death or to hasten death can be interpreted as deliberate termination of life of a newborn. This is a criminal offence, also in the Netherlands. All cases of deliberate termination of life of a newborn must be submitted to the prosecuting authorities for review. If the authorities decide that the physician acted in accordance with the criteria of due care, the physician's actions that led to deliberate termination of life are considered legally acceptable (14, 15). However, many physicians are uncertain as to where the demarcation line lies between administering medication with life-shortening effect as part of normal palliative care on the one hand, and pharmacological life-shortening that constitutes a criminal offence, on the other hand. To know where the line lies is crucial because the consequences of either action are very different. A case of deliberate termination of a newborn's life needs to be reported and reviewed. The outcome of this review is either that the physician is prosecuted for murder, or the infant's death is seen as one of the possible side-effects of good medical (palliative) practice and has no legal consequences (14, 16).

In order to differentiate between the two practices previous studies on neonatal end-of-life decisions focus on the physician's intentions (17-19). If medication is administered to the newborn with the sole intention to hasten its death, it is regarded as deliberate termination of life. The 1995 and 2001 surveys reported that intentional hastening of death causes 1% of newborn deaths in the Netherlands. This amounts to between 15 to 20 cases per year (17, 19). In the 1995 publication the reasons for hastening a newborn's death are: unbearable suffering (63%), the poor predicted quality-of-life (52%), and the poor prospects for improvement (42%) (20). The problem with physicians' intentions is that they are subjective, ambiguous, and sometimes unclear even to the physicians themselves (21, 22). Our study focused on the medical reasons for deciding to administer potentially life-shortening medication and on the clinical situation at the time of the decision. The results showed that (a) the documentation found in the medical files on the physicians' considera-

tions leading up to administrating potentially life-shortening medication was insufficient for internal and external review (b) intentional hastening of death in the NICUs occurred in 11 cases and almost exclusively because the physician wanted to stop the gasping respiratory efforts of a moribund newborn in situations were the ventilator had been withdrawn or withheld (c) physicians reported none of these deaths as having been caused by deliberate termination of life. In the interviews with the physicians we found that, in contrast to the 1995 data, they were treating directly observable symptoms without taking into consideration future quality-of-life or prospects for improvement.

There are two reasons why treating symptoms in moribund patients might be considered good palliative care. First, because there was no alternative treatment that could take away the symptoms or alleviate suffering, or both. Second, these patients were moribund, which means they were dying and death was imminent. The sight of their newborn gasping for breath can be a source of acute and long-term stress for parents. Moreover, it seems unlikely that gasping in the dying state serves the infant any purpose. In this situation, granting a parental request to stop the gasping by hastening their newborn's death will increase the parents' comfort and may contribute positively to their grieving process and should therefore be regarded as acceptable (23-27). For legal review of the physician's acts it is necessary to spell out in the medical file the reasons for causing or intentionally hastening the death of a newborn, and to include a description of the clinical circumstances prevailing when the decision was made.

In this study 16% of newborns that died (n=55) had received NMBs after the end-of-life decision had been made. The use of NMBs at the end of a newborn's life has been the subject of debate among professionals for many years (24, 26, 28-30). Those against the use of NMBs argue that (a) paralysis precludes the possibility of survival, (b) paralysis may hinder the clinician's assessment of the patient's comfort and (c) the opportunities for interaction between dying newborns and their families are diminished (28). Others argue that there is no moral difference between letting the newborn die or shortening its life by several minutes or hours by administering NMBs to prevent unnecessary suffering (24-26), and that skilled and experienced clinicians should be able to manage pain and suffering despite paralysis (2, 28). The present study described three distinct clinical situations where NMBs were administered in the Dutch NICUs. In the first situation the physician administered NMBs to a moribund newborn to stop the infant from gasping after having increased opioids and sedatives. In the second, the physician continued administering NMBs to a newborn that was already receiving these agents as part of the treatment regimen. Restoration of neuromuscular function was expected to delay the dying process and to invoke unnecessary suffering. In the third situation, the parents expressed the wish to let their child die without gasping and the physician administered the NMBs before extubating the infant and after having increased opioids and sedatives. For many physicians the first situation is controversial for any of the three reasons stated above. However, our findings pointed out for the first time that a substantial part of Dutch neonatologists thought that gasping in moribund newborns could and should be managed pharmacologically. The use of NMBs in the first situation might also be seen as proper palliative care for similar reasons as stated above with regard to causing or intentionally hastening death: no alternative treatment was

available and ending the gasping respiratory efforts might improve parental comfort and relieve their grieving.
Many physicians consider the second situation acceptable medical practice (28, 31, 32). The third situation is controversial for the same reasons as the first (28). In addition, a first important difference between the first and third situation was that no symptoms were observed in the latter and NMBs were administered solely to prevent possible future symptoms. A second difference was that the newborns were not moribund and the use of NMBs might result in shortening a substantially longer life than was the case in the first situation. Thirdly, extubation can be stressful for the infant and frequently requires increased doses of sedatives and analgesics to control pain and suffering. By administering NMBs before extubation, as was the case, the possibility of monitoring these changes were reduced.
Given the advantages and disadvantages of NMBs in the three clinical situations described above, we arrive at the following conclusion: there are compelling reasons to distinguish between the use of NMBs in moribund newborns to treat gasping and suffering and in newborns that were already receiving these agents on the one hand, and administering NMBs to newborns before extubation, on the other hand. The first and second situations are part of generally accepted medical practice in the Dutch NICUs, whereas in the third situation this may not always be the case. These end-of-life decision-making practices need to be discussed in more detail — within and probably also outside the medical profession.

— Deliberate Termination of Life and the Review Procedure

One of the important reasons for having a notification and external review procedure in place in cases of deliberate termination of life of newborns is to supervise that the physician's conduct meets the criteria of due care (14). In 2006, a committee of experts on deliberate termination of life of newborns (and on late termination of pregnancies) was appointed by the Dutch government and the procedures for reporting such cases were changed (33, 34). This happened after repeated requests by the medical profession for more transparency and clarity about the review procedure of deliberate termination of life of newborns and about the criteria and requirements of due care (35, 36). Based on the new regulations, physicians are required to report all cases of deliberate termination of a newborn's life to the public prosecutor who in turn submits the report to the committee of experts (37). The committee (consisting of a lawyer, a ethicist and three physicians specialized in the field of neonatology) reviews the case and applies the criteria of due care to assess whether the physician had acted accordingly (38). The committee's recommendations are taken into account by the prosecuting authorities who decide whether prosecution will be instituted against the physician.
During the study period the committee of experts was not yet operational but the legal obligation to report cases of deliberate termination of life to the prosecuting authorities was already in place. None of the newborn deaths following the administration of NMBs in that period were brought to the attention of the authorities. The physicians we interviewed probably considered the use of NMBs to be appropriate palliative care that did not require review. At the same time they knew that administering a NMB to a newborn would lead to respiratory arrest and result in certain death — an action that fell within the definition of deliberate termination of life. This discrepancy illustrated that for many physicians the issue of using

NMBs was as yet unresolved in relation to the obligation to report deliberate termination of life. Partly at least this is understandable because the phrase 'deliberate termination of life' was judged differently by different physicians. Another explanation could be that some medical actions were not included because they represented medical interventions that were acceptable under certain circumstances. Extubating a severely ill newborn that stands no chance to survive could serve as an example of an acceptable action to end the newborn's life. The question arises whether or not the administration of NMBs in the NICU is always an act that needs to be reported irrespective of the physician's reasons for administering it. Notifying the authorities of all cases of using NMBs in the NICU, as cases of deliberate termination of life might be consistent with the aim to ensure that medical procedures meet the criteria of due care. However, it is rather remote from the physicians' opinion on the subject and from current medical practice in the Dutch NICUs as was demonstrated here. An alternative approach could be to report only those cases in which NMBs were administered with a view to ending the newborn's life for other reasons than managing symptoms like gasping and suffering. In this approach it is assumed that NMBs are administered to secure the comfort of the dying newborn and thus qualifies as appropriate palliative care.

Although our findings suggested that consensus was reached among many neonatologists about the latter, further discussions among neonatologists, pediatricians and palliative care specialists is necessary to confirm this finding. A national consensus statement or guideline regarding the use of analgesics, sedatives and NMBs as part of end-of-life decisions could be an important tool for medical practice and would at the same time stimulate the discussion required. The findings of this study on physicians' considerations and the clinical situations at the time they administered the NMBs to newborns in the NICU, could be helpful in this discussion. These findings, however, only reflect the end-of-life practices in NICUs. Given that all the cases reported between 1997 and 2004 involved newborns that were physiologically stable, that were not given life-sustaining treatment and were not admitted to intensive care (39), the discussion about reporting deliberate termination of life of newborns should also be extended to include involve neonatal end-of-life practices outside the NICU.

Clarity is necessary about what cases qualify as deliberate termination of life and that need to be reported to the authorities for this reason. This would help physicians to report their cases. The process of external review by the multidisciplinary committee of experts is already more transparent than it was in the past. Then the prosecuting service reviewed the case without the help of medical experts and without public descriptions of the case, its considerations or of the final ruling. As soon as the first cases are reported, the reviews by the multidisciplinary committee of experts will contribute to the ongoing development and clarification of the standards regarding deliberate termination of life of newborns. This would encourage attending physicians to notify the authorities, which in turn would enhance transparency of medical practice and increase debate about what is going on at ground level.

Suggestions for Future Research

Although this thesis provided additional insight into physicians' end-of-life decision-making and its implementation in severely ill newborns, many questions about

end-of-life practices remain. Amongst them are the following, some of which are already under investigation:

1. The death of severely ill newborns is not restricted to the NICU. End-of-life decision-making also takes place in the delivery room. It appears that palliative care medication and the use of NMBs in the delivery room differ from that in NICUs (40). The different approaches to pain and suffering in the delivery room and the NICU may be a disadvantage to the infant, confuse to the parents, and may be difficult to explain. The reasons for these differences are not well understood and need to be studied in detail.
2. Not all newborn deaths occur in hospitals with a NICU. Insight into the considerations and the clinical circumstances of end-of-life decision-making in newborns that do not receive intensive care is still limited. Increased insight would provide an important contribution to the discussion on the use of analgesics, sedatives and NMBs as part of end-of-life decision-making in newborns.
3. An important criterion for legal acceptance of deliberate termination of life of newborns is the presence of hopeless and unbearable suffering. Both requirements are drawn from the standards of due care for euthanasia and need to be 'translated' to newborns. For the translation of hopelessness (being without prospects), multidisciplinary input of epidemiologists, pediatricians, neonatologists, pain specialists and others might be useful. Reporting cases of deliberate termination of life and analyzing the committee of expert's review would contribute to clarify, at least partly, about what constitutes 'unbearable suffering' in newborns.
4. End-of-life decision-making has been studied mostly with retrospective study designs. The number of prospective studies in this field is still very limited, especially with regard to the role and the experience of parents in the end-of-life decision-making process. Information about the parental perspective would be useful for neonatologists who care for severely ill newborns and would help them to better anticipate parental needs.
5. Different outcomes of the decision-making process at the end of a newborn's life can result from differences of opinion among physicians about what is in the infant's best interest. An intriguing question is whether these different outcomes as such are compatible with the intant's right to equal treatment in equal cases and protection against discrimination under international human rights law. This question needs to be investigated in more detail.
6. This study described the use of NMBs in different clinical situations in the NICU. In some situations neonatologist in the Netherlands consider the use of these agents to be part of appropriate palliative care. Many physicians, for a variety of reasons, object to using NMBs in palliative care. These reasons have yet to be studied well and more research is needed to decide whether NMBs may or may not be used as palliative care medication in the dying newborn.
7. Most studies on the use of analgesics, sedatives and NMBs as part of end-of-life decision-making stem from the Netherlands and the Flemish part of Belgium. These studies have caused intense debate both within the medical profession and in the public domain. Comparing end-of-life practices with NICUs in other countries would increase insight into the dilemmas concerning the use of

these medicines and would reveal how physicians in other countries deal with these dilemmas.

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Summary in Dutch
(Samenvatting in het Nederlands)

Het doel van dit proefschrift was tweeledig: het gedetailleerd beschrijven van de manier waarop beslissingen over het levenseinde van zieke pasgeborenen worden genomen, en het beschrijven hoe en wanneer deze beslissingen worden uitgevoerd. In dit hoofdstuk worden de belangrijkste resultaten samengevat.

Beslissingen over het levenseinde van pasgeborenen betreffen meestal het besluit om de levensverlengende behandeling te staken of te beperken. In zeldzame gevallen kan het gaan om de beslissing om tot actieve levensbeëindiging over te gaan. De pasgeborenen waarbij een dergelijke beslissing wordt genomen, kunnen worden onderverdeeld in drie categorieën. Deze categorieën, die in alle hoofdstukken van dit proefschrift terugkomen, zijn gebaseerd op de beslissing over het levenseinde in relatie tot de fysiologische toestand van de pasgeborene en diens toekomstige gezondheidstoestand (prognose).
De eerste groep omvat de pasgeborenen die geen overlevingskans hebben ondanks de inzet van alle beschikbare technologie. Als de kansloosheid van de behandeling is vast komen te staan wordt de levensverlengende behandeling, die meestal bestaat uit kunstmatige beademing, gestaakt. De tweede groep bestaat uit pasgeborenen die met inzet van maximale medisch-technische middelen theoretisch in leven zijn te houden, maar waarvan verwacht wordt dat de toekomstige gezondheidstoestand, de kwaliteit van leven, heel slecht is. Als bij pasgeborenen in deze groep een aanvaardbare gezondheidstoestand in de toekomst niet meer haalbaar is, wordt de levensverlengende behandeling gestaakt. De derde groep omvat pasgeborenen die ook zonder intensieve behandeling in leven blijven, maar niettemin een leven van zeer ernstig en uitzichtloos lijden tegemoet gaan. Als deze situatie is vastgesteld, bestaat er niet de mogelijkheid om een levensverlengende behandeling te staken zoals bij de eerder genoemde groepen. Indien de arts, samen met de ouders, van mening is dat er geen redelijke alternatieve methoden zijn om het lijden op te heffen, dan kan het besluit tot actieve levensbeëindiging worden genomen.

Hoofdstuk 1 beschrijft de praktijk van besluitvorming over het levenseinde van pasgeborenen in verschillende landen in Europa en in de Verenigde Staten en geeft een uitleg over de onderzoeksvragen.

In **hoofdstuk 2** beschrijven we de overwegingen die artsen gebruikten om actieve levensbeëindiging bij zieke pasgeborenen toe te passen in 22 gevallen die landelijk plaatsvonden tussen 1997 en 2004. Daarna beschrijven we het 'Gronings Protocol' voor actieve levensbeëindiging bij pasgeborenen dat was opgesteld om onterechte en ongecontroleerde levensbeëindiging bij pasgeborenen te voorkomen. Een bijbedoeling was om naar aanleiding van het protocol de discussie over levensbeëindiging zo openlijk mogelijk te voeren, waardoor verdere normering voor deze beslissingen kan plaatsvinden. Het Gronings Protocol omvat vijf belangrijke vereisten waaraan voldaan moet worden om van een zorgvuldig besluit tot actieve levensbeëindiging te kunnen spreken. Daarnaast zijn er nog een aantal aanvullende onderdelen beschreven die verdere verduidelijking moeten geven van de situatie waarin de patiënt zich bevindt en van de omstandigheden betreffende de besluitvorming. Al deze gegevens zijn eveneens noodzakelijk om de (verplichte) externe toetsing op een optimale wijze te laten plaats vinden.

In **hoofdstuk 3** beschrijven we de resultaten van een pilotonderzoek met een tweeledig doel: het beschrijven hoe vaak neonataal overlijden vooraf wordt gegaan door een beslissing over het levenseinde, en om gedetailleerde informatie te verzamelen over het besluitvormingsproces. Het onderzoek werd uitgevoerd in twee grote Nederlandse universiteitsziekenhuizen met een neonatale intensive care afdeling (NICU's). Het bleek goed mogelijk te zijn om de gewenste informatie te verkrijgen door systematische analyse van de medische dossiers, aangevuld met gegevens uit interviews met de behandelende artsen. De resultaten toonden aan dat gedurende de onderzoeksperiode van zes maanden het overlijden van 28 van de 30 pasgeborenen (93%) in deze centra werd voorafgegaan door een beslissing over het levenseinde. In een meerderheid van de gevallen (83%) was het overlijden het gevolg van het stoppen van de behandeling, in vier gevallen (10%) was er sprake van het beperken van de behandeling en in twee gevallen (7%) overleed het kind ondanks de maximale behandeling.
In de meeste gevallen (64%) was er voor de pasgeborene geen overlevingskans. Verlenging van de behandeling kon om die reden niet worden gerechtvaardigd. In de overige gevallen was het besluit om de behandeling te stoppen of te beperken gebaseerd op overwegingen betreffende de verwachte slechte gezondheidstoestand (sombere prognose). De meest voorkomende overwegingen in dat kader waren het verwachte ernstige toekomstig lijden en de toekomstige onmogelijkheid tot verbale of non-verbale communicatie. De toediening van medicatie met een mogelijk levensverkortend effect speelde nauwelijks een rol als doodsoorzaak.

Hoofdstuk 4 beschrijft de resultaten van een landelijke studie die was opgezet om te onderzoeken wanneer en hoe artsen in Nederland beslissingen over het levenseinde bij ernstig zieke pasgeborenen nemen. Wij beschrijven de analyse van medische dossiers van 359 pasgeborenen die overleden gedurende een periode van 12 maanden in de 10 NICU's in Nederland.
Wij vonden dat beslissingen over het levenseinde bij 95% van alle overlijdens hadden plaatsgevonden. In de overige 5% werd de behandeling doorgezet tot aan het moment van overlijden. Het stoppen van de kunstmatige beademing was de meest voorkomende beslissing die leidde tot het overlijden. Het besluit om de behandeling te staken of te beperken werd in 58% van de gevallen genomen omdat de pasgeborene geen overlevingskans had. In 42% werd dat besluit genomen vanwege de zeer slechte prognose. Er werd één geval van actieve levensbeëindiging gevonden.
Wij interviewden de behandelende artsen van 147 van de 150 overleden pasgeborenen waarbij een beslissing over het levenseinde was gebaseerd op de sombere prognose. In 92% van de overlijdens in deze groep waren de beslissingen over het levenseinde gebaseerd op de verwachte toekomstige kwaliteit van leven en betroffen vooral toekomstig lijden. In 44% van de gevallen werden deze overwegingen gecombineerd met overwegingen die betrekking hadden op de huidige kwaliteit van leven. In alle gevallen waren de ouders betrokken bij het besluitvormingsproces. In 99% van alle gevallen consulteerde de behandelende arts collega's binnen het medisch team over de besluitvorming.

De belangrijkste kenmerken van het besluitvormingsproces dat plaatsvond bij beslissingen over het levenseinde op grond van de sombere prognose, worden bespro-

ken in **hoofdstuk 5**. Wij vonden dat de ouders altijd betrokken waren bij deze beslissingen en in alle gevallen werd uiteindelijk consensus bereikt tussen de ouders en het behandelend team. In 18 van de 147 gevallen was er voorafgaand aan de consensus wel sprake van belangrijke verschillen van mening tussen de ouders en het medisch team. Deze verschillen hadden meestal betrekking op de inschatting van de ernst en van de betekenis van de neurologische prognose van het kind. Verschil van mening binnen het medisch team vond plaats in 6 van de 147 gevallen en betrof meestal onduidelijkheid rondom de prognose. Wij vonden dat verschil van mening altijd resulteerde in uitstel van de beslissing over het levenseinde. In sommige gevallen werd tijd genomen om de ouders meer informatie te geven en om consensus te bereiken tussen het team en de ouders door middel van extra bijeenkomsten. In andere gevallen werd aanvullende diagnostiek gedaan (bijvoorbeeld MRI of EEG) om de prognostische zekerheid te vergroten of werden andere intensivecareafdelingen gevraagd om een tweede of derde mening te geven.
Wij vroegen de behandelende artsen naar hun mening over (risico)factoren die bijdragen aan het ontstaan van meningsverschillen over beslissingen over het levenseinde van pasgeborenen tussen ouders en het team. De belangrijkste factoren die werden genoemd waren de religieuze overtuiging van de ouders die het stoppen of beperken van levensverlengende behandeling niet toestaat en onduidelijke communicatie tussen de ouders en het team.

In **hoofdstuk 6** beschrijven we het gebruik van analgetica, sedativa en spierverslappers als onderdeel van beslissingen over het levenseinde in de tien Nederlandse NICU's. Analgetica (meestal morfine) en sedativa (meestal midazolam) werden gegeven aan 224 van de 340 pasgeborenen voordat de beslissing over het levenseinde werd genomen en aan 292 pasgeborenen nadat die beslissing had plaatsgevonden. De medicatie werd opgehoogd na het levenseindebesluit in 94 van de 189 pasgeborenen die geen kans op overleven hadden, en in 110 van de 150 pasgeborenen met een sombere prognose. De reden om de medicatie op te hogen waren symptoombehandeling, preventie van lijden en (in 4%) het versnellen van de dood. De onderliggende overwegingen werden in 45% van de gevallen vastgelegd in het medisch dossier. Spierverslappers werden gegeven aan 55 patiënten (16%). De redenen om deze middelen te geven werden meestal niet gedocumenteerd en wij konden uitsluitend door middel van de interviews achterhalen wat de beweegredenen van de artsen waren om dit te doen. Uit de interviews bleek dat spierverslappers werden toegediend omdat (1) het stoppen van dit middel bij patiënten die het al kregen toegediend extra lijden zou veroorzaken, (2) het gaspen op die manier kon worden gestopt, of (3) omdat de ouders daarom hadden gevraagd.
Wij concludeerden dat palliatieve medicatie bij zieke pasgeborenen verhoogd wordt nadat een beslissing over het levenseinde is genomen met het doel om symptomen te bestrijden en om lijden te voorkomen, maar vrijwel nooit om de dood te versnellen. In de medische dossiers wordt onvoldoende gedocumenteerd wat de redenen zijn om medicatie te verhogen, wat (externe) toetsing van die overwegingen bemoeilijkt.

Hoofdstuk 7 beschrijft de resultaten van een vergelijkende studie over levenseindebeslissingen in vier NICU's in verschillende landen: twee in de Verenigde Staten (Comer Children's Hospital in Chicago,Illinois en Children's Hospital Wisconsin

in Milwaukee, Wisconsin), één in Canada (McGill University Health Centre met the Royal Victoria en Montreal Children's Hospital) en één in Nederland (Universitair Medisch Centrum Groningen). Wij onderzochten de medische dossiers van alle pasgeborenen met een zwangerschapsduur van >22 weken die overleden op de verloskamers en in de NICU gedurende een periode van twaalf maanden. De overleden pasgeborenen werden geclassificeerd op grond van de beslissing over het levenseinde (het stoppen of beperken van de behandeling) in relatie tot de fysiologische stabiliteit en de neurologische prognose van het kind. De meerderheid van de niet-stabiele patiënten in alle NICU's overleed in de armen van hun ouders nadat de kunstmatige beademing was gestopt. Het besluit om kinderen op grond van sombere prognoses te extuberen werd in 19-35% van de gevallen gemaakt in drie van de vier NICU's en gebeurde nooit in de NICU te Chicago. Het percentage van de patiënten dat overleed tijdens reanimatie varieerde van 4-12% in Wisconsin, Montreal en Groningen en was veel hoger in Chicago (31%). Het percentage van pasgeborenen dat overleed in de verloskamers in Wisconsin, Montreal en Groningen was 16-22%. Er waren geen overlijdens op de verloskamers in Chicago. Wij concludeerden dat het overlijden op verschillende manieren plaatsvond in de NICU's en dat verschillende beslissingen over het levenseinde goed kunnen worden onderscheiden in het classificatiemodel dat wij hebben gebruikt. Het vergelijken van de wijze waarop medische beslissingen over het levenseinde in afdelingen met een verschillende cultuur en werkwijze worden genomen is mogelijk en belangrijk om de uitkomsten tussen afdelingen te kunnen vergelijken binnen die cultuur en daarbuiten.

Hoofdstuk 8 is een samenvatting en bespreking van alle hoofdstukken. Het bevat een reflectie op de resultaten en suggesties voor toekomstig onderzoek.

Dankwoord

Dit proefschrift kwam tot stand door een uitzonderlijke samenloop van omstandigheden. Een eerste belangrijke factor was mijn (toevallige?) samenwerking met Pieter Sauer die zich altijd heeft ingezet voor openheid in beslissingen over het levenseinde van zieke pasgeborenen. Hij ondersteunde mijn plan om verder onderzoek te doen naar het neonatale levenseinde. Een tweede bijzondere omstandigheid was het ontstaan van het 'Gronings Protocol' voor actieve levensbeëindiging bij pasgeborenen. Het protocol werd in 2001 gemaakt door een aantal Groningse artsen (waaronder dr. Ko Begeer, prof. dr. Oebo Brouwer, drs. Annewies Staal, prof. dr. Pieter Sauer en ik) met de bedoeling om een lokaal richtsnoer voor een zeldzame praktijk te zijn. Geen van ons heeft, denk ik, voorzien dat dit protocol de hele wereld over zou gaan en dat het zoveel heftige reacties in sommige landen zou oproepen. Voor een aanzienlijk deel van de internationale faam van het protocol, en van de landelijke ontwikkelingen op levensbeëindiginggebied daarna zijn we dank verschuldigd aan enkele mensen in Rome die op onnavolgbare wijze een beschrijving hebben gegeven van ons werk in het kinderziekenhuis. Een derde belangrijke omstandigheid was de mogelijkheid om open en eerlijk te kunnen communiceren met het Groningse Openbaar Ministerie. Zo hebben we, met hulp van mr. dr. Pieter van Rest, kunnen leren wat de overeenkomsten en verschillen in zienswijzen waren, hetgeen bijdroeg aan het ontwerp van ons onderzoek. Ten slotte was een belangrijke factor dat de leiding van het UMCG ons in vele opzichten heeft gesteund. Eerst op het moment dat wij de wind van voren kregen in 2004 en 2005, en later bij de verdere uitwerking van onze onderzoeksplannen. Daarvoor wil ik hen graag bedanken. De afdeling Ethiek van het ministerie van VWS was gelukkig bereid een deel van het onderzoek te financieren.

De vele reacties op het protocol in combinatie met eigen klinische ervaringen maakten mij nieuwsgierig naar meer kennis van beslissingen over het levenseinde. Het was ook snel duidelijk dat belangrijke gegevens over de medische praktijk nog ontbraken. Met de hulp van een aantal mensen met ervaring in onderzoek naar levenseindeproblematiek was het mogelijk om een gericht onderzoeksplan op te stellen. Dat plan heb ik met veel plezier uitgewerkt en dit boek is daarvan het resultaat.

Veel collega's en vrienden hebben op verschillende manieren bijgedragen aan het tot stand komen van dit proefschrift. Ik wil hen allemaal daarvoor bedanken. Een paar mensen noem ik apart.

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Biography and Publications

Biography

The author of this thesis was born on May 3rd, 1962 in Haarlem, the Netherlands. He finished secondary school (Visser 't Hooft lyceum, Leiden) in 1980 after which he studied law at the University of Utrecht. He received his legal degree in 1987. In 1984 he also started to study medicine at the same university and graduated as a medical doctor in 1991. He worked for one year at the Elisabeth Hospital Amersfoort and then started the residency training program in Pediatrics at the Emma Children's Hospital/AMC in Amsterdam in 1992. He moved to Curaçao (Netherlands Antilles) for a 2-year clinical rotation at the Pediatric Department of the St. Elisabeth Hospital and returned to Amsterdam in 1994. In 1997 he was registered as pediatrician and moved back to Curaçao to work as Chef-de-Clinique at the Pediatric Department of the St. Elisabeth Hospital, on behalf of the Dutch Ministry of Interior and Kingdom Relations between 1997 and 2000. At the end of 2000 he moved to the Beatrix Children's Hospital, University Medical Center Groningen, in the Netherlands. He combined working in general pediatrics and in neonatology intensive care with departmental managerial tasks. He was one of the authors of the controversial 'Groningen Protocol' for deliberate ending of life in severely ill newborns that was published in the New England Journal of Medicine in 2005. At the same time he started working on the studies as described in this thesis. In 2008 he was appointed section head of General Pediatrics at the Beatrix Children's Hospital.

He's a member of the Editorial Advisory Board of the West Indian Medical Journal, University of the West Indies, Jamaica since 2002. He is chairman of the Committee Pediatrician, Ethics and Law (Dutch Pediatric Association), a member of the Review Committee on Late Termination of Pregnancy (Dutch Association of Gynecology and Obstetrics) and a member of the Committee for the Legal and Ethical Aspects of Health Research (CJEA) (Council of Medical Sciences of the Royal Netherlands Academy of Science and Art).

He is also the father of 4 children: Merel, Coen, Coosje and Eva and lives happily together with Gerbrich van der Meulen.

Publications

– Publications and manuscripts reprinted in this thesis

1. Verhagen E, Sauer PJ. The Groningen protocol — euthanasia in severely ill newborns. N Engl J Med 2005;352(10):959-62.
2. Verhagen AA, van der Hoeven MA, van Meerveld RC, Sauer PJ. Physician Medical Decision-making at the End of Life in Newborns: Insight Into Implementation at 2 Dutch Centers. Pediatrics 2007;120(1):e20-8.
3. Verhagen AAE, Dorscheidt JH, Hubben JH, Engels B, Sauer PJ. End-of-life decisions in severely ill newborns in the Dutch NICU's. Provisionally accepted.
4. Verhagen AAE, de Vos AM, Dorscheidt JH, Engels B, Hubben JH, Sauer PJ. Differences of opinion regarding end-of-life decisions in severely ill newborns in the NICU; results of a nationwide study in the Netherlands. Provisionally accepted.

5. Verhagen AAE, Dorscheidt JH, Engels B, Hubben JH, Sauer PJ. Analgesics, sedatives and neuromuscular blockers as part of end-of-life decisions in Dutch NICU's. Provisionally accepted.
6. Verhagen AAE, Janvier A, Leuthner S, Andrews B, Lagatta J, Bos AF, et al. Categorizing neonatal deaths; a cross-cultural study in the USA, Canada and the Netherlands. Submitted.

– Other publications and manuscripts

7. de Vries MC, Verhagen AAE. A case against something that is not the case. The Groningen Protocol and the principle of non-malifecence. Accepted for publication by Am J Bioethics.
8. Busari JO, Verhagen AAE, Muskiet FD, Duits A. Implementation of a competency-based residency curriculum: experiences from a resource-limited environment in the Caribbean. Accepted for publication by Medical Teacher.
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