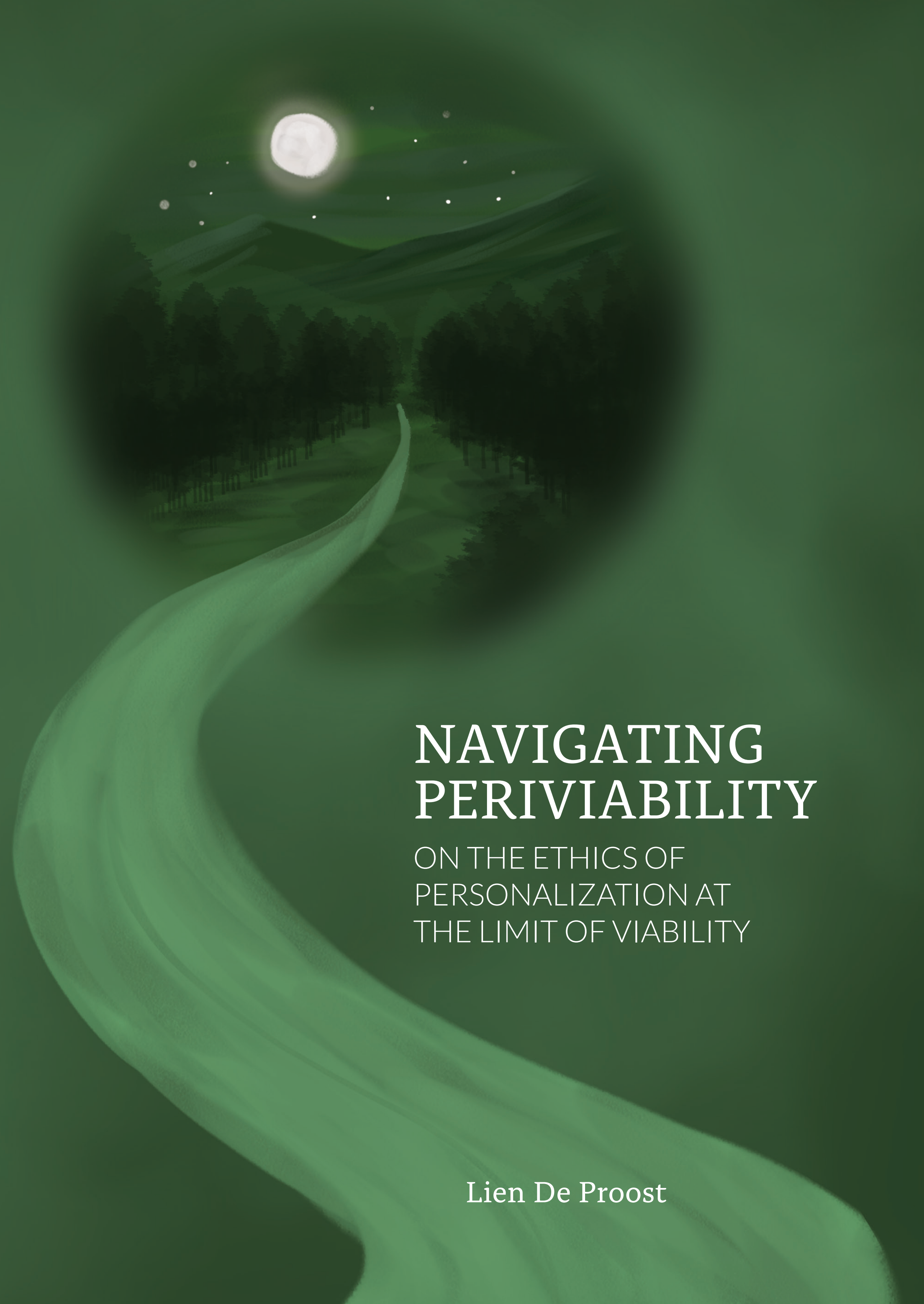

NAVIGATING PERIVIABILITY

ON THE ETHICS OF PERSONALIZATION AT THE LIMIT OF VIABILITY

Lien De Proost

NAVIGATING PERIVIABILITY:

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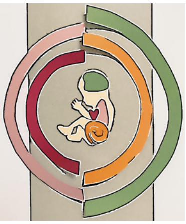

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NAVIGATING PERIVIABILITY:
ON THE ETHICS OF PERSONALIZATION AT THE LIMIT OF VIABILITY

Over de ethiek van personalisering op de grens van levensvatbaarheid

Proefschrift

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

Prof. dr. A.L. Bredenoord

en volgens besluit van het College voor Promoties.

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To the two women who have shaped my life:
my mother, whose wisdom has guided me
and my sister, whose companionship has made every step a little lighter

Table of contents

INTRODUCTION

“Breaking records
from the first second
Been fighting this lonely war
Was it that heavy?
Two pounds of sugar outweighed me
Cause I accepted the unruled game
I won’t be another blank page”

Mieke Verberkt (born at 27 weeks gestational age), in *Unruled game*

Introduction

On the opening page of this dissertation, I feature a verse from a song written by Mieke Verberkt, who was born at just 27 weeks gestational age. The verse captures the essence of the unwavering resilience and fighting spirit that characterizes those who experienced extreme prematurity. Above all, I want to honor everyone impacted by prematurity, both parents, infants, and family members, as well as the dedicated healthcare professionals who provide their care. Their concrete experiences are the basis for the academic explorations in perinatal care that form the heart of this dissertation.

This dissertation

The primary objective of this dissertation is to investigate periviability guidelines that provide guidance for prenatal decision-making and providing care at the limit of viability, with a specific focus on the concept of personalization at the limit of viability. This research project involves close collaboration with three essential stakeholders: adults who were born prematurely, parents who experienced preterm deliveries, and healthcare professionals. The study will address the following specific research questions:

1. Should there be periviability guidelines?
2. What type of guideline should be preferred?
3. How should personalization at the limit of viability be approached?

Answering these research questions, we utilize a variety of research methods: literature review, empirical research, and ethical analysis. However, before delving into the research, it is essential to provide some relevant background information.

Extreme premature birth

Extreme premature birth, as defined by the World Health Organization, refers to infants born before 28 weeks of gestational age (1). This category accounts for approximately one million infants worldwide annually, representing roughly 0,5 percent of all births (2). In the Netherlands in 2021, 611 babies were born between 24 and 28 weeks of gestation (3).[1] Despite its relatively low occurrence, extreme preterm birth remains a significant cause of neonatal morbidity and mortality on a global scale (4).

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[1] If this dissertation discusses a duration of ‘X weeks’, it refers to X weeks gestational age, measured from the first day of the last menstrual period of the pregnant person.

Extreme premature birth has significant implications for infants, parents, and healthcare professionals. Infants born extremely premature often encounter morbidities due to the underdevelopment of their organs (5). In Neonatal Intensive Care Units, prevalent morbidities include respiratory distress syndrome (related to the lungs), intraventricular hemorrhage (related to the brain), necrotizing enterocolitis (related to the intestines), patent ductus arteriosus (related to the heart), and retinopathy of prematurity (related to the eyes) (5). Over the long term, individuals born extremely premature may experience various morbidities, including neurodevelopmental and motor delays, as well as attention deficit hyperactivity disorder (6). Studies also indicate that individuals born extremely preterm may face educational and social disadvantages in adulthood (7,8).

Yet, research on the quality of life among adults born extremely preterm suggests an overall acceptable quality of life (9,10). And a recent study reveals that many individuals report positive attitudes towards their prematurity and even describe feeling stronger as a result (11). While extreme prematurity should be considered a chronic condition (12-14), not all infants or adults born extremely premature experience morbidities, and their severity and manifestation can vary significantly among individuals.

The consequences of extreme preterm birth extend beyond the infants themselves; parents may also experience long-term effects. Experiencing extreme preterm birth can be traumatic for parents, both during their time in the Neonatal Intensive Care Unit and beyond (15,16). Research indicates that parents may develop psychopathological symptoms following their premature infant's hospitalization (17). Feelings of guilt, shame, high levels of stress, mood changes, and anxiety symptoms are commonly reported by parents (18).

Healthcare professionals involved in the care of extremely preterm infants can also experience significant impact. Moral distress is commonly experienced by healthcare professionals when faced with premature infants, and neonatal nurses in particular often face moral distress related to periviable infants (19,20).

Improving care at the limit of viability

In recent years, notable progress in perinatal care has led to improved outcomes for infants born at the limit of viability. These advancements encompass various aspects, including the utilization of pharmacological interventions and changes in care-related practices. Surfactant therapy, for instance, has significantly reduced mortality and respiratory morbidity among extremely preterm infants (21). Kangaroo care has demonstrated positive impacts on maternal attachment, emotional bonding, and physiological stabilization of premature babies (22).

Another area of advancement that has garnered considerable attention is the development of artificial amniotic sac and placenta technology. This innovative technology holds great promise in offering an alternative treatment approach to conventional neonatal care, thereby potentially further enhancing outcomes for infants born at the limit of viability. Artificial placenta technology seeks to replicate the functions of the amniotic sac, amniotic fluid, and placenta, with the aim of maintaining a fetal physiological state. That way, ongoing organ development could be supported, and severe complications often observed in infants born at the limits of viability could be mitigated.

This technology is not a complete substitute for in vivo pregnancy. It still requires embryo implantation and early fetal development, as maternal-fetal interaction entails more than just providing oxygen and nutrients. The intention behind artificial placenta technology is to increase the survival rate of infants born at the limit of viability, reduce complications and severe disabilities, and enhance the quality of life for extremely premature infants. While promising results have been obtained in animal studies, the technology has not yet been tested on humans (23).

Despite these advancements, there still remains a significant degree of uncertainty regarding outcomes following extreme premature birth, and periviability decision-making.

Periviability decision-making

The literature tends to categorize extreme premature births into three distinct categories. The first category includes births for which treatment can be ‘reasonably’ considered beneficial, indicating a favorable prognosis. The second category comprises births for which treatment can be ‘reasonably’ considered medically futile, indicating a poor prognosis. The third category represents a grey zone, where significant prognostic uncertainty exists, allowing for differing opinions on the morally appropriate course of action. In these cases, decisions regarding appropriate treatment must be made during the antenatal period.

For births in the grey zone, Arbour et al. explain that due to the uncertainty surrounding outcomes, reasonable people are allowed to hold differing views on the best course of action (24). For these births, however, a decision must be made. The options typically involve providing intensive care or palliative comfort care. Intensive care may involve invasive and potentially painful procedures such as respiratory support, intubation, medication, and resuscitation, while palliative comfort care focuses on keeping the infant comfortable with pain medication, ensuring a peaceful death.

Decision-making at the limit of viability remains a complex and challenging process, mainly due to the unpredictable nature of extreme preterm birth. It involves multiple levels of consideration: the healthcare system, the healthcare professionals, and the families experiencing extreme premature birth. At the healthcare level, decisions must be made regarding resource allocation: it must be determined how much resources should be allocated to extreme prematurity care in comparison to other patient groups. At the level of healthcare professionals, there is a need to determine *which* extreme premature infants are suitable for the initiation of intensive care based on statistical or population averages of potential benefit versus futility. And at the level of families experiencing extreme preterm birth, decisions must be made on an individual basis, considering whether treatment is in the best interest of the infant, taking into account parental values related to quality of life, suffering, and so on.

Periviability decisions are emotionally charged and ethically complex. Additionally, sociocultural values may also influence these decision-making processes. This dissertation primarily focuses on addressing the decision-making processes at the levels of parents and healthcare professionals.

International heterogeneity

Decision-making at the limit of viability exhibits significant variation across countries, encompassing differences in the lower treatment limit, the zone of parental discretion, and the type of periviability guideline employed.

Firstly, countries differ in their lower treatment limits. For instance, Sweden and Japan offer intensive care to infants born at 22 weeks gestational age, while Spain and Belgium provide such care for infants born at 23 weeks (25-28). In the Netherlands, intensive care is offered to infants born after 24 weeks, while Nigeria extends this limit to 28 weeks (29,30). The availability of resources and societal and cultural values contribute to shaping these lower treatment limits (31,32). The youngest extreme premature infant to survive internationally was born at approximately 21 weeks and 5 days estimated gestational age (33).

Secondly, the zone of parental discretion varies among countries. Some countries adopt an active approach, uniformly providing intensive care to all infants born beyond a specific gestational age (34). In contrast, others follow a shared decision-making approach, where decisions at the limit of viability involve both parents and healthcare professionals (29). Prenatal counseling is commonly offered to parents to facilitate decision-making – based on prognostic information, and parental values and preferences (36-38).

Thirdly, different types of guidelines for perinatal management of extreme prematurity are utilized worldwide. Some guidelines solely rely on gestational age, suggesting the initiation of intensive care treatment for infants born later than a certain number of weeks. Palliative care is recommended for infants born earlier than this threshold. The Dutch guideline exemplifies this approach (29). Gestational age-based-plus guidelines incorporate additional prognostic factors such as birth weight and fetal sex to fine-tune an infant's prognosis, allowing for a less rigid cut-off point for offering intensive care. The British guideline is an illustration of this type (39). Prognosis-based guidelines, which calculate an infant's probability of favorable outcomes based on multiple prognostic factors, exist theoretically but are not currently employed by any country. Challenges in defining clear-cut points for treatment and individual prognoses have hindered their implementation (40-42).

In some cases, countries or medical centers lack an official guideline, and treatment decisions are made on a case-by-case basis, considering various factors and discussions among healthcare professionals and parents.

Extreme prematurity in the Netherlands

Extreme prematurity in the Netherlands is governed by a guideline established in 2010, which relies solely on gestational age as the determining factor (29). According to this guideline, palliative care is offered to infants born before 24 weeks of gestational age. For infants born between 24 and 26 weeks, a grey zone exists where parental discretion plays a role in decision-making. Intensive care is provided for infants born after 26 weeks. As a result, no infants born earlier than 23 weeks of gestational age have survived in the Netherlands. Recent Dutch research estimates a survival rate of around 50 percent for infants born at 24 weeks, with varying degrees of complications among survivors (43).

Internationally, the Dutch guideline can be considered an outlier due to its high gestational age threshold for active care initiation, the grey zone based on parental discretion, and the limited consideration of additional prognostic factors beyond gestational age (32). In 2020, a process was initiated to revise the guideline, which highlighted the complex ethical and practical considerations involved in caring for infants at the limit of viability. The revision process involves discussions on topics such as medical futility, prognostic predictions, and the assessment of quality of life.

The revision faces challenges, including the lack of national outcome data for infants born earlier than 24 weeks and the heterogeneity of care practices across countries. Resource availability, including healthcare professionals' capacity to provide intensive care, is also a concern. Another consideration is the potential impact of the termination of pregnancy policy in the Netherlands, which sets the legal abortion limit at 24 weeks gestational age based on the 'limit of viability' concept (44-47). Lowering the treatment threshold to align with international practices, potentially from 24 to 23 weeks, could have implications for the abortion framework, requiring a corresponding reduction in the abortion threshold (48). Consequently, attention is drawn to the Dutch law on abortion, particularly concerning the use of viability as a basis for the law.

The revision of the Dutch guideline could align it more closely with international guidelines, which often incorporate additional prognostic factors beyond gestational age, emphasizing a more personalized approach. This emphasis on personalization is also reflected in other literature on periviable births (49,50). However, there is currently a lack of conceptual literature and empirical research on this topic.

While research has explored the viewpoints of healthcare professionals and parents on topics such as resuscitation, counseling, decisional regret, coping mechanisms, and care practices in the Neonatal Intensive Care Unit, there is limited knowledge about their perspectives specifically regarding different types of guidelines and personalization (50-54). Moreover, there is a lack of research on the perspectives of adults who were born prematurely, and their experiences and perspectives on guidelines, treatment limits, and prognostic factors are notably absent from the existing literature. Although studies have examined the health-related quality of life of 'adult preemies', the understanding of their perspectives on guidelines and decision-making in the context of extreme prematurity remains limited (11,55-59). This dissertation aims to fill this gap.

Aims

This dissertation aims to provide answers to three research questions: whether a periviability guideline is necessary, what is the preferred type of guideline, and how personalization at the limit of viability should be approached. By addressing these questions, the dissertation will ultimately offer practical recommendations in four key areas: periviability guidelines, personalization at the limit of viability, policy on termination of pregnancy, and the further development and implementation of artificial amniotic sac and placenta technology.

Methods

To achieve these objectives, a combination of research methods is employed. A scoping review is conducted to comprehensively explore the existing literature on the topic. Both quantitative and qualitative research approaches are used to investigate the perspectives of different stakeholders. A survey study is conducted with healthcare professionals to gather their insights, while a focus group study involves adults who were born prematurely. Additionally, individual interviews are conducted with parents.[2] In addition to empirical research, ethical analysis is conducted, drawing upon the existing literature and data gathered from our own empirical studies.

Outline

This dissertation is structured into three parts to comprehensively explore the research questions.

Part one focuses on providing background information and context. It consists of two chapters that lay the necessary foundation for understanding the research questions and gaining initial insights into the topic. Chapter 1 delves into the history of Dutch periviability guidelines, offering an overview of the current Dutch guideline and discussing the sociocultural context in the Netherlands. It also reflects upon the position of the Netherlands in international discussions on treatment limits

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[2] The research involving adults born prematurely (TINY-1) and experienced parents (TINY-2) is part of the TINY study, which stands for Towards INdividualized Care for the Youngest. Currently, the TINY-3 study is also initiated, exploring the perspectives of stakeholders on artificial placenta technology as an alternative for conventional neonatal intensive care.

and perinatal treatment guidelines. Chapter 2 comprises a scoping review of the existing body of literature on prenatal counseling for extreme prematurity. The review includes an analysis of forty-six publications, aiming to synthesize the knowledge and identify gaps in the current body of research.

Part two, which consists of four chapters, presents empirical research conducted with various stakeholders to address the research questions in more detail. Chapter 3 reports the findings from individual interviews conducted with experienced parents, providing valuable insights into their perspectives and experiences related to extreme prematurity and decision-making at the limit of viability. A total of nineteen interviews were conducted. In Chapter 4, the focus shifts to the perspectives of adults who were born prematurely. The chapter presents the findings from four focus group interviews, exploring the experiences and viewpoints of these individuals. A total of twenty-three adults born prematurely participated in this study. Chapter 5 presents the results of a survey study conducted with 769 healthcare professionals from various disciplines. This quantitative research investigates the preferences of healthcare professionals for different types of guidelines at the limit of viability.

Part three of the dissertation is dedicated to ethical reflection, comprising four chapters. Chapter 6 offers a reflection on the current Dutch guideline, which is solely based on gestational age. Chapter 7 conducts an ethical reflection on a newly proposed decision-making approach for births at the limit of viability: postponed withholding. This approach was presented by Syltern et al. It involves initiating intensive care at birth by default and postponing parental decision-making about the care approach for a week. The approach aims to empower parents, improve decision-making by balancing parental bias towards ‘saving’ their infant, and providing parents with more time and space to make the decision. In Chapter 7, we briefly assess this novel approach. In Chapter 8, the concept of viability takes center stage. This chapter critically assesses the ethical legitimacy of viability as the abortion threshold in the Netherlands, raising important considerations for potential changes in the legal framework for abortion. Finally, Chapter 9 utilizes the empirical research findings and perspectives gathered throughout the dissertation to derive normative conclusions about personalization at the limit of viability. It explores the multifaceted concept of personalization and offers a breakdown of different types of personalization at the limit of viability, including personalized guidelines, counseling, and care. It concludes that personalization should be maximized in the case of counseling and care, while a balance is needed for personalized guidelines.

The dissertation ends with a general discussion that summarizes and analyzes the main findings. It also provides practical recommendations in four key areas: periviability guidelines, personalization, policy on termination of pregnancy, and artificial placenta technology.

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Table 1 Premature birth, according to the World Health Organization

Extremely premature birth	Less than 28 weeks gestational age
Very premature birth	28 to 32 weeks gestational age
Moderate to late premature birth	32 to 37 weeks gestational age

Table 2 Decision-making at the limit of viability

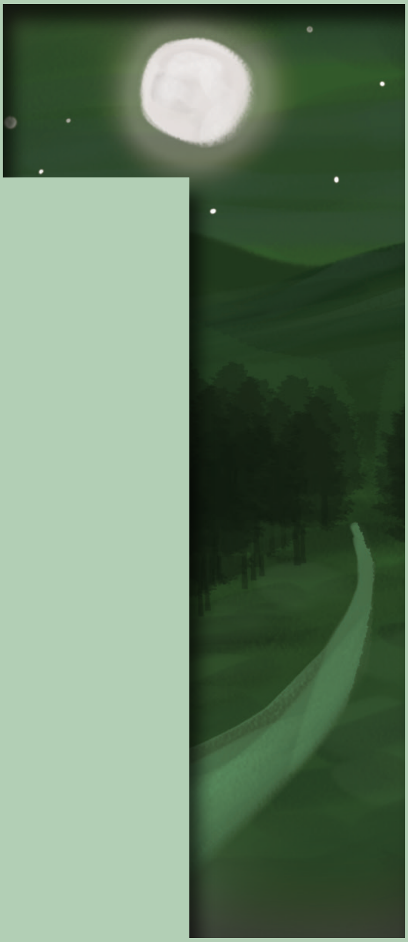
Healthcare	Extreme premature infants versus other patient groups
Healthcare professionals	Extreme premature infants versus other extreme premature infants – the *statistical* infant
Families and healthcare professionals	Intensive care at birth versus palliative comfort care – the *individual* infant

Table 3 Types of periviability guidelines

No guideline	No official guideline, decisions are made on a case-by-case basis
Gestational age-based guideline	Decisions are based solely upon gestational age
Gestational age-based-plus guideline	Decisions are based upon gestational age *and* other prognostic factors
Prognosis-based guideline	Decisions are based upon a calculation of the influence of multiple prognostic factors

PART ONE

BACKGROUND


1

THE EDGE OF PERINATAL VIABILITY: UNDERSTANDING THE DUTCH POSITION

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Abstract

The current Dutch guideline on care at the edge of perinatal viability advises to consider initiation of active care to infants born from 24 weeks of gestational age on. This, only after extensive counseling of and shared decision-making with the parents of the yet unborn infant. Compared to most other European guidelines on this matter, the Dutch guideline may be thought to stand out for its relatively high age threshold of initiating active care, its gray zone spanning weeks 24 and 25 in which active management is determined by parental discretion, and a slight reluctance to provide active care in case of extreme prematurity. In this article, we explore the Dutch position more thoroughly. First, we briefly look at the previous and current Dutch guidelines. Second, we position them within the Dutch socio-cultural context. We focus on the Dutch prioritization of individual freedom, the abortion law and the perinatal threshold of viability, and a culturally embedded aversion of suffering. Lastly, we explore two possible adaptations of the Dutch guideline; i.e., to only lower the age threshold to consider the initiation of active care, or to change the type of guideline.

Introduction

Guidelines on care at the edge of perinatal viability differ between countries. Both in terms of such guidelines and the related attitudes of healthcare professionals, the Netherlands can be considered as an outlier. Our country has a relatively high threshold of providing active care (>24 weeks of gestation), a gray zone between 24 and 26 weeks of gestational age (GA), the initiation of active management in the gray zone determined by parental discretion, and a slight reluctance to initiate active care for extremely premature infants (1-4). This Dutch position merits reflection, especially in view of the current revision of the guideline on the matter. Our article proceeds as follows. First, we provide a concise overview of the Dutch guidelines. Then, we situate the guidelines within the context of Dutch socio-cultural norms and values. Third, we will use the outcomes of this analysis to speculate on possible emendations of the current guideline.

The history of Dutch guidelines on treatment at the edge of viability

Until 2005, a Dutch consensus guideline recommended not to provide active care to extremely premature infants born before $26^{0/7}$ weeks of GA (5). A revised guideline endorsed by the Netherlands Association of Pediatrics and the Netherlands Association of Obstetrics and Gynecology was published in 2005. This guideline recommended the provision of active care to infants born at $25^{0/7}$ weeks GA and older (6). Both guidelines were strictly GA-based and left room for parental discretion: a management plan was always to be made by the healthcare team together with the parents. In the following years, it was found that the care approach for extremely premature infants was not uniform among medical centers in the Netherlands (7). Moreover, compared to other European countries, perinatal mortality for extremely premature infants in the Netherlands was found to be high (8). In response to these findings, in 2008 the Minister of Health, Welfare and Sport in the Netherlands asked the Netherlands Organization for Scientific Research - Medical Sciences to develop a new guideline on the postnatal management of extremely premature infants. The objective was to harmonize treatment and care at the edge of viability in all Dutch perinatal and neonatal centers (7).

This 'new' guideline, published in 2010 under the title Perinataal beleid bij extreme vroeggeboorte (Perinatal policy for extreme prematurity) is, again, strictly GA-based (7). The guideline accounts for spontaneous premature births only; thus, does not account for iatrogenic premature births. One of the recommendations states that, after prenatal counseling, providing active care is an option for infants from $24^{0/7}$ weeks GA onwards, unless prognostic factors clearly suggest otherwise. Importantly, the period spanning the 24th and 25th weeks GA is seen as a gray zone characterized by prognostic uncertainty. The management of infants born in this gray zone should be decided on the basis of a consensus between the healthcare professionals and the parents, provided the latter have been extensively counseled and the principles of shared decision-making have been adhered to (9). It should be noted that other countries more often identify this gray zone as a period somewhere between 22 and 24 weeks GA (10). Another guideline recommendation is that extremely premature infants from $23^{4/7}$ weeks GA should be transferred to a specialized perinatology center – where the best possible care and parental counseling can be provided. Antenatal corticosteroids are recommended to be administered from a GA of $23^{5/7}$ weeks. Lastly, a cesarean is to be considered from $24^{0/7}$ weeks GA, balancing both maternal and fetal risks as the consequence for future pregnancies (Table 1).

Unfortunately, since 2010 only few studies on Dutch management of extreme prematurity have been conducted that provide insights in the effects of the new recommendations. In 2017, the first follow-up results after implementation of the guideline were published (11). The results concern extremely premature infants at the corrected age of 2 years: of those born at 24 weeks, 20% had mild disabilities, 20% had more severe disabilities, and 60% had no disabilities at all. In comparison, 71% of the infants born at 25 weeks had no disabilities at all. Another study shows that in 2011, infants born at 24 weeks had a 43% chance to survive, while infants born at 25 weeks had a 61% chance to survive. Of those born at 24 weeks, 79% had short-term morbidities such as bronchopulmonary dysplasia and retinopathy of prematurity, while this was the case for 71% of the infants born at 25 weeks (12). In 2016, Geurtzen et al. reported that the new recommendations succeeded relatively well to harmonize physician preferences concerning the lower threshold of providing active care. However, preferences concerning the upper threshold for offering comfort care still greatly diverge, as well as practices such as offering a cesarean section and providing cardiopulmonary resuscitation (13). Finally, a recent study by van Beek et al. shows that the implementation of the 2010 guideline “resulted in increased neonatal intensive care unit admission rates and postnatal survival” (14). Although these results are useful to reflect on the guideline, more follow-up research on longer term outcomes is required.

The Dutch context

Multidisciplinary and evidence-based guidelines for centralized care
To better understand the Dutch guidelines, it is important to look at how they came about. Three factors are key. First, the aim was to have evidence-based guidelines that relied on Dutch national data. Second, the Dutch guidelines were meant to be multidisciplinarily constituted national consensus guidelines. Third, the guidelines were designed to reflect a national and not a local perspective: the approach to care was centralized. The aim was to ensure the streamlined provision of quality perinatal care in the nine level III and level IV centers in different regions in the Netherlands. As both the complex obstetric and the neonatal intensive care are concentrated in these specialized centers, care is rather well organized and coordinated.

Culture of freedom and responsibility
Historically, Dutch culture has been marked by a prioritization of individual freedom and responsibility (15). Currently, the Netherlands is known for its great variety of liberal policies concerning different aspects of life; for example, the use of soft drugs is tolerated, and prostitution is legalized and regulated (16). The Dutch also take a liberal stance in most of the widely debated bioethical dilemmas. In the Netherlands, euthanasia is legalized since 2001 for people who unbearably suffer mentally or physically (17). Euthanasia is also legalized for people who suffer from dementia, and, since 2004, for severely ill newborns (the socalled Groningen Protocol) (18, 19). Currently under debate is the legalization of euthanasia for people who are “tired of living,” people who feel their “life is completed,” and children from 1 to 12 years old who suffer unbearably (20–22). Furthermore, the Netherlands was one of the first countries in the world to legalize abortion in 1984. Currently, abortion is legalized up to 24 weeks of GA (23).

The bioethical policies discussed above might seem to contrast with the Dutch guideline on care at the edge of viability. Compared to countries such as Sweden, Japan, or Canada, which provide active care to babies born at 22 weeks (24–26), the Netherlands can be described as a late adopter: it is advised to only provide active care to infants born from 24 weeks on, after extensive counseling and a process of shared decision-making. This apparent discrepancy might be explained by the Dutch context.

Aversion to suffering and importance of quality of life
Surprisingly, the Dutch bioethical policies have a common goal that might explain, rather than conflict with, the caution of the Dutch guideline concerning treatment of extremely premature newborns. Consider the following three Dutch policies: (a) abortion is legalized up to a GA of 24 weeks (23) (b) active care is only provided to extremely premature infants born from 24 weeks on since the prognosis and or expected quality of life is not deemed hopeful below this threshold (7) (c) euthanasia is legalized for people who unbearably suffer physically or mentally and for severely ill newborns with a prognosis of severe future suffering (17, 19). It could be hypothesized that these policies have a similar goal: assuring that people do not have to suffer or do not have to live with a poor quality of life. We do not claim that these policies have been enacted for these reasons, but they do factually imply a decrease in people who are suffering or (deemed to) have a poor quality of life. Although a country wanting to avoid suffering might not in itself be remarkable, trying to structurally regulate it by laws and guidelines is.

It is instructive to look at the three policies against the background of the Dutch valuation of freedom and responsibility. The options to abort, euthanize, or to offer comfort care to a child with a poor or infaust prognosis are examples of ways in which persons can exercise their freedom over their life or the life of their offspring. The corollary of such freedom is an emphasis on the responsibility to exercise it in the way one sees fit. Dutch bioethical policies thus provide the possibility to minimize suffering as well as the possibility to exercise one's freedom. Freedom, responsibility, and the avoidance and alleviation of suffering might, in that sense, be interrelated.

The future of the Dutch guideline

As the 2010 guideline is currently under revision, it is interesting to speculate on possible changes. Let us suppose, for the sake of argument, that the guideline will change. It seems that there are two main ways that it could. The first is to continue with a strictly GA-based guideline, but with another threshold to consider the initiation of active care. This change would be in line with those of previous revisions and would better align the Dutch guideline with those in other countries. The second way is to change the type of guideline. It could become a more personalized or prognosis-based guideline, advising to take into account other factors than solely GA. But first we discuss two general challenges for revising the Dutch guideline.

The threshold of viability

A first challenge relates to the threshold of viability. Consider again the Dutch abortion policy. The Dutch abortion law is based upon the threshold of viability. In turn, the meaning of this threshold is determined in the Dutch criminal law: Article 82a states that, "Taking the life of a person or of an infant at birth or shortly afterwards shall include: the killing of a fetus which might reasonably be expected to have the potential to survive outside the mother's body" (27). Once the fetus is, in that sense, viable, abortion is illegal, and the acting physician is punishable for murder. Obviously, the guideline on care for extremely premature infants also interrelates with the threshold of viability. Importantly, it can be asked whether lowering the threshold of viability in the guideline for extreme prematurity would demand a similar change in the threshold for legal abortion. This question merits more reflection, as it seems illogical for a country to apply a threshold of viability of 24 weeks in Law X, and at the same time claim in Guideline Y that babies from 23 weeks can survive. One way to avoid such inconsistency would be to find another basis for abortion law than the threshold of viability. Some European countries do not base abortion law on a threshold of viability but refer to a certain GA: in Belgium and Germany, for example, abortion is legalized up to 12 weeks GA (28, 29), in Sweden abortion is legalized up to 18 weeks GA (30). It could be questioned whether changing the abortion law would find support: the Dutch have mostly shown great support for their abortion policy, and the support even seems to have increased over time among the younger generation (31).

Generally, a revision of the guideline on care at the edge of viability must include a reflection on the concept of a threshold of viability. The biological threshold of viability is as yet unknown. One could wonder how much technological interference is 'allowed' to still label a certain GA as threshold of viability. In practice, a set GA is actually always an estimated (e-)GA (32). Moreover, because of differences between countries in availability of technological and medical support, thresholds of viability may differ from country to country (7, 24). Of note, countries which have more resources and better infrastructure often also seem to have a lower threshold of viability (33). This raises questions of fairness and equity. All in all, the concept requires reflection. A threshold of viability is a difficult concept to base a law or guideline on. More research on this is urgently required.

Scarcity of Dutch national data

Another challenge for revising the 2010 guidelines is the scarcity of Dutch national data about survival, morbidity, and long-term outcomes of extremely premature infants. Except for the current EPI-DAF study, whose results are yet unpublished, Dutch long-term outcomes of extreme prematurity are pending (34) However, even if there would be enough national data, the self-fulfilling prophecy of a strict GA-based guideline implies that in the Netherlands, every infant born at 22 or 23 weeks will not have received active care and thus will not have survived (35). Of course, as is seen in other countries, lowering the threshold of viability is a learning curve: it demands time to get used to provide active care to such young infants: results will become better and better in time (36). Moreover, outcome data will always have to be interpreted against a national context and will always be value-loaded: the meaning of concepts such as 'surviving,' 'quality of life,' 'suffering,' and 'disability' might differ per country. In the Dutch context, aversion to suffering might color such concepts. Even with enough resources, a culture that structurally avoids suffering might refuse to utilize all technological possibilities: 'It is not because we can, that we have to'. Moreover, since the same outcomes can have different meanings in different countries, it is hard to rely on international research to construct national guidelines (37). Taking the difficulties associated with a threshold of viability and the scarcity of national data into account, let us briefly consider the two most plausible options for changing the 2010 guideline.

Lowering the threshold in a strictly GA-based guideline

The first option to change the guideline would be lowering the threshold to consider the initiation of active care to 23 or even 22 weeks GA. This would better align the Dutch guidelines with guidelines in other countries and be a similar revision to the ones in 2005 and 2010. Moreover, opting once more for a strictly GA-based guideline would make it easy to use because of its clarity and the limited room for interpretation. The problem is that changing the threshold alone can be considered an outdated measure. There is a lot of current literature stating that GA is not sufficient to come to a prognosis, and that GA is always an estimated (e-)GA (32, 38, 39). Besides, by lowering the threshold to provide active care, the ethical challenges of a strictly GA-based guideline will merely be shifted, not solved.

Changing the type of the guideline

A second option is to change the type of guideline. The decision to provide active care could be broadened to other significant prognostic factors: birth weight, the administration of antenatal corticosteroids, sex, fetal anomalies, and so on. Currently, a trend toward personalizing care at the limits of viability is becoming visible: variation in parents' values and preferences is increasing, and so does the need for a 'customization' in care (9, 40). Nevertheless, this option would imply a care approach that is less uniform. This is a downside, given that the main objective of the previous guideline was uniformity. Furthermore, the literature does not provide clear answers yet on how to actually 'personalize' in clinical practice around the threshold of viability.

Also, evidence on results of and attitudes about these sorts of guidelines is missing. An example of a more personalized type of guideline is that from the United Kingdom, published in 2019 (41). The UK guideline states that neonatal decisions should be based on all relevant prognostic factors and "the best available evidence about the prognosis for the individual baby." Results concerning the implementation and results of this guideline are not yet available. Nonetheless, opting for a personalized approach cannot avoid the challenges of the threshold of viability as mentioned above. Personalization means that some infants born at 22 weeks will receive active care, and some infants born at 26 weeks will not. If the infants born at 22 weeks survive, this raises once again the question of lowering the threshold of viability.

A guideline on care at the edge of viability must suit the Dutch cultural context, which will in turn increase support from all the stakeholders. Sufficient societal support for change is important as well. It is not just the attitudes of the public and healthcare professionals that are significant. Change should also be feasible in view of the national economic situation, the healthcare system, and the infrastructure of the nine specialized level III and level IV centers. Although one could also argue the opposite: a new guideline might imply a need for more resources, better infrastructure and or more specialized education for healthcare professionals to counsel parents according to those new guidelines. Moreover, mind that not only resources are needed to enable good quality care in the neonatal period but also care that extends into childhood and beyond. Whatever the result of the revision will be, the process should ideally include reflection on the threshold of viability, national interpretation of data, Dutch culture, the societal support base for change, and the availability of resources, infrastructure, and education.

Conclusion

Some concluding remarks are in order. First, in all its rather exceptional positions in complex bioethical dilemmas, the Netherlands seems to stay true to its own socio-cultural context. The importance of freedom and the wish to structurally avoid suffering coincide in most of its laws and guidelines. Second, the Dutch bioethical landscape stands in need of reflection on the threshold of viability: the interrelation of the abortion law and the guideline for extreme prematurity comes with serious challenges in this regard. Third, a change in the Dutch guideline concerning care at the edge of viability is likely to go one of two ways. In both ways, the new guideline would change the threshold to provide active care, either strictly GA-based or it would opt for a more personalized, prognosis-based approach. Both ways are challenging and require serious reflection.

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Table 1 GA thresholds in recommendations in Dutch guidelines

	Intra-uterine referral	Antenatal steroids	C-section	Resuscitation
<2005	$\geq 26^{0/7}$	$\geq 26^{0/7}$	$\geq 26^{0/7}$	$\geq 26^{0/7}$
2005	$\geq 25^{0/7*}$	$\geq 25^{0/7*}$	$\geq 25^{0/7}$	$\geq 25^{0/7}$
Gray area between 24$^{0/7}$ and 26$^{6/7}$: consult a tertiary center				
2010	$\geq 23^{4/7}$	$\geq 23^{5/7}$	$\geq 24^{0/7}$	$\geq 24^{0/7}$


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PRENATAL COUNSELING FOR EXTREME PREMATURITY AT THE LIMIT OF VIABILITY:

A SCOPING REVIEW

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Abstract

Objectives: To explore, based on the existing body of literature, main characteristics of prenatal counseling for parents at risk for extreme preterm birth.

Methods: A scoping review was conducted searching Embase, Medline, Web of Science, Cochrane, CINAHL, and Google Scholar.

Results: 46 articles were included. 27 of them were published between 2017 and 2021. More than half of them were conducted in the United States of America. Many different study designs were represented. The following characteristics were identified: personalization, parent-physician relationships, shared decision-making, physician bias, emotions, anxiety, psychosocial factors, parental values, religion, spirituality, hope, quality of life, and uncertainty.

Conclusions: Parental values are mentioned in 37 of the included articles. Besides this, uncertainty, shared decision-making, and emotions are most frequently mentioned in the literature. However, reflecting on the interrelation between all characteristics leads us to conclude that personalization is the most notable trend in prenatal counseling practices. More and more, it is valued to adjust the counseling to the parent(s).

Practice implications: This scoping review emphasizes again the complexity of prenatal counseling at the limit of viability. It offers an exploration of how it is currently approached, and reflects on how future research can contribute to optimizing it.

Introduction

Parents at risk for delivering an extremely premature infant receive prenatal counseling. Prenatal counseling is of major importance for the parent(s), especially when the infant is born in the so-called ‘gray zone’, that is, at the limit of viability. When infants are born at the limit of viability, only a proportion of them survives; some without disabilities, others with serious long-term disabilities (1-3). The gray zone is primarily characterized by prognostic uncertainty: no treatment option prevails based on what is known about the prognosis of the infant. The delineation of the gray zone, however, differs between countries going from – for example –22 and 23 weeks of gestational age (GA) in Sweden to 24 and 25 weeks of GA in the Netherlands (4-6).

A major goal of prenatal counseling for extreme prematurity in the gray zone is to facilitate decision-making (7,8). A decision has to be made between an active care approach and a palliative comfort care approach. When parents receive counseling for extreme prematurity beyond this gray zone, the goal of the counseling is no longer decision-making (8). Since the main goal of prenatal counseling changes beyond the gray zone, this article will focus solely on counseling for extreme prematurity in the gray zone, that is, at the limit of viability.

Overall, prenatal counseling practices are heterogenous, varying per country, medical center and physician. For example, heterogeneity has been found among trainees in regards to their use of guidelines and documentation, their education, and their provision of written material to families (9). System-based hospital variation in prenatal counseling practices has also been found (10). Without disregarding such variability, we aimed to identify main characteristics of prenatal counseling for extreme prematurity at the limit of viability that can be found in the existing body of literature on this topic.

Method

To achieve our goal, we opted for the scoping review method. Scoping reviews are considered “an ideal tool to determine the scope or coverage of a body of literature on a given topic and give clear indication of the volume of literature and studies available as well as an overview … of its focus” (11). Moreover, this relatively new method is the preferred option when the research aim is to identify main characteristics of a certain topic based on an existing body of literature (11,12). This scoping review was conducted in accordance with the scoping methodology proposed by Arksey and O'Malley in 2005 (13).

Identifying the research question

We were interested in identifying characteristics of prenatal counseling for parents at risk for preterm birth at the limit of viability. We aimed to find characteristics related to the process as well as the content of prenatal counseling. Also, we wanted to study two perspectives that are of importance in this counseling consultation: that of the parents and that of the physicians. This scoping review answers the following research question: 'What are – based upon the existing body of literature – main characteristics of prenatal counseling for extreme prematurity at the limit of viability?'

Identifying relevant studies

We systematically searched Embase, Medline, Web of Science, Cochrane, CINAHL, and Google Scholar to find relevant studies (updated until February 2021). No filter was used on date range. Only English articles were searched. Since the search string was built for a scoping review, it was construed as broadly as possible so as not to miss any relevant literature. The electronic search strategies can be found in Table 1. Additionally, we searched the reference lists of the sources that were included after full-text screening.

Study selection

Articles were included if (a) the topic was the prenatal counseling consultation for extreme prematurity at the limit of viability and (b) the perspective was either that of parents or physicians, or the study participants were either parents or physicians. Articles were excluded if they were (a) official policy statements, clinical reports or guidelines, (b) about the development of official policy statements, clinical reports or guidelines, (c) focused solely on the education or training of physicians to provide prenatal counseling.

Titles and abstracts of 1876 articles were screened by two reviewers (LDP, EJTV) that selected the articles independently for assessment against the inclusion criteria. The two researchers screened 143 articles full text and excluded 79 of them for further analysis. A screening of the reference lists of the 64 included articles yielded 6 more relevant articles. 70 articles were eventually included, of which 2 were systematic reviews. In the 2 systematic reviews, 24 articles were in total included. These 24 articles were screened full text but decided to be excluded from this scoping review. This decision was made because (a) no new substantive results were found in the included articles, (b) several of the articles were duplicates – they were included in both systematic reviews,(c) both systematic reviews had closely related results, and (d) the systematic reviews were judged to be of sufficient quality. Therefore, it was opted to only include the 2 systematic reviews and not the 24 individual articles. For the sake of completeness, however, the study characteristics of the included studies in both systematic reviews can be found in Table 3. This Table can be found in the online supplemental material.

Ultimately, 46 articles were included in this scoping review. Disagreements that arose between the reviewers at each stage of the selection process were resolved through discussion until agreement was reached. If necessary, disagreements were also mediated by a third reviewer (RG). The results of the search and the study inclusion process were reported in full and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Review (PRISMA-ScR) diagram (14). A flow diagram of the screening process can be found in Figure 1.

Charting the data

According to the methodological framework of Arksey and O'Malley, charting the data and collating the results are iterative and narrative processes: "A 'narrative review' or 'descriptive analytical' method is used to extract contextual or process oriented information from each study" (13). A scoping review protocol was designed prior to data extraction. An initial coding strategy and coding scheme were also developed. Throughout the scoping review process, the initial coding scheme was repeatedly discussed and adjusted by the reviewers. Data were charted from the included studies using a data extraction tool developed by the reviewers. The data extraction tool was made in Excel. The tool included data about the authors, the year of publication, the journal, the study design, the country in which the study was conducted or the country in which the authors of the article are based, the objective of the study, and the result or conclusion of the study.

Collating, summarizing and reporting the results

Two researchers (LDP, EJTV) then analyzed the included studies for findings relevant to the research question of this scoping revie w. In a first round of full text analysis, characteristics of prenatal counseling were identified and coded. In a second round, the studies were analyzed and coded again in reference to the characteristics that were identified in the first round. The characteristics that were mentioned most frequently in the included body of literature are discussed in the result section of this scoping review.

Results

Characteristics of the included body of literature

The included studies and their characteristics can be found in Table 2. 46 articles were included in this scoping review. The included body of literature has been published between 1998 and February 2021. Only 7 of the included articles were published before 2010, 27 articles were published between 2017 and 2021. More than half of the studies was conducted in the United States of America (n=29), of which one was conducted in Australia and the USA. The remaining studies were conducted in 4 countries: Canada (n=10), the Netherlands (n=5), Italy (n=1), and Dubai (n=1). The included studies are questionnaire studies (n=14), interview studies (n=8), literature studies or reviews (n=7), systematic reviews (n=2), retrospective reviews (n=2), commentaries, viewpoints or letters (n=7), randomized controlled trials (n=2), simulation studies (n=2), conference (36) abstracts (n=1) and editorials (n=1).

Characteristics of prenatal counseling for extreme prematurity

The following characteristics of prenatal counseling for extreme prematurity at the limit of viability were identified: personalization, parent-physician relationships, shared decision-making (SDM), physician bias, emotions, anxiety, psychosocial factors, parental values, religion, spirituality, hope, quality of life (QoL), and uncertainty. It seems that most of the characteristics cannot be said to mainly relate to the content or the process of prenatal counseling; most of them are related to both. Uncertainty, for example, seems to be a topic in prenatal counseling but at the same time influences the process of the counseling. Furthermore, most of the identified characteristics are interrelated. For example, adjusting the counseling information to parental values and discussing ideas about quality of life are aspects of personalized prenatal counseling, and taking into account the parents' religion and/or spirituality might in fact be part of taking into account their values.

It becomes clear from the result section that there is thematic overlap between the characteristics. Since our aim is to gain a thorough understanding of prenatal counseling practices, we first discuss the characteristics individually – by also providing concrete examples or quotes from the included studies. In the discussion section then, we focus on the bigger picture; the interrelation between the characteristics. For an overview of the number of included articles than mention the identified characteristics, see Table 4.

Personalization

In the past decade, personalizing prenatal counseling seems to have become increasingly important. Two articles written before 2010 refer to personalizing certain aspects of prenatal counseling, namely, the prognosis and treatment options, and the general principles of prenatal counseling (15,16). After 2010, 22 of the included articles mention personalization or individualization. The literature shows that personalization can pertain to different aspects of prenatal counseling, such as medical, parental, and informational aspects as well as aspects related to decision-making (7). Geurtzen et al. discuss personalization in relation to the preferred input of parents in decision making, the preferred amount of information shared in prenatal counseling, and the preferred use of statistics and/ or outcome data (7). In an article written by parents of extremely premature infants, one of the ten recommendations for physicians is the following: “Some parents want statistics, others want the general picture. Some parents want to make important decisions on their own, while others want recommendations. Please listen to us individually” (17). In this article, it is also advised to “have a personalized approach” (17).

Two of the included articles offer recommendations to enable personalization in practice (18,19). Haward et al., for example, advise to personalize by, among others, considering factors beyond GA, acknowledging emotions as integral in deliberations and adjust the ‘agenda’ of prenatal counseling. According to the authors, the goal of personalization is “for parents to feel like parents and to feel like they are good parents, before birth, at birth and after, either in the NICU or until the death of their child.” (18)

Parental values

The next characteristic is closely related to personalization, however, can be seen as a specific aspect of personalization; prenatal counseling can be personalized by elaborating on parental values and incorporate these into the counseling and decisionmaking. Of all the characteristics that we identified in this scoping review, parental values (n=37) were mentioned most frequently in the literature. Before 2010, parental values were mentioned in 3 (4) articles. In 2005 already, Bastek et al. discuss that “it is concerning that … families may not be receiving much assistance in identifying and discussing the nonmedical values important in making difficult decisions regarding resuscitation of their children.” (20) In the article by Staub et al., it is recommended to make prenatal counseling about values instead of abstract data. Staub et al. (17), In this regard, Srinivas states the following: “Recognition of the different values and perceptions patients and providers bring to the discussion is important to consider when counseling patients and their families. At the onset of discussion, it is critical to assess patient preferences and beliefs." (21) Although the importance of parental values is recognized in theory, almost half of the physicians participating in the study by Edmonds et al. did not elucidate values in practice (22).

SDM

28 articles referred to SDM. Conclusions about SDM seem to be divergent and changing over time. In 1998, Martinez et al. show that physicians do mostly not prefer parents to have any role in decision-making (23). Over time, this tendency seems to have changed. In 2005, for example, Bastek et al. show that 77% of the neonatologists participating in their study prefer joint decision-making with the parent(s) (20). Moreover, in a study by Geurtzen et al. in 2018, 80% of the parents felt they were involved in decision-making (24).

In most of the included papers that mention or elaborate on this characteristic, no formal definition of SDM is provided. In one study, it even shows that not all physicians know what SDM means (7). Barker et al. state however, that: "Both correct knowledge of SDM and belief in its benefit are required for this approach to perform as intended" (25). In this same article, several barriers to the use of SDM in prenatal counseling were identified, of which one was the workload: "Health care professionals described an increased workload with SDM because of the need to coordinate efforts between obstetricians, neonatologists and nurses, as well as the need for multiple encounters with some parents to clarify information and address their concerns." (25)

Parent-physician relationships

15 articles referred to the significance of the parent-physician relationship for good quality prenatal counseling. Ruthford et al. refer to the relationship as a "partnership" (26). In the literature, the importance of trust is often mentioned in this regard (18,26). For example, Haward et al. refer to the following: "Relationships begun in the antenatal consultation have been shown to be important determinants for future adaptation, by decreasing decisional regret and enhancing trust between physicians and parents. … Building relationships and focusing on trust increases the credibility of the informant and the validity of the decision" (18). Another important aspect of the parent-physician relationship is respect, as mentioned by Myers et al.: "The relationship between the counseling team and the family is healthiest in an atmosphere of respect, continued communication and a spirit of nonabandonment." (27)

Physician bias

In 19 articles, physician bias was mentioned. Two different kinds of physician bias were discussed. On the one hand, there were studies that show physician bias about parents and/or parental characteristics. Studies have, for example, shown possible effects on prenatal counseling of physician bias towards parental socioeconomic status, sociodemographic characteristics, and the desiredness of the pregnancy (28,30). Harrison then, warns for a different kind of physician bias (31). She warns for bias with regard to motives for providing active care: "… the scope of neonatal life support has rapidly expanded, professional and financial motives for its use have become more compelling, and the philosophies of aggressive interventionists have prevailed. … Perinatal and neonatal specialists should closely examine their motives for resuscitating and treating at ever-shorter gestations." (31)

QoL

22 articles mentioned QoL, even if there was no agreement in the included body of literature on whether, and if so how, to incorporate it in prenatal counseling. Harrison pleads against discussing QoL studies in prenatal counseling because of the ambiguity of such research (31). In another article however, parents are clear about their wish to discuss QoL in prenatal counseling (47). Also, one of the recommendations of the article written by parents of extremely premature infants is the following: "Tell us about what our children may, or may not, be able to do. Also tell us about the quality of life of other preterm infants have when they get older" (17). In one article then, research shows that physicians do not only discuss the QoL of the infant in prenatal counseling, but also that of the mom and/or family (33).

Psychosocial factors

The prenatal counseling consultation can include 'medical' as well as 'nonmedical' information. In 22 articles, nonmedical factors were mentioned. We will call these psychosocial factors, because they seem to be mostly related to the psychological, social or socioeconomic sphere. One of the included articles explicitly explores whether the social context of parents should matter for decision-making in prenatal counseling; the authors conclude that it should, even when it results in more directive counseling (34). They state that: "For some families, socioeconomic disadvantages, compounded by physical or mental health challenges, and chaotic living conditions exceed the parents' abilities and community resources necessary to safely bring the newborn home." (34) Janvier et al. also discuss the importance of nonmedical factors; they mention that some physicians may be hesitant to speak about such topics in prenatal counseling (35). Bastek et al. found much variability in the extent to and way in which physicians discuss nonmedical factors in prenatal counseling (20).

Religion, spirituality, hope

Religion (n=16) and spirituality (n=10) play a role in prenatal counseling. This was one of the main conclusions of both the included systematic reviews (28,36). Pedrini et al. conclude that “parents’ choices about treatment seemed to be influenced by spiritual-related aspects and/or preexisting preferences, rather than by the level of detail or by the order with which information was provided.” (36) In addition to religion and spirituality, hope (n=19) seems to be of major importance for parents. Hope can be a coping mechanism (28). In one article, parents advise the following: “Do not take away the hope we have. There is always hope that we will deliver tomorrow. There is hope that we will be able to spend some time with our child. There is hope that we can survive the death of our child with positive memories.” (17)

Emotions, anxiety

In the literature, emotions (n=26) or anxiety (n=11) were mentioned to be important for/in prenatal counseling. Srinivas, for example, writes about the emotionally charged nature of situations of threatening preterm birth (21). In a study by Boss et al., one physician states the following: “‘‘I wish (the parents) could have been less emotional and more focused on what they needed to know to make a decision.’’ (37) The same study reports however, that “aside from delivering biomedical information, physicians spent the next largest proportion of each encounter talking about and responding to emotion.” (37) The positive side of parental emotions is also stressed in the literature; emotions can be the driving force for parents to make decisions, help to elucidate values, or serve as a basis for building a strong parent-physician relationship (18).

Uncertainty

Uncertainty (n=30) was discussed in two ways in the included body of literature. Uncertainty about the prognosis, possible outcomes, the overall situation and/or the treatment decision was mentioned in the literature (35,38,39). Besides that, uncertainty was mentioned as a specific topic of discussion in prenatal counseling (7,33). Yet, a simulation study by Edmonds et al. shows that only 42% of physicians discussed uncertainties (40). Another study by Edmonds et al. finds that many physicians experience communicating uncertainty as challenging (41). In general, there seems to be agreement in the literature about the importance of addressing uncertainty in prenatal counseling: it is inevitable, so it should better be acknowledged. In their systematic review, Kharrat et al. refer to one of their included studies to state that “honesty about uncertainties and being informed that there are no guarantees regarding outcomes was valued.” (28)

Discussion

Towards personalized counseling
Parental values, uncertainty, SDM, and emotions are most frequently mentioned in the literature. However, reflecting on the interrelation between the identified characteristics may lead us to conclude that personalization is the most notable trend in prenatal counseling practices. More and more, it is valued to adjust the counseling to the parent(s) so that it optimally suits them and the unborn infant. The elucidation of parental values, the discussion of ideas about quality of life, and shared decision-making, can all be seen as aspects of personalized prenatal counseling. For example, elucidating parental values might lead to adjustments in the informational content of counseling and eventual recommendations about treatment options that best suit the parents. This, in turn, will result in more personalized prenatal counseling. Another example relates to parental views of QoL; parents can be approached differently according to their personal valuation of QoL and disabilities, and physicians can adjust treatment recommendations to parental beliefs.

An increase in personalization is a trend in time. Recommendations for personalizing prenatal counseling can also be found in more recent policy documents and guidelines for extreme prematurity care and/or counseling (42,45). The American Academy of Pediatrics, for example, advocates personalization based on fetal and maternal characteristics and on parental beliefs regarding their child's best interest (42). Canadian and UK guidelines also leave room for personalization (43,44). In the UK guideline, the following advice is provided: "Perinatal care at extremely preterm gestations will always need to be individualised (…). Decisions should be made together with parents, based on the best available evidence about the prognosis for the individual baby, and mindful of the need to act in the baby's best interests." (British Association of Perinatal Medicine. Perinatal Management of Extreme Preterm Birth before 27, 2019) Also, The National Institute of Child Health recommends that "counseling should be personalized and in the best interest of the family and their child, considering aspects beyond the gestational age" (45). Besides that, it is advised to "individualize the information to be provided, based on family preferences, wants and needs." (45)

Although there is significant thematic overlap and interrelation between the identified characteristics in this scoping review, there can also be some tensions between them. Understanding these tensions can be useful for future research in this field.

Tensions between characteristics

For example, one included article suggests a tension between SDM and personalization (18). It is suggested that instead of SDM, personalized decision-making may be better suited to reach parental decision-making preferences. Haward et al. explain that "for many, shared decision making implies that parents want to collaborate in decisions with physicians. In theory, clinicians should learn to discern between parents' informational needs for deliberation and their desires to be involved in making the decision" (18). The authors also state that: "Instead of aspiring to achieve mutual consent in shared decision making, physicians should seek to practice personalized decision making (that) would take into consideration a parent's preferences for decisional responsibility and deliberation and thereby informational and supportive needs." (18)

Haward et al. plead against SDM since parents should be allowed to defer the final decision to the doctor. However, this apparent tension seems to depend upon how SDM is interpreted. When SDM is interpreted as if the eventual decision must always be shared by the parents and the physician, there can indeed be tension with personalization. Nonetheless, this depends upon interpretation. Stiggelbout et al. describe in the last step of their SDM model, that the eventual decision may be made by the parents, the physician, or both, according to parental preferences (46). This is incorporated as such in, for example, the Dutch counseling recommendations (47). Geurtzen et al. emphasize that physicians who are asked to make treatment decisions alone must still take into account parental values (7). Interpreting SDM this way, it is compatible with personalization.

Other tensions exist as well. First, physician bias might endanger personalization and/or influence the way physicians interpret parental values. Adjustments in prenatal counseling better be prompted by family characteristics instead of physician bias about those characteristics. Second, the hesitancy of physicians to speak about nonmedical factors might be detrimental to personalization: physicians may have to speak about or take into account these factors when parents prefer so. Third, imagine highly anxious parents who decide that they do not want and/or need to hear any painful information about the long-term future of their infant. In this case, does personalized prenatal counseling mean that this information should not be told? Maybe, certain informational content just has to be shared, whether it suits the parents or not. Do we need a personalization limit?

Do we need a personalization limit for prenatal counseling?
Personalization is based upon common sense; it includes physicians sharing prognostic information that pertains to the specific child and her surroundings. Current literature provides good theoretical frameworks and grounds for personalized prenatal counseling (18,19). However, prenatal counseling should not be personalized for the sake of personalization; it needs to serve the goal of providing the best possible counseling for parents and enable ethical decision-making. Also, personalizing prenatal counseling per se has not yet been extensively and qualitatively explored with parents. Although qualitative research has been conducted on parents' perspectives on prenatal counseling (32,48), none has been done specifically on personalization and on how to personalize in practice. Given the theoretical preference for personalization, this seems to be a research gap. As becomes clear from the literature, personalizing prenatal counseling can pertain to different aspects: a personalized prognosis, a personalized relationship with the healthcare team or personalized decision-making (processes), or an overall personalized approach to the parent(s) by taking into account their values or adjusting the (amount of) information provision.

More research should be done on what aspects of prenatal counseling should be personalized according to parents and physicians. It should also be explored what are the effects of personalization at the limit of viability on parental satisfaction, decisional conflict and regret in prenatal counseling (49). Lastly, research should be done on effects of personalization at the limit of viability on neonatal mortality. It could be that a uniformly active approach such as in certain medical centers in Sweden comes with greater survival rates (50). Nonetheless, the possible differences in value prioritization between quality of life and sanctity of life may imply that this greater survival rate is not necessarily preferable.

Furthermore, the context of extreme prematurity comes with specific challenges in regards to personalization: how to resolve potential conflicts between what best suits the parent(s) and what best suits the unborn infant? Similarly, there may be conflict between personalizing the counseling for the pregnant woman, and personalizing for their partner. Concerning this last issue, it is worth mentioning that no current studies pay extensive attention for the role of the partner of the pregnant woman in prenatal counseling.

Limitations
This study is subject to certain limitations. First, it is possible that we missed gray literature or important literature that was written in other languages than English. Second, since the majority of included studies has been conducted in the USA or has been written by American researchers, there might be cultural bias in this article.

Although Canadian and Dutch perspectives are also well-represented, we know little of how prenatal counseling is practiced in the rest of the world. Third, it could be that the same characteristics appear in many of the articles because of cross-referencing in the included body of literature. Moreover, many included articles and studies were written or conducted by the same researchers. Nevertheless, similar topics have arisen in several independent qualitative interview studies with parents, and simulation studies have shown similar tendencies among physicians. Our decision to exclude the articles that were included in the systematic reviews could be a limitation. We are, however, convinced that the systematic reviews are of sufficient quality and that their results represent the most important findings of the articles that are therein included. We are confident that this methodological decision has not influenced the content of this article. Yet, it has surely influenced the number of articles in which the characteristics were mentioned.

Conclusion

In this scoping review, we explored the existing body of literature on prenatal counseling for extreme prematurity at the limit of viability. Several main characteristics were identified. Parental values, uncertainty, SDM, and emotions were most frequently mentioned. A trend in time towards an increase in personalization was found. Although personalization might seem ideal, it comes with certain challenges and an eventual limit. Especially, more research is needed on parental views of personalizing prenatal counseling, on how to personalize in practice, and on exactly what aspects of prenatal counseling should be personalized.

Practice Implications

This scoping review emphasizes again the complexity of prenatal counseling at the limit of viability. The identified characteristics are all interrelated, and at the same time relate to the trend in time that is an increase in personalization. However, this scoping review makes clear that there are some tensions that require attention in future research. Especially an eventual limit of personalization, the challenge of physician bias, and the importance and discussion of psychosocial factors requires attention. One of the conclusions of Kharrat et al. may be a great reminder for future research on prenatal counseling: “(The) quality of the antenatal consultation is not purely about information content, but also the manner in which it is provided” (28).

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Table 1 Electronic search strategies

Database	Search strategy	Years of coverage	Refe-rences	After de-duplication
Embase	('prematurity'/de OR 'extreme prematurity'/de OR 'premature labor'/de OR 'very low birth weight'/exp OR (prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) NEAR/3 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*))):ab,ti,kw) AND ('parent counseling'/de OR 'family counseling'/de OR 'counseling'/mj/exp OR (((parent* OR prenat* OR famil* OR preterm* OR pre-term* OR pre-natal* OR prematur* OR pre-matur* OR antenatal*) NEAR/3 (counsel*))):ab,ti,kw OR (counsel*):ti) AND [ENGLISH]/lim	1971-present	1200	1190
Medline ALL	(exp Infant, Premature/ OR exp Obstetric Labor, Premature/ OR exp Infant, Very Low Birth Weight/ OR (prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) ADJ3 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*))).ab,ti,kf.) AND (Counseling/ OR (((parent* OR prenat* OR famil* OR preterm* OR pre-term* OR pre-natal* OR prematur* OR pre-matur* OR antenatal*) ADJ3 (counsel*))).ab,ti,kf. OR (counsel*).ti.) AND english.la.	1946-present	716	205

Table 1 Continues

Database	Search strategy	Years of coverage	References	After deduplication
Web of Science Core Collection	TS=(((prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) NEAR/2 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*)))) AND ((((parent* OR prenat* OR famil* OR preterm* OR pre-term* OR pre-natal* OR prematur* OR pre-matur* OR antenatal*) NEAR/2 (counsel*))) OR (counsel*):ti)) AND LA=(English)	1975-present	445	57
Cochrane Central Register of Controlled Trials	((prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) NEAR/3 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*))):ab,ti) AND ((((parent* OR prenat* OR famil* OR preterm* OR pre-term* OR pre-natal* OR prematur* OR pre-matur* OR antenatal*) NEAR/3 (counsel*))):ab,ti OR (counsel*):ti)	1992-present	202	161
Google Scholar	prematurity|prematures|preterms|ELBW|VLBW|"premature|pre-mature|preterm|pre-term child|children|infant|infants|neonate|birth|baby|babies|newborn|adolescent|born|labor|labour|delivery|gestatation" counseling|counselling	100 top ranked	100	53

Table 1 Continues

Database	Search strategy	Years of coverage	Refe-rences	After de-duplication
Cinahl	(MH Infant, Premature OR MH Labor, Premature OR MH Childbirth, Premature OR MH Infant, Very Low Birth Weight OR TI(prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) N2 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*))) OR AB(prematurit* OR prematures OR preterms OR ELBW OR VLBW OR ((prematur* OR pre-matur* OR preterm* OR pre-term* OR extremely-low OR very-low) N2 (child* OR infant* OR neonat* OR birth* OR baby OR babies OR newborn* OR adolescent* OR born* OR labor* OR labour* OR deliver* OR gestat*)))) AND (MH Counseling OR AB(((parent* OR prenat* OR famil* OR preterm* OR pre-term* OR pre-natal* OR prematur* OR pre-matur* OR antenatal*) N2 (counsel*))) OR TI(counsel*))	1982-present	524	210
Total			3187	1876

Table 2: Characteristics of the studies included in this scoping review

First author et al (year)	**Journal**	**Design**	**Country**
Martinez et al (1998)[1]	*Obstet Gynecol*	Questionnaire	USA
Munro et al (2001)[2]	*Aust N Z J Obstet Gynaecol*	Questionnaire	Australia, USA
Janvier et al (2005)[3]	*J Pediatr*	Retrospective review	Canada
Bastek et al (2005)[4]	*Pediatrics*	Questionnaire	USA
Yee et al (2007)[5]	*Paediatr Child Health*	Questionnaire	Canada
Harrison (2008)[6]	*Sem Fet Neo Med*	Literature	USA

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[1] Martinez AM, Weiss E, Partridge JC, Freeman H, Kilpatrick S. Management of extremely low birth weight infants: perceptions of viability and parental counseling practices. *Obstet Gynecol* 1998;92:520-4.

[2] Munro M, Partridge JC, Martinez AM. Antenatal counseling, resuscitation practices and attitudes among Australian neonatologists towards life support in extreme prematurity. *Aust N Z J Obstet Gynaecol* 2001;41:275.

[3] Janvier A, Barrington KJ. The ethics of neonatal resuscitation at the margins of viability: informed consent and outcomes. *J Pediatr* 2005;147:532-6.

Objective	Result/conclusion
To determine physician opinions, parental counseling, and medical practices for extremely low birth weight infants	Obstetric opinions about delivery room resuscitation are influenced by birth weight and GA thresholds, infant, and parental factors. There is a limited willingness by physicians to allow a parental role in decision-making in the delivery room
To ascertain antenatal counseling, resuscitation practices, and attitudes towards life support in the extremely preterm infant of Australian neonatologists	The establishment of national guidelines would be helpful to aid Australian obstetricians and neonatologists in their clinical practice
To determine the adequacy of records of parental counseling, whether interventions at birth were consistent with recorded antenatal decisions, and whether extent of resuscitation affected occurrence of serious short-term morbidity	Records of antenatal consultations were often lacking important information. Variations in physician documentation practices are substantial and affect the care offered to infants at the threshold of viability
To determine attitudes and practices regarding prenatal counseling of neonatologists in New England	Neonatologists are consistent in discussing clinical issues but varied in discussing social and ethical issues
To explore whether the information content, process and social interaction of prenatal counseling satisfies the informational needs of women admitted to hospital in preterm and threatened preterm labor	Respondents were generally satisfied with the information provided but remained highly anxious. Recall of the discussion about disability was inconsistent. They reported needing an opportunity to express their feelings, and to talk about their baby and their anticipated interaction with their baby
To reflect on parental decision-making and information provision in prenatal counseling	The use of directives and other techniques for transparency in obstetric and neonatal care could improve the process of informed parental choice

4 Bastek TK, Richardson DK, Zupancic JA, Burns JP. Prenatal consultation practices at the border of viability: a regional survey. *Pediatrics* 2005;116:407-13.

5 Yee WH, Sauve R. What information do parents want from the antenatal consultation? *Paediatr Child Health* 2007;12:191-6.

6 Harrison H. The offer they can't refuse: parents and perinatal treatment decisions. *Semin Fetal Neonatal Med* 2008;13:329-34.

Table 2: Continued

First author et al (year)	**Journal**	**Design**	**Country**
Griswold et al (2009)[7]	*Pediatrics*	Literature	USA
Tomlinson et al (2010)[8]	*Am J Obstet Gynecol*	Clinical opinion	USA
Boss et al (2012)[9]	*Sim Healthcare*	Simulation	USA
Janvier et al (2012)[10]	*Acta Paediatr*	Viewpoint	Canada
Edmonds et al (2012)[11]	*AJOG*	Interview	USA
Srinivas (2013)[12]	*Sem Perinat*	Literature	USA
Mehrotra et al (2013)[13]	*J Perinatol*	Questionnaire	USA

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7 Griswold KJ, Fanaroff JM. An evidence-based overview of prenatal consultation with a focus on infants born at the limits of viability. *Pediatrics* 2010;125:e931-7.

8 Tomlinson MW, Kaempf JW, Ferguson LA, Stewart VT. Caring for the pregnant woman presenting at periviable gestation: acknowledging the ambiguity and uncertainty. *Am J Obstet Gynecol* 2010;202:529.e1-6.

9 Boss RD, Donohue PK, Roter DL, Larson SM, Arnold RM. “This is a decision you have to make”: using simulation to study prenatal counseling. *Simul Healthc* 2012;7:207-12.

10 Janvier A, Lorenz JM, Lantos JD. Antenatal counseling for parents facing an extremely preterm birth: Limitations of the medical evidence. *Acta Paediatr* 2012;101:800-4.

Objective	Result/conclusion
To provide an evidence-based overview of prenatal counseling	Suggestions for the incorporation of morbidity and mortality data as well as the structure and approach to discussion with parents were made
To detail problems with prenatal counseling and describe the development of a program designed to improve the process	They developed a set of guidelines to guide prenatal counseling. It resulted in a substantial improvement in the care of pregnant women
To examine how simulation might be used to engage neonatologists in reflecting on their usual prenatal counseling behaviors	Simulation can reproduce the decisional context of prenatal counseling
To analyze the complexities of parental informed consent for treatment	Personalization is preferred: doctors should try to discern what parents want and need and to adapt counseling to those needs
To examine factors that influence obstetric decision-making and counseling and to describe counseling challenges	Decision-making and counseling were influenced primarily by patient preferences. Communicating uncertainty, managing expectations, assessing understanding, and relaying consistent messages across specialties were identified as challenges
To provide a systematic approach to communicating and counseling for extreme prematurity	There is a need for a multidisciplinary approach and multiple sessions of counseling. Parents are the principle focus regarding decision-making. Information shared should be consistent and understandable. Variability between providers should be minimized
To study counselor-independent elements of prenatal counseling	Substantial system-based variability in execution was found

11 Edmonds BT, Krasny S, Srinivas S, Shea J. Obstetric decision-making and counseling at the limits of viability. *AJOG* 2012;206:248.e1-5.

12 Srinivas SK. Periviable births: Communication and counseling before delivery. *Semin Perinatol* 2013;37:426-30.

13 Mehrotra A, Lagatta J, Simpson P, Kim UO, Nugent M, Basir MA. Variations among US hospitals in counseling practices regarding prematurely born infants. *J Perinatol* 2013;33:509-13.

Table 2: Continued

First author et al (year)	**Journal**	**Design**	**Country**
Staub et al (2014)[14]	*Acta Paediatr*	Letter	Canada
Kim et al (2014)[15]	*Clin Perinat*	Literature	USA
Janvier et al (2014)[16]	*Sem in Perinat*	Literature	Canada
Boss et al (2015)[17]	*J Amer Med Assoc Pediatr*	Commentary	USA
Edmonds et al (2015)[18]	*J Perinatol*	Simulation	USA
Geurtzen et al (2016)[19]	*J Mat Fet Neo Med*	Questionnaire	Netherlands (study participants: Europe)
Geurtzen et al (2017)[20]	*Eur J Pediatr*	Interview	Netherlands
Haward et al (2017)[21]	*Clin Perinat*	Literature	Canada

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14 Staub K, Baardsnes J, Hébert N, Hébert M, Newell S, Pearce R. Our child is not just a gestational age. A first-hand account of what parents want and need to know before premature birth. *Acta Paediatr Int J Paediatr* 2014;103:1035-8.

15 Kim UO, Basir MA. Informing and educating parents about the risks and outcomes of prematurity. Clinics in Perinatology 2014;41:979-91.

16 Janvier A, Barrington K, Farlow B. Communication with parents concerning witholding or withdrawing of life-sustaining interventions in neonatology. *Semin Perinatol* 2014;38:38-46.

17 Boss RD, Henderson CM, Wilfond BS. Decisions regarding resuscitation of extremely premature infants: should social context matter? *J Amer Med Assoc Pediatrics* 2015;169:521-2.

Objective	Result/conclusion
To help clinicians understand what parents want and need from them	Ten concrete recommendations for healthcare providers
To elaborate on communicating risks and outcomes of prematurity in prenatal counseling	Efforts in prenatal counseling must focus on improving communication and not on decreasing information provided to parents
To suggest ways to personalize prenatal discussions with parents	The mnemonic “SOBPIE” may help providers have fruitful discussions
To answer the question whether social context should matter when responding to parents’ requests for resuscitation	The contextual realities of family circumstances should influence counseling, in an active way, towards directive counseling
To compare the management options, risks and the content that obstetricians and neonatologists discuss in prenatal counseling	Both specialties organized decision-making around medical information, survival, quality of life, time and support. Neonatologists also introduced themes of values, comfort or suffering, and uncertainty
To evaluate current practices in prenatal counseling amongst European trainees	Wide variation in content and organization was observed
To gain insight into professionals’ preferences on three domains of counseling: content, organization and decision-making	There is limited familiarity with SDM although it is the preferred model
To present practical recommendations for antenatal counseling	Personalized decision-making empowers parents and should replace SDM

18 Edmonds BT, McKenzie F, Panoch JE, Barnato AE, Frankel RM. Comparing obstetricians’ and neonatologists’ approaches to periviable counseling. *J Perinatol* 2015;35:344-8.

19 Geurtzen R, van Heijst AFJ, Babarao S, Molloy E, Draaisma JMT, Hogeveen M. Practices in antenatal counseling for extremely premature infants amongst European trainees. *J Matern Fetal Neonatal Med* 2016;29:3956-9.

20 Geurtzen R, van Heijst A, Draaisma J, Ouwerkerk L, Scheepers H, Woiski M, et al. Professionals’ preferences in prenatal counseling at the limits of viability: a nationwide qualitative Dutch study. *Eur J Pediatr* 2017;176:1107-19.

21 Haward MF, Gaucher N, Payot A, Robson K, Janvier A. Personalized Decision-making: Practical Recommendations for Antenatal Counseling for Fragile Neonates. *Clin Perinatol* 2017;44:429-45.

Table 2: Continued

First author et al (year)	Journal	Design	Country
Haward et al (2017)[22]	*AJOB Empirical Bioethics*	Interview	USA
Kharrat et al (2017)[23]	*J Pediatr*	Systematic review	Canada
Kunkel et al (2017)[24]	*J Perinat*	Questionnaire	USA
Pedrini et al (2017)[25]	*BioMed Res Inter*	Systematic review	Italy
Ruthford et al (2017)[26]	*Pediatrics*	Commentary	USA
Moore et al (2017)[27]	*J Perinatol*	Field testing, questionnaire	Canada
Geurtzen et al (2018)[28]	*BMC Pregnancy Childbirth*	Questionnaire	Netherlands

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[22] Haward MF, Janvier A, Lorenz JM, Fischhoff B. Counseling parents at risk of delivery of an extremely premature infant: Differing strategies. *AJOB Empir Bioeth* 2017;8:243-52.

[23] Kharrat A, Moore GP, Beckett S, Nicholls SG, Sampson M, Daboval T. Antenatal consultations at extreme prematurity: a systematic review of parent communication needs. *J Pediatr* 2018;196:109-15.e7.

[24] Kunkel MD, Downs SM, Edmonds BT. Influence of Maternal Factors in Neonatologists' Counseling for Periviable Pregnancies. *Am J Perinatol* 2017;34:787-94.

Objective	Result/conclusion
To explore neonatologists' views on decision-making processes and their own roles in counseling	Neonatologists are concerned that parents understand the decision facing them. They differ on what information they offer and how they balance parents' need for cognitive and affective support
To synthesize and describe parental expectations on how healthcare professionals should interact with them during prenatal counseling	Six themes emerged: perception of support, degree of understanding, hope, spirituality, and decision-making influences
To determine the relative influence of maternal factors in counseling	Parity and intendedness had the highest importance scores, followed by race, education, and age
To describe the outcomes of prenatal counseling for preterm delivery	Parents' choices about treatment seemed to be influenced by spiritual-related aspects and or pre-existing preferences rather than by the level of detail or by the order with which information was provided
To reflect on a couple's experience of prenatal counseling and premature birth	Physicians should try to understand the values and motivations that influence parental decision-making
To assess and modify an existing decision aid and field-test decision coaching with the modified aid during prenatal counseling	Consultations using the aid with decision coaching were feasible, reduced decisional conflict and may facilitate SDM
To explore preferred prenatal counseling by Dutch professionals and compare this to current care	Dutch professionals would prefer more protocolized counseling, joint counseling, supportive material and local outcome statistics

25 Pedrini L, Prefumo F, Frusca T, Frusca T, Ghilardi A. Counseling about the Risk of Preterm Delivery: A Systematic Review. *BioMed Res Int* 2017:7320583.

26 Ruthford E, Ruthford M, Hudak ML. Parent-physician partnership at the edge of viability. *Pediatrics* 2017;139.

27 Moore GP, Lemyre B, Daboval T, Ding S, Dunn S, Akiki S, et al. Field testing of decision coaching with a decision aid for parents facing extreme prematurity. *J Perinatol* 2017;37:728-34.

28 Geurtzen R, Van Heijst A, Hermens R, Scheepers H, Woiski M, Draaisma J, et al. Preferred prenatal counseling at the limits of viability: a survey among Dutch perinatal professionals. *BMC Pregnancy Childbirth* 2018;18:7.

Table 2: Continued

First author et al (year)	Journal	Design	Country
Geurtzen et al (2018)[29]	*Pat Educ Counsel*	Questionnaire	Netherlands
Lantos (2018)[30]	*J Pediatr*	Editorial	USA
Myers et al (2018)[31]	*Sem Fet Neo Med*	Literature	USA
Drago et al (2018)[32]	*Mat Child Health J*	Interview, simulation	USA
Shapiro et al (2018)[33]	*J Pediatr*	Questionnaire	USA
Barker et al (2018)[34]	*Paediatr Child Health*	Interview	Canada

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[29] Geurtzen R, Draaisma J, Hermens R, Scheepers H, Woiski M, van Heijst A, et al. Various experiences and preferences of Dutch parents in prenatal counseling in extreme prematurity. *Patient Educ Couns* 2018;101:2179-85.

[30] Lantos JD. What is the Purpose of Antenatal Counseling? J Pediatr 2018;196:8-10.

[31] Myers P, Andrews B, Meadow W. Opportunities and difficulties for counseling at the margins of viability. *Semin Fetal Neonatal Med* 2018;23:30-4.

Objective	Result/conclusion
To investigate experienced and preferred prenatal counseling among parents	Parents want to be involved in the decision-making process but differed on the preferred extent of involvement
To reflect on the purpose of prenatal counseling	Doctors should strive to understand what parents want: less talking, more listening. Discussions should be individualized and respond to the family's needs
To address opportunities and difficulties for prenatal counseling	Multi-timepoint counseling provides the opportunity to address important goals and continue communication as the trajectories of infants, families, and the counseling team change
To characterize Latino parental perceptions of antenatal counseling in order to construct and validate a Spanish decision-aid	A decision-aid for Latino parents may improve comprehension of antenatal counseling
To assess whether neonatologists show implicit racial and/or socioeconomic biases and whether these are predictive of recommendations at extreme periviability	Unconscious socioeconomic bias influences recommendations when counseling at the limits of viability. Physicians who display a negative socioeconomic bias are less likely to recommend resuscitation when counseling women of high socioeconomic status
To explore health care providers' perceptions of using SDM and to identify facilitators of and barriers to its use in prenatal counseling	Nine facilitators and sixteen barriers were identified that can be used to inform development of tailored strategies to facilitate future implementation of SDM in prenatal counseling

32 Drago MJ, Guillén Ú, Schiaratura M, Batza J, Zygmunt A, Mowes A, et al. Constructing a Culturally Informed Spanish Decision-Aid to Counsel Latino Parents Facing Imminent Extreme Premature Delivery. *Maternal and Child Health Journal* 2018;22:950-7.

33 Shapiro N, Wachtel EV, Bailey SM, Espiritu MM. Implicit Physician Biases in Periviability Counseling. *J Pediatr* 2018;197:109-15.e1.

34 Barker C, Dunn S, Moore GP, Reszel J, Lemyre B, Daboval T. Shared decision making during antenatal counseling for anticipated extremely preterm birth. *Paediatrics & Child Health* 2019;24:240-9.

Table 2: Continued

First author et al (year)	Journal	Design	Country
Geurtzen et al (2019)[35]	*Pat Educ Counsel*	Interview	Netherlands
Edmonds et al (2019)[36]	*J Mat Fet Neo Med*	Interview	USA
Guillén et al (2019)[37]	*J Pediatr*	Randomized controlled trial	USA
Tysdahl et al (2019)[38]	*Pediatrics*	Commentary	USA
Feltman et al (2020)[39]	*Am J Perinatol*	Retrospective review	USA

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35 Geurtzen R, van Heijst A, Draaisma J, Ouwerkerk L, Scheepers H, Hogeveen M, et al. Prenatal counseling in extreme prematurity - Insight into preferences from experienced parents. *Patient Educ Couns* 2019;102:1541-9.

36 Edmonds BT, McKenzie F, Panoch J, Litwiller A, DiCorcia MJ. Evaluating shared decision-making in periviable counseling using objective structured clinical examinations. *J Perinatol* 2019;39:857-65.

37 Guillén Ú, Mackley A, Laventhal N, Kukora S, Christ L, Derrick M, et al. Evaluating the Use of a Decision Aid for Parents Facing Extremely Premature Delivery: A Randomized Trial. *J Pediatr* 2019;209:52-60.

Objective	Result/conclusion
To analyze parental preferences in prenatal counseling	Various preferences were found related to the content, the organization, and decision-making
To examine prospective parents' perceptions of management options and outcomes and the values they apply in decision-making	Over half desired a shared decision-making role. The potential for disability influenced decision-making to variable degrees
To assess decisional conflict and knowledge about prematurity when the counseling clinicians were randomized to counsel using a validated decision aid compared with usual counseling	Use of a decision aid did not impact maternal decisional conflict, but it significantly improved knowledge of complex information.
To share delivery stories and let parents offer advice to clinicians developing care approaches for families like theirs	Careful decision-making should be shared by physicians and parents. Parents and physicians must engage in discourse to make treatment decisions aligned with parental values and appropriate expectations
To describe periviability counseling practices and decision-making	Areas requiring improvement include delivery/content of neonatology consultations, social work support, consideration of centers' patient populations, and opportunities for shared decisions

38 Tysdahl C, Tysdahl T, Wendt J, Wendt L, Feltman DM. Helping Families Navigate Center Variability in Antenatal Counseling for Extremely Early Births. *Pediatrics* 2019;144:e20191625.

39 Feltman DM, Fritz KA, Datta A, Carlos C, Hayslett D, Tonismae T, et al. Antenatal Periviability Counseling and Decision Making: A Retrospective Examination by the Investigating Neonatal Decisions for Extremely Early Deliveries Study Group. *Am J Perinatol* 2020;37:184-95.

Table 2: Continued

First author et al (year)	**Journal**	**Design**	**Country**
Rau et al (2020)[40]	*BMC Medical Informatics and Decision-making*	Questionnaire, interview	USA
Mardian et al (2020)[41]	*The Journal of Maternal-Fetal & Neonatal Medicine*	Interview	Canada
Reed et al (2020)[42]	*J Perinatol*	Questionnaire	USA
Abusalah (2020)[43]	*Archives of Disease in Childhood*	Conference abstract	Dubai

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[40] Rau NM, Basir MA, Flynn KE. Parental understanding of crucial medical jargon used in prenatal prematurity counseling. *BMC Med Inform Decis Mak* 2020;20:169.

[41] Mardian E, Bucking S, Dunn S, Lemyre B, Daboval T, Moore GP. Evaluating parental perceptions of written handbooks provided during shared decision-making with parents anticipating extremely preterm birth. *J Matern - Fetal Neonatal Med* 2020;1-8.

Objective	Result/conclusion
To look into parental understanding of medical jargon commonly used during prematurity counseling	Cognitive interviews provided empirical testing of parental understanding of crucial medical jargon and highlighted that language commonly used during prenatal prematurity counseling is not understood by many parents. For parents to participate in shared decision-making, plain language should be used to maximize their understanding of medical information.
To explore parental perceptions of written handbooks provided to them during antenatal counseling for anticipated extremely preterm birth	Overall, parents positively evaluated the handbooks, supporting their utility for parents anticipating extremely preterm birth. Concrete suggestions for improvement were made; the handbooks will be modified accordingly. Parents at other perinatal centers may bene-fit from receiving such handbooks
To investigate the frequency with which neonatal and maternal–fetal medicine (MFM) providers perform joint periviability counseling (JPC), compare content of counseling, and identify perceived barriers to JPC	JPC is recommended but infrequently performed, with both specialties interested in further collaboration to strengthen the counseling provided
To highlight the importance of effective communication with parents and to suggest a structured approach for counseling	The paper will advocate the adoption of the SPIKES protocol (with permission) that was originally described to disclose unfavourable clinical information to patients with cancer. The six steps of Modified SPIKES: S— Setting up the interview P— assessing the parents' Perception I—obtaining the parents' Invitation K —giving Knowledge and information E — addressing the parents' Emotions with empathic responses S— Strategy and Summary

42 Reed R, Grossman T, Askin G, Gerber LM, Kasdorf E. Joint periviability counseling between neonatology and obstetrics is a rare occurrence. *J Perinatol* 2020;40:1789-96.

43 Abusalah Z. Counseling parents of premature babies. a novel approach. *Archives of Disease in Childhood* 2020:9924.

Table 2: Continued

First author et al (year)	Journal	Design	Country
Fish et al (2021)[44]	*J Perinatol*	Randomized controlled trial	USA
Arnolds et al (2021)[45]	*The Journal of Pediatrics*	Commentary	USA
Georgescu et al (2021)[46]	*J Pediatr Intensive Care*	Questionnaire	USA

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[44] Fish R, Weber A, Crowley M, March M, Thompson C, Voos K. Early antenatal counseling in the outpatient setting for high-risk pregnancies: a randomized control trial. *J Perinatol* 2021;41:1595–1604.

[45] Arnolds M, Laventhal N. Perinatal Counseling at the Margin of Gestational Viability: Where We've Been, Where We're Going, and How to Navigate a Path Forward. *J Pediatr* 2021;233:255-62.

Objective	Result/conclusion
To determine if antenatal counseling delivered in the outpatient setting improves parental knowledge and satisfaction without contributing to anxiety	Antenatal counseling in the high-risk outpatient setting improved parental knowledge and satisfaction without leading to increased anxiety
To support clinicians seeking consistent strategies for counseling and shared decision-making in the gray zone by exploring the moral and practical dimensions at the margin of gestational viability, with emphasis on contemporary normative and empirical work	Compassionate and up-to-date counseling of expectant parents at the margin of gestational viability requires the clinician to take into account contemporary outcome data, current ethical frameworks, and modern approaches to value based SDM. A structured approach to prenatal consultation at the margin of gestational viability is essential as it does not simply improve communication and clinician and parent satisfaction, but also serves to reduce the encroachment of unconscious biases and structural inequities for already vulnerable babies and families
To describe the characteristics and content of intrapartum counseling provided to women hospitalized for premature birth between 23 and 34 weeks of GA	The authors found that the duration of most sessions is 30 minutes; the father of the baby is not present during counseling for most premature births, and the topics discussed are fairly similar and extensive irrespective of the GA. These findings highlight the existing contrast between the recommended counseling practices and the actual practice reported by counselors

46 Georgescu A, Muthusamy A, Basir MA. The 30-Minute Sprint: Recognizing Intrapartum Prematurity Counseling Limitations. *J Pediatr Intensive* Care 2021;10.1055/s-0041-1724096.

Table 3: Characteristics of the studies included in the identified systematic reviews (Kharrat et al (2017) and Pedrini et al (2017))

First author et al (year)	Journal	Design	Country
Young et al (2012)[47]	*Paediatr Child Heal*	Interview	Canada
Payot et al (2007)[48]	*Soc Sci Med*	Interview	Canada
Grobman et al (2010)[49]	*Obstet Gynecol*	Interview	USA
Kavanaugh et al (2009)[50]	*J Perinatol Neonatal Nurs*	Case study	USA

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[47] Young E, Tsai E, O'Riordan A. A qualitative study of predelivery counseling for extreme prematurity. *Paediatr Child Heal* 2021;17:432-6.

[48] Payot A, Gendron S, Lefebvre F, Doucet H. Deciding to resuscitate extremely premature babies: how do parents and neonatologists engage in the decision? *Soc Sci Med* 2007;64:1487-500.

Objective	Result/conclusion
To ascertain from parents of neonates born before 27 weeks' gestational age how to improve predelivery counseling for delivery room resuscitation	Information about prematurity should be offered when the pregnancy is deemed high risk, with repeat counseling opportunities for both parents to discuss options. Once the decision is made to resuscitate, parents want the neonatal team to convey a message of hope and compassion
To explore how parents and neonatologists engage in decision-making in a context of imminent and unplanned delivery at the threshold of viability	Results highlight how neonatologists and parents engage in decision making from different standpoints: while neonatologists focus on the management of the unborn baby, parents have yet to fully conceptualize their infant as a distinct entity since they are in a process of grieving their pregnancy and their parenthood project. Parents express the need to receive more than just factual information from neonatologists. They also require support and engagement from caregivers to manage the uncertainty
To better understand preferred approaches that health care professionals could use when caring for parents who are at risk of giving birth to an extremely premature infant	Both patients and providers agree about the centrality of information provision and emotional support for women at risk of periviable delivery. This study not only elucidates preferred approaches and methods by which this information and support could be optimized, but also shows pitfalls that, if not avoided, may impair the relationship between provider and patient
The authors describe a case from a larger collective case study that examines the decision making and the decision support needs of parents regarding life support decisions made over time (prenatally and postnatally) for extremely premature infants from the perceptions of parents, physicians, and nurses	The findings in this case study demonstrate the importance of the nurse being present when information is given to parents, of informing with compassion, and helping parents to understand treatment options and decisions

49 Grobman WA, Kavanaugh K, Moro T, DeRegnier R-A, Savage T. Providing advice to parents for women at acutely high risk of periviable delivery. *Obstet Gynecol* 2010;115:904-9.

50 Kavanaugh K, Moro TT, Savage TA, Reyes M, Wydra M. Supporting parents' decision making surrounding the anticipated birth of an extremely premature infant. *J Perinatol Neonatal Nurs* 2009;23:159-70.

Table 3: Continued

First author et al (year)	Journal	Design	Country
Daboval et al (2016)[51]	*PloS One*	Interview	Canada
Roscigno et al (2012)[52]	*Qual Health Res*	Interview	USA
Moro et al (2011)[53]	*J Perinat Neonatal Nurs*	Interview	USA
Bohnhorst et al (2015)[54]	*Am J Perinatol*	Questionnaire	Germany

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[51] Daboval T, Shidler S, Thomas D. Shared decision making at the limit of viability: a blue print for physician action. *PloS One* 2016;11:e0166151.

[52] Roscigno CI, Savage TA, Kavanaugh K, Moro TT, Kilpatrick SJ, Strassner HT, et al. Divergent views of hope influencing communications between parents and hospital providers. *Qual Health Res* 2012;22:1232-46.

Objective	Result/conclusion
To document interactions during the antenatal consultation between parents and neonatologist that parents linked to their satisfaction with their participation in shared decision making for their infant at risk of being born at the limit of viability	Parent descriptions indicate that the opportunity to participate to their satisfaction in the clinical antenatal consultation depends on how the physician interacts with them
To evaluate parents' and health care providers' descriptions of hope following prenatal counseling	Divergent views of hope were found between parents and providers
To describe how parents make life support decisions for extremely premature infants from the prenatal period through death from the perspectives of parents, nurses, and physicians	Mothers were found to exhibit these characteristics: desire for and actual involvement in life support decisions, weighing pain, suffering and hope in decision making, and wanting everything done for their infants. All mothers received decision making help and support from partners and family, but relationships with providers were also important. Finally, external resources impacted parental decision making in several of the cases
This article aims to investigate the impact of prenatal counseling on subsequent parents' experiences during in-patient care of their infant(s) and whether feelings of parents with deceased infants are different in principle	This study stresses the impact of prenatal counseling and shows that, regardless of outcome, the course of a trusting relationship between parents and health care team is already set before birth

53 Moro TT, Kavanaugh K, Savage TA, Reyes MR, Kimura RE, Bhat R. Parent decision making for life support decisions for extremely premature infants: from the prenatal through end-of-life period. *J Perinat Neonatal Nurs* 2011;25:52-60.

54 Bohnhorst B, Ahl T, Peter C, Pirr S. Parents' prenatal, onward, and Postdischarge experiences in case of extreme prematurity: when to set the course for a trusting relationship between parents and medical staff. *Am J Perinatol* 2015;32:1191-7.

Table 3: Continued

First author et al (year)	Journal	Design	Country
Boss et al (2008)[55]	*Pediatrics*	Interview	USA
Partridge et al (2005)[56]	*Pediatrics*	Interview	USA, Australia, Hong Kong, Japan, Malaysia, Taiwan, Singapore
Zupancic et al (2002)[57]	*Arch Dis Child Fetal Neonatal Ed*	Nonrandomized controlled trial	Canada

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[55] Boss RD, Hutron N, Sulpar LJ, West AM, Donohue PK. Values parents apply to decision-making regarding delivery room resuscitation for high-risk newborns. *Pediatrics* 2008;122:583-9.

[56] Partridge JC, Martinez A, Nishida H, Boo N-Y, Tan KW, Yeung C-Y, et al. International comparison of care for very low birth weight infants: parents' perceptions of counseling and decision-making. *Pediatrics* 2005;116:e263-71.

Objective	Result/conclusion
The aim of this study was to characterize parental decision-making regarding delivery room resuscitation for infants born extremely prematurely or with potentially lethal congenital anomalies	The values that parents find most important during decision-making regarding delivery room resuscitation may not be addressed routinely in prenatal counseling. Parents and physicians may have different interpretations of what is discussed and what decisions are made. Future work should investigate whether physicians can be trained to address effectively parents' values during the decision-making process and whether addressing these values may improve physician-parent communication and lead to better post-decision outcomes for parents
To characterize parent perceptions and satisfaction with physician counseling and delivery-room resuscitation of very low birth weight infants in countries with neonatal intensive care capacity	Counseling differs by center among these centers in Australasia and California. Given that parents desire to play an active role in decision-making for their premature infant, physicians should strive to provide parents the medical information critical for informed decision-making. Given that parents do not seek sole decision-making capacity, physicians should foster parental involvement in life-support decisions to the extent appropriate for local cultural norms
To assess outcome of counseling in a routine setting of care	The agreement score correlated negatively with the level of anxiety. The agreement for obstetric variables was good, while concordance on potential neonatal problems was generally poor

57 Zupancic JA, Kirpalani H, Barrett J, Stewart S, Gafni A, Streiner D, et al. Characterising doctor-parent communication in counseling for impending preterm delivery. *Arch Dis Child Fetal neonatal Ed* 2002;87:F113-7.

Table 3: Continued

First author et al (year)	Journal	Design	Country
Kavanaugh et al (2005)[58]	*J Pediatr Nurs*	Interview	USA
Keenan et al (2005)[59]	*Pediatrics*	Interview	USA
Guillén et al (2012)[60]	*J Pediatr Nurs*	Nonrandomized controlled trial	USA

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[58] Kavanaugh K, Savage T, Kilpatrick S, Kimura R, Hershberger P. Life support decisions for extremely premature infants: report of a pilot study. *J Pediatr Nurs* 2005;20:347-59.

[59] Keenan HT, Doron MW, Seyda BA. Comparison of mothers' and counselors' perceptions of predelivery counseling for extremely premature infants. *Pediatrics* 2005;116:104-11.

Objective	Result/conclusion
To describe decision making and the decision support needs of parents, physicians, and nurses regarding life support decisions made over time prenatally and postnatally for extremely premature infants	Most parents wanted a model of shared decision making and perceived that they were informed and involved in making decisions. Parents felt that to be involved in decision making they needed information and recommendations from physicians. Parents also stressed the importance of encouragement and hope. In contrast, physicians informed parents but most physicians felt that parents were the decision makers. Physicians used parameters to offer options or involve parents in decisions and became very directive at certain gestational ages. Nurses reported that they believed that parents needed information from the physician first, then they would reinforce information
To understand mothers' and counselors' perceptions of their roles in decision-making about resuscitation of extremely premature infants at delivery and to assess mothers' and counselors' satisfaction with the counseling and decision-making process	The decision-making process in this study conforms most closely to a model of informed assent. Mothers may have been satisfied with this type of counseling because they felt informed and included in the decision-making process. Physicians and nurses need to elicit mothers' preferences to incorporate them into the treatment plan, as counseling about the resuscitation of extremely premature infants at delivery is considered directive by mothers even when it is not intended to be directive
To assess outcome of a decision-aid to counsel parents facing premature delivery	Participants found the cards useful and easy to understand. The level of knowledge improved after counseling both for "experienced" parents and "naïve" parents

60 Guillén U, Suh S, Munson D, Posencheg M, Truitt E, Zupancic JA, et al. Development and pretesting of a decision-aid to use when counseling parents facing imminent extreme prematur delivery. *J Pediatr* 2012;160:382-7.

Table 3: Continued

First author et al (year)	Journal	Design	Country
Kavanaugh et al (2015)[61]	*Palliat Support Care*	Interview	USA
Guillén et al (2016)[62]	J Perinatol	Mixed methods	USA
Kett et al (2016)[63]	J Clin Neonatol	Randomized controlled trial	USA
Kaempf et al (2009)[64]	Pediatrics	Nonrandomized controlled trial	USA

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[61] Kavanaugh K, Roscigno CI, Swanson KM, Savage TA, Kimura RE, Kilpatrick SJ. Perinatal palliative care: parent perceptions of caring in interactions surrounding counseling for risk of delivering an extremely premature infant. *Palliat Support Care* 2015;13:145-55.

[62] Guillén U, Suh S, Wang E, Stickelman V, Kirpalani H. Development of a video decision aid to inform parents on potential outcomes of extreme prematurity. *J Perinatol* 2016;36:939-43.

Objective	Result/conclusion
When infants are at risk of being born at a very premature gestation (22-25 weeks), parents face important life-support decisions because of the high mortality for such infants. Concurrently, providers are challenged with providing parents a supportive environment within which to make these decisions. Practice guidelines for medical care of these infants and the principles of perinatal palliative care for families can be resources for providers, but there is limited research to bridge these medical and humanistic approaches to infant and family care. The purpose of this article is to describe how parents at risk of delivering their infant prior to 26 weeks gestation interpreted the quality of their interpersonal interactions with healthcare providers	Parents' expectations for caring included: (a) respecting parents and believing in their capacity to make the best decisions for their family (maintaining belief); (b) understanding parents' experiences and their continued need to protect their infant (knowing); (c) physically and emotionally engaging with the parents (being with); (d) providing unbiased information describing all possibilities (enabling); and (e) helping parents navigate the system and creating a therapeutic environment for them in which to make decisions (doing for)
The objective of the study is to develop and validate a video-based parental decision aid about the outcomes of extremely premature infants	A short video showing the range of outcomes of extreme prematurity has been produced. It is well accepted and does not increase levels of anxiety as measured by the STAI. This video may be a useful and non-stress-inducing aid at the time of counseling parents facing extreme prematurity
To assess whether a written information provided after the prenatal consultation could improve recall and satisfaction	The two groups did not differ in factual recall (within 72h) of satisfaction with the prenatal consultation
To assess the outcome of consensus medical staff guidelines for counseling woman at risk of premature birth	The woman felt comfortable asking questions. About 60% of the mothers mentioned the written guidelines as the most useful information given to them

63 Kett J, Mohamed M, Bathgate S, Larsen J, Aly H. Written information may not improve factual recall after verbal counseling of mothers in premature labor – a randomized controlled trial. *J Clin Neonatol* 2016;5:39-45.

64 Kaempf JW, Tomlinson MW, Campbell B, Perguson L, Stewart VT. Counseling pregnant women who may deliver extremely premature infants: medical care guidelines, family choices, and neonatal outcomes. *Pediatrics* 2009;123:1509-15.

Table 3: Continued

First author et al (year)	Journal	Design	Country
Kavanaugh et al (2014)[65]	Neonatal Netw	Interview	USA
Kakkilaya et al (2011)[66]	Pediatrics	Randomized controlled trial	USA
Muthusamy et al (2012)[67]	Pediatrics	Randomized controlled trial	USA
Haward et al (2012)[68]	Pediatrics	Randomized controlled trial	USA
Edmonds et al (2014)[69]	Simul Healthc	Randomized controlled trial	USA
Geurtzen et al (2014)[70]	Simul Healthc	Nonrandomized controlled trial	USA, The Netherlands

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[65] Kavanaugh K, Nantais-Smith LM, Savage T, Schim SM, Natarajan G. Extended family support for parents faced with life-support decision for extremely premature infants. *Neonatal Netw* 2014;33:255-62.

[66] Kakkilaya V, Groome LJ, Platt D, Kurepa D, Pramanik A, Caldito G, et al. Use of a visual aid to improve counseling at the threshold of viability. *Pediatrics* 2011;128:e1511-9.

[67] Muthusamy AD, Leuthner S, Gaebler-Uhing C, Hoffmann RG, Li SH, Basir MA. Supplemental written information improves prenatal counseling: a randomized trial. *Pediatrics* 2012;129:e1269-74.

Objective	Result/conclusion
To outline parents' descriptions of extended family involvement and support surrounding decision making for their extremely preterm infant	Most parents did not seek advice from family members for life-support decisions made prenatally. Instead, parents made the decision as a couple with their physician without seeking family input. Family members provided certain types of support: emotional support, advice and information, prayer, and instrumental help such as child care. Most parents described at least one way their family supported them. For postnatal and end-of-life decisions, parents were more likely to seek advice from extended family in addition to the other forms of support
To assess outcome of a visual aid to counsel parents facing premature delivery	Women counseled with visual aid recalled more short-term problems, more long-term disability, and longer NICU stay than controls. Attitudes toward resuscitation did not change after counseling in either group
To assess the effect of providing written information during counseling	Written information improved knowledge of long-term problems and numerical outcome data, and it also decreased anxiety
To examine whether choices between comfort care and intensive care are affected by the details and the order of presentation	Order had no effect on final choice. Participants were significantly less likely to choose comfort care if they were highly religious or values preservation of life over quality of life
To assess the feasibility of simulation to test the effect of maternal race and insurance status on shared decision-making in periviable counseling	Information regarding diagnosis and prognosis was heavily emphasized, while attempts to elicit goals and values were often lacking. Shared decision-making occurs differentially based on patients' race and insurer
To compare the contents and styles of counseling as delivered by subjects from two cultural backgrounds in a highly standardized scenario	American and Dutch neonatologists diverged in the discussed and emphasized options for immediate care in the delivery room

68 Haward MF, John LK, Lorenz JM, Fischhoff B. Effects of description of options on parental perinatal decision-making. *Pediatrics* 2012;129:891-902.

69 Edmonds BM, Mckenzie F, Fadel WF, Matthias MS, Salyers MP, Barnato AE, et al. Using Simulation to Assess the Influence of Race and Insurer on Shared Decision Making in Periviable Counseling. *Simul Healthc* 2012;9:353–9.

70 Geurtzen R, Hogeveen M, Rajani AK, Chitkara R, Antonius T, van Heijst A, et al. Using simulation to study difficult clinical issues: prenatal counseling at the threshold of viability across American and Dutch cultures. *Simul Healthc* 2014;9:167-73.

Table 4 Overview of the number of included articles than mention the identified characteristics

Characteristic	Number of articles
Parental values	N=37
Uncertainty	N=30
Shared decision-making	N=28
Emotions	N=26
Personalization	N=24
Quality of life	N=22
Psychosocial factors	N=22
Personalization	N=24
Hope	N=19
Physician bias	N=19
Religion	N=16
Parent physician relationship	N=15
Anxiety	N=11
Spirituality	N=10

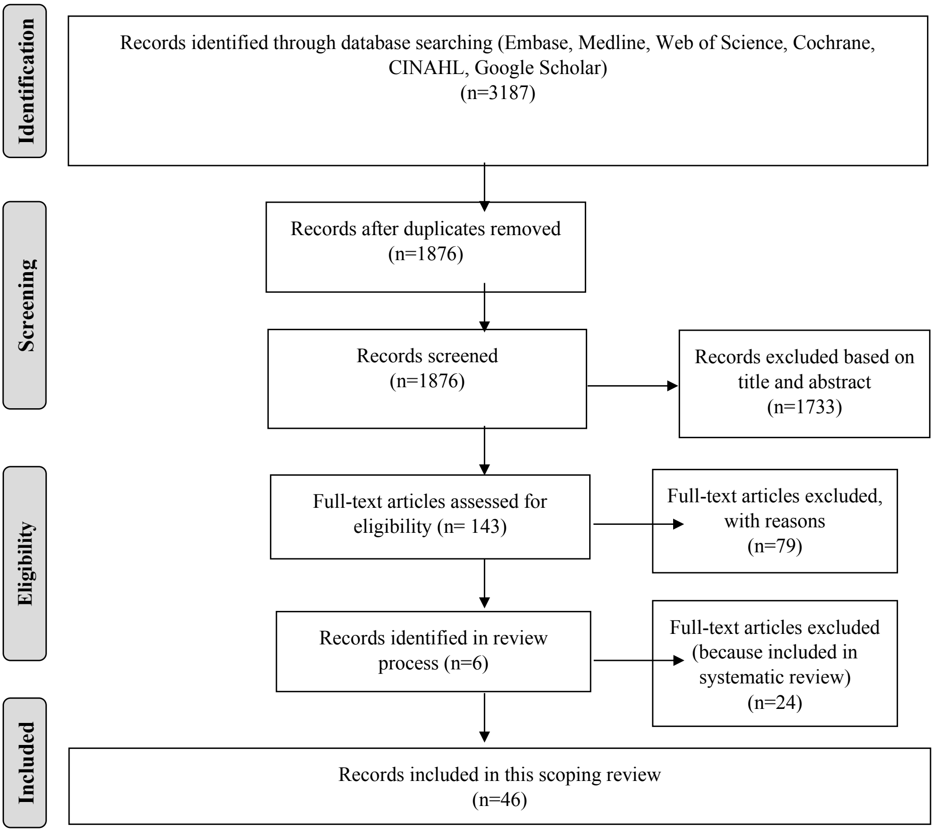

Figure 1 PRISMA flow diagram

PART TWO

EMPIRICAL RESEARCH


3

VOICES OF EXPERIENCE: INSIGHTS FROM PARENTS ON PERIVIABILITY GUIDELINES AND PERSONALIZATION

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To be submitted

Introduction

When an infant is born at the limit of viability, a critical decision must be made regarding the provision of intensive care or palliative care. Periviability guidelines serve as a framework for making these decisions. In the Netherlands, the current periviability guideline, established in 2010, primarily considers gestational age (GA) and sets a lower treatment limit of 24+0/7 weeks. (1) However, within the GA range of 24 to 26 weeks, a 'grey zone' exists where shared decision-making between parents and caregivers is recommended. (2)

Guidelines for treatment at the limit of viability vary significantly across countries (3), with many adopting a lower treatment limit than 24 weeks or considering multiple prognostic factors instead of relying solely on GA (4,5). For example, the British and Canadian guidelines for periviability care incorporate additional prognostic factors such as birth weight, sex, and the administration of corticosteroids. (4,5) And while countries like Canada and Spain provide intensive care from 23 weeks GA, Sweden and Japan offer intensive care from 22 weeks GA. (5-8) While there is a considerable amount of research available on treatment limits and resuscitation involving healthcare professionals (9,10), the literature currently lacks research specifically focusing on this topic from the perspective of parents.

Recent literature on the care and guidelines for extreme prematurity has emphasized an emerging trend towards personalization or individualization at the threshold of viability. (11,12) Generally, personalization is defined as adapting interventions, communications, and opportunities to meet parents' unique needs, moving away from a uniform approach. (13) Periviability personalization, however, may encompass different dimensions of extreme preterm birth. There is a lack of systematic exploration of personalization in the context of extreme preterm birth, and research focusing on personalization with parents is limited.

This qualitative research aims to explore parental perspectives regarding periviability guidelines and personalization. The research objectives encompass understanding whether experienced parents perceive a guideline as necessary, examining the preferred type of periviability guideline preferred, and exploring parental perspectives on and experiences with personalization at the limit of viability. By gaining insights into these areas, this study seeks to contribute to the ongoing discourse on optimizing periviability counseling and supporting parents in their decision-making process.

Methods

Study design and setting

This study is part of the Dutch research project called Towards INdividualized care for the Youngest (TINY), led by researchers from three level III-IV perinatal centers in the Netherlands (Erasmus MC, Rotterdam; LUMC, Leiden; and Radboudumc, Nijmegen). The research topics of TINY include periviability guidelines, personalization at the limit of viability, and values in decision-making for extreme premature birth. The TINY project encompasses quantitative research with healthcare professionals (TINY) (14,15), focus group interviews with adults born prematurely (TINY-1) (16), and individual interviews with experienced parents (TINY-2).

This paper focuses on the results of TINY-2 on guidelines and personalization. The manuscript followed the COnsolidated criteria for REporting Qualitative research (COREQ) checklist to report methods and results. (17) Ethical approval was obtained from the Medical Ethics Committee Leiden-Den Haag-Delft, the Netherlands, on November 4, 2021.

A semi-structured interview guide was developed, consisting of two sections. Section I explored the participants' perceptions of guidelines, their views on the necessity of guidelines, and their preferences for different types of guidelines: no guideline, GA-based guideline, GA-based-plus guideline, or prognosis-based guideline. For an explanation of these types of guidelines, see Table 1.

PowerPoint slides were used during the interviews to explain the different types of guidelines to the participants.

In section II of the interview, the study focused on examining the participants' perception of personalization and its connection to guidelines. The objective was to gain insights into how personalization is understood and should be implemented in the context of extreme premature birth. The study aimed to explore the various understandings and interpretations of the term among the participants by utilizing open-ended and exploratory questions. Rather than providing a specific definition or framework, we encouraged participants to share their perspectives on what personalization could mean, how it is meaningful to them, and its potential relevance to extreme premature birth. This approach aimed to encompass the wide range of meanings and interpretations associated with personalization.

Study participants

As part of the TINY studies, a database was created in Castor to include parents who had experienced a threatening or actual extremely premature birth and expressed interest in participating in research on this topic. The database facilitated purposive sampling to select participants for our research group. Recruitment for this study involved various channels, including the Dutch patient organization Care4Neo (for parents of extremely preterm infants and adults born extremely preterm), the Dutch patient organization Stille Levens (for parents who have lost their child), physicians' networks, clinical contacts, and the social media channels of the participating hospitals and researchers.

To be included in the aforementioned database, participants had to meet one of two criteria: (a) they needed to be parents of extremely premature infants born between 23 and 26 weeks of gestation after the 2010 guideline revision in the Netherlands, or (b) they should be parents who had experienced an imminent extreme premature birth between 2010 and the present, with a gestational age between 23 and 26 weeks, but did not deliver prematurely. The inclusion process involved interested parents expressing their interest via email, after which they were added to the database. Subsequently, all parents in the database were asked to complete a brief online questionnaire to provide demographic information.

For the TINY-2 study, purposive sampling was employed to ensure a diverse range of participants. Our goal was to select participants who exhibited variation in terms of treatment decisions, treating hospitals, infant outcomes, socioeconomic backgrounds, and whether they had a singleton or multiple birth. Parents in the database were approached based on the gathered information, and their consent to participate in the TINY-2 study was obtained. Upon obtaining consent, interviews were scheduled with the participating parents.

Data collection

The interviews for this study were conducted in three different settings, depending on the participants' preferences: the participants' homes, the hospital, or online using Microsoft Teams. Two researchers, LP (with a background in philosophy and bioethics) and AB (with a background in medicine), conducted the interviews. Prior to the interviews, participants were asked to provide both written and oral informed consent. The interviews were recorded using a digital recorder and had an average duration of approximately 60 minutes each. To ensure accurate documentation, a professional transcription service was employed to transcribe the recordings verbatim.

Data analysis

Prior to the analysis, two researchers, LP and AB, collaborated to develop an initial codebook. The interviews were then coded and independently analyzed by LP and AB using a thematic content analysis approach, following the guidelines proposed by Braun and Clarke. (18) This approach involved a systematic process that included becoming familiar with the data, generating initial codes, identifying patterns and themes within the data, reviewing and refining themes, updating the codebook, and finally, defining and naming the themes.

Throughout the analysis, LP and AB conducted multiple iterations of reviewing and adjusting the codebook and analysis until a consensus was reached. In cases of disagreements, discussions involving JV and RG were held to resolve them. In the results section, each quote is accompanied by a number indicating the interview from which it was derived.

Results

This study involved conducting nineteen semi-structured qualitative interviews in the Netherlands between September 2022 and April 2023. The participants were parents who had experienced extreme premature births or faced the threat of extreme premature births between 23+5 and 26+2 weeks of gestation. Out of the nineteen interviews, twelve involved only the mother, while seven interviews included both parents. Additionally, seven parents had twins. Among the participants, four parents opted for palliative care, while fifteen parents chose intensive care resulting in the survival of the infant in nine cases. The interviews were conducted in the participants' homes (n=11), in the hospital (n=2), and online via Microsoft Teams (n=6). For further demographic information about the participants, please refer to Table 2.

In the subsequent sections, we delve into the parental perspectives regarding the necessity of a guideline, their preferred type of guideline, and their views on periviability personalization.

Do we need a periviability guideline?

The overwhelming consensus among the study participants was that a periviability guideline is necessary. The main argument put forth by the majority of parents was that guidelines offer crucial support to both healthcare professionals and parents in making difficult decisions at the limit of viability. Participants also expressed that guidelines serve a protective function. They emphasized that in the absence of a guideline, parents might be inclined to pursue aggressive treatment regardless of the infant's gestational age. Concerns were raised about the potential dangers of making decisions based solely on parental instincts without considering the long-term perspectives for the child.

"*Without a guideline, I think the danger would be that people would be too quick to say… 'treat anyway', when it's really not wise to do so.*" [6]

> *"If you don't have guidelines and only look as a parent, I think you would always want to go for it, but you would overlook many important future perspectives for the child."* [12]

Additional reasons provided for the necessity of a guideline included minimizing the chances of medical errors, acknowledging the practicality of having a guideline for physicians, facilitating physician-parent communication by providing a common reference point, and preventing an imbalance of decision-making power in favor of physicians. The need for uniformity in health care professionals' decision-making processes was also emphasized.

Guideline preferences

Most of the participants expressed criticism of the current Dutch guideline, which solely relies on GA. This type of guideline was described as 'too black and white' and 'short-sighted'. Parents shared anecdotes illustrating that GA is an estimated factor and may not always be accurate in their specific situations.

> *"There was much discussion about the estimated gestational age in my situation… It would still have been around 24 or 25 weeks, but then I think: what if we had counted it differently, it might have been 24+6."* [7]

Parents were also well-informed about stories of children born before 24 weeks GA who have a good quality of life, and they referred to these stories in their criticism of GA-based guidelines.

> *"You can't make a treatment decision based solely on gestational age. There are success stories these days of babies who were born just under the current limit anyway."* [2]

Participants also frequently mentioned the variation in treatment limits across different countries. They were aware that neighboring countries had lower treatment limits, and some found it strange that a drive to Belgium or Germany would result in their infant receiving intensive care treatment, while in the Netherlands, she might not be eligible for treatment. As a result, some parents expressed a preference for 'European guidelines'.

> *"When I drive five kilometers, they receive treatment. I think you must have a good story to go with that: why can they offer care at 23 weeks in Belgium and Germany? And what makes the Dutch policy different? What are the underlying reasons?"* [10]

During one interview, parents shared their experience of their baby being born extremely prematurely while they were on vacation in a country with a lower treatment limit than the Netherlands. They mentioned that if they had been in the Netherlands at that time, their child would not have survived due to the treatment limit in place.

> *"It's bizarre, such big differences... So we made a plan for ourselves when I was pregnant with our second child: if this situation arises again ... we will drive to [country X]. That was the idea."* [6]

According to the parents interviewed, the strict '24-week limit' also creates a narrative that implies 'smooth progress' once the infant reaches this milestone. While some appreciate this narrative and find it motivating, others express concerns that it may be detrimental because it sets unrealistic expectations and overlooks individual differences in prognosis and outcomes.

> *"I really struggle with, for example, websites about gestational ages that state: yay, you've reached 24 weeks! Like: if he's born now, it's all going to be okay..."* [1]

According to most parents interviewed, there is a strong desire for the periviability guideline to consider multiple prognostic factors. The GA-based-plus guideline, which goes beyond gestational age and considers individualized factors, was particularly favored. Parents appreciated the focus on their child's specific chances and the factors involved, rather than relying solely on a strict number or percentage.

> *"I have the idea that with this, gestational age-based-plus, there is no strict number or percentage attached to it, but more attention is given to the child: what are the chances for that child and which factors are important here? This really appeals to me."* [6]

> *"Because you still have the support of a guideline, but you don't make it so black and white by only looking at gestational age."* [18]

There was somewhat more hesitation regarding a prognosis-based guideline that relied on the calculated prognosis as the determining factor for treatment. Parents expressed concerns about reducing the decision to a single numerical percentage, as they believed it failed to capture the complexity of the situation and the uniqueness of each case. They emphasized the importance of discussing the prognosis with parents but questioned the idea of offering intensive care treatment only to infants with a prognosis above a certain threshold.

> *"I think, ultimately, this is a human decision. So to let an algorithm calculate it in a cold manner, I find it a bit simplistic."* [10]

> *"Making a complete prognosis: I am also very much into data and such. In that regard, I think it might actually be helpful, but at the same time, I'm not sure - because it is, of course, very much an emotional thing - whether it would be correct to attach a specific percentage to it."* [18]

Parents also shared the view that an abundance of information and prognostic factors might not necessarily simplify the decision-making process. In fact, it could potentially make it more challenging, leading to doubts and regrets afterward. Some parents stressed the need to respect the preferences of those who may not want to be overwhelmed with detailed prognostic information.

> *"If you have to decide based on multiple factors of which you don't really know much yourself, … it might become even more difficult for yourself afterwards. Because then you think: …maybe I should have read more about that. … I think the more factors there are, the more you have to think about it and discuss it."* [1]

During the interviews, fathers seem to be more inclined than mothers to mention statistics and numbers, emphasizing their significance in decision-making.

Furthermore, many anecdotes were shared highlighting the importance of sensible communication about prognostic factors and prognoses.

> *"'If they had been girls, they would have had a better chance'. Well… We don't have girls, but these boys will make it too!"* [14]

> *"I think that, for example, discussing socioeconomic status with parents during such a challenging time might make the conversation even more difficult. It could potentially add another layer of stress, especially for parents who come from less privileged backgrounds. Hearing that socioeconomic status could also have an impact may not be very helpful in that moment."* [18]

In general, the majority of parents expressed a preference for a GA-based-plus guideline. Some parents mentioned that they felt they *had* already received counseling aligned with the GA-based-plus approach, despite the current Dutch guideline in place.

Personalization
To our open-ended question about personalization, parents provided the following descriptions and interpretations: 'considering the story behind the person,' 'being seen and heard,' 'engaging in dialogue with parents,' 'being taken seriously,' 'providing support and facilities to cope with the situation,' 'being humane,' 'taking the time,' 'thinking together with parents,' 'showing empathy,' 'focusing on parental needs,' 'adapting to the situation,' 'recognizing the uniqueness of each situation,' 'providing one-on-one interactions,' and 'involving parents in the care process.'

During the interviews, parents shared various examples of personalization, such as offering opportunities for exercise to distract from the situation, placing remembrance cards on the incubator if the baby had lost a sibling, or celebrating gestational age milestones with the nurses.

Parents primarily associated personalization with building relationships with healthcare professionals and having empathetic and sensitive communication. They shared anecdotes about 'addressing doctors by their first names', 'receiving information in everyday language', and 'making decisions as a team'. They emphasized that personalization is not just about the content of the communication, but also about the way it is conveyed. In the words of the parents:

> *"If a bomb of information is thrown at you, and it explodes, you may have all the information, but it may not be the best way to deliver it."* [2]
>
> *"You may be skilled at giving injections, but having a conversation is also part of it."* [4]
>
> *"There's a difference between the compassionate communication of the nursing staff and that one doctor telling us, '[Your son] is making a mess of things' … There's not much gentleness in that."* [10]

When discussing personalization in relation to guidelines, parents frequently expressed concerns about the challenges of incorporating personalization within a guideline that has a rigid cut-off limit for treatment, such as a GA-based guideline.

Discussion

This interview study aimed to explore parental perspectives on periviability guidelines and personalization. Several notable findings emerged from the analysis.

Firstly, it was found that all participants unanimously agreed on the necessity of having a guideline in place to provide decision-making support and to act as a safeguard against the natural instinct to prioritize 'saving' their child. These findings align with the results obtained from the TINY and TINY-1 studies, which focused on the perspectives of adults who were born extremely premature as well as healthcare professionals. (14-16) The adults born prematurely believed that guidelines are crucial to prevent arbitrary treatment decisions and counter physician bias. Additionally, only 13.4 percent of healthcare professionals supported the absence of guidelines, indicating a widespread recognition among Dutch stakeholders involved in extreme premature birth that guidelines can offer support and protection.

Secondly, none of the participants in this study agreed with the utilization of a GA-based guideline, which is currently in use in the Netherlands. This finding is consistent with the earlier TINY studies conducted on the same topic. Furthermore, this study revealed that parents recognized the significance of considering multiple prognostic factors when making periviability decisions. However, they did not necessarily believe that increasing the number of factors would simplify the decision-making process. In fact, an abundance of complex information presented within a short timeframe could further complicate the decision-making process. Recent studies also support this conclusion, suggesting that additional information may complicate decisions for parents, particularly when provided during the challenging and emotionally charged period of imminent extreme premature birth. (19,20)

It is worth noting that a 2017 study involving Dutch physicians expressed similar sentiments regarding the challenges of decision-making and the need for personalization in cases of extreme premature birth. (21) These physicians acknowledged the difficulties in involving parents in the decision-making process, particularly when there is an overload of information. They emphasized the importance of personalizing the information provided, as not all parents can effectively handle or process a large amount of information, even though various aspects of the decision may be crucial.

Thirdly, in terms of personalization at the limit of viability, our findings indicate that parents primarily associate it with the quality of relationships and communication between parents and healthcare professionals. Parents mainly emphasized the importance of feeling heard and seen. These findings align with existing literature on prenatal counseling for extreme prematurity, highlighting the significance of sensible communication, individualizing the approach to parental circumstances, and tailoring information based on parental preferences. (12,13,22,23) The examples shared by our participants underscored the value parents place on small gestures that demonstrate empathy and sensitivity. These examples are reminiscent of what has been referred to as ‘Mangomoments’ in a 2018 Lancet article, which describes the profound impact of unexpected, small acts or gestures on the care experience for patients, families, residents, and healthcare professionals. (24) “These micro-moments of positive resonance can foster stronger connections and contribute to the fabric of our communities,” the authors explain.

Based on the findings of this study, it can be concluded that personalization and the avoidance of a one-size-fits-all approach are highly valued in the context of periviability decision-making. The study highlights the importance of recognizing and addressing the unique needs and circumstances of individual parents, rather than reducing them to mere statistical figures. It is crucial to ensure that conversations with parents are tailored to their specific situation, characterized by empathy and a focus on their individual needs. However, these results should not be interpreted as a dismissal of research on prognostic factors and individualized predictions. Rather, they emphasize the need for a thoughtful and ethical approach in utilizing prognostic knowledge within the framework of prenatal counseling. While an excessive reliance on numerical data may not be beneficial during conversations with parents, individualized predictions can still provide valuable information and help parents prepare for the potential outcomes they may face.

Moving forward, it is essential to focus on effectively incorporating and communicating individualized predictions within the context of prenatal counseling. This requires a balanced approach that recognizes the significance of personalization, while also ensuring that parents receive the necessary information and support to make informed decisions regarding periviability. Additionally, it is important to consider the ethical implications of certain prognostic factors in predictions, such as socioeconomic status and ethnicity, which may raise ethical concerns and require careful consideration in the decision-making process.

Generally, this study provides further evidence of the critical role that effective communication skills play in periviability decision-making for healthcare professionals. A recent study has revealed that many parents do not understand the language commonly used during prenatal prematurity counseling. (25) Moreover, other recent studies emphasize the significance of enhancing training programs to equip healthcare professionals with the necessary skills for effective communication during periviability discussions. (26,27) The findings of our study highlight the significance of addressing training gaps to enhance the quality of care and support offered to parents making periviability decisions, particularly in the domain of communication. It is essential to recognize that effective communication extends beyond the content of the information shared but also encompasses the manner in which it is conveyed.

Strengths and limitations

This study possesses several notable strengths. Firstly, it emphasizes the crucial inclusion of parents' perspectives in the development and implementation of periviability guidelines. To the best of our knowledge, this the first qualitative interview study with parents on this topic. The use of purposive sampling is another strength of this study. By purposefully selecting participants with diverse backgrounds, including variations in hospitals, family backgrounds, educational levels, and geographic regions within the Netherlands, the study successfully captures a wide range of parental perspectives. This diversity enhances the generalizability and applicability of the study's findings, allowing for a more comprehensive representation of parental viewpoints. Furthermore, the interdisciplinary nature of the research team contributes to the study's strength. The involvement of both medical and non-medical professionals in the design and execution of the study brings a comprehensive and well-rounded approach. The team's diverse expertise and viewpoints enrich the study's analysis and interpretation, ensuring a broader understanding of the complex issues surrounding periviability guidelines.

This study is also subject to limitations. First, the findings of this study are specific to the Dutch context, which may limit their generalizability to other countries or healthcare systems. The Dutch periviability guidelines are shaped by the sociocultural context of the country, and therefore, the perspectives and experiences of parents may differ in other cultural or geographical settings. (3,28) Conducting international comparisons would be valuable to gain a broader understanding of periviability guidelines and personalization. Secondly, it is important to acknowledge that despite our efforts to ensure a diverse participant population, we faced challenges in recruiting parents from various religious backgrounds, members of the LGBTQIA+ community, and individuals from non-white ethnicities. Despite our best attempts to reach out to these communities and provide an inclusive environment, their representation in the study was limited. Future research should make additional efforts to include a more diverse sample of participants to ensure a comprehensive understanding of periviability decision-making across various cultural and ethnic groups. By acknowledging these limitations, we recognize the contextual boundaries of the study and the need for further research to explore periviability decision-making in different cultural and international contexts, as well as the importance of inclusivity in participant recruitment.

Conclusion

This study sought to understand the perspectives of experienced parents regarding periviability guidelines and personalization. The findings highlight the importance of having a guideline in place to provide decision-making support and to address the natural urge of parents to save their child. The majority of participants expressed a preference for a guideline that consider multiple prognostic factors. Personalization was defined by participants as being seen and heard, emphasizing the significance of effective communication and building relationships with healthcare professionals. This study emphasizes the pivotal role of healthcare professionals in developing empathetic and sensitive communication skills to deliver high-quality personalized care for families in periviability situations.

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Table 1 Explanation of the different types of guidelines

No guideline	Treatment decisions are made on a case-by-case basis without a specific cut-off limit for offering intensive care treatment
Gestational age-based guideline	Relies solely on GA to determine the cut-off limit for providing intensive care treatment
Gestational age-based-plus guideline	Considers GA along with other prognostic factors like birth weight or sex to fine-tune individual prognosis. This type of guideline allows for a less strict cut-off point for offering intensive care treatment
Prognosis-based guideline	Incorporates multiple prognostic factors and utilizes a prediction model to calculate the prognostic influences. This type of guideline sets a cut-off point to determine whether intensive care treatment should be offered. Currently, no countries are known to employ a prognosis-based guideline. Attempts have been made, however, establish a prognostic cut-off for treatment. Several tools are currently available for estimating prognosis.

Table 2 Demographic information of the participants

Participant characteristics	**N = 19**
Place of interview	
Home	11
Hospital	2
Online	6
Participants	
Mother	12
Mother and father	7
Year of (first) experience with extreme premature birth	
2009-2015	7
2016-2020	8
2021-2023	4
Gestational age at birth[1]	
<24 weeks	1
$24^{+0/7}$ – $24^{+6/7}$	7
$25^{+0/7}$ – $25^{+6/7}$	5
>26 weeks	6
Multiple birth	
Yes	7
No	12
Treatment decision	
Active care	15
Palliative care	4
Survival	
Infant survived	9
Multiple birth; one of the infants survived	4
Infant did not survive	6
Religion	
No religion	16
Christian	3

[1] The study involved parents who had encountered either extreme premature birth or the imminent risk of extreme premature births occurring between 23+5 and 26+2 weeks of gestation. The table indicates the gestational age at which the infants were born.


4

ADULTS BORN PREMATURELY PREFER A PERIVIABILITY GUIDELINE THAT CONSIDERS MULTIPLE PROGNOSTIC FACTORS BEYOND GESTATIONAL AGE

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Abstract

Aim: The aim of the study was to explore the perspectives of adults born prematurely on guidelines for management at extreme premature birth and personalisation at the limit of viability.

Methods: We conducted four 2-h online focus group interviews in the Netherlands.

Results: Twenty-three participants born prematurely were included in this study, ranging in age from 19 to 56 years and representing a variety of health outcomes. Participants shared their perspectives on different types of guidelines for managing extremely premature birth. They agreed that a guideline was necessary to prevent arbitrary treatment decisions and to avoid physician bias. All participants favoured a guideline that is based upon multiple prognostic factors beyond gestational age. They emphasised the importance of discretion, regardless of the type of guideline used. Discussions centred mainly on the heterogeneity of value judgements about outcomes after extreme premature birth. Participants defined personalisation as 'not just looking at numbers and statistics'. They associated personalisation mainly with information provision and decision-making. Participants stressed the importance of involving families in decision-making and taking their care needs seriously.

Conclusion: Adults born prematurely prefer a periviability guideline that considers multiple prognostic factors and allows for discretion.

Introduction

Guidelines for managing threatening extremely premature birth exhibit significant variations across different countries, influenced by factors such as available resources, infrastructure, and cultural and societal values (1,2). This variation is not only observed among high- and low-income countries but also among high-income countries, and even within countries or hospitals (1,3-5). Types of periviability guidelines vary internationally (6-10). Some guidelines recommend that the initiation of intensive care treatment should only be offered to infants born at an advanced gestational age (GA) (6), while others take into account multiple prognostic factors when making this decision (7-10). In addition, some guidelines provide a zone of parental discretion, allowing parents to make the decision (6-10), while others have a uniformly active approach for births at the limit of viability (11,12).

In the Netherlands, the current guideline for management after extremely premature birth dates back to 2010 and is based solely on GA (6). The limit for offering intensive care is 24+0/7 weeks GA. Between 24 and 26 weeks GA, there is a grey zone of significant prognostic uncertainty: based on the valuation of evidence on long-term outcomes, no option can be considered the 'best' choice. In the grey zone, the Dutch guideline advises shared decision-making (SDM) between parents and healthcare professionals (HCPs). Currently, the periviability guideline is under revision, which may result in a lower treatment threshold. This practice is already common in other countries. For instance, in Spain and Belgium, the limit for offering intensive care is 23 weeks GA (7,13), while in Japan and Sweden, the limit is 22 weeks GA (11,12,14-16).

The existing literature on periviability guidelines, care, and counselling emphasizes the importance of personalisation at the limit of viability (17-21). Personalisation can be applied to many aspects, such as the individual prognosis, the provision of information, facilitating shared decision-making (SDM), building relationships, determining the care process at birth (22). Regarding guidelines, personalisation is related mainly to making decisions based on factors beyond just GA, aiming to individualize the infant's prognosis (10,21). There is agreement in the literature that personalisation is crucial for providing high-quality care in the case of extreme premature birth (23).

Although periviability guidelines and decisions about management at birth significantly impact the lives of individuals born extremely premature, there is currently a lack of information available on their perspectives regarding this matter. The aim of this study is to gain an understanding of their perspectives.

Methods

Study design

This focus group study elicited perspectives of adults born between 24 and 30 weeks GA on periviability guidelines and personalisation. Four focus group sessions were conducted online between January and February 2022, utilizing Microsoft Teams as a measure to comply with COVID-19 pandemic protocols. This study is part of the Dutch study: Towards INdividualized care for the Youngest (TINY), initiated by researchers from three level III-IV perinatal centres in the Netherlands (Erasmus MC, Rotterdam; LUMC, Leiden and Radboudumc, Nijmegen). TINY consists of quantitative research with HCPs (TINY), focus groups interviews with adults born prematurely (TINY-1), and individual interviews with experienced parents (TINY-2). The topics of TINY are periviability guidelines, personalisation at the limit of viability, and values in decision-making for extreme premature birth.

This paper presents the results of TINY-1 on guidelines and personalisation. The COnsolidated criteria for REporting Qualitative research (COREQ) checklist was used to report methods and results (online supplemental material, Appendix 1) (24). Ethical approval was obtained from the Medical Ethics Committee Leiden-Den Haag-Delft, the Netherlands, 4 November 2021.

A semi-structured interview guide was developed (online supplemental material, Appendix 2) and consisted of two sections. Section I was on the participants' perceptions of guidelines, whether guidelines are necessary, and their guideline preference: no guideline, a GA-based guideline, a GA-based-plus guideline or a prognosis-based guideline.

If there is no guideline, treatment decisions are made on a case-by-case basis, looking at each case individually; there is no official cut-off limit for offering intensive care treatment. A GA-based guideline is based solely on GA, which means the cut-off limit for offering intensive care treatment is a certain weeks GA. An example is the current Dutch guideline (6). Another guideline option is a GA-based-plus guideline. This type of guideline takes into consideration GA but *also* other prognostic factors like birth weight or sex. So, GA is still an important prognostic factor, but other factors are used to fine-tune an individual prognosis. This means that there is a less strict cut-off point for offering intensive care treatment than in GA-based guidelines. This guideline may recommend providing intensive care to infants born at a GA later than a certain number of weeks but *only* if all other prognostic factors are exceptionally favourable, for instance, if an infant is born at 23 weeks GA but has a high birth weight and the mother has received corticosteroids. The British guideline is an example of a GA-based-plus guideline, as it takes into account potentially controllable like location of birth or the administration of antenatal corticosteroids, and non-controllable factors like birth weight or sex (8). A prognosis-based guideline also considers multiple prognostic factors but is based on a calculation of the prognostic influences of these factors, that is, a prediction model. This calculation is used as a cut-off point to determine whether intensive care treatment should be offered: for instance, such a guideline could advice comfort care below a certain percent chance on intact survival, and active care above a certain percent chance for a good outcome. As far as we know, no countries currently use a prognosis-based guideline, but several tools are available to estimate a prognosis (25,26). To learn more about prognosis-based guidelines, please see Table 1 for additional background information.

PowerPoint slides (Online supplemental material, Appendix 3) were utilised to educate the participants on the various types of guidelines and the advantages and disadvantages associated with each type of guideline, drawing upon the existing body of literature. The goal was to enable the participants to form an *informed* opinion about the different types of guidelines.

In section II of the focus group session, the participants' perception of personalisation, and the relation between personalisation and guidelines were explored. We aimed to understand how personalization is perceived and (should be) applied in the context of extreme premature birth by exploring the various meanings and interpretations of the term among our study participants. Our open-ended and exploratory questions in relation to personalization did not provide a specific definition or framework, but rather asked participants to share their perspectives on what it *could* mean, what it means to them and how it might be relevant to extreme premature birth. Our approach aimed to capture the diverse range of meanings and interpretations that personalization can hold.

Study participants

The study comprised twenty-three participants, among whom eighteen identified as female and five as male. Participants' ages were diverse, with one under 20 years old, nine between 21-30 years old, nine between 31-40 years old, three between 41-50 years old, and one between 51-60 years old. Education levels varied, with one participant completing secondary school, four completing secondary vocational education, ten completing higher professional education, and eight completing university education. Most participants had no religious affiliation (n=17), and six reporting to be Christian. Participants were born between 24-30 weeks of gestational age. Regarding the long-term consequences of extreme premature birth, the majority of participants reported (neuro)motor function issues, with eight reporting motor disability. Five participants reported cognitive disability, learning disabilities, or problems at school. Eight participants reported psychosocial issues such as concentration problems or symptoms of autism spectrum disorder. Other consequences included vision or hearing problems, respiratory problems, reduced immunity or susceptibility to infection, easily fatigued, growth restriction, feeding problems, intestinal problems, feeling misunderstood, attachment issues, anxiety disorder/performance anxiety, insecurities, and stimulus processing problems. Participants reported varying numbers of comorbidities. For further information on participant demographics, see Table 2 and Table 3.

Participants were recruited through the Dutch patient organization Care4Neo and the social media channels of the involved hospitals and researchers. Inclusion criteria for this study were age above eighteen years and being born prematurely. Individuals who were interested to participate contacted the researchers via email. The researchers collected demographic and health-related information through an online questionnaire. Participants were divided into focus groups, ensuring diversity in age, gender, and health status. Due to the potential sensitivity of the topic, we used a smaller group size than typically recommended in the literature (32,33). The number of focus groups conducted in this study is consistent with the existing literature on focus group methodology (33,34).

All individuals who signed up were included in the study. One participant had to cancel at the last moment due to illness. There was no reimbursement for participation in the study, but a small gathering with food and drinks was organised afterward to thank all participants and provide an opportunity for them to meet each other.

Data collection

One week before the study, an individual online session with a duration of 15 minutes was conducted with each participant (LP, AB) to facilitate general acquaintance, to provide general information about the study, and to answer any questions. During each individual session, identical information was shared, including the number of participants, the structure of the focus groups, the duration, and other relevant details. All participants who took part in the initial encounter agreed to participate in the focus groups. Saturation was reached after four focus groups, so recruitment was stopped at that point.

Two researchers moderated the focus group sessions: one has a background in philosophy and bioethics (LP), and one has a background in medicine (AB). A third researcher (either EV, maternal-fetal medicine specialist or RG, neonatologist) was also present during the sessions but did not participate in the discussion and kept their camera turned off. Their presence was for the purpose of answering any (clinical) questions from the participants that the researchers were unable to answer. While research suggests that online focus groups may pose specific challenges, such as the loss of subtle visual cues, they also offer advantages, such as greater and easier access to a diverse pool of research participants (35).

At the start of each focus group session, the participants were provided with information on consent, privacy, and withdrawal. After obtaining written and oral informed consent, the rest of the sessions were recorded using both a digital recorder and Microsoft Teams. The topics for discussion were then introduced to the participants, which included guidelines, personalisation, and values in decision-making.

During the first hour, the participants were asked about their initial ideas on guidelines, without any prior information being provided. They were asked whether a guideline is necessary. Next, PowerPoint slides were shared to explain the four different types of guidelines and their advantages and disadvantages, after which the participants were given the opportunity to discuss them. A closing question was asked to summarize their preferences in this part of the session. In the second part of the focus group sessions, the topic of personalisation was discussed, following the questions in the interview guide.

Each session had a duration of approximately 120 minutes. A professional service was employed to transcribe the recordings verbatim. Individual debriefing meetings were offered to the participants two weeks after the sessions to allow them to reflect on their study experience. A 30-minute meeting was held with 15 participants, led by LP and AB.

Data analysis

Prior to analysis, two researchers (LP, AB) developed an initial codebook (online supplemental material, Appendix 4). The focus group sessions were coded and independently analysed by LP and AB using a thematic content analysis approach as proposed by Braun and Clarke (36-39). This approach involved a systematic process of identifying patterns and themes in the data, familiarizing ourselves with the data, generating initial codes, searching for themes, reviewing and refining themes, defining and naming themes, and finally, producing a report of the themes identified. The codebook and analysis were reviewed and adjusted in multiple rounds until a consensus was reached among LP, AB, EV, and RG. In the results section, each quote is accompanied by a number indicating the focus group session and a letter indicating the participant.

Results

A total of 23 participants took part in four focus groups. Details on their demographic and self-reported clinical information can be found in Table 2 and Table 3.

Do we need a periviability guideline?
All participants agreed that a guideline is necessary, primarily to avoid arbitrariness in providing treatment and to counter physician bias. When describing the absence of a guideline, participants used words such as ‘guesswork’, ‘gambling’ and ‘blurry’.

> *“I’m afraid it will be arbitrary. Doctors will be biased by their own preferences. If a doctor has dealt with three premature babies dying, the next time he or she will be more inclined to tell parents that ‘it will not work out’, while objectively that doesn’t really say anything. It will also be difficult to retrospectively evaluate the decision, or find out how a decision came about. I don’t think that’s desirable.”* (2B)

There were also concerns about the impracticality of HCPs not having any guideline to follow.

> *“Even if there’s no guideline, you still have to base your decision on something. Or will doctors then don’t give any advice at all, will it be fully up to the parents? Or will it differ per doctor, who has the final say in this? Or that in (city X) the doctor says, ‘fine, I’ll try it with those lungs’, but in (city Y) they say, ‘no way, I only have bad experiences with this’. I think it’s nice, in a way, that a doctor has something to hold on to for making decisions.”* (3D)

However, participants stressed the importance of allowing for discretion.

> *"It's a good thing that guidelines exist, because health care needs it and insurance companies need it, but (HCPs) shouldn't hold on to them in a very definitive way. I think they always have to consider whether to go along with it."* (1C)

Guideline preferences

None of the participants expressed a preference for GA-based guidelines, citing their 'narrow focus', and them being 'too rigid'.

> *"I find the GA-based guideline difficult. In my case, I was 27 weeks in my mother's womb, but I was not 27 weeks fully grown… I would indeed include multiple factors."(1D)*

Instead, the participants believed that guidelines relying on multiple prognostic factors would be 'a better starting point for discussion' of the situation, possible outcomes, and future quality of life with parents. It was assumed that such guidelines would leave more room for parental involvement in the decision-making process and encourage more nuanced conversations about long-term outcomes and quality of life.

During discussions about guidelines relying on multiple prognostic factors, however, there were concerns raised about *which* factors should be considered and *how* they should be disclosed to parents. Some participants expressed that factors such as 'sex', 'socioeconomic status', or 'ethnicity' could be stigmatizing, and there was discussion about whether to consider them. Many personal anecdotes were shared during these sessions.

> *"I know from my parents that they were told to 'be glad it's a girl, she'll fight'. My parents found that quite difficult. They knew, however, that it was said with good intentions - but maybe you shouldn't say things like that. Now, 31 years later, my parents are still talking about that. (…) This comment still haunts us so many years later."* (4C)

Critical comments about the discussion of prognostic factors were often focused on the language used rather than the actual predictor itself. During the discussions, participants emphasised the importance of clear communication and counselling about these factors.

> *"I think it's really important that doctors are transparent in counselling about the meaning and weighing of the 'plus'-factors, whatever they are. (…) [GA-based-plus] could be a very flexible type of guideline. But that's why you have to communicate it very well to parents. And educate doctors to be able to do that."* (2C)

Similar concerns were also raised about using an estimated prognosis as a cut-off point for treatment. Participants described prognosis-based guidelines as being 'too black and white', 'unfair to extreme premature infants', and 'giving too much decision-making power to estimated outcomes'. During these discussions, several personal anecdotes were shared about estimated prognoses.

> *"I had 10 % chance of survival and wasn't going to be able to talk. Well, I can talk fine… Of course, I have my issues. (…) But still, a prognosis can turn out very different."* (2D)

The lack of data on long-term outcomes after premature birth was also noted by participants, who highlighted it as an additional challenge for developing prognosis-based guidelines.

> *"If more research like this is done, and more data is collected from adult preemies, … then it may well be that estimated prognoses will be very different."* (2A)

Nonetheless, some participants mentioned that collecting more data would not necessarily result in better or easier decision-making.

> *"I think it's dangerous to state so simply that when more data is collected, better decisions are made. … That's not necessarily true at all. I personally would find it very scary to decide about whether to go for treatment depending entirely on data. Without – if you put it very sharply – leaving room for discussion or nuance or a conversation about preferences."* (2B)

Some participants raised the question of *which* types of prognoses should be considered. On several occasions, a distinction was made between 'medical' and 'non-medical' or 'social' prognoses.

> *"Even if the medical prognosis is that 'your child is going to be severely disabled', within this category there are many degrees. Even if they can say with reasonable certainty, 'we expect that your child will never be able to walk or eat or…', a child can still live a good life, if the parents give good care. I think you should look at the medical prognosis in combination with the social and socioeconomic prognosis."* (1A)

Another great point of discussion that arose in all focus group sessions was the heterogeneity of value judgments that accompany estimated prognoses. As one participant stated,

> *"For example, being able to walk … how does that relate to your happiness and well-being? One person ends up in a wheelchair and accepts it, being super happy, and another person deals with it very differently."* (3E)

Participants also reflected on the context in which a prognosis is valued.

> *"It matters in what kind of society you value a prognosis – to what extent there is inclusion of people with disabilities, for example. … I think it matters in what kind of society a child ends up in."* (3C)

It was difficult for some participants to accept that a prognosis-based guideline uses a cut-off for offering treatment that is based on 'a calculation', 'a mathematical model' or 'statistical calculations'.

> *"How does this work in practice? With a kind of score? Okay, you can breathe on your own: +3. You can't walk: -5. That's problematic."* (3A)

As a result of these concerns, only few participants were in favour of prognosis-based guidelines. However, the importance of discussing prognoses in counselling was emphasised.

> *"Whether the prognosis is important is a very different question than whether you must base the guideline on it."* (1F)

Based on the question round at the end of the discussion in every focus group session, most participants expressed a preference for GA-based-plus guidelines. They described this type of guideline as 'a good mix between physician judgment and parental values' and 'a full-package approach to extremely premature birth'.

Personalisation

Mainly, participants defined personalisation as ‘looking at the human being rather than the numbers’.

> *“Of course it matters how much I weigh when I am born, but that is not who I am. … Personalisation means that it is less about the number and more about the human being.”* (4D)

> *“I do know that I was told, including by my neonatologist, ‘If you had not been a twin, you would not have been treated based on the statistics.’ Then you don’t deliver personalised care either.” (4C)*

They linked personalisation mostly to information provision, SDM, and the relationships between families and HCPs.

> *“Our society is very much ‘you decide, you think along’. But maybe there are also people who, of course, want to be heard and seen, but perhaps don’t have the need to make the decision. It must be a choice whether to participate in the decision. … Also, you can ask people, ‘do you want to know everything or not?’. That’s not a strange question at all.”* (1F)

> *“… you can offer information in different layers. Some people may want to know a lot about the current state of science, while others want much more information about how to make the best choice based on their feelings.”* (1A)

> *“I couldn’t breathe independently, but at some point, when I was off the ventilator, I apparently made quite a loud sound, and a nurse wrote in my diary: “You’re making nice sounds, maybe you have a beautiful voice, maybe you’re musical.” … In the end, I got into music, so for me, that was really personalised care in hindsight. … It was very important for my parents at the time, and now that diary is especially important to me.” (4C)*

For personalisation at the limit of viability, participants noticed the importance of considering the social context. They mentioned, for example, that factors such as care for existing or future siblings and the financial situation of the family should be considered by HCPs when counselling and caring for them.

> *"Also the rather practical things should be personalised, based upon the entire family situation. Do the parents wish to stay near the hospital while their infant is in the NICU? Do they have daycare for siblings? And so on."* (3C)

Participants were convinced of the compatibility of personalisation and guidelines.

> *"A guideline lays a general foundation and then you can individually build the house; how you are going to build that house, you decide and do it together."* (1C)

Discussion

We analysed focus group discussions with 23 participants who were born prematurely to explore their views on periviability guidelines and personalization. Our findings showed that guidelines are seen as necessary to ensure consistent treatment and prevent bias. According to the participants, a periviability guideline should consider various prognostic factors and not have strict cut-off limits for providing intensive care. It should be flexible enough to allow for discretion by physicians and parents.

The participants emphasized that involving parents in the decision-making process is an integral part of personalization at the limit of viability. To achieve this, prognostic factors should be clearly communicated and discussed with parents while considering their preferences regarding the sharing of information. As part of personalization, HCPs should also make an effort to get to know parents, build a relationship with them, and customize their care approach to meet the specific needs of the family.

These findings are interesting in the context of other research on periviability guidelines and prenatal counselling for extreme premature birth. Firstly, while GA-based guidelines have traditionally been used to predict the likelihood of survival and developmental outcomes, recent literature on periviability guidelines suggests that relying solely on GA for making periviability decisions may be (morally) problematic (29,40,41). Secondly, the participants in our study exhibited a sensitivity towards appropriate communication and language use in discussing prognostic information, which is consistent with findings from previous research involving experienced parents (42,43). Finally, the importance of providing personalized information, supporting decision-making, and building relationships in prenatal counselling is well-documented in the literature (44-47).

Janvier et al., for example, concluded that HCPs should aim to identify individual needs and preferences of parents on a case-by-case basis, and provide personalized information accordingly (44). Similarly, Gaucher and Payot emphasized the importance of considering each family's unique situation, context, and emotions in stressful health emergencies, and tailoring antenatal consultations to address these issues (45). And Haward et al. noted that parents approach decision-making for extremely premature infants in a personal manner, and require support that is customized to their unique circumstances and emotional state (47). It is noteworthy that, without prior knowledge of the existing literature, participants in our study expressed similar views regarding personalisation at the limit of viability.

Nonetheless, the findings of this study raise some considerations. First, while the participants recognized the importance of guidelines in preventing physician bias, they also believed that physicians should have some discretion to deviate from the guidelines. Regardless of the type of guideline, however, the decision to follow or deviate from it will be at the discretion of the physician to some degree – and may therefore be subject to physician bias.

Secondly, the factors related to personalisation mentioned by the participants are more pertinent to the counselling context rather than guidelines or prognostic calculations. However, periviability personalisation can also be associated with the prognosis itself – by considering all relevant factors to provide an accurate individual prognosis. It is noteworthy that none of the participants in this study *directly* connected personalisation with prognostic calculations.

Thirdly, a significant observation from the study was that many participants did not favour a prognosis-based guideline because it was primarily based on calculations and statistical information. However, it is crucial to note that GA-based guidelines and GA-based-plus guidelines are also based on calculations and statistics, albeit to a lesser – or rather, less explicit – extent. In fact, every periviability guideline necessarily involves some level of calculations or statistical information. It is possible that the participants' reluctance towards prognosis-based guidelines is due to other factors, such as their perspective on personalization and the concern of being viewed as 'just a statistic or number'.

Strengths and limitations

While there have been several studies that have examined the quality of life of premature infants (48-51), only three previous qualitative studies were conducted involving this particular stakeholder group (52-54). The significant strength of this study is that it was the first to investigate the attitudes of adults born prematurely regarding periviability guidelines and personalisation at the limit of viability.

However, several limitations need to be considered. One such limitation is the online format of the focus groups, which may have affected group dynamics and influenced participant responses (35). Another limitation could be the format of focus groups themselves, which may not always allow for a full expression of thoughts or feelings (33). However, during the debriefing sessions, none of the participants reported any issues related to these limitations.

Second, the study was conducted solely in the Netherlands, where cultural and societal values may have influenced the results. The Dutch context emphasizes decisional autonomy and prioritizes quality of life (2), which may have impacted the guidelines surrounding periviability care and the perspectives of the participants. To assess the generalizability of the findings, it would be useful to compare them with results from international studies conducted in different cultural and societal contexts.

Third, it should be noted that recruiting participants born at the limit of viability presents several challenges; it is not feasible to have a fully representative group due to non-survivors and adults with severe cognitive impairments being unable to participate. Furthermore, individuals with a generally high quality of life may be more inclined to engage in this type of research, potentially impacting the results of the study. Additionally, the recruitment of participants through patient organisations and hospitals may have influenced the sample of participants. The variability in the participants' gestational ages at the time of birth must also be considered. Although all participants were born prematurely, treatment limits, guidelines, and the concept of the 'limit of viability' have evolved over time. We do not have information on whether the participants' parents had to make a decision at birth between intensive care and palliative care. Nonetheless, all participants were born in the (then) grey zone in the Netherlands.

Last, providing the participants with PowerPoint slides and information on different types of guidelines could have introduced bias. However, our aim was to gain insight into the *informed* opinions of the participants. To minimize any potential bias, we ensured that there was time at the beginning of the focus group study for participants to discuss their initial ideas and thoughts about guidelines, as well as about the necessity of guidelines. Only after this initial discussion did we show the slides to the participants to deepen the discussion further, based upon the existing body of literature on the topic.

Conclusion

This empirical study aimed to collect the viewpoints of adults who were born prematurely on guidelines and personalization at the limit of viability. The participants of this study expressed a preference for a guideline for managing extreme premature birth that considers various prognostic factors and allows for parental and physician discretion. They generally defined personalization as ‘more than just relying on numbers and statistics’, and emphasized its association with information, decision-making, and relationships with HCPs. The perspective of adults born premature is not yet extensively explored but highly significant for future guideline development.

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Table 1: Prognosis-based guidelines

Prognosis-based guidelines have been suggested in the literature as an alternative to GA-based guidelines for making decisions about neonatal care.[27-29] However, implementation of such guidelines has been shown difficult due to the challenge of defining clear cut-off points; in the United States, attempts to develop prognosis-based guidelines were unsuccessful due to disagreements among the committee about what constituted 'good' or 'bad' outcomes.[30] In Canada also, a guideline was developed using mortality and major neurodevelopment disability risk as cut-offs for intensive care and palliative care[10], but exact percentages were not provided in the final guideline.[9] A survey of neonatologists from the UK, Netherlands, and Sweden showed a wide variety of preferred prognosis thresholds for treatment, with some respondents unwilling to provide a prognosis cut-off at all.[31]

Table 2: Self-reported sociodemographic and clinical characteristics of the participants

Participant characteristics	**N = 23**
Gender	
Male	5
Female	18
Age	
<20yr	1
21-30yr	9
31-40yr	9
41-50yr	3
51-60yr	1
Education	
Secondary school	1
Secondary vocational education	4
Higher professional education	10
University education	8
Religion	
Christian	6
None	17
Gestational age at birth	
24-25w	1
25-26w	2
26-27w	6
27-28w	7
28-29w	4
29-30w	3
Multiple pregnancy:	
Yes (*twins*)	3
No	20
Location of birth:	
Academic hospital	14
General hospital	6
Other	3
- Hospital abroad	2
- At home	1

Table 3: Self-reported long-term consequences of extreme preterm birth

Consequences	N = 17
Cognitive	
- Cognitive disability / learning disability / problems at school	5
(Neuro)motor function	
- Motor disability (e.g., due to hypo / hypertonia)	8
Psychosocial	
- Concentration problems / ADHD*	8
- (symptoms of) autism spectrum disorder	2
Physical	
- Vision / hearing problems	7
- Respiratory problems	7
- Reduced immunity / susceptible to infection	5
- Easily fatigued	5
- Growth restriction	4
- Eating / feedings problems	4
- Intestinal problems	3
Other named consequences:	
- Feeling misunderstood	1
- Attachment issues	1
- Anxiety disorder / performance anxiety	1
- Insecurities	1
- Stimulus processing problems	1
Number of comorbidities:**	
- 1	1
- 2	3
- 3	6
- >3	7

*ADHD = Attention Deficit Hyperactivity Disorder

**Based upon the list of comorbidities in this Table


5

DUTCH GUIDELINES ON CARE FOR EXTREMELY PREMATURE INFANTS: NAVIGATING BETWEEN PERSONALIZATION AND STANDARDIZATION

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Abstract

Objective: There is no international consensus on what type of guideline is preferred for care at the limit of viability. We aimed to conceptualize what type of guideline is preferred by Dutch healthcare professionals: 1) none; 2) gestational-age-based; 3) gestational-age based-plus; or 4) prognosis-based via a survey instrument. Additional questions were asked to explore the grey zone and attitudes towards treatment variation.

Finding: 769 surveys were received. Most of the respondents (72.8%) preferred a gestational age-based-plus guideline. Around 50% preferred 24+0/7 weeks gestational age as the lower limit of the grey zone, whereas 26+0/7 weeks was the most preferred upper limit. Professionals considered treatment variation acceptable when it is based upon parental values, but unacceptable when it is based upon the hospital's policy or the physician's opinion.

Conclusion: In contrast to the current Dutch guideline, our results suggest that there is a preference to take into account individual factors besides gestational age.

Introduction

In most countries there are guidelines for perinatal care at the limit of viability. Worldwide however, much heterogeneity exists regarding these guidelines; there is no consensus on both the type and the content of these guidelines. (1,2) Different types of guidelines are used in different countries and clinical settings. Mainly, three types of guidelines can be distinguished: gestational-age-based guidelines, gestational-age-based-plus guidelines, and prognosis-based guidelines. Besides this, it can be preferred to have no guideline at all.

The different types of guidelines all have their advantages and disadvantages. First, a clear gestational age (GA) cut-off may be preferred by some because of its clarity and unambiguity in practice. (3) However, GA-based guidelines are called self-fulfilling prophecies. Furthermore, they ignore other prognostic factors besides GA (4) and the gradualness of prognostic changes. Also, determining the exact GA is always prone to error; a GA of 24 weeks and 2 days may in fact be a GA of 23 weeks and 5 days or a GA of 24 weeks and 4 days. For this reason, the term estimated gestational-age (e-GA) was introduced. (5)

A second type of guideline that integrates more prognostic factors than just GA, could be called a GA-based-plus guideline. An example of such a guideline is the recent UK guideline from 2019. (6,7) It is recommended in the guideline to make a risk assessment and take into account the GA, but also other important prognostic factors such as birth weight, the administration of corticosteroids, the sex of the infant, and whether or not it is a single or multiple birth.

A third type of guideline is prognosis-based. (3,8) The cut-off points are then based on the expected prognosis – the chance of a “good” or “poor” outcome. This might be the most unbiased approach. No consensus is reached however, about the value-laden definition of what a “poor outcome” entails. (9) Besides, some but not all could find consensus about prognostic cut-off points. (8,10,11) It is difficult to determine correct prognostic figures and there is currently no internationally validated model. (12) Furthermore, the prognostic figures vary greatly between centres, countries and cultures. (13,14)

The importance of parental values, preferences and goals, and the process of shared – or personalised – decision-making is highly emphasized in the literature. (15-19) These parental preferences should be incorporated in ‘grey zone’ decision-making, or the so-called zone of parental discretion, in either

GA-based, GA-based-plus or prognosis-based guidelines. (20,21) However, some authors are convinced that no guideline is in fact needed for care at the limit of viability. (4,22) According to them, the existence of such a guideline contributes to treating extremely premature infants at the limit of viability morally different than other patient groups: for no other patient group with comparable survival and morbidity rates guidelines decide whether or not intensive care can be offered. This, they say, is unjust to the infants and their parents. (3,4,23,24)

In the Netherlands, nine level III perinatal care centres provide care for extreme prematurity. The Dutch guideline on care for extremely premature infants born earlier than 26 weeks GA is a national and interdisciplinary consensus guideline. It is strictly GA-based with a lower treatment limit of 24+0/7 weeks GA, and only refers to spontaneous preterm deliveries. (25) The 24-to-26-week GA period is considered to be the grey zone in which shared decision making by parents and healthcare professionals (HCPs) is advised. (18)

The current Dutch guideline dates from 2010 and is now being revised. (25) Therefore, we want to explore Dutch perinatal HCPs' attitudes on different possible types of guidelines. The views of HCPs on guidelines for perinatal care at the limit of viability have been studied before but these studies mostly focused on the GA-related content of these. (26) In this study, we aimed to conceptualize what type of guideline is preferred by most Dutch HCPs. Throughout the online survey, we provided background information on the different types of guidelines because we aimed to explore the informed opinion of Dutch HCPs.

Methods

Study design

Cross-sectional, multi-center study using an online survey.

Setting and population

The online survey was sent to a broad scope of HCPs involved: all obstetricians, neonatologists, obstetric nurses, neonatology nurses, clinical midwives (obstetrics) and physician assistants or nurse practitioners (neonatology) from the nine level III centers in the Netherlands. The Dutch framework recommends joint counselling by an obstetrician and neonatologist together. Shared decision making between

HCPs and parents is advocated to reach a decision. The survey was sent to (one or two) gynecologists and pediatricians for each level II hospital, involved in either referring pregnant women to the tertiary care center, or in receiving premature neonates after their period of neonatal intensive care.

Survey design

The anonymous online survey was designed to obtain information on HCPs opinions on actual issues relating to the guideline for extreme prematurity. Since not all HCPs may be familiar with the latest literature on the topic of extreme prematurity guidelines and decision-making, we provided background information and references for the various questions. We purposely choose to ask for their 'informed' opinion. Topics of interest were: (a) the current Dutch guideline, potential guideline types and guideline development (Table 1 is an example of information given before answering a question, a total overview can be found in supplement (1) (b) the grey zone: limits and acceptance for treatment variation and (c) counselling and decision-making. Next to multiple choice questions, open textboxes for comments were provided in each section. In this manuscript, results of section (a) and (b) will be described.

The first version of the survey was created by the authors, based on published literature. In a second round, comment from an expert in survey-development was used for further improvement. In a third round, a pilot-test was done by HCPs, one or two from each professional group, who would not receive the final survey since they were either just retired or switched jobs. The final version was approved by all authors. The original Dutch survey was translated to English by a professional translational service for publication purposes and can be found in the online supplemental material.

Not all survey results will be discussed in this manuscript because of the extensive nature of the survey. For this manuscript, we chose to focus on the survey results for topics (a) and (b). The survey results for topic (c) will be discussed in a separate paper.

Data collection

All neonatology and obstetrics department heads of the level III perinatal centres were approached by the authors and supported this survey, which was then spread to the target population in both their own centre and the regional level II centres by the administrative office, using a web-link. One reminder was sent. The survey was anonymized, e.g., no names or e-mail addresses were collected. Institutional Review Board consent was waived.

Data analysis
Descriptive statistics were given as proportions of the respondents for each completed question. Statistical analyses were conducted using IBM SPSS Statistics (Version 25, Armonk, NY: IBM Corp.).

Results

A total of 297 complete and 472 incomplete surveys were received. Each level III perinatal centre and its region level II centre was represented. The exact response rate could not be calculated since feedback from a few centres feedback was incomplete. However, an estimated total of 2000 to 2200 surveys was sent, meaning a response rate of 35% to 40%. Demographic questions were asked at the very end of the survey, so these were mostly missing for the incomplete surveys. Demographic characteristics of the respondents can be found in Table 2.

Upper and lower limits of the grey zone
Exploration of the preferred upper and lower limits of the grey zone (if the guideline were to be based on GA of a well-grown, singleton pregnancy in a level III centre) revealed that 196 (48.6%) of the participants preferred 24+0/7 weeks gestation as the lower limit and 26+0/7 weeks gestation was the most preferred upper limit (197, 49.4%). Figure 1 shows the opinions on the upper and lower limit of the grey zone.

Many additional comments were made about the lower limit. The few participants who choose 22+0/7 weeks as a lower limit added that they found it important to provide similar care as in neighbouring countries. Comments of participants with a preference for a lower limit at 23+0/7 weeks added consequently that active management only should be offered without additional risk factors like a well-grown baby. An argument given to lower the threshold to 23+0/7 weeks was the presumed improvement of the quality of care for all neonates, mainly the slightly older preemies. The most important comments of participants preferring to keep the 24+0/7 weeks lower limit were their “lack of good outcomes” and the “lack of improvement in outcomes over the years”. Another problem frequently reported was the capacity problem for the Dutch neonatal intensive care units (NICUs) if more neonates are admitted. For the preferred upper limit, some participants noted that it would be logical to lower the upper limit too, if the lower limit is lowered. On the other hand, some participants noted that personalised care should also include the willingness to withhold neonatal intensive care beyond the upper limits in cases of severe growth restriction. Interestingly 11 participants, mostly obstetrical nurses, felt the lower limit should be 26 weeks' GA. One comment is noted, summarized 'we shouldn't give care too early, but I am not an expert on this topic'.

Opinions on the current Dutch guideline

Most of the participants (82.7%, n = 593) were familiar with the Dutch guideline, however only 10.3% (n = 74) were familiar with foreign guidelines. The majority 87.7% (n = 427) agreed with the recommendations in the current guideline and most participants (94.8%, n = 435) found the guideline feasible in practice. A summary of the most mentioned comments in open text boxes were: there is more need for personalization; decision-making in the grey zone is challenging; the current guideline is too strict; the 24-week threshold is too low; the influence of parental wishes is too high; and finally, there were comments regarding worries about the capacity of NICU beds and about the ongoing variety between different hospitals. Only 32.5% (n = 105) of the participants said to follow the guideline strictly while 65.3% (n = 205) of the participants did deviate from the guideline in some cases. Though the Dutch guideline strictly describes what to do in cases of spontaneous preterm birth, 77.8% (n = 397) indicated that they also use it for iatrogenous preterm birth.

Possible guideline types

Participants were asked to give their opinion on different types of guidelines. The questions were prefaced by information on national and international discussions on the exact boundaries of the grey zone and the discussion on the type of guideline. Four types of guidelines were presented including the benefits and disadvantages; (1) no guideline; (2) a GA-based guideline (the limits of the grey zone are based on duration of pregnancy); (3) a GA-based-plus guideline (based on duration of pregnancy plus other factors); and (4) a prognosis-based guideline (the limits of the grey zone based on the expected prognosis). Participants ranked each type of guideline (Table 3). After scoring each guideline type, participants were asked for their personal favorite. Most respondents preferred a GA-based-plus guideline (72.8%, n = 295). The most important comments on the GA-based-plus guideline were: a GA-based-plus guideline is a good balance between personalisation and evidence-based medicine, the 'plus' should be used especially for borderline cases, clear thresholds give less discussion with the parents, and there is often no time for individualised care. Several other comments were on the lack of validated models for a prognosis-based guideline and on the preference to add criteria for withdrawal of intensive care treatment after birth.

Scenarios: acceptance for treatment variation

The participants were asked to indicate their opinion on similar scenarios of extreme prematurity with only a different motivation for varying treatment (see Table 4 and Figure 2, a total overview can be found in the only supplementary material). In the open text boxes, many participants commented on the cases. Many emphasized the importance of parental values. Participants recommended that counselling should be done well and honestly. Some respondents believed that parents often do not realise the possible complications of extreme prematurity. Others noted that counselling is often too positive. It was also noted that it is very understandable that parents want this chance and that 'we should not judge them for that'.

For different treatment decisions based on medical judgement of the social background, the comments are mostly supporting the opinion that it is highly unacceptable for a physician to judge someone's social situation. Participants frequently labelled this explanation as 'discrimination' or 'paternalism'. A few participants commented that the difference is acceptable since, for example, a young teenage mother and her extreme premature child will both face a difficult future.

For different treatment decisions based on variation in hospital policies most comments were about the wish to have a comparable policy in all hospitals, which is also important in the context of possible transfers between hospitals due to space limitations. An equal chance on starting active care for similar cases is considered important. A few comments underline the importance of transparency on the differences in policy between hospitals.

Finally, different treatment decisions based on varying personal opinions of individual physicians is found highly unacceptable. Most commented that there should be a unanimous policy for the entire health care team. Moreover, it was often mentioned that the counselling should be neutral, uninfluenced by the physicians' personal values, and based on facts. Some participants underlined the importance of a strict guideline, as this will reduce treatment variation based on physicians' opinions.

Discussion

The results of our survey yield three important findings: (1) the majority of Dutch HCPs still find the current Dutch guideline which recommends the provision of early intensive care for premature babies from 24+0/7 weeks GA and above acceptable; (2) many professionals however, prefer a different type of guideline; the GA-based-plus guideline which advises to take into account other prognostic factors than just GA is mostly preferred. In addition, we found that (3) most study participants find variation in treatment between similar infants acceptable only in situations where the variation is based upon individual parental values or wishes, and unacceptable when it is based upon differences in the hospital policy or the physician's preferences.

Revising the Dutch guideline

As mentioned earlier, compared to most other international guidelines on this matter the Dutch guideline may be thought to stand out. The Netherlands can be considered an outlier for "its relatively high age threshold of initiating active care, its grey zone spanning weeks 24 and 25 in which active management is determined by parental discretion, and a slight reluctance to provide active care in case of extreme prematurity." (27) Although the current Dutch guideline was already published in 2010, our survey shows that the majority of HCPs still agree with the recommendations made in this guideline. Only a minority of around 30% find that the threshold should be lowered to 23+0/7 weeks of gestational age. In the light of the current revision of the Dutch guideline, these are important findings. More importantly, we noted that the results of our survey demonstrate an interesting shift in Dutch HCP attitudes. The wish for personalization or individualization of care at the limit of viability is increasing. Personalization and related terms are often mentioned in the comment sections of several survey questions. The importance of integrating more prognostic factors in the guideline and focusing on parental wishes and values were often mentioned. At the same time however, the participating HCPs underline the importance of a clear guideline while including more prognostic factors.

Personalisation and guidelines

From the survey results it became clear that personalisation or individualization of care at the limit of viability can have different meanings for HCPs. It can mean 'to take into account other prognostic factors than GA', but also 'to take into account parental wishes and values' or 'to adjust the information shared in counselling to the parents being counselled', and so on. A number of HCPs believe that optimal individualization is accomplished if no guideline is present, while others seem to believe that personalisation is independent of a guideline. It may therefore be that the importance of parental values is transcendent of the guideline type; no matter the type of guideline, parental values are significant. Then, there should also be room for parental values when there is, for example, a strictly GA-based guideline.

Furthermore, the wish to individualize care seems to have limits for Dutch HCPs. As said, according to the responses, treatment variation that is based upon parental values is acceptable whereas variation due to differences between (values of) a hospital or physician is not. Also, almost all HCPs wish to have a guideline, a lower treatment limit, and an upper treatment limit. The wish for national uniformity of treatment and standardization of care may be influenced by the fact that in the Netherlands, typically, all national guidelines to date are consensus-based.

A potential way to have more 'uniformity in personalisation' could be the organization of training in counselling or an up-to-date decision aid to help parents understand outcome data (when preferred) and to help parents discern their own values and preferences. Already, nationwide consensus on important counselling aspects has been reached. (18) Furthermore, since some comments showed several factually unnuanced assumptions, efforts to increase knowledge on treatments and outcomes of extreme prematurity among healthcare providers should be made. Examples of these assumptions are: 'barely good outcome for children born at 24+ weeks GA' and 'only start with active management if the child shows a good start'. Especially the last comment, mentioned several times, is not recommended, as literature shows that 'clinical assessment in the delivery room is a poor predictor of survival'. (28,29) Also, a national training on prenatally counselling parents is lacking in the Netherlands. First steps are made however, to organize such a training for fellows in neonatology and maternal-fetal medicine.

Strengths and limitations

This is the first study to conceptualize what type of guideline is preferred by HCPs. We asked for their informed opinion by providing background information on different possible types of guidelines. All HCPs involved in the daily care practice around the limit of viability were represented in our survey respondents; this is a strength of this study. The results or our survey may of course be influenced by the Dutch context and the strictly GA-based, national consensus guideline in the Netherlands. The responses might therefore be biased and may not fully apply internationally. Yet, we notice a general trend towards personalisation at the limit of viability also in the international literature. (6,19,28)

Future research

It is clear that more research is needed to define the preferred personalisation for the specific field of extreme prematurity at the limit of viability. It is also unknown what patients and their families think about this matter. Studies showed that there is variation in parental preferences regarding how they want to be counselled.(29-33) Parental views on treatment guidelines however, are largely unknown. Although one article shows that – at least some – parents find it hard to cope with variety between institution, we need more studies to confirm this. (34)

Conclusion

Further reflection is needed on the relationship between personalisation and the wish for uniformity in guidelines on care at the limit of viability. Also, facilitators and barriers to personalising care and counselling in practice must be explored. An important knowledge gap is the patient and family perspective on this matter. Qualitative research with patients, parents and healthcare providers on preferred guidelines and personalisation is therefore urgently needed.

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Table 1 Background characteristics of the participants

Background characteristics		**N (%)**
Years of experience (*)	Mean 13,2y (SD 8,9) Median 12y (IQR 5 – 19)	
Age (years)	20-30	28 (9)
	30-40	83 (28)
	40-50	93 (31)
	50-60	75 (25)
	60-70	18 (6)
Profession	Neonatal nurse	92 (30)
	Obstetric nurse	53 (17)
	Nurse (not otherwise specified)	5 (2)
	Clinical midwife	13 (4)
	Physician assistant or nurse practitioner neonatology	15 (5)
	Gynaecologist	39 (13)
	Pediatrician	82 (27)
	Other	6 (2)
Gender	Female	241 (82)
	Male	49 (17)
	Other	0
	Prefer not to answer	3 (1)
Working in level III hospital (with NICU facility)?	Yes	266 (90)
	No	30 (10)
Exposure extreme prematurity (GA $23^{+0/7}$ - $25^{+6/7}$), (**) frequency in past year	None	9 (4)
	<5	0
	5-10	70 (34)
	10-20	69 (33)
	20-30	32 (15)
	>30	28 (14)
Counseling conversations for imminent extreme premature birth <$26^{+0/7}$ weeks GA, (***) frequency in past year	None	0
	1-10	117 (68)
	10-20	41 (24)
	20-30	12 (7)
	>30	3 (2)

Table 1 Continued

Background characteristics		**N (%)**
Children	Yes	219 (75)
	No	69 (24)
	Prefer not to answer	5 (2)
Religion	Yes	75 (26)
	No	203 (72)
	Prefer not to answer	6 (2)
Type of religion (only in those answering YES to religion)	Christianity	72 (96)
	Islam	2 (3)
	Judaism	0
	Buddhism	1 (1)
	Hinduism	0
	Prefer not to answer	0
	Other	0

(*) for physicians including fellowship, for physician assistants and nurse practioners including education part in neonatology, for clinical midwifes including education part in level III hospital, for neonatal & obstetric nurses including education part in level III hospital (**) depending on profession: trajectory of hospitalization neonate, mother, deliveries or referrals to and from level II hospital (***) depending on profession: presence at counselling conversation as counsellor or as observer / supportive person

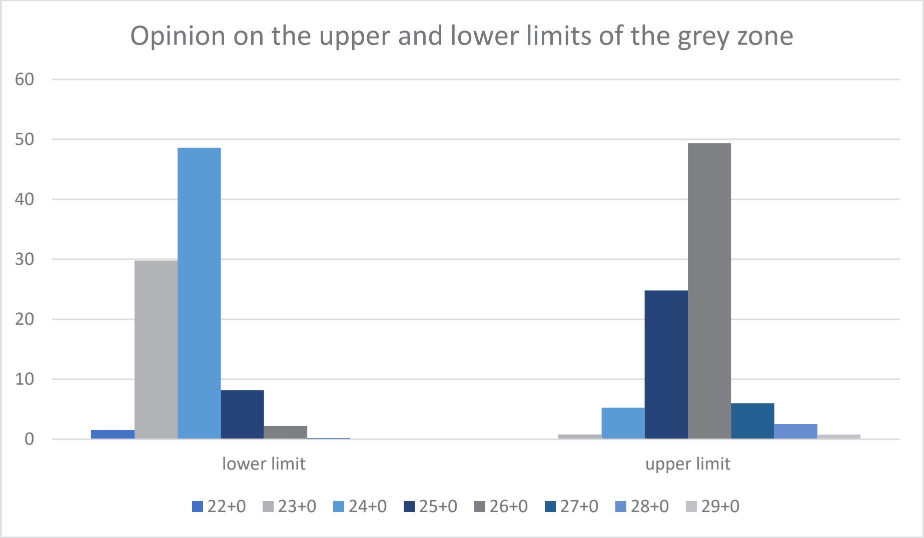

Figure 1 Opinions on the upper and lower limits of the grey zone

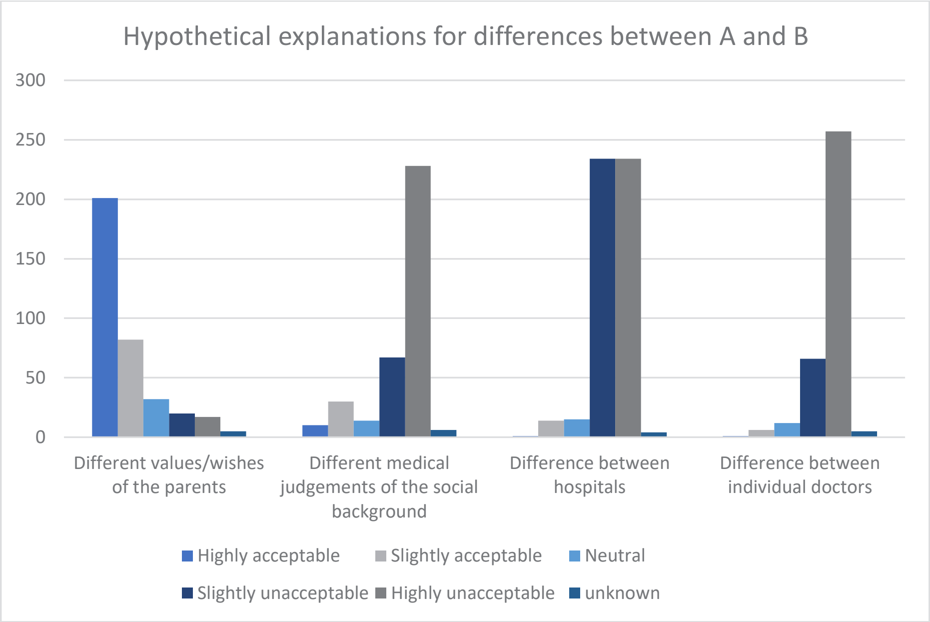

Figure 2 Hypothetical explanations for different treatment decisions for similar cases

Table 2 Opinions per type of guideline, *highest percentage

Type of guideline	Fully agree	Agree	Neutral	Disagree	Fully disagree
	N (%)	N (%)	N (%)	N (%)	N (%)
No guideline	8 (1,7)	55 (11,7)	50 (10,6)	226 (48,1)*	131 (27,9)
GA-based guideline	7 (1,6)	130 (29,2)	112 (25,2)	178 (40)*	18 (4)
GA-based-plus guideline	78 (18,4)	280 (65,9)*	51 (12)	16 (3,8)	0 (0)
Prognosis-based guideline	19 (4,7)	143 (35,3)*	118 (29,1)	111 (27,4)	14 (3,5)

Table 3 Scenarios of cases of extremely premature birth but variation in treatment

We would like to know to what extent you are willing/able to accept certain differences in strategy. Please forget the current guideline for a moment and imagine the following hypothetical case: it is November 2020, a pregnant woman (G1P0) has been admitted to a specialized center with cervical shortening and contractions. She is carrying a single female fetus and at 23+5/7 weeks gestational age. Corticosteroids have not been administered yet.
In situation A the choice is made to implement palliative comfort care if the labor progresses today.
In situation B the choice is made to implement active neonatal care if the labor progresses today, and corticosteroids are administered.
We have provided a number of (hypothetical) explanations for the difference between situation A and situation B. Please indicate whether you find this acceptable or not.
Motivations of varying treatments:
Scenario 1: based on values/wishes of the parent(s) Scenario 2: based on social background of the parent(s) Scenario 3: based on differences between hospitals Scenario 4: based on differences between caregivers

PART THREE

ETHICAL EXPLORATIONS


6

POSTPONED WITHHOLDING: HARMFUL FOR THE INFANT AND INCREASING THE COMPLEXITY OF DECISION-MAKING

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Syltern et al. (2022) propose a new approach to decision-making at the limit of viability: by default, intensive care will be initiated for every infant born in "the gray zone" of viability. This will be redirected toward palliative care in the second week unless the parents request otherwise. This novel approach is called postponed withholding (PPWH). PPWH is proposed by the authors to facilitate fair and balanced decision-making at the limit of viability. Furthermore, it is said to contribute to empowering parents in the highly vulnerable situation of extreme preterm birth, and to better support healthcare personnel (HCP) in making life-and-death decisions. Although facilitating balanced decision-making is a commendable goal, we are not convinced that the proposed change in choice architecture is the way to go. Firstly, PPWH might lead to over- as well as undertreatment, which is not in the best interests of extremely premature infants. Secondly, decision-making in the second week might be more complex than before birth, ethically, legally and psychologically. Finally, our own empirical research with adults who were born at the limit of viability illustrates that the harm of intensive care at birth must not be underestimated.

Decision-making for extreme prematurity

In what Syltern et al. call the "traditional approach" for decision-making for extreme prematurity, high-quality prenatal counseling should provide parents with information on treatment options, survival, risks of (long-term) consequences, uncertainty, and the possibility for multiple future decision moments, and should include a discussion on parental values and preferences (Geurtzen et al. 2019). A shared decision between intensive care and palliative care is then made by the parents and HCP, prenatally. Thus, some infants born in the gray zone-i.e., roughly between 22 and 25 weeks of gestation (Wilkinson, Verhagen, and Johansson 2018)—will receive palliative care, and others will receive intensive care. In the PPWH approach, all children will receive intensive care. The default initiation of intensive care in the gray zone is seen as a non-decision, and decision-making in the second week is seen as pertaining still to withholding rather than withdrawing of life-supporting treatment. The aim of PPWH is to buy time for parents to be better informed and prepared to take part in the shared decision-making process about the appropriate treatment for their premature infant.

The complexity of decision-making

Syltern et al. argue that PPWH contributes to balancing decision-making at the limit of viability. For several reasons, however, we think that PPWH increases rather than decreases the complexity of decision-making, ethically, legally and psychologically, and does not support parental autonomy. Literature suggests that a subgroup of parents wants to avoid suffering due to NICU treatment for their extremely premature infant (Jager et al. 2020; Keenan, Doron, and Seyda 2005; Moro et al. 2011; Tucker Edmonds et al., 2019). In the PPWH approach, these parents will not be given the freedom to do so, and are thus denied a valuable option. Also, while in the traditional approach, decision-making takes place prenatally, when the mother is still pregnant and the infant has not yet been born, in the PPWH approach, it takes place one week after birth, when the infant has become a patient. Toward their patients, HCP have fiduciary duties. Because of this, HCP have a stronger say in the decision. Despite the heterogeneity in legal frameworks surrounding the status of the (un)born infant, it does matter for decision-making whether the infant is born; HCP must act in the best interests of patients, even if the parents may wish otherwise.

Furthermore, PPWH may give rise to conflicts and increase the complexity of decision-making psychologically. While it is possible that after one week of intensive care, the prognosis is still as uncertain as it was before (or at) birth, it is also possible that it is more hopeful. In this situation, HCP might experience conscientious objections when parents adhere to (dis)- continuation of intensive care as planned. Even if the prognosis does not improve and the parents merely comply with planned redirection of care, they may feel responsible for ending the life of their infant, as they could have requested continuation of intensive care. In the traditional approach, intensive care would not have been initiated at all, and parents would have been spared having to make the postponed decision. Moreover, it is not clear whether the extra time will in fact strengthen parental decision-making. Decisions about continuation or discontinuation of intensive care may be guided largely by parental feelings and intuitions rather than explicit deliberation about values, and those feelings and intuitions may not be based on underlying values at all, but colored by the emotional rollercoaster parents are in after extreme prematurity (de Vries et al. 2013). Postponing decision-making for one week may fail to change intuitive decision-making into deliberative decision-making. Altogether, changing the choice architecture so that there are default options at birth and after one week, does not make it a less difficult decision for parents or HCP to (dis)continue intensive care after one week. Also, it may come at the expense of the infant.

Over- and undertreatment

In the PPWH approach, every infant born in the gray zone receives intensive care at birth. This means that a group of infants that would traditionally have received palliative care at birth in accordance with parental intuitions or values, will now receive intensive care for one week. As it is not clear that intensive care benefits extremely premature infants (Walker 2019; Vinall and Grunau 2014), this results in overtreatment. At the same time, the introduction of a default option of redirecting to palliative care after one week means that life-supporting treatment will be withdrawn from a higher number of extremely premature infants than it currently is. Syltern et al. claim that their aim is to “permit parents to grasp the situation before any irreversible action is taken.” If, however, one week does not suffice to empower parents, they may comply with the default option, even if their infant stands a good chance of survival. Thus, a default to withdraw may also lead to undertreatment. For these reasons, we do not believe that PPWH solves the problem of over- and undertreatment at the limit of viability.

Harm and needless suffering

PPWH may be harmful to the infant. Based upon our own recent qualitative studies, we have concerns about the harm that comes with the initiation of intensive care and one week of treatment in the Neonatal Intensive Care Unit (NICU). In January 2022, four focus groups were held in the Netherlands with 23 adults who were born at the (then) limit of viability. The participants were aged 19–59 years. Our aim was to gain a more comprehensive understanding of extremely prematurely born adults’ perspectives on (a) guidelines for extreme prematurity care, (b) personalization of care and, (c) values in decision-making about extreme prematurity care. Preliminary results of this focus group study illustrate that the impact of NICU treatment should not be underestimated. Respondents reported on the trauma that NICU treatment had caused for them as well as for their parents. Comprehensive results of this Dutch focus group study will soon be submitted for publication. They will suggest that intensive care at the limit of viability is associated with harm and suffering, and that there are reasons for being hesitant about initiating it for all extremely premature infants.

Syltern et al. state the following about harm and suffering: “[I]ntroducing the postponed-withholding concept may lead to more infants receiving initial life support, and potentially more needless suffering. However, this is justified by both the medical and moral uncertainty […]. The burden of intensive care will be of limited duration, and many parents who suffer a loss in the NICU, express their gratitude for the days they got to spend with their baby.” The importance for parents of spending time with their extremely premature infant must indeed not be underestimated either. We disagree, however, with PPWH being the way to go for gaining this time, as we do not believe that the possible benefits for the parents outweigh the harms and suffering for the infant.

Facilitating balanced decision-making

To strive toward balanced decision-making, it may be better not to abandon, but to strengthen the traditional approach. Decision-making about extreme prematurity care should be preceded by high-quality prenatal periviability counseling that not only relays information about treatment options and outcomes, and elucidates parental values, but also paints a very clear picture of what might happen after birth. It should be underlined that intensive care is associated with harm and suffering, and that the infant may die from complications, or survive with severe, lasting impairments. Also, parents should understand that decision-making is not a one-off event but a continuous process. After one week of intensive care, parents and HCP together may decide that withdrawal of intensive care is in the best interest of the infant. To help parents overcome withdrawal resistance, they may need to know that after one week, redirection to palliative care is possible and sometimes preferable. Ideally, parents and HCP should find agreement in advance about criteria for withdrawal of lifesupporting care and about the process of redirecting care, especially when the odds of benefit are low (Bunnik and Aarts 2018). Altogether, for enabling balanced decision-making for extreme prematurity, high-quality prenatal periviability counseling is of utmost importance.

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7

ON THE LIMITS OF VIABILITY: TOWARD AN INDIVIDUALIZED PROGNOSIS-BASED APPROACH

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Consider two fictional cases in The Netherlands: (a) a 41- year-old woman, 233/7 weeks pregnant with a female fetus of estimated 600 g, and (b) a 25-year-old woman, 241/7 weeks pregnant with a male fetus of estimated 500 g. Both women are in imminent labor. Although the chances for survival of the girl might be better compared to the boy, no neonatal intensive care is offered to the parents of the girl because of the GA of 233/7 weeks. Instead, palliative comfort care will be offered. The parents of the boy will be offered full counseling and if desired, after a process of shared decision-making, initiation of neonatal intensive care (1).

Decisions about early intensive or palliative comfort care at the edge of neonatal viability are challenging. Despite international efforts to emphasize the importance of not focusing solely on gestational age (GA) to make these decisions (2–5), The Netherlands still relies on a GA-based guideline: the earliest GA for offering neonatal intensive care is strictly 240/7 weeks. We, as Dutch professionals, would like to substantiate our criticism of these national guideline as complex decisions about intensive neonatal care should not be based on GA alone (6–9). Moreover, we plea for a review of the Dutch, and other strictly GA-based guidelines, on a multidisciplinary basis. In what follows, four arguments will be provided to support this statement.

First, uncertainty is inevitable when it comes to objectively pinpointing the correct GA. Since determining the GA of a fetus is challenging and unsure, it should preferably be referred to as an estimated GA (e-GA). An e-GA being 24 weeks could be $24^{2/7}$ weeks but also $23^{5/7}$ weeks (10). Thus, we need to factor in these possible measurement errors. Due to this uncertainty, it seems unjustifiable to only provide neonatal intensive care to those estimated to be born from 24 weeks, especially when GA is the only factor taken into account to decide about a future care process. As Wilkinson et al. state: “this might lead to changes in the permissibility of resuscitation from 1 day to the next, a phenomenon that could be compared to a “Cinderella effect” (referencing the impact of the stroke of midnight in the Cinderella fairy-tale)” (6). This does not entail that we should not consider e-GA at all or that we should lower the guideline toward an e-GA of 22 or 23 weeks. It entails that e-GA should be considered as one amongst other prognostic factors to be taken into consideration in decisions about care at the edge of neonatal viability.

Second, the cut-off at 24 weeks gestation is chosen because of statistics about survival. This insight however may be based on a “self-fulfilling prophecy” (11). As Hendriks and Lantos claim: if no foetuses are treated at 22 or 23 weeks, then no such babies will survive (12). The same authors refer to local hospital data claiming that there is a hundred percent mortality rate for extremely premature infants born earlier than 24 weeks. Such reported low survival rates then seem to justify the policy of not treating babies born earlier than 24 weeks, creating a self-justifying circle.

Third, it has been argued that GA-based guidelines reduce the complexity of a decision as it is clear-cut and available for every pregnant woman (12). This, however, raises serious issues of fairness. It is instructive to take Aristotle's rule of thumb into consideration, for something to be fair we have to: "treat like cases as like" (13). Important to note is that we have to identify what makes cases alike from a morally relevant perspective. An infant of 232/7 and one of 240/7 who may have equal chances to survive "in reasonably good health" are not treated equally when a GA-based guideline of 24 weeks is in place. Fairness seems to demand that infants with equal chances for survival "in reasonably good health" are treated equally. For this purpose, a guideline based solely on e-GA is inadequate and therefore unfair (5). Albeit, considering that surviving "in reasonably good health" might have various meanings for different people, applying this in practice could be challenging. Moreover, parental values are of significance here (1, 11–13). More research is needed on how to apply this rule of fairness, the idea of surviving "in reasonably good health", and the role of parental values in practice at the neonatal limits of viability.

Lastly, a guideline solely based on GA might evoke moral pressure because of the implicit default to treat when the GA threshold is reached. For example, even if the prognosis of fetus B, being born the 24th week is poor because of additional factors such as for example birthweight, the mother and the caregivers might still be more inclined to opt for neonatal intensive care. The existence of a sharp cut-off standard might implicitly communicate that one should always treat neonates when this threshold is exceeded. In other words, mothers and caregivers might be pressured into providing neonatal intensive care to a certain infant only because the limit of GA has been reached. Because of the possible harmful effects of such a "threshold bias", it is important to also take into account other relevant factors. Factors such as weight, gender, and fetal development, but also parental values, should be taken into account in the decision-making process (1, 14–16). Moreover, a sharp cut-off might not be consistent with shared decision-making—which is explicitly recommended for making periviable decisions (1). What justifies not sharing the decision just below the 24-week GA cut off, in which situation the interpretation of benefit-harm ratio also depends on personal values (1, 14–16)?

It is important to provide the parent(s) with useful prognostic information enabling them to make an informed, well-considered decision. More research is needed about what factors are significant when it comes to a prognosis, how to predict these, and whether these are cross-culturally applicable. Then, this could come with reduced moral pressure for the parent(s) as well as the caregivers to provide neonatal intensive care to all babies born from 24 weeks. Note that providing palliative comfort care is a not less significant option compared to neonatal intensive care and that both options should thus always be presented equally (1). Especially for cases in the "gray zone" where prognostic uncertainty is often inevitable, presenting both options as being morally justifiable is of major importance.

Overall, every parent and future child is entitled to an individual evaluation of her medical situation. This, in combination with a process of shared decision-making with both parents and caregivers, has to lead to an individual care plan providing the future child with the best possible prospects that connect well to parental norms and values. Nonetheless, more research is needed to find the most feasible way to reach this required revision of the guidelines and overarching cultural change, taking into consideration all important stakeholders and society.

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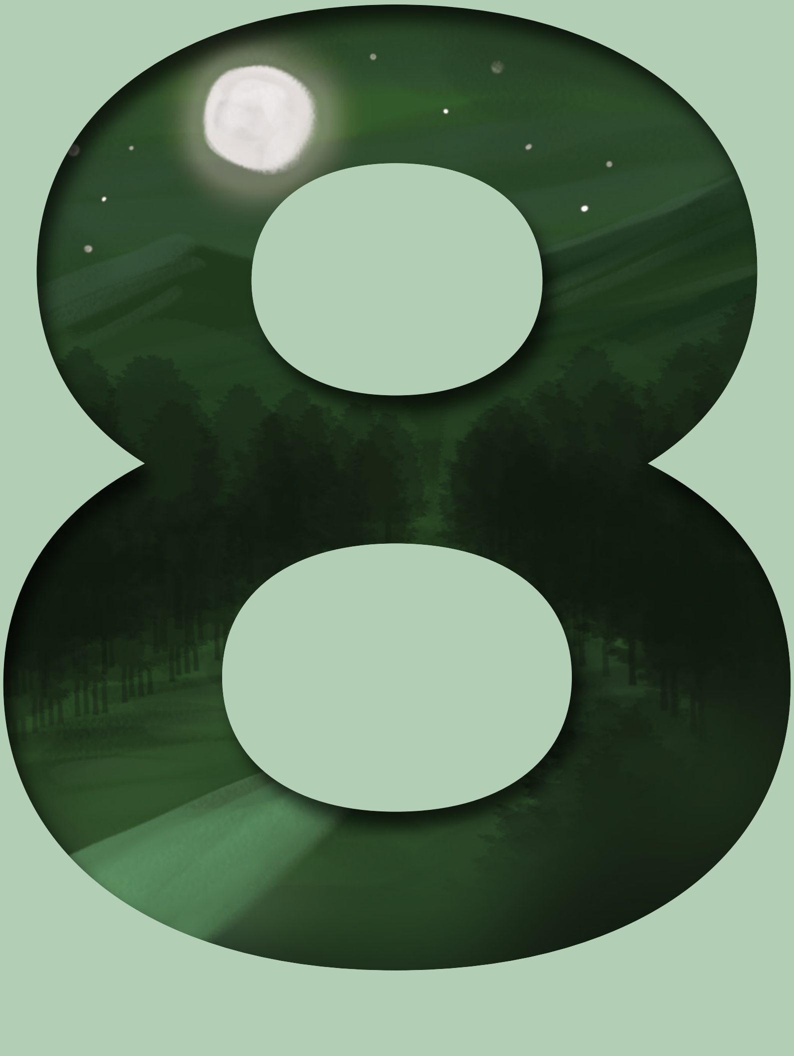

VIABILITY, ABORTION AND EXTREME PREMATURITY:
A CRITIQUE

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Abstract

This article examines the ethical validity of using viability as the cutoff point for abortion in the Netherlands, in view of potential changes to the Dutch perinatal care guideline. According to the Dutch Penal Code, abortion is permitted until viability: the point at which a fetus can survive outside the womb with technological assistance. Since the law was enacted in 1984, viability has been set at 24 weeks gestational age. Currently, in the Netherlands, the treatment limit for extreme prematurity is also set at 24 weeks. The potential revision of the guideline could lower this threshold. Such a change could have implications for abortion in the Netherlands. We critically evaluate the use of viability within the Dutch context and offer recommendations for modifying the legal framework concerning abortion. We conclude that relying on any interpretation of viability is morally problematic for abortion regulation, as it is too indeterminate a concept to establish a threshold in a morally relevant way.

Abortion in the Netherlands: an introduction

Recently, the legal regulation of abortion in the Netherlands has received renewed attention. This is largely because the Dutch treatment guideline on perinatal care in case of extremely premature birth is currently in the process of being revised. The current Dutch guideline, which dates back to 2010, restricts the provision of intensive care to infants born before 24 weeks and 0 days gestational age ($24^{+0/7}$ weeks GA) (1). At present therefore, infants born below this 24-week threshold do, in general, not survive in the Netherlands. Internationally, the Netherlands is considered an outlier for its rather high treatment limit for extremely premature infants (2-5). The revision of the Dutch guideline may result in a lower threshold for providing intensive care, as this practice is already common elsewhere. The treatment limit may eventually be lowered to $23^{+0/7}$ instead of $24^{+0/7}$ weeks GA. This revision could have unforeseen repercussions for abortion because of how the legal framework is constructed in the Netherlands. The 24-week threshold is not only the threshold for providing intensive care for extremely premature infants but also the threshold for legal abortion. That is, Dutch law allows abortion until 'fetal viability'. If the guideline on perinatal care for extremely premature infants is changed to apply a lower treatment threshold, the abortion threshold may also have to change to the same GA, to avoid legal and ethical inconsistency. Hence the renewed attention for Dutch abortion law and more specifically, for the use of viability as a basis for this law.

Abortion in the Netherlands is regulated by the Dutch Penal Code, the Termination of Pregnancy Decree 1984, and the Dutch Termination of Pregnancy Act 1981/84 (6-8). Section 296, Subsection 1 of the Penal Code states that: "Any person who gives a woman treatment, when (s)he knows or has reasonable cause to suspect that this treatment may terminate the pregnancy, shall be liable to a term of imprisonment not exceeding four years and six months or a fine of the fourth category". Concurrently, the law determines a non-punishable form of termination of pregnancy in Section 296, Subsection 5: "The offence (…) shall not be punishable, if the treatment is performed by a medical doctor in a hospital or clinic in which such treatment may be performed under the Termination of Pregnancy Act". The Explanatory Memorandum to the Act elaborates on two underlying aims of the Act: to protect unborn human life, and to provide assistance to women in an emergency situation because of an unwanted pregnancy (9). Oddly enough, the Dutch legal framework for abortion means that the emergency situation of women is only relevant when the fetus is not viable.

Section 82a of the Penal Code states that: “Taking the life of a person or of an infant at birth or shortly afterwards shall include: the killing of a fetus which might reasonably be expected to have the potential to survive outside the pregnant person’s body”. In the Explanatory Memorandum, Dutch lawmakers clarified that viability should be understood as the point in time at which a fetus can survive outside the womb, with medical technological support if necessary (9). Yet, what it means to ‘survive’ is not further specified; neither the duration of survival nor the quality of life after survival are discussed. This contrasts with the way viability is understood in, for example, the Japanese Motherhood Protection Act. There, viability is interpreted as “the quality or state of being able to live, grow and develop” (10). Viability in the Netherlands, on the other hand, aligns with the interpretation of viability provided by the Supreme Court of the United States in *Roe v. Wade* in 1973, where viability is defined as “the interim point at which the fetus becomes (…) potentially able to live outside the womb, albeit with artificial aid” (11).

The Dutch Termination of Pregnancy Act was enacted in 1984 (8). This Act does not contain a definition of viability in terms of GA. The Dutch Ministry of Health, Welfare and Sport is responsible for concretizing the concept of viability by defining it as a certain GA. Thirty-nine years ago, the Ministry determined that the point in time at which fetal viability is reached is 24 weeks GA. The Explanatory Memorandum to the Act specifies that this GA is explicitly based on the consensus in medical science (9-12). Obviously, the medical consensus has shifted since 1984, given that babies born before 24 weeks now regularly survive.

Yet, the 24-week viability threshold has not been changed over the years. 24 weeks GA is still used as the viability (and thus the abortion) threshold in the Netherlands (13). Yet, as we have written elsewhere (14), the Dutch Burial and Cremation Act of 1991 does acknowledge the possibility of viability below 24 weeks GA. The Act defines stillbirth as a fetus born at a gestational age of at least 24 weeks or earlier, if it survives for more than 24 hours after birth (15).

In principle, terminations of pregnancy later than 24 weeks are not possible in the Netherlands, although there is room for exceptions. Requests for the termination of a pregnancy beyond 24 weeks are evaluated by the Ministerial Regulations of the Assessment Committee for Late Terminations of Pregnancy and Termination of Life in Neonates (16). This regulation makes it possible to terminate pregnancies later than 24 weeks GA, on the basis of foetal abnormalities. The Regulation is applicable only when one of the following categories applies: (1) when the fetus is expected to die immediately after birth, and therefore considered not viable, and (2) when the fetus can be considered viable but has a condition which would lead to “serious and irreparable functional disorders” (16). Around 5-10 cases of late termination of pregnancy are reported each year (17-19). Late Terminations of Pregnancy in the Netherlands are punishable by law *unless* one of the two categories applies, and a number of ‘due care criteria’ are met. Whether this was the case is retrospectively assessed by the Assessment Committee.

The entire legal framework for termination of pregnancy in the Netherlands (Penal Code, Termination of Pregnancy Act, Termination of Pregnancy Decree, Regulation Late Termination of Pregnancy) is centred around the concept of viability. More specifically, around the viability limit of 24 weeks GA. Because of the current revision of the guideline on perinatal care for extreme prematurity, the entwinement of the regulations on abortion and prematurity in the Netherlands becomes very clear for the first time in the history of legal abortion (see Table 1).

In this paper, we examine the ethical legitimacy of fetal viability as the threshold for abortion in the Netherlands. First, we discuss the multi-interpretable concept of viability. Then, we investigate how viability has been interpreted and applied in the Netherlands and how it is a pivotal concept for the provision of care for infants born extremely prematurely as well as for the regulation of abortion. Third, we show that for abortion regulation it is morally problematic to rely on *any* interpretation of viability, because it is too indeterminate a concept to be of use to establish an abortion threshold in a morally relevant way. Lastly, we provide recommendations for changing the Dutch legal framework for abortion.

The concept of fetal viability

The concept of fetal viability is complex and can be interpreted in many ways. Di Stefano et al. provide a helpful overview of different ways in which viability can be understood (20). The authors differentiate between *absolute* viability (the GA at which the youngest extremely premature infant has ever survived), *median* viability (the GA at which around 50 percent of the infants born extreme prematurely survive with medical intervention, with or without disabilities), *median intact* viability (the GA at which around 50 percent of the infants born extreme prematurely survive with medical intervention, without disabilities), and *natural* viability (the GA at which around 50 percent of the infants survive without medical intervention, with or without disabilities). The variables between these interpretations are the number of infants that survive when born at X weeks GA, the use of medical technological support at birth, and the account of eventual disabilities. In all the above interpretations, viability is a 'statistical property': not every fetus will survive when born at the so-called limit of viability.

Except for natural viability, viability in these interpretations depends on advances in perinatal medicine, insights in fetal development, and pharmacological innovation. These are contextual variables. Globally, there are differences in the availability of resources, infrastructure and knowledge. We will therefore add a new level of interpretational difference: viability can be understood either as '*actual* viability' or 'viability *in principle*'.

Actual viability is the GA at which a country offers neonatal intensive care to extremely premature infants. Below this threshold, offering neonatal intensive care is considered medically futile, or simply not feasible, and therefore morally problematic. Actual viability depends upon (a) the national availability of resources, infrastructure and knowledge and (b) treatment guidelines for perinatal care at the limit of viability. Of course, (b) also depends upon (a). That is, guidelines are dependent upon the available resources; if a country does not have the resources to provide intensive care, the national guideline will presumably not advise to do so. Because (a) and (b) differ between countries, actual viability also differs between countries. For example, actual median viability is around 22 weeks GA in Sweden and Japan, and around 26 weeks GA in Nigeria (2,21-23). The limit of viability is typically lower in high-income countries than in low-income countries (24). Besides resources, treatment guidelines can also be influenced by societal and cultural values. In the Netherlands, for example, values such as independence and quality of life may explain the 'higher' treatment limit for extreme prematurity (25).

Viability in principle (as opposed to actual viability) is independent of (a) and (b). In Zaitchik's words, what we call viability in principle does not rely on the "medical technology actually available to the particular fetus in question (but the) medical technology in principle available, perhaps only somewhere else in the world and only to the wealthy."(26) Viability in principle takes no notice of the "deliverability" of the fetus (26). For a schematic representation of the different interpretations of viability, see Figure 1.

Viability in the Netherlands

In the Netherlands, viability has been an important concept for extreme prematurity as well as abortion, although from contrasting perspectives. For the case of extreme prematurity, it refers to the point at which it is considered medically meaningful and ethically desirable to offer intensive care. Viability functions as a necessary but not sufficient condition for offering intensive care treatment. That is, if a fetus is not deemed viable, it is medically futile to offer intensive care treatment. However, if a fetus is deemed viable, it is not necessarily medically meaningful to offer intensive care; the possibility of survival is not the only consideration for deciding to offer intensive care treatment. According to research involving parents and healthcare professionals with experience of extreme preterm birth, factors such as the infant's (long-term) health outcomes and the quality of life for the family are also highly important for periviability decision-making (27). In a recent study by Edmonds and colleagues, parents shared their perspectives on what was crucial when deciding on the management of periviable birth. Important considerations mentioned included 'the best interest of their infant', 'having a healthy baby', or 'avoiding pain and suffering' (28).

For abortion, viability is used as the legal cut-off point for legal prosecution in case of pregnancy termination. In the past, however, viability has always been defined as a different GA for both neonatal care and abortion. In the Dutch history of abortion, the meaning of the 24-week GA cut-off in relation to the definition of viability has evolved over time. In 1984, when the Termination of Pregnancy Act was enacted, no infants born at 24 weeks GA survived in the Netherlands. At that time, the Dutch Ministry of Health, Welfare and Sport seemed to understand viability as viability in principle: at that moment, somewhere in the world, infants born at 24 weeks GA were surviving outside the pregnant person's womb. At present, however, around half of the extremely premature infants born at 24 weeks GA survive in the Netherlands, with medical technological support, with or without disabilities (21). In the Netherlands, the meaning of viability seems to have evolved, implicitly, from absolute viability in principle in the 1980s (at that time, somewhere in the world, the youngest survivor of extreme prematurity was born around 24 weeks GA), to actual median viability in the 2020s (at present, around 50 percent of Dutch infants born at 24 weeks survives).

The Dutch framework for abortion, and care practice at the limit of viability are intrinsically linked. On the one hand, keeping a certain fixed interpretation of viability results in a continuous change of the corresponding GA – due to innovation in perinatal care. On the other hand, keeping a certain fixed GA for viability results in a change of the corresponding interpretation of viability (see Table 2).

Although these shifts in meaning have caused little debate so far, a revision of the guideline on perinatal care would likely change this, because determinations of viability in cases of perinatal care and abortion would differ explicitly. Concretely, a fetus of, say, 23 weeks GA would be considered viable in one medical context (perinatal care) and not viable in another (abortion). Since viability in extreme prematurity functions as a necessary condition for offering treatment, a lower treatment limit seemingly implies a lower abortion threshold.

Viability as the criterion for (dis)allowing abortion

To understand what it means to base abortion regulation on viability, consider the following hypothetical cases of extreme prematurity and abortion. In these cases, abortion regulation is based upon actual viability.

Person A and Person B are both 23 weeks pregnant. A lives in high-income country X, B lives in low-income country Y. In country X, viability is set at 24 weeks GA. In country Y, viability is set at 29 weeks GA; highly specialized care is lacking. A and B both deliver their baby at 24 weeks GA. A's baby survives. B's baby does not. If B would have been on vacation in country X at the time of labor, her baby may have survived. In this case, an extremely premature baby dies because of the lack of availability of medical technology. In the case of extreme prematurity, the availability of medical technology matters: it determines what can be done for an extremely premature infant. The availability of resources, infrastructure and knowledge is morally relevant in case of extreme prematurity.

Consider now that country X and country Y both have actual viability as their abortion threshold. Given the available medical technology, the abortion threshold in country X is set at 24 weeks GA and in country Y it is set at 29 weeks GA. A and B both find out that they are pregnant at 24 weeks GA. They both want to terminate their pregnancy. For B this is no problem. A, however, is not allowed to have an abortion. Oddly enough, the possibility for A to have an abortion is linked to the available medical technology of country X, but the available medical technology has no relation to the possibility of terminating the pregnancy. The availability of resources, infrastructure and knowledge is, prima facie, morally irrelevant in case of abortion.

Given that a request for abortion is not a request for providing neonatal care, the availability of said care is a morally arbitrary criterion for (dis)allowing abortion. It does not matter whether the fetus would have received neonatal care if it was born extremely premature in deciding whether having an abortion should be allowed.

In other words, basing the admissibility of abortion on actual viability (as appears to be the case in the Netherlands) is morally problematic as the availability of medical technology is irrelevant for the proper establishment of the limit to abortion. Other authors have made similar points (26,29). One author writes that: "No one would want to say that by flying from Cambridge to Calcutta a woman suddenly gained the right to destroy a formerly "viable" but now "pre-viable" fetus, or that the fetus suddenly ceased to be a person or human, or that it suddenly lost a "right to life" (26).

Now this objection might be worked around by opting for a different interpretation of viability, which is independent of the (national) availability of resources, infrastructure and knowledge, and treatment guidelines for perinatal care at the limit of viability, that is, either viability in principle or natural viability. Before we are in position to evaluate these options, however, we need to consider why viability is deemed morally relevant for abortion in the first place.

In the literature, the main argument in favor of viability as a morally relevant cut-off point for abortion, is that it indicates the point in time at which a fetus can survive independently of the pregnant person's body (30). That is, referring to the illustrious thought experiment of Thomson, the point at which the 'detaching' of the fetus no longer equals the 'killing' of it (31). Our discussion of viability has already shown that this point in time is notoriously hard to determine. Accordingly, independent survival suffers from the same problems as viability when it comes to determining an abortion threshold: it can be understood as actual or in principle, technological or natural, etc. To be viable is to be able to survive independently and vice versa. But the problem here is that we have used one underdetermined concept to explain another underdetermined concept. No insights are gained.

So why do scholars consider independent survival morally relevant to determine abortion thresholds? Usually, because it is construed as a necessary condition or marker of personhood, or some other form of moral status from which the right to life follows. Now given the (near-)synonymity of independent survival and viability, can independent survival function as such a condition or marker?

In light of the above, an actual interpretation of independent survival is out of the question. Just like actual viability, it would be determined by the (national) availability of resources, infrastructure and knowledge, and treatment guidelines for perinatal care at the limit of viability, with all the ethical consequences detailed above. On other interpretations of viability, independent survival fares no better, but for different reasons.

Recall that every interpretation of viability is to be understood as a statistical property. It usually ranges from 21 weeks GA (absolute viability – N=1) to 34 weeks GA (natural viability – around 50 percent of infants survive without medical intervention, with or without disabilities), but can logically be extended even further. For interpretations of viability that rely upon long-term survival, even birth does not equal viability, as infants sometimes do not survive (the first days after) delivery. Furthermore, because of advancements in neonatal medical technologies, it is imaginable that infants born before 21 weeks GA can one day be ‘viable’. Over the years, younger and younger extremely premature infants can receive intensive care at birth and survive (32). One day, we may reach an absolute biological limit of viability. Irrespective of medical science, fetal organ growth and development will take a minimum of time (32). However, innovative medical technological inventions might even then lower the limit of viability. An example of this is artificial amniotic sac and placenta technology often referred to as artificial womb technology (33,34). In the future, this innovation might make it possible for fetuses to be independent from the pregnant person’s body earlier than they currently are.

Furthermore, there is no logically compelling reason to limit concepts of viability to 50 percent of infants rather than, say, 60, 75 or even 90 percent of infants surviving without medical intervention, with or without disabilities. Now in view of this extensive range of interpretations, it is unclear how a concept as indeterminate as viability could serve as a marker or condition of determinate concepts like personhood, or right to life. There is no compelling moral argument to prefer one moment in the viability range over another (although there can be legitimate pragmatic or political reasons to choose one). Viability, therefore, cannot serve as a moral basis to decide whether a fetus is (to be treated as) a person. As a result, independent survival loses its moral relevance as a cut-off point for abortion.

For extreme prematurity, the availability of neonatal care and the percentage of extremely premature survivors are morally relevant. We are in favor of relying upon technological actual viability for this field of health care. For abortion however, contextual factors such as the availability of technology but also the personalized prognosis of viability for the fetus are not morally relevant. It does not matter whether the fetus *would have* received neonatal intensive care *if* it was born extremely premature in deciding about the permissibility of abortion. The point in time that is usually considered morally relevant for abortion is when the detaching of the fetus no longer equals the killing of the fetus, that is, the possibility of independent survival. Given the (near-)synonymity of independent survival and viability and the underdetermined nature of both concepts, independent survival cannot serve as a morally relevant criterion. If the argument does not work with viability it will also not work with independent survival.

Changing the Dutch legal framework for abortion

Scholars have put forward that viability is not an ideal abortion threshold as it is morally problematic, conceptually and or practically ambiguous, and a slippery slope towards an abortion ban (26,29, 34-37). It has also been suggested that the viability-threshold implies an unjustified conflation between the fetus' interests and the pregnant person's duties. Already in 1995, Gert pointed out that the viability-threshold is peculiar in relation to the pregnant person's duties: "As long as (the fetus) needs you, you are not responsible to it; when it doesn't need you anymore, you are." (38) After viability, however, the pregnant person does no longer need to carry sole responsibility to pursue the fetal interest of surviving; technology can promote this interest as well. Yet, in more recent literature, it has been argued that inducing birth for post-viability abortions brings about another conflict, one with the pregnant person's autonomy; "(…) The process of birthing a fetus makes use of the body of the pregnant person in significant ways. (…) Just as it is sometimes morally permissible to choose to have an abortion rather than continue a pregnancy, it is sometimes morally permissible to choose to have an abortion rather than undergo an induction or cesarean."(36) Still, a viability-based abortion threshold could overall be the 'least bad' option, out of all similarly 'bad' options. We are convinced, however, that – especially for the Dutch situation – there are better options.

Another moral ground for abortion in the Netherlands

As explained, the Dutch legal framework for abortion aims to serve two principles: protecting unborn human life and relieving the emergency situation of the woman. These aims result in a viability-based abortion threshold; only abortions of viable fetuses are punishable by law. We have shown that a viability-based abortion threshold is morally problematic. It is beyond the scope of this paper to fully develop a normative alternative framework for an abortion threshold. Yet, in what follows we will outline what are morally relevant grounds for developing such a framework, namely, the autonomy of the pregnant person to decide what happens to her body and the fetus' interest to survive.

Whatever abortion threshold is chosen, it should weigh or balance the interests of its two stakeholders, both the fetus and the pregnant person. From the viewpoint of autonomy, the pregnant person's interest is to have the option to abort open for as long as possible. In this way, their opportunity to exercise autonomy is maximized. The fetus' interest is to survive, and thus to be protected (we leave questions about whether there are circumstances in which it would be better for the fetus not to be born unaddressed). If we consider *only* the interests of the pregnant person, abortion should be permissible throughout the entire pregnancy. The same goes for the protection of the fetus. If we consider *only* the fetus' interest to be protected, abortion should be banned. Assigning relative weight to these interests (respect for the autonomy of the pregnant person to decide what happens to her body and the protection of life) constitutes a relevant moral ground for abortion regulation.

It could be argued that this moral ground is, like viability, subject to interpretation. This is correct. Unlike viability, however, the weighing of both interests is morally relevant for the moral justification of an abortion threshold. That is, if we consider when it is justifiable to terminate a pregnancy and thereby terminate the life of one subject to promote the autonomy, prevent harm or promote the good of another subject, it is paramount that the stakeholders' potential gains and harms register on the moral scale. Internationally differing interpretations might raise practical concerns but are not ethically problematic. The corresponding GA for the point of balance can be influenced by differing sociocultural values and convictions related to reproductive autonomy, personhood and the right to life. Just as different countries have different speed limits but similar reasons for having these limits in place, we think that having different points of balance is not problematic as long as they take into account the relevant moral grounds. Deciding about the abortion threshold thus may have an empirical component. An abortion threshold that is based upon a balance between the interests of the pregnant person and the interests of the fetus has a defensible moral ground, and is therefore preferable to one based on viability.[1]

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[1] It is possible for a state to weigh the interests of the fetus and the pregnant person and conclude that the appropriate balance is best served by a threshold of viability. However, to support this position, it would be necessary to clarify (a) which interpretation of viability is being used, and (b) under what conditions that interpretation can be changed (e.g., advancing assisted reproductive technology). There should not be a problem with viability as long as it is very clearly defined, but in practice, it often just comes down to a certain number of weeks of gestational age within the viability range. This raises the question of what the concept of viability adds, if anything, to the discussion.

Conclusion

In the Netherlands, viability has been an important concept for extreme prematurity as well as abortion. Yet, we have shown that viability can be interpreted in many ways. For extreme prematurity, viability should be interpreted as technological actual viability. For abortion, however, it is morally problematic to rely upon this or any other interpretation of viability. This leaves the Netherlands with the following choice of policy options in view of the proposed revision of the guideline on perinatal care for extreme prematurity. The 24-week GA abortion threshold in Dutch law was based on absolute viability. If this interpretation of viability is to be retained the Dutch abortion threshold should be lowered. If this is deemed undesirable, the Dutch could either abandon viability as a marker for personhood or opt explicitly for another interpretation of viability in the case of abortion. Another option would be to change the basis of Dutch abortion regulation entirely. A set GA could be incorporated in the Penal Code or the Termination of Pregnancy Act. Or another moral ground for abortion can be introduced: the balancing of the interests of the pregnant person and the fetus – which would be our recommendation for the Dutch practice.

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Table 1: Treatment limits and the abortion threshold in the Netherlands throughout the years

Perinatal guideline	Treatment limit	Abortion threshold
<2005	$26^{+0/7}$ weeks GA	$24^{+0/7}$ weeks GA
2005-2010	$25^{+0/7}$ weeks GA	$24^{+0/7}$ weeks GA
2010-2022	$24^{+0/7}$ weeks GA	$24^{+0/7}$ weeks GA
>2023	$<24^{+0/7}$ weeks GA?	$<24^{+0/7}$ weeks GA?

Table 2: Viability and interpretations of viability

A: Viability fixed, interpretation changing

	1980s	2000s	2020s
Viability in terms of GA	24 weeks	24 weeks	24 weeks
Interpretation of viability	Absolute viability in principle	Median viability in principle	Actual median viability

B: Viability changing, interpretation fixed

	1980s	2000s	2020s
Interpretation of viability	Absolute viability in principle	Absolute viability in principle	Absolute viability in principle
Viability in terms of GA	24 weeks	23 weeks	21/2 weeks

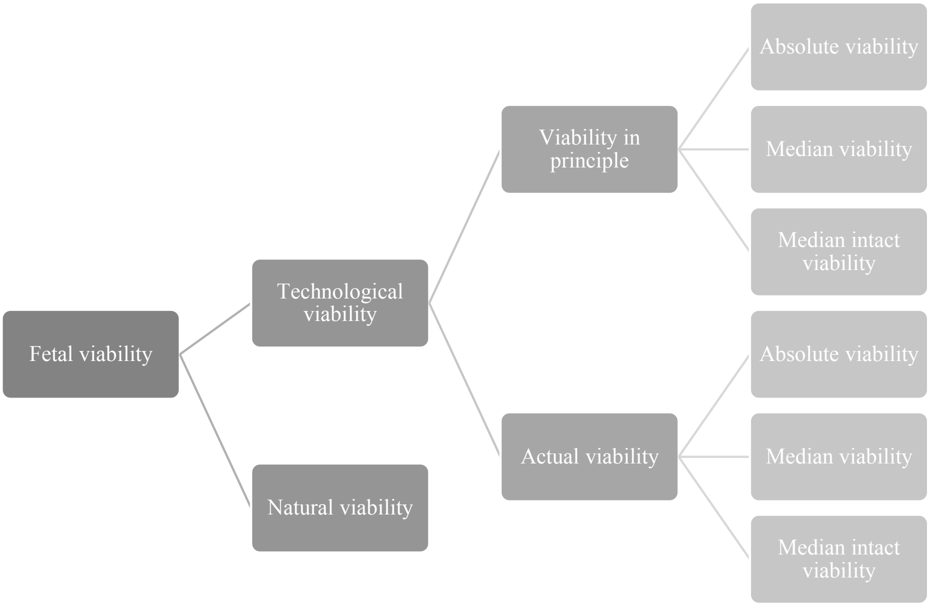

Figure 1: Interpretations of fetal viability


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PERSONALIZATION AT THE LIMIT OF VIABILITY:

STRIKING THE RIGHT BALANCE

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Under review

Introduction

Decision-making regarding periviable birth remains a critical issue that receives considerable attention in current literature.(1-3) For extreme premature births, prognostic uncertainty is high, especially for those born in the so-called 'grey zone'. For births in the grey zone, there is no clear medical nor moral consensus on the preferred treatment option: intensive care or palliative care. Arbour et al. define the grey zone as a category of births where 'reasonable people' may have differing opinions regarding the appropriate course of action.(4) Most often, a shared decision-making approach is used for decision-making at the limit of viability, where healthcare professionals and parents jointly decide on the treatment plan.(5,6) Periviable birth has significant (lifelong) consequences for both infants and parents(7,8), underscoring the importance of ongoing research and innovation to enhance outcomes, care and decision-making for these families.

The existing body of literature on extreme prematurity shows a growing interest in 'personalization' or 'individualization' at the limit of viability. (9-11) Haward et al. summarize personalization as "tailoring interventions, communication, and opportunities to meet parents where they are, rather than taking a "one size fits all" approach". (12) Generally, personalization is discussed as considering the specific characteristics, preferences and needs of individual families. In the context of extreme prematurity, it is driven by two main objectives: enhancing decision-making for parents and healthcare professionals, and promoting parental well-being.

Personalization at the limit of viability is, however, a multifaceted concept. A more systematic untangling is lacking. In this article, we will start by identifying three types of periviability personalization: personalized care, personalized counseling, and personalized guidelines. Each type of personalization should be evaluated separately in terms of its ability to achieve the two objectives mentioned earlier.

The central argument of this article is that, while personalized counseling and personalized care inherently enhance decision-making and promote parental well-being, the same cannot be guaranteed for personalized guidelines. Personalized guidelines can lead to information overload, and complicate rather than simplify the decision-making process. Furthermore, they potentially harm parents in two ways. First, the process of obtaining individual prognostic predictions may require parents to disclose sensitive information, which could lead to discomfort and in some cases even stigmatization. Second, if a poor prognosis is determined based on individual prognostic factors, this could result in 'victim-blaming', by implying that the infant's prognosis would have been better if the parents had, for example, a higher socioeconomic status.

In this article, therefore, it will be argued that personalized guidelines should be approached with caution. Periviability guidelines must be personalized for the sake of enhancing decision-making and promoting parental well-being, not just for the sake of personalization.

Different types of periviability personalization

Personalized care

The first type of periviability personalization is personalized care. Parents view personalized care as being 'seen and heard' by healthcare professionals, developing a trusting relationship with them, and receiving various forms of support beyond medical care. (9,12-14) This requires considering the unique needs and circumstances of each family. For example, by acknowledging the fact that the premature infant has siblings, by assisting parents in finding accommodation close to the hospital during their infant's hospitalization, or by referring them to psychological counseling when necessary. (14) The 'persons' in *person*alized care are the parents: the care (process) is tailored to their specific characteristics, preferences and needs.

Personalized counseling

The second type of periviability personalization is personalized counseling. In the existing body of literature on prenatal counseling for extreme prematurity, there is a growing trend towards personalization.(10) Personalized counseling involves, among others, adjusting the (amount of) information and the decision-making approach to better meet the individual parents.(9,12) Some parents prefer to make treatment decisions more autonomously, while others seek guidance from healthcare professionals or defer the decision to them.(15) Similarly, some parents prefer detailed discussions about statistical outcome information, while others prefer a general overview of the situation and possible consequences of extreme preterm birth.(16) Therefore, information and decision-making can be personalized by adapting it to the parents rather than, for example, following a predetermined checklist.(9,12,15,16) The importance of parental values in personalized counseling for extreme preterm birth is emphasized in the literature.(10,17-20) While some parents prioritize 'quality of life', others may prioritize 'the sanctity of life' – and even among parents who prioritize quality of life, perspectives may vary greatly.(17)

Different values may lead to different conversations and decisions. The ‘persons’ in *person*alized counseling are, again, the parents, with information and decision-making tailored to their unique circumstances.

In a sense, personalized care and personalized counseling are two sides of the same coin. They are closely intertwined, as both rely on healthcare professionals to get to know, understand and connect with the family, and adapt their approach accordingly to the family’s characteristics, values, preferences and needs.

Personalized guidelines

A third type of periviability personalization is personalized guidelines. In a personalized guideline, a range of prognostic factors which go beyond the ‘conventional’ factor gestational age are considered to forecast the prognosis of an extremely premature infant.(21,22) Research shows that several prognostic factors can influence an infant’s prognosis.(23,24) Currently, the most prevalent prognostic factors in personalized guidelines are gestational age, estimated birth weight, prenatal corticosteroids, multiplicity, and fetal sex.(25) Research is also conducted to assess the impact of other (potential) prognostic factors, such as socioeconomic status and ethnicity, or maternal factors such as stress or pre-pregnancy body mass index.(26-30)

An example of a personalized guideline can be found in the United Kingdom with the 2019 framework for *Perinatal Management of Extreme Preterm Birth Before 27 weeks of Gestation*. (21) It is stated that “(d)ecisions should be (…) based on the best available evidence about the prognosis for the individual baby (…). It is essential that such decisions reflect all relevant prognostic information and not simply gestational age”. In the UK framework, the following prognostic factors are considered: gestational age, fetal growth, fetal sex, multiplicity, prenatal corticosteroids, and the setting for birth.

Another example can be found in Canada. (22) The Canadian position statement on *Counselling and Management for Anticipated Extremely Preterm Birth* outlines the use of a prognosis-based approach that considers factors such as gestational age, estimated birth weight, prenatal corticosteroids, multiplicity, fetal status and anomalies on ultrasound, and place of birth. The statement emphasizes that: “The (healthcare professionals’) expertise lies in recognizing major biological and medical factors influencing survival and long-term prognosis, while the family knows most about the socioenvironmental and familial characteristics that will influence their infant’s outcomes (e.g., finances, resource availability, support from extended family). Such characteristics are difficult to measure but must all be considered in the (shared decision-making) process”.

Personalized guidelines can take two distinct approaches regarding the use of prognostic factors. The first approach, as outlined in the Canadian statement, involves healthcare professionals considering multiple prognostic factors during prenatal counseling and the decision-making process with parents. Healthcare professionals utilize this information to collaborate with parents and assess their unique circumstances, instead of relying on these factors to provide a calculated or estimated prognosis or establish a specific cut-off limit for offering intensive care treatment. The second approach involves using a prognostic model to forecast the chances of a positive outcome for the infant, presented as a percentage or range of possibilities. This approach utilizes statistical models based on large datasets to provide information about an infant's chances of survival or other outcomes.

There are numerous prognostic models available worldwide. In 2021, van Beek and colleagues conducted a systematic review that identified 144 prognostic models for predicting mortality in very preterm infants. (31) These models use various prognostic predictors, and different models weigh the prognostic factors differently. The review found that gestational age, Apgar score, estimated birth weight, fetal sex, multiplicity, prenatal corticosteroids, and ethnicity were used as predictors in more than forty models. The National Institutes of Health calculator is a well-known example of a prognostic model that provides information on survival rates and developmental delays based on multiple factors. (25) The calculator suggests that relying solely on gestational age to predict outcomes after extreme preterm birth is not a reliable approach for predicting outcomes. For instance, a girl born at 24 weeks from a multiple pregnancy, weighing 490 grams, and receiving corticosteroids has a 52 percent chance of survival after intensive care treatment and a 31-46 percent chance of cognitive developmental delay. Meanwhile, a boy born at 24 weeks from a singleton pregnancy, weighing 420 grams, and not receiving corticosteroids has a 23 percent chance of survival and a 46-67 percent chance of developmental delay. (25)

The use of prognostic models is, however, not without its limitations. Firstly, there is no international consensus on which factors to consider and how to weigh them. Secondly, prognostic predictions are based on population averages and, therefore, are unavoidably limited in their ability to accurately predict an individual's prognosis. (4) Furthermore, there is significant variability in management practices among different institutions (32,33), which can further impact the accuracy of these predictions.

The ‘person’ in *person*alized guidelines is the extremely preterm infant. In personalized guidelines, individual characteristics of the infant that may impact her prognosis and future quality of life are considered.

The objectives of periviability personalization

Personalization in the context of extreme prematurity has two primary objectives: to enhance decision-making for parents and healthcare professionals, and to promote parental well-being.

Decision-making at the limit of viability is a complex, emotionally charged, and time-sensitive process. (1-3) There is ongoing research to further understand and improve parental decision-making. For example, one recently proposed approach is ‘postponed withholding’, where intensive care at birth is initiated by default and parental decision-making about (a redirection of) the care approach is postponed for a week.(34) While the traditional approach involves prenatal counseling to inform parents about treatment options, risks, and potential outcomes, leading to a shared decision between intensive care and palliative care, the postponed withholding approach suggests initiating intensive care for all infants, redirecting to palliative care after one week *unless* the parents request otherwise. This approach aims to empower parents, improve decision-making by balancing parental bias towards ‘saving’ their infant and providing parents with more time and space to make the decision.

As we have written elsewhere (35), however, postponed withholding may lead to both over- and undertreatment, which is not in the best interest of extremely premature infants. Moreover, decision-making in the second week, after intensive care has already begun, may be ethically, legally, and psychologically even more complex. It could create conflicts and psychological burdens for healthcare professionals if the prognosis improves, or it may make parents feel responsible for ending their infant’s life. It may be that, instead of finding new approaches to decision-making for extreme prematurity, the traditional approach should be strengthened – by opting for a personalized approach, perhaps.

Before discussing *how* personalization may enhance parental decision-making, it is important to clarify what is meant by this phrase. Enhancing decision-making means empowering parents and making them feel more confident in making a decision that aligns with their values or enabling a decision-making process that results in a decision that is better adjusted to the family’s values, needs, and preferences.

A second objective of personalization in the periviability context is to promote parental well-being. Numerous studies have demonstrated that preterm birth can be a traumatic experience for parents (and infants) and can have long-lasting psychological and social consequences. (7,8) As in all areas of medicine, it is crucial to prioritize beneficence and non-maleficence, that is, promoting parental well-being as much as possible, and avoiding any additional harm to parents in this already vulnerable situation.

In the upcoming section, we will begin by very briefly discussing how personalized care and personalized counseling inherently enhance decision-making and promote parental well-being. Following that, we will argue that personalized guidelines *may* have the potential to achieve these objectives but are not guaranteed to do so.

Achieving the objectives

Personalized care and personalized counseling inherently achieve the objectives of personalization. Adjusting counseling helps parents to better understand the information being shared with them, which can increase their comfort and confidence in decision-making, and better allows them to express any concerns or questions they may have.(9,12,14) Additionally, personalized counseling can better accommodate individual differences and cultural backgrounds, which can lead to parents feeling more respected, supported, and empowered to make decisions that are best for themselves and their families. Personalized care, also, is inherently beneficent because it tailors the care process to the unique needs and preferences of the parents. When implemented in a thoughtful way, personalized care and personalized counseling are powerful tools for enhancing decision-making and promoting well-being.

This is, however, not necessarily the case for personalized guidelines. Let us first examine the advantages of personalized guidelines, or, how they can indeed enhance decision-making and promote parental well-being.

Personalized guidelines may have some benefits. The general consensus in the literature is that it is ethically preferable to consider more factors than solely gestational age when developing guidelines and making treatment decisions at the limit of viability.(36,37) Gestational age-based guidelines have been criticized in the literature for being ethically problematic because gestational age is an estimated factor, and does not on its own provide a prediction of outcomes.(38) Additionally, they are criticized for risking a self-fulfilling prophecy: if babies born at a certain gestational age are not treated, they will inevitably not survive.(39) Empirical research also suggests that guidelines considering additional prognostic factors are preferred by healthcare professionals, experienced parents, and adults born extremely premature.(14,40,41) Personalized guidelines are seen as fairer, less rigid, and more informative for families regarding the expected quality of life.

Personalized guidelines can indeed benefit parents, infants, and healthcare professionals. They may benefit parents by providing them with the most accurate information about their infant's possible outcomes. This may enable them to better align their decision with their values and perspectives on factors such as disabilities, care needs, and quality of life. Extremely preterm infants can benefit from improved prognostic accuracy by, for example, avoiding painful NICU procedures if there are too limited or no prospects for an acceptable quality of life. And healthcare professionals can benefit from more precise prognostic predictions, enabling them to better anticipate possible consequences and guide parental decision-making more effectively[1]. In a way, personalized guidelines have the potential to better protect against medically futile treatment by helping to identify which infants would benefit from treatment. That is, these guidelines may more effectively differentiate between infants who have a higher likelihood of responding positively to treatment and those for whom the chances of positive outcomes may be limited or unlikely.

So, personalized guidelines can be advantageous. However, they could also impair parental decision-making, and there are at least two ways in which they potentially harm parents.

Impairing decision-making

Presenting intricate details regarding numerous prognostic factors can potentially result in information overload, which is a substantial issue.(42) Studies indicate that parents encounter considerable difficulty when attempting to comprehend information during prenatal counseling.(43) Moreover, it is crucial to acknowledge

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[1] It is crucial that the prognostic factors considered in personalized guidelines are evidence-based in order for these advantages to be meaningful. Currently, evidence is lacking for some prognostic factors, and it is unclear whether the accumulation of prognostic factors that individually may lead to a more accurate prognosis also produces a more accurate prognosis. More research is needed to demonstrate their influence, explain underlying mechanisms, and weigh them relative to other prognostic factors. Only with sufficient evidence can personalized prognoses truly benefit parents, infants, and healthcare professionals.

the specific context of prenatal counseling in this regard, as parents often experience heightened stress levels, and mothers may endure physical discomfort. (44) Comprehending all relevant information during prenatal counseling may become even more demanding when additional prognostic information is introduced, and multiple individual factors are considered.

Furthermore, there is doubt as to whether the additional focus on prognostic information is a valuable use of time. In a recent vignette study, it was found that the data presented to parents did not have any significant impact on their decisions. (45) The study revealed that presenting a 30 per cent or 60 per cent survival probability to a randomly selected group of 1000 women had no effect on their decision-making. Additionally, the data presented did not impact their *perception* of the chance of survival, as participants seemed to believe the survival rate to be over 50 per cent even when informed of a 30 per cent survival rate. Also Laventhal and colleagues have pointed out that although there are many tools for calculating per cent survival and disability, there is no good data to show that such percentages align with parents' desires or affect their decisions.(46) The same authors conclude, however, that this does not necessarily mean that the information has no value: some parents may still want to know what happens to babies like theirs, and framing the information in the right way remains a key area of study.

Furthermore, an excessive amount of information on prognostic factors during prenatal counseling may take up valuable time that could better be used to discuss parental values and perspectives. For some parents, values or intuition may be more crucial for decision-making than prognostic information. Additionally, providing extra prognostic information must be viewed in the context of the unavoidable uncertainty that remains for births in the grey zone. Even if all prognostic information is considered, uncertainty remains. (47)

Taken together, personalized guidelines do not lead to an unqualified improvement of parental decision-making.

Harming parents

Personalized guidelines may also fail to achieve the second objective, to promote parental well-being.

First, they can have negative effects because parents may be required to share sensitive information for individual predictions. Some parents may not feel comfortable sharing information about their education, family history, ancestry, financial situation, housing conditions, and more. And second, personalized guidelines may unfairly place blame on parents, suggesting that their child's chances of a positive outcome depend on factors such as their financial status or (psycho)social context. Families who are already marginalized may be further stigmatized. Additionally, including these individual characteristics may lead to bias. Recent research has found that, for example, physicians with implicit bias towards socioeconomics are more likely to recommend comfort care when advising women of higher socioeconomic status. (48) There is also evidence of racial bias in healthcare professionals providing counseling at the limit of viability. (49) Incorporating such factors in personalized guidelines can increase the risk of bias and, therefore, harm parents and infants.

The effect of disclosing information on sensitive factors, such as socioeconomic status or ethnicity, to parents is still unclear. Studies have demonstrated, however, that some adults born extremely premature and their parents have perceived it as harmful that they were told to "be grateful that it is a girl, because they are fighters". (40) It is important to further investigate how parents and adults born preterm perceive information on possible prognostic factors.

While personalized guidelines based solely on 'medical' factors may seem like a solution, this approach may create an artificial distinction. In reality, medical factors are often intertwined with non-medical factors, as for example demonstrated by the existing body of literature on 'social determinants of health'. (50)

Striking a balance

Personalized guidelines should be developed with a focus on the objectives of personalization. The aim should be to parental decision-making and promote parental well-being, rather than solely pursuing personalization for its own sake. However, determining the practical implications of these objectives requires further crucial research. Future studies should prioritize investigating parental perspectives on potential prognostic factors and their discussion, and assessing the additional prognostic value of specific factors and how they should be weighed against one another.

While incorporating additional prognostic factors can provide valuable insights for parents and healthcare professionals, it is crucial to carefully consider the potential benefits against the risks and complexities they may introduce to decision-making. Maintaining proportionality is essential, as the added prognostic value must be substantial enough to justify any potential harm to parents or the increased complexity of decision-making. Striking the right balance for personalization at the limit of viability is therefore a delicate task. It is important to acknowledge that maximum personalization does not necessarily equate to optimal personalization in this particular context.

Conclusion

The aim of periviability personalization is to improve decision-making and to promote parental well-being. This article has identified three types of personalization at the limit of viability: care, counseling, and guidelines. While personalized care and counseling inherently support the objectives of personalization, personalized guidelines may not do so. Therefore, it is essential to approach personalized guidelines with caution. Proportionality is crucial: the added personalization by adding a prognostic value must be significant enough to justify any potential harm to parents or the added complexity to decision-making. Further research with parents is necessary to determine this balance.

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GENERAL DISCUSSION

General discussion

Every 40 seconds, a death related to prematurity occurs, highlighting the ongoing challenge of reducing premature births worldwide (1,2). Despite efforts over the past decade, no region has made substantial progress in this regard, with prematurity remaining the leading cause of neonatal mortality and health complications, as highlighted in a recent report by the World Health Organization (1). Over the years, there have been ongoing modifications to international periviability guidelines and treatment limits for managing extreme preterm births. On the one hand, several countries have lowered the limit for providing intensive care treatment (3,4). On the other hand, there is a trend to consider additional prognostic factors beyond the 'conventional' one: gestational age (5,6).

The primary focus of this dissertation has been to examine periviability guidelines and delve into the concept of personalization through three specific research questions: the need for a periviability guideline, the characteristics of such a guideline, and the aspect of personalization.

This research project started from the assumption that maximal personalization would result in optimal health care: 'the more personalization, the better'. This assumption appeared logical, as customized guidelines and care would likely lead to improved outcomes. However, the research conducted for this dissertation presents a more nuanced perspective. Specifically, in the context of extremely premature birth, achieving optimal personalization does not necessarily align with maximal personalization, particularly regarding periviability guidelines. This conclusion was informed by empirical research involving parents with experience of preterm birth and childrearing, and adults who were born prematurely.

In the discussion section, we begin by summarizing the key findings derived from the research conducted for this dissertation, and by examining significant patterns observed across all stakeholder groups, including the results from the survey study involving healthcare professionals. Subsequently, we present practical recommendations based on this research, with a specific focus on four areas: periviability guidelines, personalization at the limit of viability, policy on termination of pregnancy, and the further development and implementation of artificial amniotic sac and placenta technology.

Let me briefly explain why recommendations will be provided for these four areas, instead of solely focusing on periviability guidelines and personalization. The main research question in this dissertation centered around the ‘24-week infant’. This significant figure connects seemingly unconnected medical and bioethical discussions concerning periviability, perinatal care, personalization, and pregnancy termination. The ‘24-week limit’ has become a prominent concept when discussing prematurity and viability. And since 2010, the treatment limit in the Netherlands has been set at 24 weeks (7,8). The literature also addresses the ‘24-week fetus’ in the context of pregnancy termination (9). This is particularly relevant in the Netherlands, where the legal limit for abortion aligns with fetal viability and is set at 24 weeks of gestational age (10). Figure *x* represents the central place of the 24-week infant at the intersection of these divergent care practices.

Our work on personalizing periviability guidelines by considering multiple prognostic factors beyond just gestational age, inevitably leads to discussions about a lower treatment limit. These discussions raise important questions not only for extreme prematurity but also for the policy on termination of pregnancy in the Netherlands, assuming nothing would change in the current legal framework for abortion. Given the potential ramifications of a lower treatment limit in the Netherlands, it became imperative to explore the ethical validity and understand the conceptual basis of the interrelation between prematurity and abortion, especially given their potential impact on healthcare decision-making.

Similarly, the topic of artificial placenta and amniotic sac technology emerged as highly significant throughout the research process. Artificial placenta technology aims to replicate the essential functions of the amniotic sac, amniotic fluid, and placenta. Its primary objective is to maintain a fetal physiological state to support ongoing organ development and maturation. While the technology has demonstrated positive outcomes in animal studies (11,12), human trials are yet to be conducted. Artificial placenta technology aims to provide an alternative approach to neonatal care for infants born at the limits of viability, typically between 23 and 28 weeks of gestation (13). It is hypothesized that these infants would benefit from an environment resembling the womb during the critical early weeks, as they are not yet prepared for the challenges of an air-filled environment. By facilitating continued organ growth and development, particularly of the lungs, the artificial placenta aims to prevent organ damage. Ultimately, the objective is to improve the survival rates of extremely premature infants, minimize complications and disabilities, and enhance their overall quality of life.

As noted above, recent reports from the World Health Organization, as well as previous studies, have highlighted that outcomes for prematurity have not improved as intended (1,2,14). The introduction of new artificial placenta technology could be a game-changer. It holds the potential to significantly enhance outcomes at the limit of viability, thereby revolutionizing the field of extreme prematurity (15). While it may be premature to draw definitive conclusions about the impact of artificial placenta technology at this stage, it is crucial to engage in the debate due to its potential influence on the limit of viability and parental decision-making in cases of premature birth. Furthermore, if artificial placenta technology enables infants to 'survive independently from the womb' at an earlier stage, it could potentially have repercussions for the limit of legal abortion in the Netherlands. Given the interconnectedness of this topic with the other research conducted in this dissertation, we will provide further recommendations regarding the continued development and implementation of this innovative technology. But let me first present the research results.

Reflections on the key findings

During our research, we posed similar sets of questions to various stakeholder groups, including healthcare professionals, parents who have experienced extreme preterm birth, and adults who were born prematurely. On a collective analysis of the data, several trends emerged. But before we discuss them, two important methodological caveats are in order.

First, it is crucial to acknowledge the inherent divergence in the roles and perspectives of these stakeholders, because it significantly influences the interpretation of the data. In the context of births at the limit of viability, healthcare professionals and parents serve as the primary decision-makers, while adults who were born preterm approach the matter from the perspective of living with the long-term consequences of these decisions, and the conversations that took place between them, their parents, and their caregivers. When interviewing adults who were born extremely preterm, it is important to recognize the potential bias stemming from the fact that the decisions made during their birth were instrumental in their survival. Nonetheless, including this stakeholder group in qualitative research is vital to capture their unique perspectives, as they have firsthand experience of the long-term ramifications of periviability guidelines and decisions.

Second, we acknowledge that our participant sample could have been more diverse, which is a limitation of our study. Despite our conscious efforts to ensure diversity by utilizing a comprehensive database and purposive sampling techniques, there was an underrepresentation of individuals who identified as religious. The existing literature emphasizes the significance of religious considerations in periviability decision-making (16-18), thus this limitation may impact the comprehensiveness of our findings. Additionally, there was a lack of representation from non-white ethnicities. Research suggests that ethnic differences may play a role in perspectives on death, disability, and quality of life in periviable decision-making (19). For example, a study conducted by Edmonds et al. in the United States found that non-white women primarily focused on immediate survival and perseverance, whereas white women expressed concerns about the quality of life beyond the Neonatal Intensive Care Unit (20).

Future research endeavors should strive for greater diversity in the sample. By doing so, a more comprehensive understanding of the perspectives and considerations of various stakeholders involved in periviability decision-making could be attained. It is worth considering alternative research methods that may be more suitable for some individuals. For example, some parents may be less inclined to participate if they have to directly engage with researchers in an individual interview setting. Exploring different approaches, such as group discussions or online surveys, could facilitate broader participation and enhance the inclusivity of the research.

Despite the limitations of our study, a careful analysis of the collective data revealed several trends across the different stakeholder groups. These trends provide valuable insights into the three research questions: the necessity of a guideline, the nature of such a guideline, and the topic of personalization.

Is a periviability guideline necessary?

Regarding the necessity of a guideline, the data indicated a consensus among healthcare professionals, experienced parents, and adults born prematurely that a periviability guideline is crucial, albeit for different reasons. Adults who were born prematurely emphasized the importance of a guideline to prevent arbitrary treatment decisions and mitigate potential physician bias. They highlighted that having a clear guideline in place provides a safeguard against subjective judgment, ensuring that decisions are based on objective criteria and consistent standards of care. This is particularly significant considering the potential long-term consequences of periviability decisions on the lives of individuals born extremely premature.

Parents, on the other hand, expressed a preference for a guideline to assist them in decision-making and to provide a sense of security and guidance during a highly emotional and challenging time. They acknowledged the presence of their own biases, such as the parental 'instinct of saving', which can influence decision-making (21). Having a guideline in place helps parents rely on an established framework.

Among the healthcare professionals surveyed, a significant majority disagreed or strongly disagreed with the notion of not having a guideline. Their perspective aligns with the need for standardized protocols and consistent approaches in periviability decision-making. While guidelines cannot entirely resolve the ethical complexities inherent in these decisions, they provide valuable support for healthcare professionals in navigating the challenges and ensuring consistent and evidence-based care.

What type of guideline should be preferred?
Across all stakeholder groups, there was a consensus favoring a guideline that incorporates multiple prognostic factors rather than relying solely on gestational age. The current Dutch guidelines, which primarily rely on gestational age, received limited support among the stakeholders. Their concerns centered around the inflexibility and arbitrary nature of using gestational age as the sole determinant of treatment decisions.

However, when discussing the option of lowering the treatment limit and allowing intensive care treatment at, for example, 23 weeks in the Netherlands, stakeholders displayed hesitation. Their reservations often revolved around considerations related to the quality of life for infants born at such an early gestational age.

Most stakeholders preferred a gestational age-based approach supplemented by considering other prognostic factors to fine-tune the prognosis. This 'GA-based plus' approach considers both gestational age and additional factors, allowing for a more personalized assessment of the infant's prognosis. Only a few participants favored a strictly prognosis-based approach with a cutoff limit based on a certain percentage chance for a hopeful outcome. The hesitation towards a prognosis-based approach may stem from stakeholders' perspectives on personalization and their reluctance to be 'treated as mere statistics'.

Another notable trend among stakeholders was their preference for maintaining some degree of decision-making discretion for both parents and healthcare professionals. While stakeholders recognized the importance of a guideline as a protective measure against bias, they also emphasized the need for flexibility and individualized decision-making within the framework of the guideline. This recognition reflects the complex nature of periviability decisions and the desire to balance standardization with the unique circumstances and values of each case.

How should we personalize at the limit of viability?
The data obtained from stakeholders highlighted the significance of personalization in periviability decision-making. Stakeholders consistently emphasized the importance of being treated as individuals rather than being reduced to medical cases or statistics. They stressed the need for healthcare professionals to consider factors beyond strictly medical aspects and to consider the broader context of their lives. Effective communication and the establishment of meaningful relationships with healthcare professionals were identified as key components of personalization by the stakeholders.

This perspective on personalization helps explain the stakeholders' reluctance towards a guideline that strictly adheres to a predetermined cut-off limit for treatment. They expressed that true personalization cannot be achieved if a numerical value solely dictates the treatment decision. Stakeholders emphasized the significance of being recognized as unique individuals with their own specific circumstances and needs, rather than being reduced to mere data points.

Both parents and adults who were born prematurely demonstrated hesitation when it came to personalizing the prognosis based on factors such as sex, socioeconomic status, and ethnicity. There was a collective recognition of the complexities involved in personalizing these aspects and the potential ethical implications that arise from doing so. Stakeholders acknowledged the risk of discrimination, stigmatization, and feelings of guilt if certain factors were taken into consideration in the prognosis. They expressed concerns about assigning blame to parents based on these factors and recognized the need for a fair and unbiased approach to decision-making.

Implications and reflections
Two reflections emerge from these results. The first revolves around the different types of guidelines and the factors influencing stakeholder preferences. It is important to acknowledge that all guidelines, whether based on gestational age,

multiple prognostic factors, or a prognostic cut-off limit, rely on statistical data and numbers (22). Each type of guideline considers certain statistical thresholds or probabilities as significant indicators. For example, a treatment cut-off at 24 weeks may be determined because a 50 percent chance for survival at that gestational age is deemed 'good enough' to offer intensive care treatment. Similarly, a gestational age-based-plus guideline incorporates population statistics to fine-tune the prognosis beyond gestational age.

This brings us to the second reflection: statistical frameworks and numerical cut-offs for treatment are compatible with personalized care, provided there is sufficient attention to nuanced communication. Prognostic information is necessary, but the manner in which it is shared becomes paramount. The way healthcare professionals convey this information to patients and families significantly impacts their care experience, their understanding, and their decision-making process (23,24). By recognizing the statistical basis of guidelines but at the same time embracing effective communication, healthcare professionals can strike a balance between objective statistical data and personalized, empathetic care.

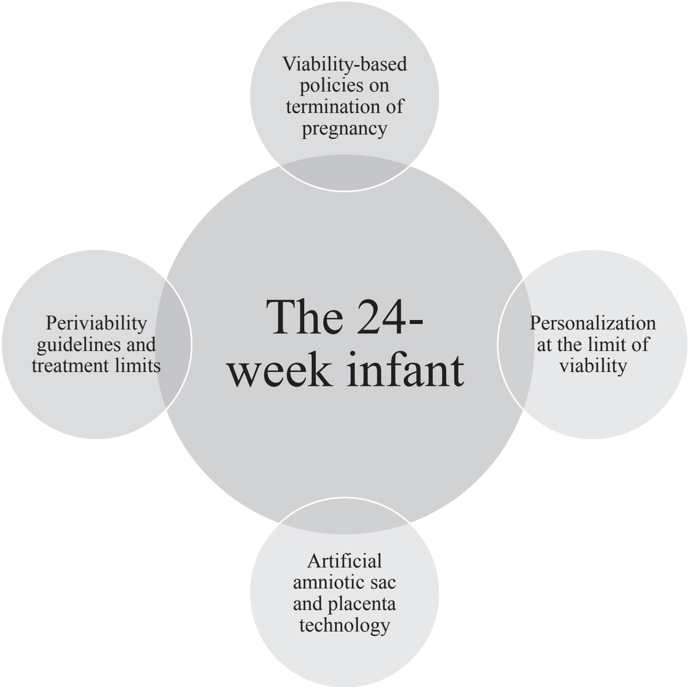

Figure *x:* The central place of the 24-week infant at the intersection of divergent care practices

Recommendations

Based on the valuable insights obtained from the empirical research conducted for this dissertation, several recommendations can be made in four specific research areas: periviability guidelines, personalization at the limit of viability, termination of pregnancy, and artificial amniotic sac and placenta technology. These recommendations aim to provide guidance for practice and future research, leveraging the empirical findings.

Periviability guidelines

Based on our research, we present the following recommendations regarding periviability guidelines. Periviability guidelines are necessary for multiple reasons. They offer decision-making support, ensure uniformity, and provide protection for parents, adults born prematurely, and healthcare professionals. Furthermore, it is imperative to move beyond relying on gestational age as the sole determining factor in periviability guidelines. The arbitrary nature of gestational age estimation raises ethical concerns (25,26) and conflicts with stakeholders' perspectives of personalized care, which can have adverse effects. By incorporating additional factors, guidelines can better capture the complexity of periviability decision-making.

Including an element of discretion is crucial, allowing parents to actively participate in the decision-making process and ensuring their perspectives are considered. Involving parents fosters empowerment and collaboration, recognizing their unique circumstances.

Our research highlights the Netherlands as an outlier with its relatively high treatment limit. Yet, we recommend lowering the treatment limit *only if* accompanied by enhanced attention to long-term follow-up care. A lower treatment limit should not be implemented in isolation but should be part of a comprehensive framework that includes robust systems for long-term follow-up care. Our findings reveal a lack of ongoing support for adults who were born prematurely, leaving them feeling neglected beyond a certain stage in life. Prematurity is a lifelong condition (27,28), and individuals requiring continued care should have access to lifelong follow-up support. The existence of these guidelines directly contributes to the survival of these individuals, establishing a societal responsibility to provide ongoing care for those whose lives have been sustained by them.

Furthermore, parents of infants born at the limit of viability also require comprehensive support. They may encounter emotional, psychological, and practical challenges in navigating the complexities associated with their child's care (29). Ensuring access to counseling, support groups, and resources can assist parents in coping with the unique demands of parenting an extremely premature infant and facilitate their decision-making process (30).

Recommendations with regard to periviability guidelines
A periviability guideline should not rely solely on gestational age as the determining factor
Periviability guidelines should encompass an element of discretion and avoid rigid cut-off points for providing treatment
Establishing a lower treatment limit for extreme prematurity can only be deemed ethically responsible if it is coupled with adequate attention to long-term follow-up care for both infants and parents

Personalization at the limit of viability

The second area in which we provide recommendations is personalization at the limit of viability. Our research, as presented in Chapter 9 of this dissertation, underscores the significance of personalization in the context of care and counseling. Healthcare professionals should aim to deeply understand the parents and infants they are caring for, enabling them to tailor their approach accordingly. Effective communication and the development of strong relationships between healthcare professionals and families are crucial, as highlighted by both parents and adults born preterm. It is important to recognize that personalization goes beyond the mere execution of tasks and encompasses a caring attitude that cannot be replaced by machines or algorithms.

While personalization of care and counseling is essential, finding the optimal level of personalization for guidelines requires striking a balance. Future research in this area should directly involve parents, specifically exploring their perspectives on prognostic factors and their preferences for communication. Understanding how parents perceive and value different factors can inform the development of personalized guidelines that align with their needs and preferences.

To achieve this, it is also necessary to be clear about the definition and objectives of personalization at the limit of viability. Healthcare professionals should have a clear understanding of the rationale and methods behind (the different types of) personalization to ensure its appropriate and effective implementation in practice.

By emphasizing effective communication, compassionate relationships, and trust, healthcare professionals can enhance the experience of receiving quality care, recognizing that personalization extends beyond guidelines and encompasses the relational aspects of care provision. By striking a balance between personalization and standardized practices, healthcare professionals can deliver care that meets the individual needs of parents and infants while upholding ethical and evidence-based standards.

Recommendations with regards to personalization at the limit of viability
Personalization at the limit of viability is a multifaceted concept that should be approached with clarity regarding its definition and objectives. It is essential to explicitly outline what is meant by personalization and establish clear goals when implementing personalized approaches
Personalization should be prioritized in prenatal counseling, encompassing information provision, decision-making processes, and building strong relationships between healthcare providers and parents
Finding the right balance is crucial when it comes to personalization in guidelines, as optimal personalization does not always equate to maximal personalization. Future research should involve parents and prioritize high-quality epidemiological studies to help identify this balance

Termination of pregnancy

Based on the analysis conducted in this dissertation, particularly in Chapter 8, regarding the termination of pregnancy policy, we propose the following recommendations.

First, there is a need to reevaluate the viability-based limit for pregnancy termination. Our research has demonstrated that relying solely on viability as a criterion for abortion raises moral concerns. The Netherlands should explore alternative options to ensure a more ethically grounded approach. These options include adopting a more explicit interpretation of viability for abortion or completely revising the basis of Dutch abortion regulation. This could involve incorporating a specific gestational age in the Penal Code or the Termination of Pregnancy Act, or introducing a new moral ground that explicitly balances the interests of the pregnant person and the fetus. Our recommendation is to consider the latter option. Following this, we strongly recommend that policies regarding the termination of pregnancy should be treated as a separate matter, distinct from policies concerning the management of infants born extremely premature. These are two entirely different care practices that require their own considerations and approaches. Giving each of them individual attention and consideration is essential to ensure appropriate and ethical decision-making in both situations.

Furthermore, it is crucial to improve access to appropriate care within the Netherlands for women who require late-term pregnancy termination due to therapeutic reasons beyond 24 weeks gestational age. Currently, Dutch women are compelled to seek care in neighboring countries due to limitations in the domestic healthcare system (31,32). This situation not only poses challenges to the well-being of pregnant individuals (and their partners) but also creates difficulties for treating physicians. Efforts should be made to establish comprehensive and accessible care pathways for women who require late-term pregnancy termination due to therapeutic reasons, ensuring that they can receive the necessary support and services within the country. Additionally, it is worth considering the development of a *specific* policy category for termination of pregnancy in cases of fetal abnormalities throughout the entirety of the pregnancy, recognizing the unique circumstances involved (33).

Lastly, the current abortion law, particularly the Regulation for late-term abortions, in the Netherlands creates uncertainty for physicians. The law allows abortion until the gestational viability limit is reached, after which it is equated with killing a child. This legal framework puts physicians in a potentially precarious position as they navigate the boundaries of the law when providing medically indicated terminations after the viability limit. To address this issue, a thorough review and clarification of the legal aspects surrounding late-term pregnancy termination is essential. Another viable option would be to implement a prospective assessment rather than a retrospective one to determine compliance with the legal framework surrounding termination of pregnancy.

Recommendations with regards to termination of pregnancy policy
Termination of pregnancy for fetal abnormalities requires its own distinct category, warranting the development of specific policies
The legal framework for termination of pregnancy should not be based upon the concept of fetal viability
Policies regarding termination of pregnancy should be addressed as a distinct matter, separate from policies concerning the management of infants born extremely premature

Artificial amniotic sac and placenta technology

In conclusion, let us consider the future implications of artificial amniotic sac and placenta technology, which holds promise for improving care for extreme prematurity. It is crucial to explore the ethical dimensions surrounding this technology and consider its impact on our perspectives on birth, healthcare responsibilities, and the concepts of fetus and neonate (34). Engaging in critical thinking and conducting empirical research with stakeholders are essential steps before widespread implementation.

The impacts of this technology can be categorized as ‘hard’ and ‘soft’ (35). Hard impacts involve measurable and factual aspects such as mortality rates, morbidity rates, and the impact on healthcare infrastructure and costs. Soft impacts, on the other hand, are more subjective and pertain to changes in practices, identities, morals, conceptions of a good life, and worldviews. Understanding and evaluating both types of impacts from an ethical perspective is crucial in shaping the technology and integrating it into society and the healthcare system.

In recent discussions on this technology various terms have been coined to describe its subject, such as ‘fetonate’, ‘gestateling’ or ‘perinate’, but there is no consensus on the appropriate nomenclature (36-39). However, the focus on terminology seems to obscure rather than clarify the ethical debate (39). Physiologically, the subject is a fetus, but morally we treat it as a neonate, due to the aim of providing optimal care for extremely premature infants. It is important to recognize this moral distinction and avoid getting entangled in debates over terminology. Moreover, treating the subject of the technology as a fetus could lead to paradoxical or nonsensical conclusions: the subject could potentially have fewer legal protections than a neonate, despite requiring better neonatal care (39). Such an outcome would not align with the interests of the fetus.

To further develop and implement artificial placenta technology, it is imperative to conduct empirical research that actively involves stakeholders, particularly parents. The literature currently lacks research that explores their perspectives and experiences, which are fundamental for informing the development and implementation of this technology. Parents are the ones who will be directly impacted by the technology and will have to navigate the emotional challenges of, for example, not being able to see or hear their child during the initial months. Understanding the perspectives of parents is essential for ensuring that the design and implementation of artificial placenta technology align with their needs and expectations. Their insights can provide valuable guidance in addressing concerns, optimizing user experience, and addressing any potential ethical considerations.

Another crucial recommendation is to ensure that ethical research on artificial placenta technology remains rooted in science rather than speculative fiction. The primary objectives of artificial placenta technology are to reduce mortality and morbidity rates in cases of extreme prematurity at the limit of viability. However, a significant portion of the existing literature on artificial placenta technology either explores applications that are unrelated to extreme prematurity or delves into applications of the technology that are not technologically feasible at the moment (40, 41). To truly harness the value of ethics in interdisciplinary research, it is essential to firmly ground it in scientific reality rather than relying on science fiction.

Considering the above, the following recommendations are offered regarding artificial amniotic sac and placenta technology:

Recommendations with regards to artificial amniotic sac and placenta technology
Prioritize empirical stakeholder research, especially with parents, to guide the further development and implementation of artificial placenta technology
Reduce excessive focus on terminology as it diverts attention from the core ethical debate surrounding the technology: the subject of the technology is a fetus, and morally, we treat it as a neonate
Ensure that ethical research on artificial placenta technology remains grounded in scientific principles rather than speculative fiction

Concluding remarks

While it may be tempting to envision a near future where the World Health Organization presents improved figures for prematurity outcomes, it is important to remain humble in the face of the complexities of extreme prematurity. Despite advancements in medical knowledge and technology, uncertainties persist, making it challenging to predict outcomes and provide optimal care for extremely premature infants, regardless of available prognostic information or sophisticated medical care. Despite these uncertainties, this dissertation presents potential avenues for improving guidelines and implementing personalized approaches to enhance stakeholder experiences. It is vital to recognize that the most valuable insights emerge from actively listening to the stakeholders involved, as their lived experiences and unique perspectives offer invaluable knowledge that should shape the future of care for extreme prematurity. By incorporating their voices and experiences, we can drive the development of policies, healthcare practices, and research initiatives, striving for meaningful change. This inclusive approach holds the promise of continually improving the care provided to extremely premature infants and their families in the years to come.

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APPENDICES

ENGLISH SUMMARY

English summary

The primary objective of this dissertation is to investigate periviability guidelines that provide guidance for prenatal decision-making and providing care at the limit of viability, with a specific focus on the concept of personalization at the limit of viability. This research project involves close collaboration with three essential stakeholders: adults who were born prematurely, parents who experienced preterm deliveries, and healthcare professionals. The study will address the following specific research questions: (a) should there be periviability guidelines? (b) what type of guideline should be preferred? And (c) how should personalization at the limit of viability be approached? Answering these research questions, we utilize a variety of research methods: literature review, quantitative and qualitative empirical research, and ethical analysis.

This dissertation is structured into three parts to comprehensively explore the research questions. **Part one** focuses on providing background information and context. It consists of two chapters that lay the necessary foundation for understanding the research questions and gaining initial insights into the topic. *Chapter 1* delves into the history of Dutch periviability guidelines, offering an overview of the current Dutch guideline and discussing the sociocultural context in the Netherlands. It also reflects upon the position of the Netherlands in international discussions on treatment limits and perinatal treatment guidelines. *Chapter 2* comprises a scoping review of the existing body of literature on prenatal counseling for extreme prematurity. The review includes an analysis of forty-six publications, aiming to synthesize the knowledge and identify gaps in the current body of research.

Part two, which consists of three chapters, presents empirical research conducted with various stakeholders to address the research questions in more detail. *Chapter 3* reports the findings from individual interviews conducted with experienced parents, providing valuable insights into their perspectives and experiences related to extreme prematurity and decision-making at the limit of viability. A total of nineteen interviews were conducted. In *Chapter 4*, the focus shifts to the perspectives of adults who were born prematurely. The chapter presents the findings from four focus group interviews, exploring the experiences and viewpoints of these individuals. A total of twenty-three adults born prematurely participated in this study. *Chapter 5* presents the results of a survey study conducted with 769 healthcare professionals from various disciplines. This quantitative research investigates the preferences of healthcare professionals for different types of guidelines at the limit of viability.

Part three of the dissertation is dedicated to ethical reflection, comprising four chapters. *Chapter 6* offers a reflection on the current Dutch guideline, which is solely based on gestational age. *Chapter 7* conducts an ethical reflection on a newly proposed decision-making approach for births at the limit of viability: postponed withholding. This approach was presented by Syltern et al. It involves initiating intensive care at birth by default and postponing parental decision-making about the care approach for a week. The approach aims to empower parents, improve decision-making by balancing parental bias towards 'saving' their infant, and providing parents with more time and space to make the decision. In Chapter 7, we briefly assess this novel approach. In *Chapter 8*, the concept of viability takes center stage. This chapter critically assesses the ethical legitimacy of viability as the abortion threshold in the Netherlands, raising important considerations for potential changes in the legal framework for abortion. Finally, *Chapter 9* utilizes the empirical research findings and perspectives gathered throughout the dissertation to derive normative conclusions about personalization at the limit of viability. It explores the multifaceted concept of personalization and offers a breakdown of different types of personalization at the limit of viability, including personalized guidelines, counseling, and care. It concludes that personalization should be maximized in the case of counseling and care, while a balance is needed for personalized guidelines.

The dissertation ends with a general discussion that summarizes and analyzes the main findings. It also provides practical recommendations in four key areas: periviability guidelines, personalization, policy on termination of pregnancy, and artificial placenta technology.

NEDERLANDSTALIGE SAMENVATTING

Nederlandstalige samenvatting

Deze dissertatie onderzoekt richtlijnen voor perinatale zorg op de grens van levensvatbaarheid, met een specifieke focus op het concept van personalisatie. Het onderzoeksproject omvat nauwe samenwerking met volwassenen die zelf te vroeg geboren werden, ouders die ervaring hebben met extreme vroeggeboorte, en verleners. De dissertatie behandelt de volgende specifieke onderzoeksvragen: (a) moeten er perinatale richtlijnen zijn? (b) welk type richtlijn moet de voorkeur hebben? En (c) hoe moet personalisatie op de grens van levensvatbaarheid worden benaderd? Bij het beantwoorden van deze onderzoeksvragen wordt gebruik gemaakt van verschillende onderzoeksmethoden: literatuuronderzoek, empirisch onderzoek en ethische reflectie.

De dissertatie bestaat uit drie delen. **Deel één** richt zich op het verstrekken van achtergrondinformatie en context. Het bestaat uit twee hoofdstukken die de nodige basis leggen voor het begrijpen van de onderzoeksvragen en het onderwerp. *Hoofdstuk 1* duikt in de geschiedenis van Nederlandse perinatale richtlijnen, geeft inzicht in de huidige Nederlandse richtlijn en bespreekt de socioculturele context in Nederland. Het reflecteert ook op de positie van Nederland in internationale discussies over behandelingsgrenzen en -richtlijnen. *Hoofdstuk 2* omvat literatuuronderzoek over prenatale counseling voor extreme vroeggeboorte. Het betreft een analyse van 46 publicaties, met als doel de huidige kennis te synthetiseren en hiaten in het onderzoeksveld te identificeren.

Deel twee, dat bestaat uit drie hoofdstukken, presenteert empirisch onderzoek. *Hoofdstuk 3* rapporteert de bevindingen van individuele interviews met ervaren ouders. In totaal werden 19 interviews gehouden. In *Hoofdstuk 4* verschuift de focus naar de perspectieven van volwassenen die zelf te vroeg zijn werden. Het hoofdstuk presenteert de bevindingen van 4 focusgroepen met in totaal 23 participanten. *Hoofdstuk 5* presenteert de resultaten van een enquêteonderzoek uitgevoerd onder 769 zorgprofessionals uit verschillende disciplines. Dit onderzoek gaat in op de voorkeuren van zorgverleners voor verschillende soorten perinatale richtlijnen en ondergrenzen.

Deel drie van de dissertatie is gewijd aan ethische reflectie en bestaat uit vier hoofdstukken. *Hoofdstuk 6* biedt een eerste reflectie op de huidige Nederlandse richtlijn, die uitsluitend is gebaseerd op de zwangerschapsduur. *Hoofdstuk 7* gaat in op een nieuw voorgestelde benadering voor besluitvorming op de grens van levensvatbaarheid: *postponed withholding*. Deze benadering werd gepresenteerd door Syltern en collega's. Het houdt in dat intensieve zorg bij de geboorte standaard wordt gestart en dat de besluitvorming door ouders over de zorgbenadering een week wordt uitgesteld. Het doel is om besluitvorming van ouders te verbeteren door ze meer tijd en ruimte te geven om de beslissing te nemen. In dit hoofdstuk beoordelen we kort deze nieuwe benadering. In *Hoofdstuk 8* staat het concept van levensvatbaarheid centraal. Dit hoofdstuk beoordeelt kritisch de ethische legitimiteit van levensvatbaarheid als de abortusdrempel in Nederland en brengt belangrijke overwegingen naar voren voor mogelijke veranderingen in het juridisch kader voor abortus. Ten slotte gebruikt *Hoofdstuk 9* het empirische onderzoek en de eerdere ethische reflecties om normatieve conclusies te trekken over personalisatie op de grens van levensvatbaarheid. Het verkent het veelzijdige concept van personalisatie en biedt een uiteenzetting van verschillende soorten personalisatie, waaronder gepersonaliseerde richtlijnen, counseling en zorg. Het concludeert dat personalisatie gemaximaliseerd moet worden in het geval van counseling en zorg, maar dat er gezocht moet worden naar een balans nodig in gepersonaliseerde richtlijnen.

De dissertatie eindigt met een algemene discussie die de belangrijkste bevindingen samenvat en analyseert. Het geeft ook praktische aanbevelingen op vier kerngebieden: perinatale richtlijnen, personalisatie op de grens van levensvatbaarheid, beleid inzake zwangerschapsafbreking en artificiële placenta-technologie.

PUBLICATIONS

Publications

1. De Proost L, Verweij EJT, Ismaili M'hamdi H, et al. The Edge of Perinatal Viability: Understanding the Dutch Position. *Front Pediatr*. 2021;9:634290.
2. De Proost L, Geurtzen R, Ismaili M'hamdi H, et al. Prenatal counseling for extreme prematurity at the limit of viability: A scoping review. *Patient Educ Couns*. 2022;105(7):1743-60.
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ABOUT THE AUTHOR

About the author

Lien De Proost, born on December 11, 1996, in Turnhout, Belgium, initiated her academic journey in 2014 at the Catholic University of Leuven, Belgium, where she pursued a bachelor's and a master's degree in philosophy. Her enduring fascination with ethics led her to further specialize in the subject, culminating in the completion of a second master's degree in bioethics, supported by the Roger Dillemans fund. Following the completion of her studies, Lien briefly explored journalism for half a year before embarking on an academic journey. In 2020, she commenced her PhD research in Rotterdam. Concurrently, Lien worked part-time at the Institute of Philosophy in Leuven, contributing to the development of postgraduate education in applied ethics and instructing a course on care ethics. In April 2023, Lien transitioned into the role of a postdoctoral researcher at the Department of Ethics and Law at Leiden University Medical Center.

PHD PORTFOLIO

PhD portfolio

Name PhD student: Lien De Proost
Erasmus MC Department: Department of Neonatology, Department of Obstetrics and Gynecology, Department of Medical Ethics and Philosophy of Medicine

PhD period: 2020-2023
Promotor(s): Prof. dr. E.A.P. Steegers and Prof. dr. I.K.M. Reiss
Supervisor(s): dr. E.J.T. Verweij and dr. H Ismaili M'hamdi

PhD training

	Year	Workload (ECTS)
Courses		
Pubmed	2020	0.4
Embase	2020	0.2
LimeSurvey	2020	0.4
EndNote	2020	0.2
Kwalitatief interviewen	2021	1
Philosophy of responsible innovation	2021	5
Wetenschappelijke integriteit	2021	0.3
Academisch Engels	2021	3
Kwalitatieve analyse	2021	1
Atlas.ti voor beginners	2021	1
Biomedical Ethics OZSW	2022	6
Workshop Kinderpalliatieve zorg	2022	0.1
Kwalitatief onderzoek LUMC	2022	0.1
Docentprofessionalisering Diversiteit en Inclusie	2022	0.1
Summer School Empirical Bioethics	2022	3
Teaching		
Begeleiding stage 6 weken: 'kwaliteit van leven na extreme vroeggeboorte'	2020	1
Begeleiding stage 4 maanden: 'perinatale palliatieve zorg'	2021	2
Minor *Mystery of creation*: scriptiebegeleiding en onderwijs	2020-2022	3
Nakijken tweedejaarsessays Ethiek, Erasmus MC	2020-2022	2
Nakijken bacheloressays Ethiek, Erasmus MC	2020-2022	3
Discussienota onderwijs BA3 Geneeskunde, Erasmus MC	2022	1
Minor Innovatieve gezondheidszorg: onderwijs	2023	0.2
Double Degree Program, Erasmus MC: onderwijs	2023	0.2

PhD training

	Year	Workload (ECTS)
Presentations		
Neo aan de kust, Nederland. Oral presentation	2021	1
World Conference on Bioethics, Medical Ethics and Health Law, Portugal. Oral presentation	2021	1
Congress of the European Academy of Paediatric Societies, Spain. Oral presentation	2022	1
Gynaecongres NVOG, Nederland. Oral presentation	2022	1
Amsterdam Kindersymposium, Nederland. Oral presentation	2022	1
Landelijke Neonatale Follow-up Symposium, Nederland. Oral presentation	2022	1
Gesellschaft für Neonatologie und Pädiatrische Intensivmedizin, Germany. Oral presentation	2023	1
Symposium Zorg rond de pasgeborene, Nederland. Oral presentation	2023	1
Symposium De veilige kribbe, Nederland. Oral presentation	2023	1
Ideeënwedstrijd Centrum voor Ethiek en Gezondheid, Nederland. Oral presentation	2023	1
Other		
TULIPS PhD Curriculum	2021-2023	5
Expert meeting evaluatie LZA/LP	2022	0.1
Participant Brocher Foundation Workshop *Realistic Ethical, Legal and Social Implications of LiFE-S*, Switserland	2022	1
Leiden City of Science, Nederland. Oral presentation	2022	0.5
Research meetings Erasmus MC, Radoudumc, LUMC	2020-2023	3

DANKWOORD

Dankwoord

“Het is zo mooi om als denker tussen de mensen te fietsen, in plaats van aan een luchtballon te hangen en naar hen te kijken” - stelde een filosoof op de eerste conferentie die ik meemaakte. De afgelopen jaren mocht ik op die manier leren wat het is om ethicus te zijn *in* de geneeskunde. Om echt goed te kunnen begrijpen over wie (en wat) ik schreef, mocht ik weleens meelopen op de NICU, of zat ik in een hoekje van de spreekkamer te luisteren bij counselingsgesprekken. Ik leerde zelfs over prematurenretinopathie, en over waarom die ductus per se moet sluiten. Als iemand nog vragen heeft over necrotiserende enterocolitis? Ik moest weten waarover ik sprak, weg van de ivoren toren. Veel dank aan mijn promotieteam om dit mogelijk te maken: Joanne Verweij, Hafez Ismaili M’hamdi, Irwin Reiss en Eric Steegers. Verder wil ik de gehele lees- en promotiecommissie bedanken voor de zinvolle feedback en gedachtenwisseling.

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[1] ‘We’ zeggen dat niet per se, maar het is een soort Vlaams cultureel erfgoed.

mijn verhalen over kleine baby's, kunstbaarmoeders, en stamcel-embryo's. Voor je begrip dat mijn hoofd soms vol zat, en de hulp om het weer leeg te maken.

Naast ethicus in de geneeskunde, was ik de afgelopen jaren ook Belg in Nederland. Hoewel mijn Brabantse *roots* zeker hebben geholpen, was er toch de cultuurshock. 'Dat ik net zo praat zoals Hanne van K3!', liet een van de kinderen tijdens Leiden City of Science me weten. En toen ouders in een interview overwogen om eventueel de grens over te rijden naar Luik, omdat de behandelgrens in België lager ligt, nuanceerden ze toch: 'Hm, maar dan zou ons kind een Belg zijn...' De verschillen tussen België en Nederland zijn veel groter dan 'zeker en vast' versus 'vast en zeker', maar ik ben de afgelopen jaren met plezier *die Belg* geweest, en zal dat hopelijk nog wat jaren blijven.

En dan echt tot slot nog - naar voorbeeld van een groot denker[2] - wil ik mezelf nog bedanken; ik heb echt hard gewerkt.

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[2] Dit is betwistbaar, het gaat over Snoop Dogg. Maar leest iemand echt voetnoten?