

## Lay Summary

### End-of-life decision-making in extremely preterm infants in Switzerland

#### Project team

##### *Project leader*

Prof. Dr. med. Thomas M. Berger  
Brambergstrasse 25  
6004 Luzern  
E-Mail: [thomas.berger@bluewin.ch](mailto:thomas.berger@bluewin.ch)  
Tel: 079/359 4784

##### *Other project team members*

Dr. theol. Ruth Baumann-Hölzle  
Prof. Dr. med. Jean-Claude Fauchère  
PD Dr. med. Riccardo Pfister

#### Contact address

##### **Prof. Dr. med. Thomas M. Berger**

Former address (until 31.12.2016): no longer active  
Director Neonatal and Pediatric Intensive Care Unit  
Children's Hospital of Lucerne  
Spitalstrasse  
6000 Luzern 16

Current address:  
Brambergstrasse 25  
6004 Luzern  
Tel: 079/359 4784  
E-Mail: [tmberger@bluewin.ch](mailto:tmberger@bluewin.ch)

##### **Prof. Dr. med. Jean-Claude Fauchère**

Klinik für Neonatologie  
Universitätsspital Zürich  
Frauenklinikstrasse 10  
8091 Zürich  
Phone: 044/255 35 84  
E-Mail: [jean-claude.fauchere@usz.ch](mailto:jean-claude.fauchere@usz.ch)

April 5, 2017

## 1. Background

Despite enormous progress made in the field of neonatology over the past 30-40 years in highly developed countries, mortality and morbidity rates of extremely low gestational age neonates (defined as infants born with a gestational age less than 28 completed weeks) have remained substantial; infants born at the limit of viability, frequently defined as 22-26 weeks, are at particularly high risks.

In Switzerland, approximately 200-250 extremely preterm infants are born alive after less than 28 weeks of gestation every year (normal pregnancy duration is 40 weeks). Some of these infants die in the delivery room, while others are admitted to a neonatal intensive care unit to save their lives. As long as their prospect for a good outcome remains intact, life-sustaining therapies are continued and many will survive and be discharged after many weeks of hospitalization. If, on the other hand, the use of life-sustaining therapies only appears to be prolonging pain and suffering and death has become inevitable, redirection of care from therapies aimed at prolonging life to therapies aimed at providing maximum comfort (i.e. palliative care) is discussed. Similarly, if severe complications occur that are likely to severely lower the future quality of life of the patient, the health care team and the parents will need to decide whether the burden of ongoing intensive care now outweighs the patient's benefit; if this is the case, the decision-makers must consider redirection of care as well. End-of-life decision-making for extremely preterm infants is challenging for several reasons.

First, not uncommonly, decisions must be made in the face of significant prognostic uncertainty. This includes uncertainty about ultimate survival, but also uncertainty about the ultimate consequences of severe neonatal complication on the future quality of life. If no decisions are made as long as any uncertainty remains (i.e., the "wait until certain" approach), there is a significant risk of overtreatment; on the other hand, life-sustaining therapies are withdrawn even if significant doubts about the patients' prognosis persist, some patients will die who otherwise would have been able to survive with an acceptable quality of life.

Second, the patients cannot decide for themselves and decisions must be made by proxy. In this context, the question arises of who should have the authority to be the proxy decision-maker. In Switzerland, a model of shared decision-making (between health care professionals and parents) is mostly favored; however, how should one proceed if no consent can be reached? Is it the authority of the physician or the authority of the parents that should be decisive?

Third, in many studies, center of care was shown to be an important determinant of infant outcome even after adjustment for a variety of risk factors. How can such center-to-center variations in outcome be explained? Since most extremely low gestational age neonates die following end-of-life decision-making, analysis of causes and circumstances of death may shed some light on center-to-center outcome variability.

## 2. Goals of the project

The goal of this study was to analyze causes and circumstances of all deaths among extremely low gestational age neonates in Switzerland over a three-year-period. To understand its full scope, information on both stillbirths and livebirths were to be collected, regardless of whether deaths occurred in a delivery room or in a neonatal intensive care unit. Attempts were made to determine the bases for end-of-life decision-making and to collect information on the precise circumstances of death.



### 3. Methods

Detailed information on all delivery room and neonatal intensive care unit deaths before discharge among extremely preterm infants with a gestational between 22 to 27 completed weeks born in Switzerland over a 36-month-period (July 1, 2012 to June 30, 2015) was collected. Both stillborn and liveborn infants were included. Data collection was organized on-site in the level III NICUs at the University Hospitals of Basel, Bern, Geneva, Lausanne and Zurich, and the level III NICUs at the Cantonal Hospitals of Aarau, Chur, Lucerne and St. Gallen.

Patients were identified using clinical records, electronic data bases as well as birth log books. De-identified data was entered by trained research assistants on-site into REDCap™ (Research Electronic Data Capture), a secure on-line database. The system featured easy-to-use online screen forms and electronic data validation checks to minimise data entering errors. Confidentiality was assured by password protection.

For each patient, date and time of birth as well as the perinatal centre where the infant was born were registered. Additional demographic data included GA in weeks and days, birth weight, sex and whether the infant was a singleton or child from a multiple birth. Pregnancy complications such as premature rupture of membranes, clinical chorioamnionitis and maternal hypertension were recorded. The use of prenatal steroids as well as the type of delivery were assessed. Deliveries occurring after spontaneous labour or induction of labour for maternal reasons or with the objective to increase chances of infant survival were distinguished from late terminations of pregnancy.

For stillborn infants, apart from basic demographic data, it was assessed whether labour occurred spontaneously or was induced for late termination of pregnancy. For liveborn infants, DR resuscitation measures (intubation, use of surfactant, chest compressions, use of epinephrine) were noted. The reason for death in the DR was classified as either primary non-intervention, limited resuscitation or full resuscitation. For infants who received palliative care only, the use of sedatives or analgesics was recorded.

For infants admitted to the NICU, information on severe neonatal complications that potentially influence the future quality of life and age at death were noted. Daily data on cardiovascular and respiratory system performance as well as the degree of cardiorespiratory support were recorded for three days prior to death. Based on this information, it was determined whether the primary cause of death was related to severe congenital malformations, refractory cardiovascular or respiratory failure, sepsis, gastrointestinal complications or severe neurological injury. In addition, it was recorded whether death occurred despite ongoing unrestricted intensive care or whether death was preceded by withholding or withdrawing of life-sustaining therapies. Reasons for any redirection of care decisions were classified as being due to medical futility or concerns regarding the anticipated future quality of life. Finally, the use of any medication to alleviate pain and suffering after redirection of care was noted.

### 4. Results

Overall, 594 deaths of extremely low gestational age neonates were recorded over the three-year-study period. Of these, 280 (47%) infants were stillborn (median gestational age and birth weight 23 5/7 weeks and 537 g, respectively) and 314 (53%) died after livebirth. Of the latter, 185 (59%) died in the delivery room, and 129 (41%) died in the NICU following provisional intensive care. Median gestational age and birth weight were higher in the infants who died in the neonatal intensive care unit (25 2/7 weeks and 690 g) than in infants who were born alive but died in the DR (23 3/7 weeks and 560 g).



Obstetrical and delivery room interventions were used only rarely in liveborn infants after spontaneous labor at 22 and 23 weeks, and almost all deaths occurred in the delivery room (22 weeks: 100%, 23 weeks: 89%). A more active approach was seen at 24 weeks and the proportion of delivery room deaths decreased to 35%. At more than 24 weeks, most deaths (more than 95%) were observed after admission to a neonatal intensive care unit.

Regardless of gestational age, active perinatal interventions were used only in a minority of liveborn infants after spontaneous labour who later died in the delivery room. Failed resuscitation attempts were rare. A total of 129 infants died following admission to a neonatal intensive care unit. To analyse whether the degree of immaturity had an impact on the circumstances of death among these patients, two groups of extremely preterm infants were compared: infants with a gestational age < 25 weeks (group 1) and infants with a gestational age  $\geq$  25 weeks (group 2).

For both groups, medical futility was the predominant reason given for end-of-life decision-making in the neonatal intensive care unit (mentioned in 65% and 72% of group 1 and group 2 patients, respectively); quality of life considerations was the reason for redirection of care decisions in 33% and 26% of these patients.

Independent of their gestational age, most infants were on invasive respiratory support in the three days preceding death (> 90%); however, at the time of death, the majority ( $\geq$  85%) was extubated. Once a decision had been made to redirect care, palliative care measures were used in many patients: analgesics (mostly morphine) were given to > 50% of the dying patients, whereas sedatives (e.g., benzodiazepines) were administered less commonly ( $\leq$  15%).

## 5. Significance of the results for science and practice

In Switzerland, almost 50% of all extremely preterm infants with a gestational age between 22-28 weeks are stillborn. Most extremely preterm infants who are born alive but ultimately die, do so following end-of-life decision-making. For delivery room deaths after livebirth (59%), the major factor for decision-making appears to be gestational age only. In contrast, once infants when infants are admitted to a neonatal intensive care unit prior to their deaths (41%), decisions to redirect care are based on more comprehensive information and assessments. Once health care professionals and parents conclude that either ongoing intensive care would be futile or the future quality of life would no longer justify the burden of intensive care, care is redirected from attempts to guarantee survival to comfort or palliative care only.

The study did not identify any significant differences between the 9 level III perinatal centers. This could either be due to the limited number of cases (n=594), variations in the quality of medical documentation (particularly of delivery room deaths), or reflect the fact that previously observed center-to-center differences in the approach to infants born at the limit of viability have indeed decreased in recent years.

The results of this and related NRP 67 studies will need to be considered when the Swiss recommendations for perinatal care between 22 and 26 weeks will be revised (planned for 2017/2018).

