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Prognose for og oppfølging av ekstremt premature barn

Systematisk oversikt

Prognosis and follow-up of extreme preterm infants: a systematic review
This is an excerpt from the full technical report, which is written in Norwegian.
The excerpt provides the report's main messages in English.

folkehelseinstituttet

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Key messages

In Norway, approximately half a percentage of all births happen before 27 weeks' gestational age (GA). These extremely preterm infants have an increased risk of mortality and disabilities like cerebral palsy, sight and hearing impairment as well as learning and psychological difficulties.
The treatment of extremely preterm infants has changed since 2000, and the survival rate has improved in high income countries. In addition, the limits of offering life-saving treatment has changed.
This systematic review summarises studies of prognosis of extremely preterm children who have received life-saving treatment on survival and function until three years age.

We have summarised 52 studies, where 47 studies have estimated the prognosis of survival and 22 studies have estimated the risk of impairment in children born at 22-27 weeks of GA.

This systematic review shows that:

- The prognosis of survival among live birth infants was 9% (95% Confidence interval (CI) 3-22)) for children born at 22 weeks of GA, and 55% (95% CI 39-70) for children born at 24 weeks of GA. The quality of evidence was moderate and low.
- About two of three children born at 25-27 weeks of GA survived. These prognosis estimates were less heterogeneous than in week 22-24 GA.
- The risk estimates of severe and less severe disabilities among children born at week 22-24 GA are very uncertain. The quality of evidence was low and very low.

Title:
Prognosis and follow-up of extreme preterm infants

Type of publication:
Systematic review

Doesn't answer everything:
This systematic review does not answer questions about prognosis and follow-up of children born after gestational week 27 and/or born in low and middle income countries. The follow-up in included studies was only until three years of age.

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Executive summary (English)

Background

In Norway, approximately half a percentage of all births happens before 27 weeks' gestational age (GA). These extremely preterm infants have an increased risk of mortality around and after birth. They also have an increased risk of severe and less severe disabilities. Children born before week 23 GA are seldom offered active life-saving treatment in Norway. According to the consensus conference in 1998, active life-saving treatment was not recommended to children born less than week 24 GA. In 2005, this limit was lowered to week 23 GA. The method on how to determine when a woman is due to deliver might affect the treatment limits. In Norway, responding physicians from different maternity and neonatal intensive care units report similar treatment limits for offering acute life-saving treatment.

The National council for priority setting in healthcare gave the Knowledge centre in the Norwegian Institute of Public Health the assignment to summarize studies of prognosis of extremely preterm children that have received life-saving treatment. During the last decades, the survival of children born before week 28 GA in high-income countries has increased. Some studies also show improvement in risk of severe disabilities among children born before week 28 GA.

Objective

To summarise national and international research where prognosis and follow-up was measured for survival from birth and health-related outcomes after discharge from hospital among children born before week 28 GA.

Method

We conducted a systematic review based on cohorts published from year 2000. We ran literature searches in Cochrane central, PubMed, MEDLINE, Embase, PsycINFO, CINAHL, ISI Web of Science, SveMed+ and Maternity and Infant Care. The following inclusion criteria were used:

Population: Children born from week 22 GA to week 27 GA, born as of 1998. The included children had received life-saving treatment. Context: High-income countries. Outcome measures: Survival, and disabilities as cerebral palsy, autism, AD/HD, impaired sight, lung problems, cognitive skills and other health related outcomes. Exclusion criteria were studies published before year 2000, studies that only reported birth weight, effects of interventions (as medication, nutrition and medical equipment) and studies that were not available in full-text.

Two persons independently examined the search results. This selection was based on the titles and abstracts. Five hundred and six articles were relevant and assessed in full text against our inclusion criteria. We also critically assessed the risk of bias according to a checklist for cohort studies reported in the Knowledge centre's handbook. We extracted relevant information from included studies as survival rate and risk of disabilities at the different weeks of GA. Meta-analyses and balance charts were conducted in R "metaphor." RevMan was used for other analyses. We used the GRADE-methodology (Grading of Recommendations Assessment, Development, and Evaluation) to assess our confidence in the estimates of survival among children born in week 22 to 24 GA. GRADE was also used to appraise the likelihood of no disabilities, and the risk of severe disabilities among children born at week 22-24 GA, assessed at 1.5 to three years after birth.

Results

We included 53 articles of which 47 studies estimated the survival among children born at week 22 to 27 GA. Twenty-two studies reported morbidity among extremely preterm children. The studies came from Australia, Austria, Belgium, Canada, Germany, Great Britain, Finland, France, Japan, The Nederland, Norway, Portugal, Singapore, Spain, Switzerland, Sweden, Taiwan, and US. Twenty-six of the forty-seven studies that estimated the prognosis of survival had low risk of bias. Twelve of 22 studies that estimated the prognosis of morbidity had high risk of bias. This was due to small or non-representative population, not reporting method of determination of GA and not reporting blinded outcome assessors.

Survival

The survival rate among children born in week 22 (22^0 – 22^6) and transferred to neonatal intensive care unit (NICU) was estimated to 33% (95% CI 27 to 40), whereas the prognosis of live births, born in week 22 GA was 9% (95% CI 3 to 22). The prognosis estimates varied between the included studies. The certainty of the evidence was moderate to low.

The survival rate among children born in week 23 (23^0 – 23^6) and transferred to NICU, was estimated to 48% (95% CI 31 to 66). The prognosis of live births, born in week 23 GA was 27% (95% CI 12 to 51). The prognosis estimates varied between the included studies. The certainty of the evidence was moderate.

The survival rate among children born in week 24 (24^0 – 24^6) and transferred to NICU, was estimated to 68% (95% CI 51 to 81). The prognosis of live births, born in week 24

GA was 55% (95% CI 39 to 70). The prognosis estimates varied between the included studies. The certainty of the evidence was moderate.

The survival rate among children born in the weeks 25 to 27 (25^0 – 27^6) was significantly higher, than among children born in the weeks 22 to 24 GA. The prognosis estimates in these analyses were less heterogeneous. The prognosis of children born in week 27 GA was estimated to 90%. We did not assess the certainty of the evidence of these outcomes.

Disability
We conducted meta-analyses based on cohort studies that had followed the surviving children from 1.5 to 3 years age. In these studies, the risk of disability was assessed with Bayleys Scales of Infants Development (BSID) II or III. This test assesses the likelihood of disability as none, mild, moderate or severe.

It was not possible to estimate the likelihood to avoid disability for children born in week 22 GA. This evidence was based on two studies including seven children. Four cohorts including 24 survivors found a risk of severe disability of 37% (95% CI 21 to 58). The risk of severe disability among children born in week 23 GA was estimated to 20% (95% CI 5 to 52). This meta-analysis included six studies of 125 survivors, whereas the risk of severe impairment among children born in week 24 varied between 5 to 44%. This meta-analysis was based on eight studies including 299 surviving children. The certainty of the evidence for these outcomes was low to very low.

The risk of cerebral palsy was estimated to 22% among children born in the weeks 22 and 23 GA, and 17% among children born in week 24 GA. The risk of blindness on one or both eyes among children born at week 23 GA was 10% and assessed at two to three years. Among children born at weeks 24 to 25 GA the risk of blindness was estimated to 2%. Regarding severe hearing loss including the need of hearing aids, the risk was estimated to 2-3% among children born in week 22 to week 26 GA.

Discussion

The evidence in our analyses for survival was based on meta-analyses with seven to 18 cohort studies with 3429 to 9185 live births in gestational week 22 to 27. The evidence for the likelihood of no disability and serious disability for children born in gestational weeks 22 to 24 was based on two to nine studies with seven to 299 children. The certainty of the evidence is very low to moderate which means that we are very unsure about the results (prognosis estimates). However, we know that children born in gestational weeks 22 to 24 have a significant risk of death and disabilities, and that the prognosis improves after birth in gestational week 24.

Methods to calculate gestational age in pregnancy vary. The methods to predict due date were poorly described in many of the included studies. Because of this, the prognosis estimates may not be reliable and this may explain some of the heterogeneity be-

tween studies. Inadequate descriptions of the intensive treatment the children received and why it was given might explain different prognoses across studies. Even though all the studies were from high-income countries, there are cultural differences concerning how much intensive treatment the most extremely preterm are given. There may be many other explanations for the heterogeneity between studies and countries. The studies we included poorly described factors that can affect survival and morbidity, such as socioeconomic conditions, smoking, overweight, multiple pregnancies. In countries where, at a certain gestational age, there are significant differences in survival for all born children (stillbirths included), for live births and for children admitted to neonatal wards, this variation can probably be partly explained by different attitudes to providing acute life-saving treatment.

The findings in this systematic review will, in addition to other input, be the basis of discussion for the professional community and The National Council for Priority Setting in Health Care. Intensive treatment for extremely preterm children is a field that has changed during the past twenty years and it would be interesting to look more closely at the differences between centres and countries that have been revealed in our meta-analyses. A strength to our review is that we have involved Norwegian experts who along the way have commented on the protocol, literature search, analyses, evidence grading, and report drafts. A limitation to the review is that the literature search is more than a year old, and that the follow-up time in the included studies is short.

To predict accurate and reliable prognosis estimates in the future we need studies that report variables such as methods to predict due date, the life-saving and intensive treatments that were given, and a clear report of the numbers used to estimate survival.

Conclusion

Extremely preterm children born in gestational week 22 to 24 have a significant risk of death; about half of them do not survive. For children born in gestational weeks 25 to 27 the survival rate is significantly higher. Among the most extremely preterm children who survive, the evidence for disability is uncertain, but the risk decreases the more mature the baby is at birth. The proportion of children who develop a severe disability is approximately 37% in gestational weeks 22 and between 20% and 11% for gestational weeks 23-25.