



THE EPICE PROJECT

(Effective Perinatal Intensive Care in Europe)

BACKGROUND

Babies born very preterm (before 32 weeks of pregnancy) are only 1 to 2% of all births, but these vulnerable newborn infants constitute half of all deaths during the first year of life.^{1,2} Compared to babies born at full term, they also face higher risks of health problems and developmental delays in childhood.²⁻⁴ In Europe, there are differences across countries in mortality and severe neonatal health complications among very preterm babies.⁵ Reasons for this variation might be related in part to individual characteristics (degree of prematurity or presence of other problems such as congenital malformations or poor intrauterine growth) but also to the care provided to these babies, including the organisation of health services⁶ and the use of evidence-based practices in maternity and neonatal wards.

STRUCTURE OF THE PROJECT

In the EPICE (Effective Perinatal Intensive Care in Europe) project, a research group (consortium) investigated the use of **evidence-based***⁰¹ interventions for the care of very preterm infants in 19 regions from 11 EU member states (Figure 1). Data were collected for a 12 months period in each region (except France with 6 months) from April 2011 to September 2012. In total, 10.329 births from 22 to 31 completed weeks of gestation (live births, stillbirths) and 335 maternity units as well as 242 neonatal units were included in the analysis. The multi-disciplinary approach brings together expertise in obstetrics, paediatrics, epidemiology, biostatistics and health services research.



Figure 1:
The 19 EPICE regions (yellow) representing 11 EU member states (blue): Belgium, Denmark, Estonia, France, Germany, Italy, the Netherlands, Poland, Portugal, Sweden, United Kingdom



evidence-based refers to care practices that are based on results of systematic research rather than based solely on expert opinion or usual practice.

01 Evidence-based

MAIN RESEARCH QUESTIONS

The following main research questions (RQ) were addressed in the EPICE project by conducting 4 different studies:

RQ 1:

Are all very preterm babies in Europe receiving state-of-the-art evidence-based care?

RQ 2:

Does evidence-based care contribute to differences in mortality and morbidity?

RQ 3:

What are facilitators and barriers to implement evidence-based care and best clinical practices in neonatal intensive care units?

DATA COLLECTION METHODS

The EPICE project included 4 different related studies. Within these studies, a broad range of tools was used to collect **quantitative and qualitative***02 data after informed consent of the parents. This approach helps to provide a deeper insight into the use of evidence-based care on a patient, unit, and regional level.

 quantitative research aims at quantifying the problem by generating numerical data or data that can be transformed into usable statistics to generalise results of usually a lot of participants. Qualitative research is used to gain a deep understanding of underlying reasons, opinions, feelings, and motivations and is carried out using individual personal interviews, focus groups (group discussions), or even direct observation.

02 Quantitative and qualitative

STUDY 01



Population-based **prospective cohort study***03 of all very preterm stillbirths and live births from 22+0 weeks to 31+6 weeks of gestation to collect data on medical practices, clinical characteristics, and health outcomes up to 2 years of age

- Medical records to collect data on medical practices, clinical characteristics, and health outcomes
- Parental questionnaires

STUDY 02

Survey of maternity and neonatal units on structural characteristics, policies, protocols, and practices

- Maternity unit questionnaires
- Neonatal unit questionnaires



Qualitative study in selected units on facilitators and barriers to adopt evidence-based innovations in neonatal care

- Semi-structured interviews and focus groups with neonatal physicians and nurses

 a type of study where participants are enrolled before they develop a certain outcome (here: consequences of preterm birth) and accompanied through time

03 Prospective cohort study

STUDY 03



Case studies on regional, national, European, and international governance structures

- Document analysis

STUDY 04

EVIDENCE-BASED PRACTICES INVESTIGATED

To get a broader understanding of the use of evidence-based practices in the care of very preterm babies, the EPICE consortium agreed on 17 practices related to both obstetric and neonatal care to be included in the project. These interventions (see boxes) were selected based on the following criteria:



Clinical importance:
the intervention has a significant impact on health and/or is commonly used



Quality of evidence:
there is a high level of evidence for the use or non-use of the intervention



Comparable indicators:
the intervention can be measured the same way in all participating units



Variability in intervention use:
inter-regional and inter-unit variability exists, which suggests that non-clinical factors such as the organisation of care or provider characteristics have an impact

Before birth (antenatally)



- Administration of antibiotics (to reduce preterm labour)
- Administration of tocolysis (to suppress preterm labour)
- Administration of corticosteroids before birth (to improve the maturation of the baby's lungs)*
- Administration of magnesium sulphate for neuroprotection (e.g. to reduce the risk of cerebral palsy/brain damage in the baby)

Around birth (perinatally)



- Delivery in maternity units with appropriate on-site neonatal intensive care services**
- Optimal mode of delivery for very preterm babies
- Timing of cord clamping (late clamping increases the baby's blood volume and reduces the risk of cerebral haemorrhage)**
- Prevention of low body temperature (hypothermia)**
- **Surfactant****⁰⁴ replacement therapy (to prevent respiratory failure)**

After birth (postnatally)



- Management of patent ductus arteriosus (the short vessel that connects the pulmonary artery with the aorta in the fetus fails to close after preterm birth)
- Inhaled nitric oxide (to prevent bronchopulmonary dysplasia (BPD))
- Non-use of corticosteroids after birth (they were widely used to treat and prevent BPD in preterm babies until studies showed an increased risk for cerebral palsy and neurodevelopmental impairment)**
- Strategies to prevent Bronchopulmonary Dysplasia (BPD)
- Screening for and treatment of retinopathy of prematurity (ROP) (too much oxygen can cause abnormal blood vessels to grow in the retina, and can lead to blindness)**
- Administration of **probiotics****⁰⁵ (to reduce the risk of necrotising enterocolitis (NEC); NEC is a rare but severe gastrointestinal disease with a high mortality rate)
- Breastfeeding and breastmilk use**
- Skin-to-skin care (direct skin contact between mother and baby, can include father, other family member)

**based on a high level of evidence



a naturally produced substance that is important for the lungs to function. Fetuses develop surfactant from the 24th week of pregnancy, and it builds up to its full level by the 37th week of pregnancy

04 Surfactant



live bacteria and yeasts that are good for the digestive tract and therefore also for the immune system

05 Probiotics



Continuous Positive Airway Pressure: a respiratory support method that delivers a constant flow of air into the baby's lungs to keep the air sacs open after each breath.

06 CPAP



a method to quickly determine the health of an infant by evaluating the newborn baby directly after birth on five simple criteria: Appearance, Pulse, Grimace, Activity, Respiration

07 Apgar score

RESULTS

RQ 1: Are all very preterm babies receiving optimal evidence-based care?

- The study first identified 4 widely accepted evidence-based practices that improve the survival of very preterm babies: delivery in a specialised maternity unit with on-site neonatal intensive care, administration of antenatal steroids to promote fetal lung maturation, prevention of hypothermia after birth and optimal respiratory management (use of surfactant or early **CPAP**^{*06}) at birth.
- Across the study regions, only 58.3% of babies received all of these selected evidence-based practices for which they were eligible.
- Babies with lower gestational age, growth restriction, lower **Apgar scores**^{*07} were less likely to receive these elements of evidence-based care.

Other examples:

The project has also investigated other evidence-based interventions and found that sub-optimal use of many practices is widespread:



Postnatal corticosteroid use in preterm babies

Postnatal corticosteroids increase the risk for cerebral palsy and neurodevelopmental impairment among children born very preterm and therefore best practice guidelines call for restricted use of this treatment. The EPICE project showed that postnatal corticosteroids are still frequently used in Europe, but with wide regional variation that was not explained by the characteristics of the newborn infants. Having a unit policy to restrict corticosteroid administration contributed to lower use, and this finding highlights the importance of guidelines to promote use of evidence-based practices.



Breastmilk feeding

Breastmilk feeding is associated with lower neonatal morbidity in very preterm babies and is beneficial for maternal health. The EPICE group analysed the association between maternal, obstetric, and infant clinical factors (e.g. type of birth), maternal education, neonatal and maternal care unit policies and breastmilk feeding at discharge from the NICU. Overall, 58% of the babies received any breastmilk at discharge, but there were large variations between regions (range 36-80%). Units with a Baby Friendly Hospital accreditation and protocols for using breast- and donor milk had higher rates of exclusive breastmilk feeding at discharge. A positive association between maternal education and the likelihood of receiving mother's own milk at discharge was found. In light of the proven benefits of maternal milk, strategies to support breastfeeding should be targeted also to mothers with less education.



Administration of magnesium sulphate

Magnesium sulphate has long been used in obstetric care for the prevention of eclampsia, but also acts as a neuroprotective agent for the baby. Recent best practice guidelines promote use of magnesium sulphate for neuroprotection when the birth of a very preterm baby is anticipated. The EPICE consortium explored unit policies of use of magnesium sulphate and the actual use in European obstetrical units. This study found that the use of magnesium sulphate for neuroprotection was still rare in Europe. The reason for this might be that European obstetricians are not convinced by available evidence on magnesium sulphate's neuroprotective effect. Therefore, more research evidence is needed to feed in national guidelines for use of magnesium sulphate for neuroprotection.

RQ 2: Does evidence-based care contribute to differences in mortality and morbidity?

Data from the EPICE project show wide disparities in preterm birth rates, mortality rates (e.g. stillbirth rate, survival to discharge), short-term morbidity (frequency of diseases or complications) and longer term development for very preterm babies across the study regions. However, these disparities could only slightly be explained by pregnancy, maternal, or infant characteristics.

Babies who received all of 4 selected evidence-based practices were 28% less likely to die.

If all babies received all of 4 selected evidence-based practices, then 11.3% of deaths and/or severe morbidity would be avoided.

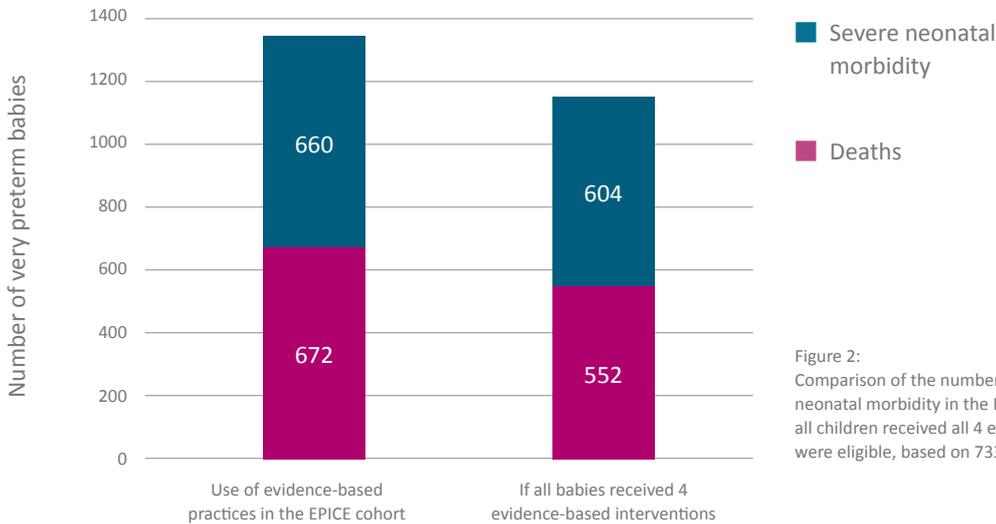


Figure 2: Comparison of the number of babies who died or who had a severe neonatal morbidity in the EPICE cohort with the ideal situation where all children received all 4 evidence-based interventions for which they were eligible, based on 7336 very preterm infants included in the study.

This means that although patient characteristics such as maternal age at birth, gestational age, the occurrence of multiple births, or the prevalence of pre-eclampsia (also known as “toxaemia of pregnancy”) vary across regions, this could not completely explain the differences in mortality and morbidity found across regions.

- The finding suggests an inequity in the quality of care and treatment provided to very preterm babies across Europe.
- Results reveal that mortality and morbidity were lower in babies, who received evidence-based practices. Differences in the use of evidence-based care practices across regions and units were found, e.g. for hypothermia prevention or the non-use of corticosteroids after birth.
- These findings show that there is still space for improvement, and that changes in the organisation and quality of the care delivered is called for.

RQ 3: What are barriers and facilitators to adopt evidence-based care?

When the 44 physicians and nurses from 6 EPICE regions were asked to tell about the last change in policies or practices introduced in their unit, they reported the following barriers and facilitators:

Barriers and difficulties



- Seeking agreement within the team
- Time, resources, and workload
- Communication and dissemination difficulties within the team
- People’s attitudes and resistance to change
- Poor quality of the evidence or of the guideline

Facilitators



- Quality of the guideline
- Perceived benefit to patients
- Perceived benefit to staff work
- “Bottom-up” decision by staff to change
- Presence of a key staff member promoting and/or facilitating the process

WHAT DO THE RESULTS MEAN?



The EPICE project showed that evidence-based care practices are not always used for the care of very preterm babies in Europe. Importantly, EPICE demonstrated that practices shown to be effective in research studies were effective in real-life environments as mortality and morbidity were lower among babies receiving evidence-based care.

The study also found wide variability in the use of some interventions across obstetrical and neonatal units, highlighting the absence of a consensus on best practice. This shows the need to improve guidance for clinicians, which in turn requires better evidence for the interventions needed to care for very preterm babies. The relation found in this study between the presence of specific unit guidelines and the percentage of uptake of such practice confirms the usefulness of such guidelines. Thus, it is important to translate research results into guidelines that are unambiguous, clearly written, and easy to interpret. These should point out the benefits for patients and healthcare professionals.

Randomised controlled trials are needed when there is uncertainty about the real value and benefits of interventions.

The overall message from EPICE is that better use of evidence-based care could result in significant health gains for very preterm babies.

NEXT STEPS

EPICE explored how evidence-based care affected outcome for very preterm infants at birth and during their neonatal hospitalisation. How these practices affect longer term development and health of very preterm children is currently investigated in the on-going studies in the SHIPS and RECAP preterm projects.

OUTLOOK

The European Foundation for the Care of Newborn Infants (EFCNI) together with many experts and parent representatives develops European Standards of Care for Newborn Health for key topics in newborn health to establish a reference framework for developing guidance on a country, region, and unit level.

Within the European Standards of Care for Newborn Health project the whole range of issues associated with preterm birth and neonatal morbidity is covered.

The multi-disciplinary project brings together more than 220 healthcare professionals of different professions, parent representatives and selected industry specialists, from more than 35 countries. Representatives from national parent organisations play an important role in all phases of the project – from the development to the implementation of the standards.

All stakeholders can help to promote this reference framework in their country. For more information about the project, see <https://newborn-health-standards.org/> or <http://www.efcni.org/>.





THANK
YOU!

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PLEASE NOTE:

- Further evaluation of the EPICE data is still ongoing and more details and results are to be expected.
- For further details and information on the EPICE and SHIPS project, please visit: <http://www.epiceproject.eu/en/>
- For further details and information on the RECAP preterm project, please visit: <https://recap-preterm.eu/>



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PUBLICATIONS FROM THE EPICE PROJECT

Main papers

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