Swedish EXPRESS Study

Karel Maršál
Department of Obstetrics and Gynecology
Lund University, Sweden
Swedish national prospective study

Extremely Preterm Infants in Sweden (EXPRESS)

Inclusion criteria:
• All live-born infants < 27 gestational weeks
• Stillbirths 22+0 – 26+6 weeks

April 1, 2004 – March 31, 2007

Exclusion criteria:
• Births outside Sweden
• Pregnancy terminations
• Neonatal care outside Sweden
SWEDEN:

7 health care regions

with large differences in size and population density
Study protocol and basic design

- Previously recorded information on pregnancy and delivery collected
- Data stored in a web-based database
- Database accessible for all team members with personal accounts

Data from the first visit at antenatal clinic
Data from ultrasound measurements
Clinical data on pregnancy and labor
Information on placental histomorphology
Prospectively collected clinical data from NICU

In cases of stillbirths or infant deaths: Information from post mortem reports

One-year survival assessed using data from Statistics Sweden
Study protocol and basic design

- Data from the first visit at antenatal clinic
- Data from ultrasound measurements
- Clinical data on pregnancy and labour
- Information from placental histomorphology
- Prospectively collected clinical data from NICU

Follow-up at 2.5 years
Follow-up at 6.5 years

Data ready for analysis

+ matched term controls
Study protocol and basic design

Data from the first visit at antenatal clinic
Data from ultrasound measurements
Clinical data on pregnancy and labour
Information from placental histomorphology
Prospectively collected clinical data from NICU
Follow-up at 2.5 years
Follow-up at 6.5 years
Follow-up at 11 years
Protocol being planned
+ matched term controls
Number of registered infants  

- live-born  707  (70 %)  
- stillborn  304  (30 %)  

Incidence  
- total  3.3  per 1000 infants  
  - live-born  2.3  per 1000 infants  
  - stillborn  1.0  per 1000 infants
Live births <27 weeks

Per thousand births in MBR

EXPRESS-study
N=707

Medical Birth Register
N=615

+15%
Gender

- Boys: 55%
- Girls: 45%

Singleton / multiple birth

- Singleton: 78%
- Multiple: 22%

(live-born infants n=707)
SURVIVAL AT 1 YEAR

(live-born infants n=707)
Survival in Sweden 2004-07 vs recent national studies
Survival – live-born infants (n = 707) acc. to gestational age at birth
## Obstetric factors - infant mortality within the first 24 h

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chorioamnionitis/PPROM</td>
<td>2.4</td>
<td>(1.1 – 5.4)</td>
</tr>
<tr>
<td>Placenta abruption</td>
<td>2.7</td>
<td>(1.0 – 7.3)</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>2.2</td>
<td>(1.2 – 4.3)</td>
</tr>
<tr>
<td>Birth at level III hospital</td>
<td>0.3</td>
<td>(0.2 – 0.5)</td>
</tr>
<tr>
<td>Tocolysis</td>
<td>0.3</td>
<td>(0.2 – 0.5)</td>
</tr>
<tr>
<td>Antenatal steroids</td>
<td>0.1</td>
<td>(0.1 – 0.2)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>0.2</td>
<td>(0.1 – 0.3)</td>
</tr>
<tr>
<td>Apgar score &lt;4 at 5 min</td>
<td>50.4</td>
<td>(28.2 – 90.2)</td>
</tr>
</tbody>
</table>

OR adjusted for gestational age
Is there a risk that better survival has been bought at the expense of increased neonatal morbidity?
SURVIVAL WITHOUT MAJOR MORBIDITY

(IVH ≥ gr.3, ROP ≥ st.3, NEC, CLD)

No major neonatal morbidity at 1 year: 43% of survivors
Survivors without major morbidity - infants <26 weeks

<table>
<thead>
<tr>
<th>Country</th>
<th>Per cent of live-born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epicure</td>
<td>38</td>
</tr>
<tr>
<td>New Zealand</td>
<td>38</td>
</tr>
<tr>
<td>Canada</td>
<td>23</td>
</tr>
<tr>
<td>EpiBel</td>
<td>30</td>
</tr>
<tr>
<td>Netherlands</td>
<td>30</td>
</tr>
<tr>
<td><strong>Express</strong></td>
<td><strong>30</strong></td>
</tr>
<tr>
<td><em>(Swedish study)</em></td>
<td></td>
</tr>
</tbody>
</table>

Major morbidity: IVH ≥grade 3, PVL, ROP ≥stage 3, NEC, CLD
Conclusions I

The Swedish national EXPRESS study showed a further improvement of the survival also at the boarder of viability.

The neonatal morbidity was considerable, however, not more frequent than in other studies.
Neurodevelopmental outcome at 2.5 years of age

Infants born alive n = 707

Alive at 1 year, n = 497

Could not be located, n = 30

Died, n = 6

Eligible for assessment, n = 461

Refused, n = 5

Only chart review, n = 41

Formally assessed at 30 months of corrected age n = 415

Formally assessed or assessed by chart review n = 456

Control groups, n = 922

controlgroup 1, incl Bayley

controlgroup 2, no Bayley

Declined n = 207

Assessed at 30 months n = 715

Telephone interview, n = 327

Bayley 3rd ed, n = 370
Examinations at 2.5 years of corrected age

- **Pediatrician**: Structured examination and medical history:
  - Motor development/CP
  - Vision
  - Hearing
  - Communication (speech)

- **Psychologist**: Developmental testing
  - Cognition, language, motor development (Bayley 3rd ed)

- **Ophthalmologist**:
  - Visual acuity
  - Strabismus and other eye problems

- **Parents**:
  - Behavior (CBCL)

- **Nurse**: Telephone interview on medical history
Bayley III scores compared with term controls
Rate of cerebral palsy in the index children (n=456) vs control group (n=715)

<table>
<thead>
<tr>
<th></th>
<th>Index n</th>
<th>Index %</th>
<th>Control n</th>
<th>Control %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral palsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulant</td>
<td>26</td>
<td>5.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non-ambulant</td>
<td>6</td>
<td>1.3</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>7.0</td>
<td>1</td>
<td>0.1</td>
</tr>
</tbody>
</table>
## Overall disability

<table>
<thead>
<tr>
<th>Disability:</th>
<th>Extremely preterm (&lt; 27 wks) n=456</th>
<th>Controls (37-41 wks) n=366</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>192 (42)</td>
<td>286 (78)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>140 (31)</td>
<td>68 (19)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>74 (16)</td>
<td>11 (3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Severe</td>
<td>50 (11)</td>
<td>1 (0.3)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

At 2.5 years, 73 % survived without moderate or severe disability
Outcome at 2.5 years
EPICURE 1995 vs. EXPRESS 2004-07

(Infants < 26 wks)
Conclusions II

In spite of high survival compared with other studies, the morbidity rate at 2.5 years was similar or lower. Few children were severely impaired. Thus, the reduced mortality was not bought at the expense of increased morbidity among survivors.
<table>
<thead>
<tr>
<th>Mats Blennow</th>
<th>Marius Kublickas</th>
<th>Petra Otterblad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uwe Ewald</td>
<td>Karin Källén</td>
<td>Grozda Pajic</td>
</tr>
<tr>
<td>Vineta Fellman</td>
<td>Hugo Lagercrantz</td>
<td>Jens Schollin</td>
</tr>
<tr>
<td>Orvar Finnström</td>
<td>Ricardo Laurini</td>
<td>Fredrik Serenius</td>
</tr>
<tr>
<td>Thomas Fritz</td>
<td>Eva Lindberg</td>
<td>Marija Simic</td>
</tr>
<tr>
<td>Ingrid Hansson</td>
<td>Anita Lundqvist</td>
<td>Gunnar Sjörs</td>
</tr>
<tr>
<td>Lena Hellström-Westas</td>
<td>Pia Lundqvist</td>
<td>Lennart Stigson</td>
</tr>
<tr>
<td>Per-Åke Holmgren</td>
<td>Karel Maršíál</td>
<td>Karin Stjernqvist</td>
</tr>
<tr>
<td>Gerd Holmström</td>
<td>Tore Nilstun</td>
<td>Bo Strömberg</td>
</tr>
<tr>
<td>Stellan Håkansson</td>
<td>Solveig Norden-Lindeberg</td>
<td>Margareta Wennergren</td>
</tr>
<tr>
<td>Annika Jeppsson</td>
<td>Mikael Norman</td>
<td>Magnus Westgren</td>
</tr>
<tr>
<td>Bengt Jönsson</td>
<td>Elisabeth Olhager</td>
<td>Ingrid Östlund</td>
</tr>
</tbody>
</table>