



# Intensity of perinatal care in Switzerland: Does it affect outcome?

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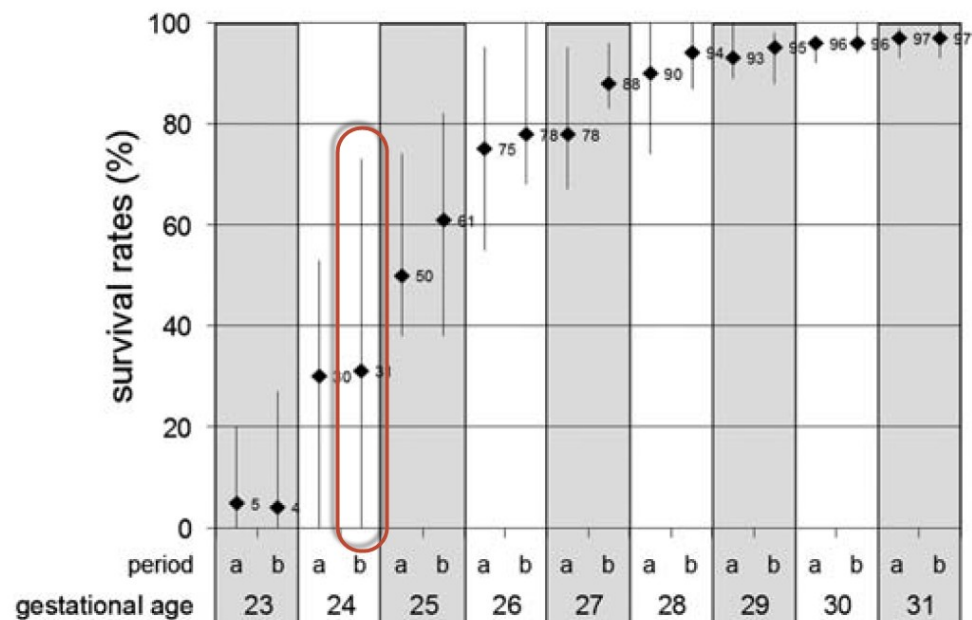
# Background

- Survival of extremely preterm born neonates below 26 gestational weeks ↑
- Unit to unit variability constantly high: why?
  
- Extremely preterm:
  - At limit of viability: 22 - 25 weeks gestation
  - Control group: 26 - 27 weeks gestation

# Restrictive use of perinatal intensive care in Switzerland

- Prior to 2002:
  - restrictive intensive care < 25 weeks gestational age
- Guidelines in 2002:
  - increased survival,
  - conditional intensive care 24 - 25 weeks
- Revisions in 2011:
  - intensive care at 24 weeks
  - provisional intensive care as of 23 weeks
  - a priori palliative care at 22 weeks

# Large variability in mortality



**Figure 3** Unadjusted centre-to-centre variability of gestational age-specific survival rates in two time periods: (A) 2000–2004 and (B) 2005–2009 (black diamonds: average overall survival rate in Switzerland; vertical lines indicate range of survival rates observed).

Berger et. al, Arch Dis Child Fetal Neonatal Ed 2012.

# Small variability in morbidities

- **Morbidities:** variability ↓[1]
  - Variability: Culture positive sepsis
  - No variability: NEC, IVH, BPD, ROP
- **Conclusion:**
  - major differences in ethical approach [2]
  - not quality of care

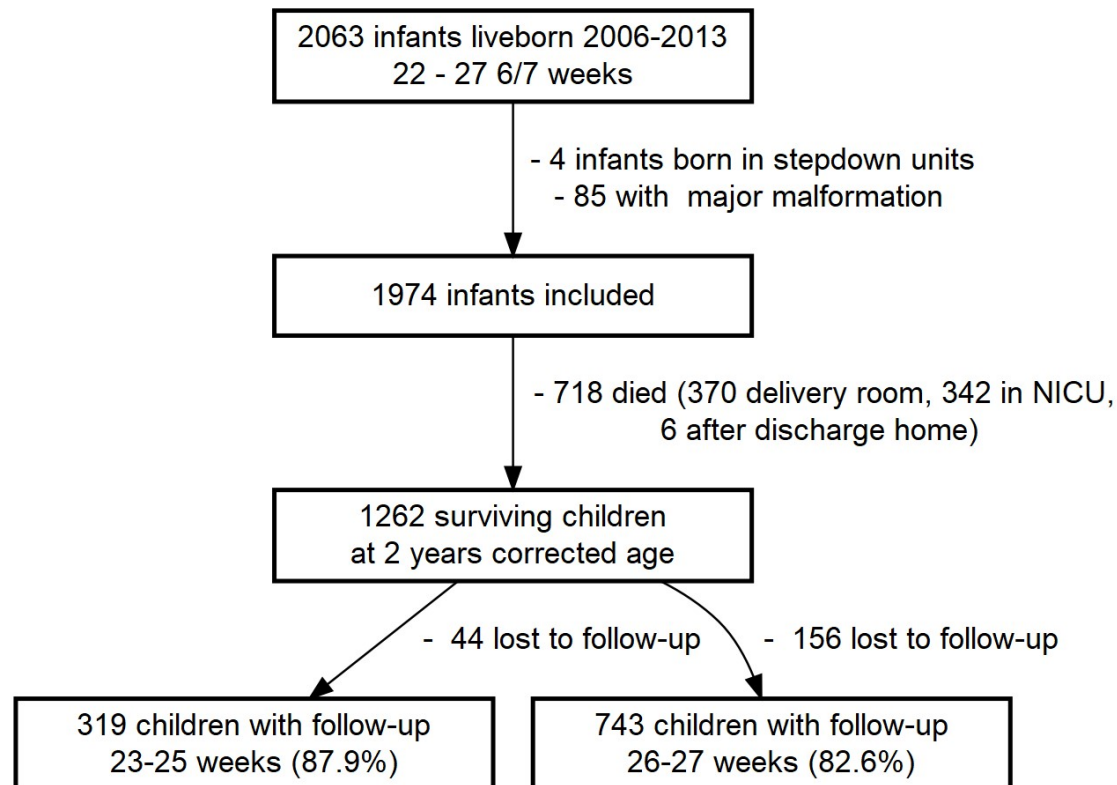
[1] Adams et al., BMC Ped. 2013.

[2] Steurer et al., Acta Paed. 2015.

# Intensity of perinatal care vs. increased neurodevelopmental impairment?

- providing intensive care < 25 weeks
  - **Against:** suffering until death ↑, quality of life ↓
  - **In favor:** chances for survival ↑, quality of life =;

# Prospective data collection from live-birth to 2 years



# Aim is comparison of low versus high activity

- perinatal activity - versus - outcome at 2 years of life
- low versus high activity:
  - 22 - 25 weeks gestation
  - 26 - 27 weeks gestation



# Numerical unit activity score based on key indicators

- 3 key obstetric indicators:
  - Delivery at perinatal center
  - Complete course antenatal steroids
  - Caesarean delivery
- 4 key neonatal indicators:
  - Surfactant within 2 hours after birth
  - Delivery room CPAP or intubation
  - No decision for primary non-intervention
  - infants admitted for intensive care

Based on: Serenius et. al, Pediatrics 2015.

# Outcomes

1. Mortality at 2 years
2. Death or moderate to severe neuro-developmental impairment (NDI) at 2 years\*
3. Favorable outcome at 2 years (survivors only)

- \*Moderate to severe NDI:
  - Developmental test  $< -2$  SD
  - Cerebral Palsy (GMFCS  $> 1$ )
  - moderate to severe visual or hearing impairment

# Hypothesis

- Main:
  - High activity centers: Mortality ↓
  - High activity centers: Favorable outcome ↓
- Side:
  - High activity centers: hours until death ↑
  - 26 - 27 weeks: outcome = for all units

# Center activity score 22 - 25 weeks

	Center 1	Center 3	Center 5	Center 7	Center 2	Center 6	Center 4	Center 9	Center 8
Obs. Activity	64.8	80.9	80.4	78.0	91.4	93.3	97.6	93.7	95.5
Neo Activity	48.7	55.4	67.1	77.5	77.1	81.7	80.9	91.7	99.8
Activity Score	56.8	68.2	73.8	77.8	84.2	87.5	89.2	92.7	97.7
Rank	1	2	3	4	5	6	7	8	9
Unit group	low	low	low	low	high	high	high	high	high

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# Baseline characteristics 22 - 25 weeks

	low activity	high activity
N	461 (49.7%)	466 (50.3%)
Gestational age (iqr)	24.7 (24 - 25.3)	24.6 (23.6 - 25.3)
Small for gestational age	11.9 %	<b>16.1 %</b>
Male sex	51.6 %	<b>57.6 %</b>
Multiple births	28.2 %	27.5 %
Activity Score (iqr)	68.2 (68.2 - 73.8)	<b>89.2 (87.5 - 92.7)</b>

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# Crude outcome 22 - 25 weeks

	low activity	high activity
Mortality	70.9 %	50.9 %
- Died in delivery room	41.9 %	34.1 %
- Mortality on ward	29.1 %	16.7 %
Death or NDI	79 %	66.7 %
Favorable Outcome (survivors)	78.3 %	72.9 %
Hours until death (iqr)	2 (1 - 72)	2 (1 - 25)

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# Adjusted OR for high activity centers

Collective	Outcome	adjusted OR	adj. 95% CI
22 - 25 6/7w GA	Mortality	0.22	0.15 to 0.31
	Death or NDI	0.37	0.26 to 0.53
	Favorable outcome (survivors)	0.78	0.45 to 1.35

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Adjusted for: gestational age, birth-weight z-score, Male sex, Multiple births, Outborn, SES

# Baseline characteristics 26 - 27 weeks

	low activity	high activity
N	554 (52.9%)	493 (47.1%)
Gestational age (iqr)	26.9 (26.4 - 27.4)	27 (26.4 - 27.4)
Small for gestational age	11.7 %	12.8 %
Male sex	52.1 %	55.8 %
Multiple births	24.2 %	28.2 %
Activity Score (iqr)	84.2 (83.3 - 85.9)	<b>91.1 (90.2 - 92.3)</b>

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# Crude outcome 26 - 27 weeks

	low activity	high activity
Mortality	18.1 %	9.7 %
- Died in delivery room	1.6 %	1.8 %
- Mortality on ward	16.4 %	7.9 %
Death or NDI	34.9 %	29.1 %
Favorable Outcome (survivors)	82.1 %	80.2 %
Hours until death (iqr)	120 (24.8 - 312)	216 (11.3 - 504)

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# Adjusted OR for high activity centers

Collective	Outcome	adjusted OR	adj. 95% CI
26 - 27 6/7w GA	Mortality	0.47	0.32 to 0.69
	Death or NDI	0.74	0.55 to 0.99
	Favorable outcome (survivors)	0.81	0.54 to 1.22

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Adjusted for: gestational age, birth-weight z-score, Male sex, Multiple births, Outborn, SES

# Conclusions

- Main:
  - Higher activity centers: Mortality ↓
  - Higher activity centers: Favorable outcome NOT ↓
- Side:
  - Higher activity centers: duration of dying for infants 26 - 27 weeks ↑
  - 26 - 27 weeks: outcome ≠ for all units

# Limitations

- Incomplete data between 22-25 weeks
- Missing power to determine difference in favorable outcome at 2 years?
- Infants born between 26-27 weeks cannot serve as control group

# Outlook

- Lower activity units are changing approach:
  - Mortality since 2014 ↓
- Revision of guidelines for care at 22 - 25 weeks
- Revision of guidelines for antenatal steroids (Obs / Neo)
- Outcome difference at 26 - 27 weeks to be discussed in network

# Acknowledgements

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**Thank you!**

**Extra Slides**



# In literature AGAINST

**Table 3. Acute Interventions Provided for Infants Admitted to the NICU**

	No. (%)		RR (95% CI) <sup>a</sup>
	EE (1993-1995) (n=35)	LE (2001-2003) (n=55)	
High-frequency ventilation	9 (26)	47 (86)	3.57 (1.93-6.61)
Chest tube(s)	4 (11)	16 (29)	1.44 (1.06-1.94)
Dopamine	20 (57)	49 (89)	2.49 (1.24-4.97)
Hydrocortisone for blood pressure support	2 (6)	30 (55)	2.18 (1.60-2.92)
Umbilical catheter(s)	30 (86)	55 (100)	1.17 (1.02-1.36)
Blood cultures	29 (83)	55 (100)	1.21 (1.04-1.40)
Antibiotics	30 (86)	54 (98)	3.86 (0.64-23.25)
Postnatal steroids for lung disease	16 (46)	34 (62)	1.30 (0.91-1.84)
Cardiopulmonary resuscitation	3 (9)	8 (15)	1.22 (0.82-1.83)
Epinephrine	3 (9)	6 (11)	1.10 (0.68-1.81)

Abbreviations: CI, confidence interval; EE, early epoch; LE, late epoch; NICU, neonatology intensive care unit; RR, relative risk.

<sup>a</sup>In the LE compared with the EE.

**Table 4. Comparison of Mortality at Each Week of Completed Gestation**

	No./Total No. (%)		RR (95% CI) <sup>a</sup>
	EE (1993-1995)	LE (2001-2003)	
Total cohort	54/75 (72)	72/104 (69)	0.93 (0.63-1.36)
22-wk GA	25 (100)	26 (100)	0.00
23-wk GA	16/22 (73)	22/26 (85)	1.43 (0.76-2.67)
24-wk GA	13/28 (46)	24/52 (46)	1.00 (0.73-1.39)

Abbreviations: CI, confidence interval; EE, early epoch; GA, gestational age; LE, late epoch; RR, relative risk.

<sup>a</sup>In the LE compared with the EE.

Donahue et al., ARCH PEDIATR ADOLESC MED 2009.

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# In literature IN FAVOR

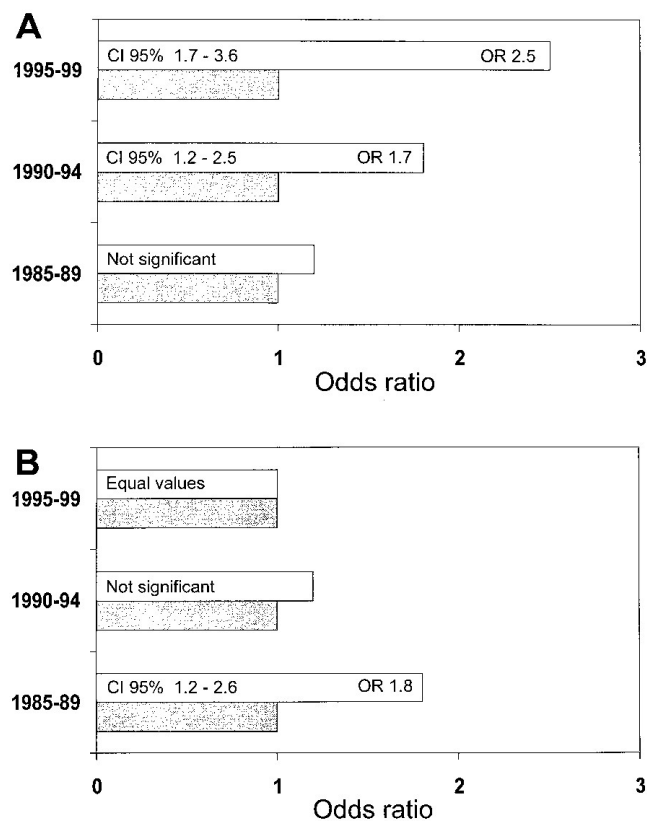


Fig 2. Graph illustrating OR for survival at 1 year of age per time period, GA, and region of birth. White bars, North; gray bars; South (reference). Upper panel, 22 to 25 weeks; lower panel, 26 to 27 weeks.

Hakansson et al., PEDIATRICS 2009.

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# Serenius et al. Pediatrics 2015

## Intensity of Perinatal Care for Extremely Preterm Infants: Outcomes at 2.5 Years

Fredrik Serenius, MD, PhD<sup>a,b</sup>, Mats Blennow, MD, PhD<sup>c</sup>, Karel Maršál, MD, PhD<sup>d</sup>, Gunnar Sjörs, MD, PhD<sup>e</sup>, Karin Källen, PhD<sup>f</sup>,  
for the EXPRESS Study Group

- All live fetuses as of 22 0/7
- 7 regions: low versus high perinatal activity

# Regional activity score

**TABLE 1** Intensity of Perinatal Care as Measured With GA-Specific and Aggregated Activity Scores in Swedish Health Care Regions

	Health Care Region						
	A	B	C	D	E	F	G
Aggregated scores (22–26 weeks)							
Obstetric	74	93	87	100	88	82	99
Neonatal	72	98	69	96	75	78	100
Perinatal	74	96	78	98	82	80	100

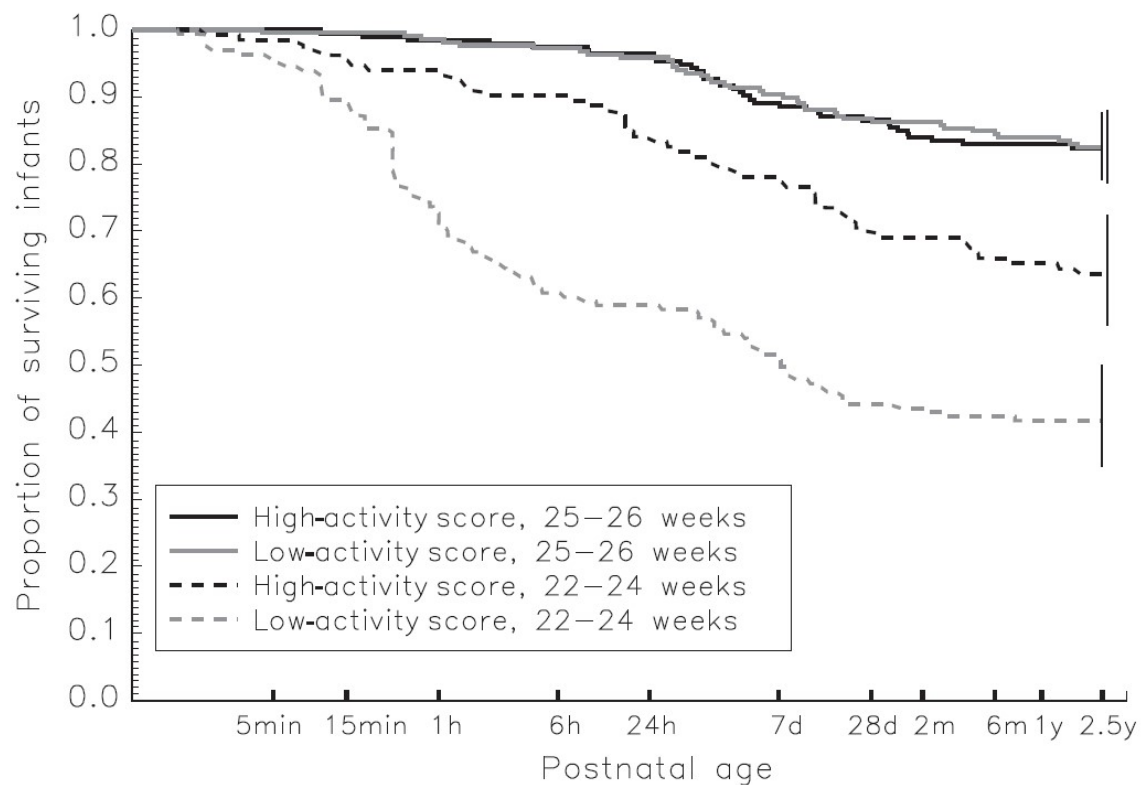
The activity score is a regional measure of intensity of perinatal care. See Methods for definitions. Actual regional intervention rates are shown in Supplemental Fig 2.

- **4 obstetric indicators** (delivery at level III hospitals, complete course of antenatal steroids, cesarean delivery, tocolytic treatment) and
- **4 neonatal indicators** (surfactant within 2 hours after birth, delivery attended by a neonatologist, intubation immediately after birth, infants admitted for intensive care)

# Their hypothesis

1. the intensity of perinatal care would be associated with a reduced risk of death up to 1 year
2. death or NDI at 2.5 years' CA would be reduced in health care regions with a higher intensity of perinatal care

# Their outcome



**FIGURE 1**

Survival curves from birth to 2.5 years' CA for infants born alive in high- and low-activity regions by GA group. Error bars are 95% Kaplan-Meier estimates.

# Lost to Follow-up

	with FU	w/o FU
N	1062 (84.2%)	200 (15.8%)
Gestational age (iqr)	26.6 (25.7 - 27.3)	26.9 (26 - 27.4)
Small for gestational age	9.9 %	5.5 %
Male sex	53.2 %	54 %
Multiple births	25.4 %	25 %
Activity Score (iqr)	85.9 (84.2 - 91.1)	87.5 (84.2 - 91.1)
Major morbidity	46.1 %	40 %

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# Data imputation

- 5-fold imputation for logistic regressions