EPIDEMIOLOGIC RESEARCH UTILISING NEONATAL DATABASES

- SNQ-dagarna 12-13.3.2020
- Kjell Helenius/University of Turku, Finland

COI

- No conflicts of interest

FINNISH MEDICAL BIRTH REGISTER

Finnish institute for health and welfare

- Active since 1987
- Governmentally funded and maintained
- All delivery units in the country are by law obliged to submit data on all stillborn and live born infants
  - 100% national coverage

https://thl.fi/sv/web/thlfi-sv/statistik/datainsamlingar/registret-over-fodelser

FINNISH MEDICAL BIRTH REGISTER

Finnish institute for health and welfare

- Small Preterm Infants data file since 2005 (piloted in late 2004)
- Includes all infants born < 32 weeks GA or birth weight <1501 grams
- Part of the Medical Birth Register

https://thl.fi/sv/web/thlfi-sv/statistik/datainsamlingar/registret-over-fodelser

THE INTERNATIONAL NETWORK FOR EVALUATING OUTCOMES IN NEONATES (INEO)

- International collaboration including 10 national/regional neonatal networks
- Aim: population-based epidemiologic VPT neonatal research platform
- Limitations
  - Not fully population-based
  - Different inclusion criteria
  - Data only from level 3 units in some networks

http://ineonetwork.org/

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Survival in Very Preterm Infants: An International Comparison of 10 National Neonatal Networks

Kjell Helenius, Gunnar Sjörs, Prakesh S. Shah, Neena Modi, Brian Reichman, Naho Morisaki, Satoshi Kusuda, Kei Lui, Brian A. Darlow, Dirk Bassler, Stellan Håkansson, Mark Adams, Maximo Vento, Franca Rusconi, Tetsuya Isayama, Shoo K. Lee, Liisa Lehtonen and on behalf of the International Network for Evaluating Outcomes (iNeo) of Neonates

Pediatrics 2017;140;
DOI: 10.1542/peds.2017-1264 originally published online November 21, 2017;

MATERIALS AND METHODS

Network	Aus/NZ	Canada	Finland	Israel	Japan	Spain	Sweden[a]	Swiss	Tuscan[b]	UK[c]	Total
Approximate number of births per year	360,000	380,000	60,000	160,000	1,080,000	480,000	90,000	80,000	30,000	690,000	3,410,000
Number of units from which data are included in iNeo[b]	56	28	30	27	73	61	28	12	24	131	470
Number of tertiary neonatal units in the country/region	29	28	5	23	93	50	7	9	7	49	300
Delivery room deaths included in database	No	Partial	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	N.A.
Data from step-down units included	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	N.A.
Proportion of infants in network compared to national birth statistics[d]	92.5%	92.5%	99.1%	95.0%	61.1%	76.1%[e]	100%	99.7%	100%	73.5%	75.6%

Helenius et al. Pediatrics. 2017 Dec;140(6). pii: e20171264

MATERIALS AND METHODS

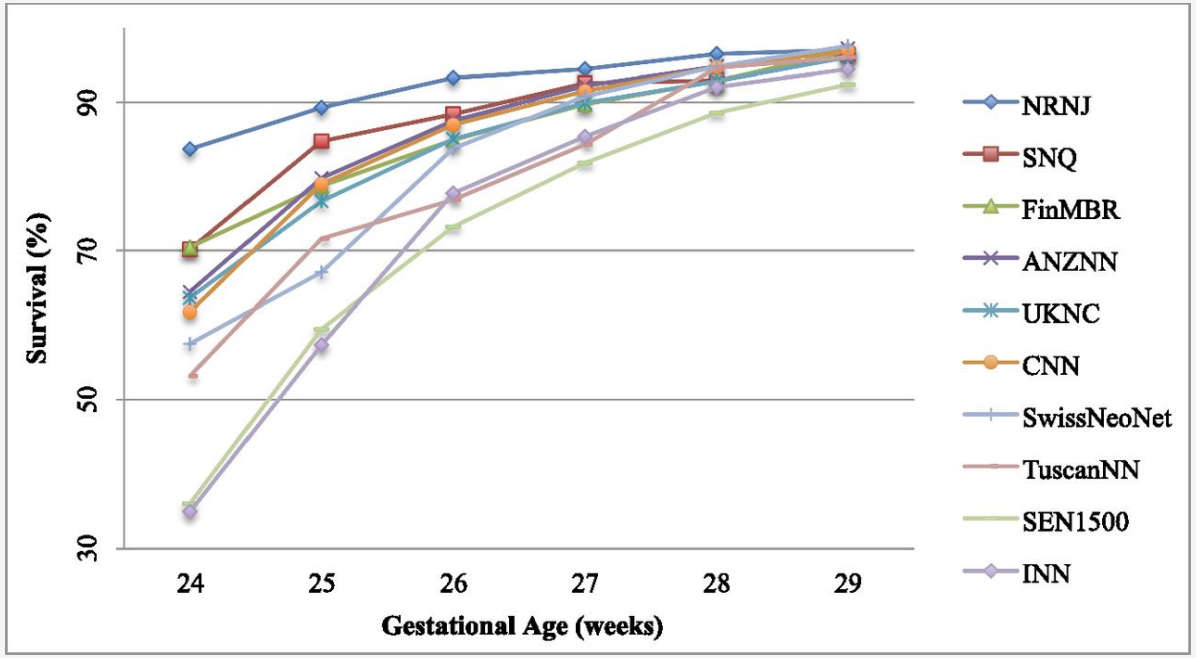
- 88,000 infants born alive at 24-29 weeks in 2007-2013 and admitted to neonatal care
- Main outcome measures: Survival until discharge and age at death
- Adjustment for sex, GA, birth weight z-score and multiple birth
  - NB! No adjustment for antenatal steroids, mode of delivery or non-tertiary birth

Helenius et al. Pediatrics. 2017 Dec;140(6). pii: e20171264

MATERIALS AND METHODS

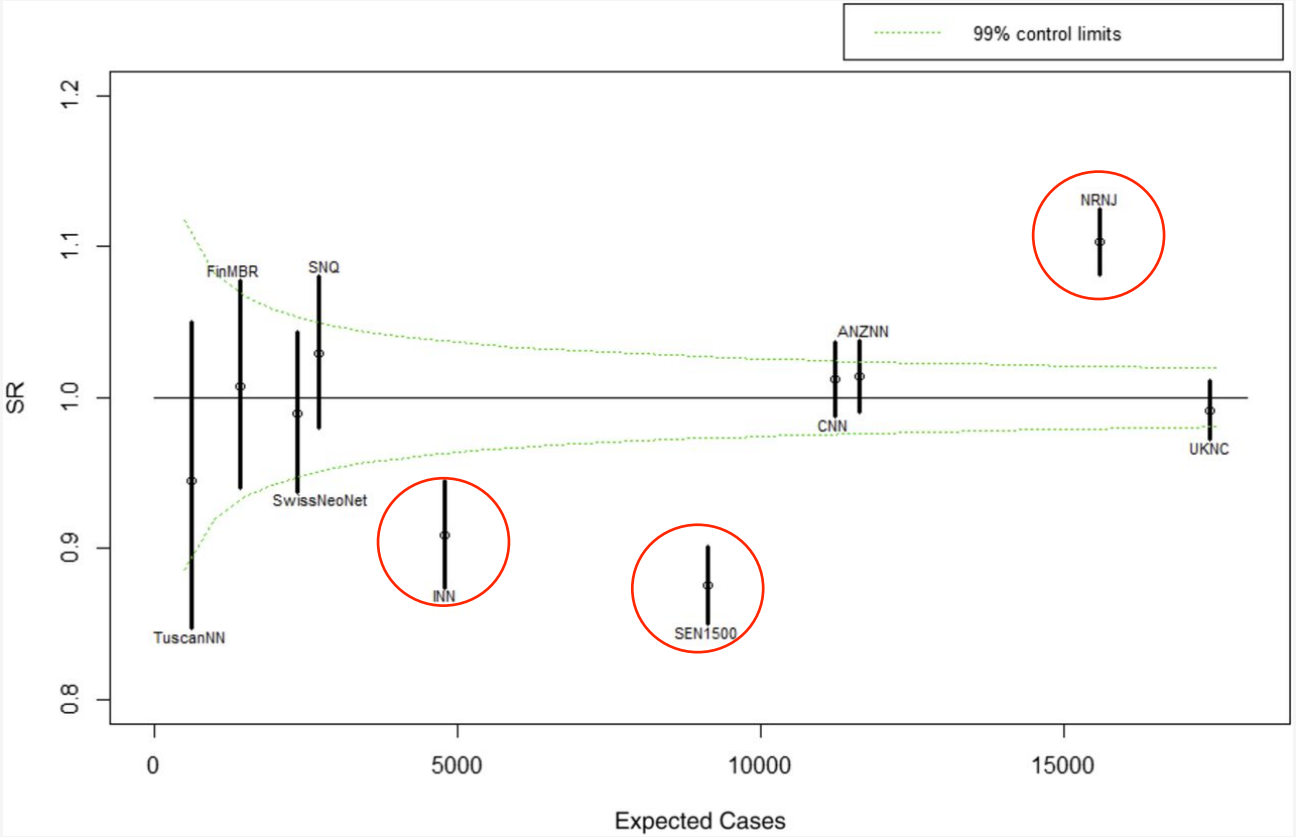
Network	Aus/NZ	Canada	Finland	Israel	Japan	Spain	Sweden[a]	Swiss	Tuscan[b]	UK[c]	Total
Number of neonates in database	13,265	12,971	1,633	5,441	18,426	10,547	3,124	2,678	705	19,975	88,765
Characteristics											
GA (weeks), mean (sd)	27.0 (1.6)	26.9 (1.6)	27.0 (1.6)	27.0 (1.6)	26.9 (1.7)	27.1 (1.6)	27.0 (1.6)	27.1 (1.6)	27.0 (1.7)	27.0 (1.6)	27.0 (1.6)
Birth weight (grams), mean (sd)	993 (251)	986 (246)	980 (259)	972 (247)	927 (256)	978 (247)	986 (256)	961 (254)	940 (257)	976 (243)	969 (251)
Birth weight z-score, mean (sd)	0.01 (0.95)	-0.09 (0.83)	-0.18 (0.91)	-0.10 (0.83)	-0.17 (0.99)	-0.08 (0.98)	-0.12 (0.86)	-0.17 (0.82)	0.07 (0.97)	-0.18 (0.93)	-0.11 (0.93)
Multiple births, n (%)	3,758 (28.4)	3,706 (28.8)	484 (29.6)	2,133 (39.2)	3,809 (20.7)	3,071 (30.0)	898 (28.8)	802 (30.0)	222 (31.5)	5,305 (26.6)	24,188 (27.3)
Male sex, n (%)	7,064 (53.4)	6,985 (54.2)	862 (52.8)	2,952 (54.3)	9,877 (53.6)	5,461 (53.4)	1,697 (54.3)	1,401 (52.4)	363 (51.5)	10,740 (53.8)	47,402 (53.6)
Any antenatal steroid, n (%)	11,818 (89.3)	10,994 (85.3)	1,537 (94.1)	4,098 (75.3)	9,901 (53.8)	8,700 (85.1)	2,616 (83.7)	2,400 (89.7)	607 (86.1)	16,585 (83.0)	69,256 (79.2)
Cesarean birth, n (%)	8,101 (61.2)	7,703 (59.8)	1,144 (70.1)	3,877 (71.3)	14,132 (76.7)	6,592 (64.5)	2,159 (69.1)	2,146 (80.2)	492 (69.8)	9,903 (49.6)	56,249 (60.0)
Born in non-tertiary hospital, n (%)	1,791 (13.5)	2,234 (17.3)	79 (4.8)	63 (1.2)	1,193 (6.5)	562 (5.5)	321 (10.3)	127 (4.8)	115 (16.3)	N.A.	6,485 (9.5)

RESULTS: SURVIVAL RATE VS. GA



Helenius et al. Pediatrics. 2017 Dec;140(6). pii: e20171264

RESULTS: SURVIVAL, STANDARDISED RATIO



Helenius et al. Pediatrics. 2017 Dec;140(6). pii: e20171264

RESULTS: AGE AT DEATH

Network	Aus/NZ	Canada	Finland	Israel	Japan	Spain	Sweden	Swiss	Tuscan	UK	All
	N=1450	N=1531	N=194	N=1091	N=1206	N=1986	N=311	N=347	N=102	N=2621	N=10839
Median (IQR) age at death, days	8 (3, 30)	10 (3, 26)	4 (1, 15)	7 (3, 19)	13 (3, 42)	8 (3, 20)	7 (2, 24)	6 (2, 16)	8 (2, 19)	8 (2, 28)	8 (3, 26)
Age at death <1 day[c]	146 (10.0)	139 (9.1)	52 (26.8)	179 (16.4)	155 (12.9)	266 (13.4)	52 (16.7)	34 (9.8)	7 (6.9)	554 (21.1)	1,584 (14.6)
Age at death[c] 1-27 days	908 (62.6)	1,036 (67.7)	112 (57.7)	701 (64.3)	657 (54.5)	1,359 (68.4)	189 (60.8)	263 (75.8)	78 (76.5)	1,398 (53.3)	6,701 (61.8)
Age at death[c] ≥28 days	396 (27.3)	356 (23.3)	30 (15.5)	211 (19.3)	394 (32.7)	361 (18.2)	70 (22.5)	50 (14.4)	17 (16.7)	669 (25.5)	2,554 (23.6)

Helenius et al. Pediatrics. 2017 Dec;140(6). pii: e20171264

DISCUSSION

- Marked differences in survival between networks
- ”Ranks” largely unchanged as GA increases
- Variation in age at death: different attitudes to end-of-life care?
- How representative are the data in networks with suboptimal coverage?
  - Selection bias: only top-performing centres participate?
  - Would inclusion of stillborn and DRD infants alter the results?

END-OF-LIFE CARE IN INEO

Received: 21 May 2019 | Revised: 3 October 2019 | Accepted: 18 October 2019

DOI: 10.1111/apa.15069

REGULAR ARTICLE

ACTA PÆDIATRICA NURTURING THE CHILD | WILEY

Survey shows marked variations in approaches to redirection of care for critically ill very preterm infants in 11 countries

Kjell Helenius[1] | Naho Morisaki[2] | Satoshi Kusuda[3] | Prakesh S. Shah[4,5] | Mikael Norman[6] | Liisa Lehtonen[1] | Brian Reichman[7] | Brian A. Darlow[8] | Akihiko Noguchi[9] | Mark Adams[10] | Dirk Bassler[10] | Stellan Håkansson[11] | Tetsuya Isayama[12] | Elettra Berti[13] | Shoo K. Lee[4,5,14] | Maximo Vento[15] | Kei Lui[16] | on behalf of the International Network for Evaluation of Outcomes of neonates (iNeo)

MATERIALS AND METHODS

- Survey on care practices for VPT infants distributed to all NICUs participating in iNeo (N=390)
- Questions regarding end-of-life care in two domains

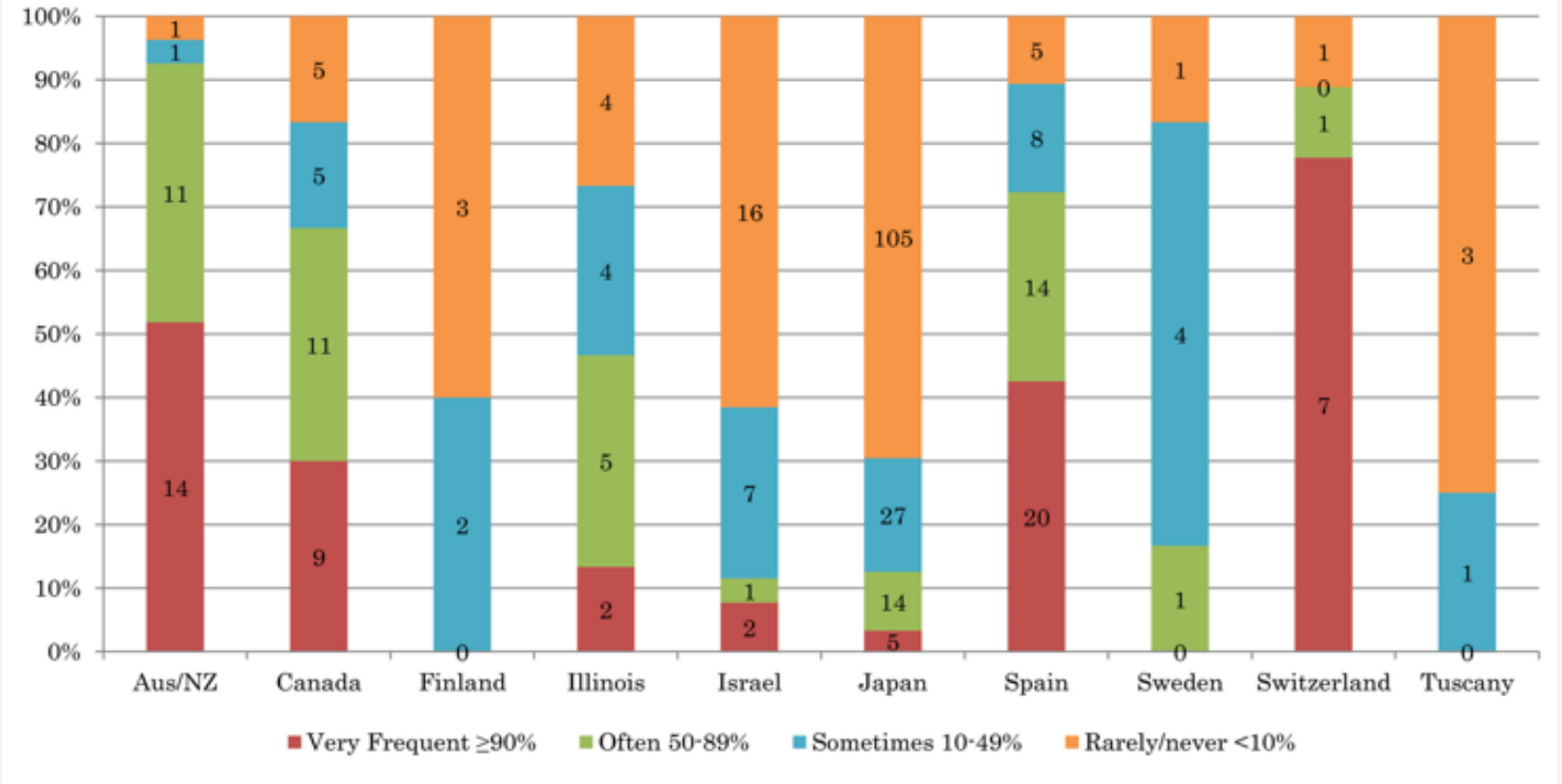
Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

MATERIALS AND METHODS

- Frequency of offering withdrawal for stable VPT infants with severe IVH
  - Very frequent (>90%)
  - Often (50-89%)
  - Sometimes (10-49%)
  - Rarely or never (<10%)
- Critically ill VPT infants where intensive care is considered futile
  - Redirection (withdrawal) of care
  - Withholding care
  - Continuing full intensive care

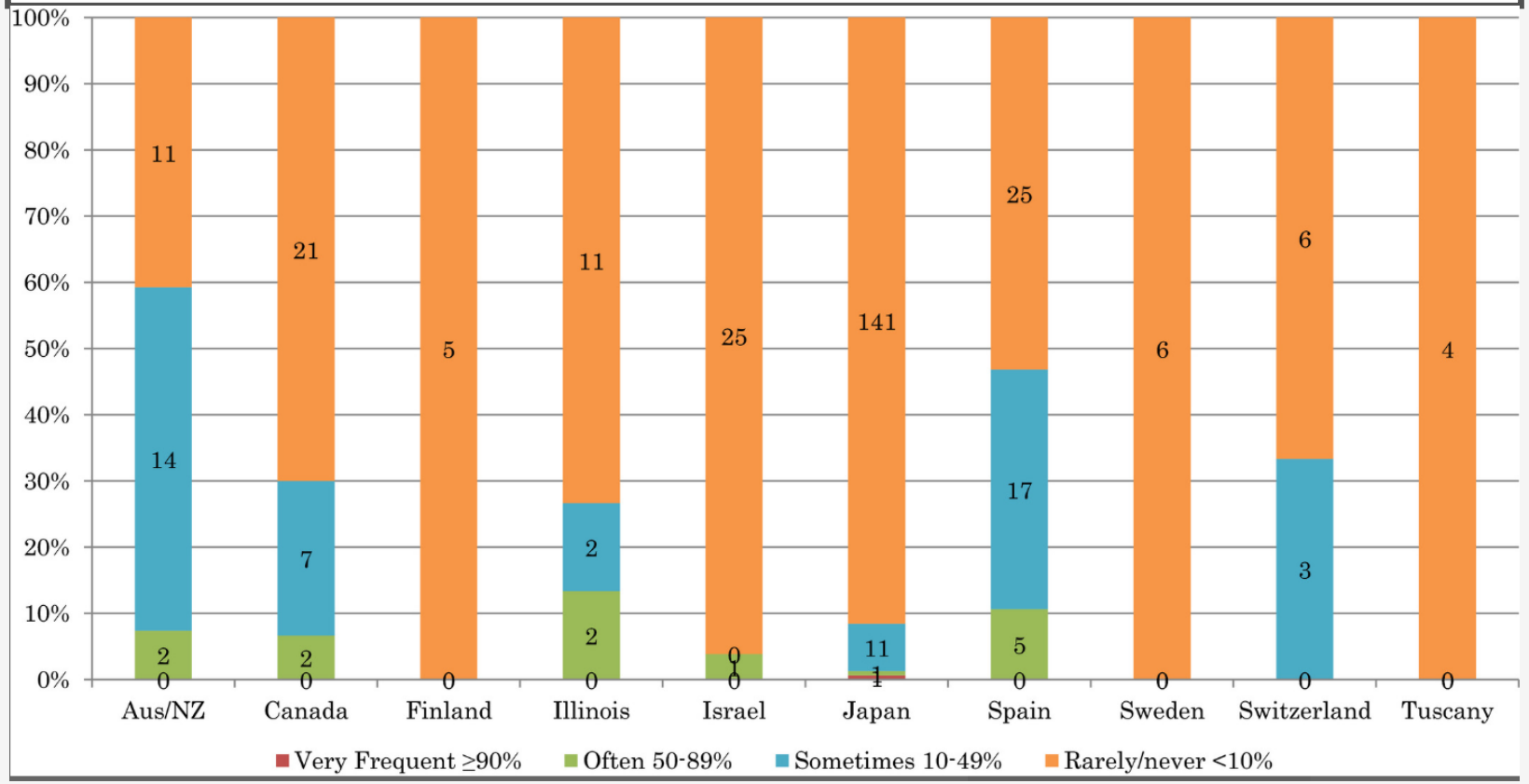
Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

RESULTS: OFFERING WITHDRAWAL FOR BILATERAL GR 4 IVH



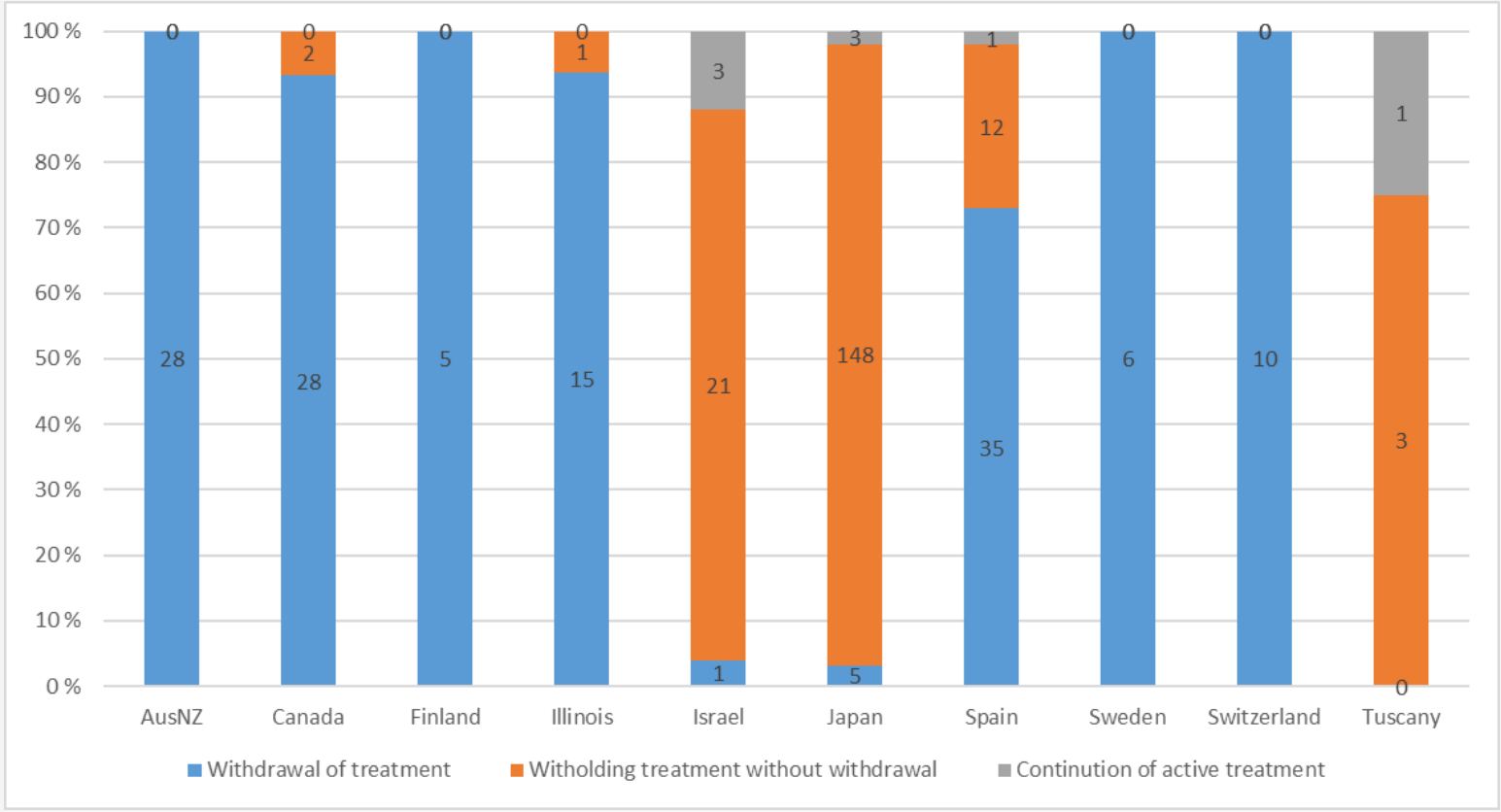
Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

RESULTS: OFFERING WITHDRAWAL FOR UNILATERAL GR 4 IVH



Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

RESULTS: CARE OF CRITICALLY ILL VPT INFANTS



Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

DISCUSSION

- Frequent withdrawal for severe IVH in Australia/New Zealand and Switzerland
- Withdrawal rare even when intensive care is considered futile in Japan, Israel and Tuscany
  - Survival of severely impaired infants
  - Ethical aspects of withdrawing care for severe IVH only
  - Religious/cultural views on quality of life
  - Legislation related to withdrawing intensive care

Helenius et al. Acta Paediatr. 2019 Oct 20. doi: 10.1111/apa.15069. [Epub ahead of print]

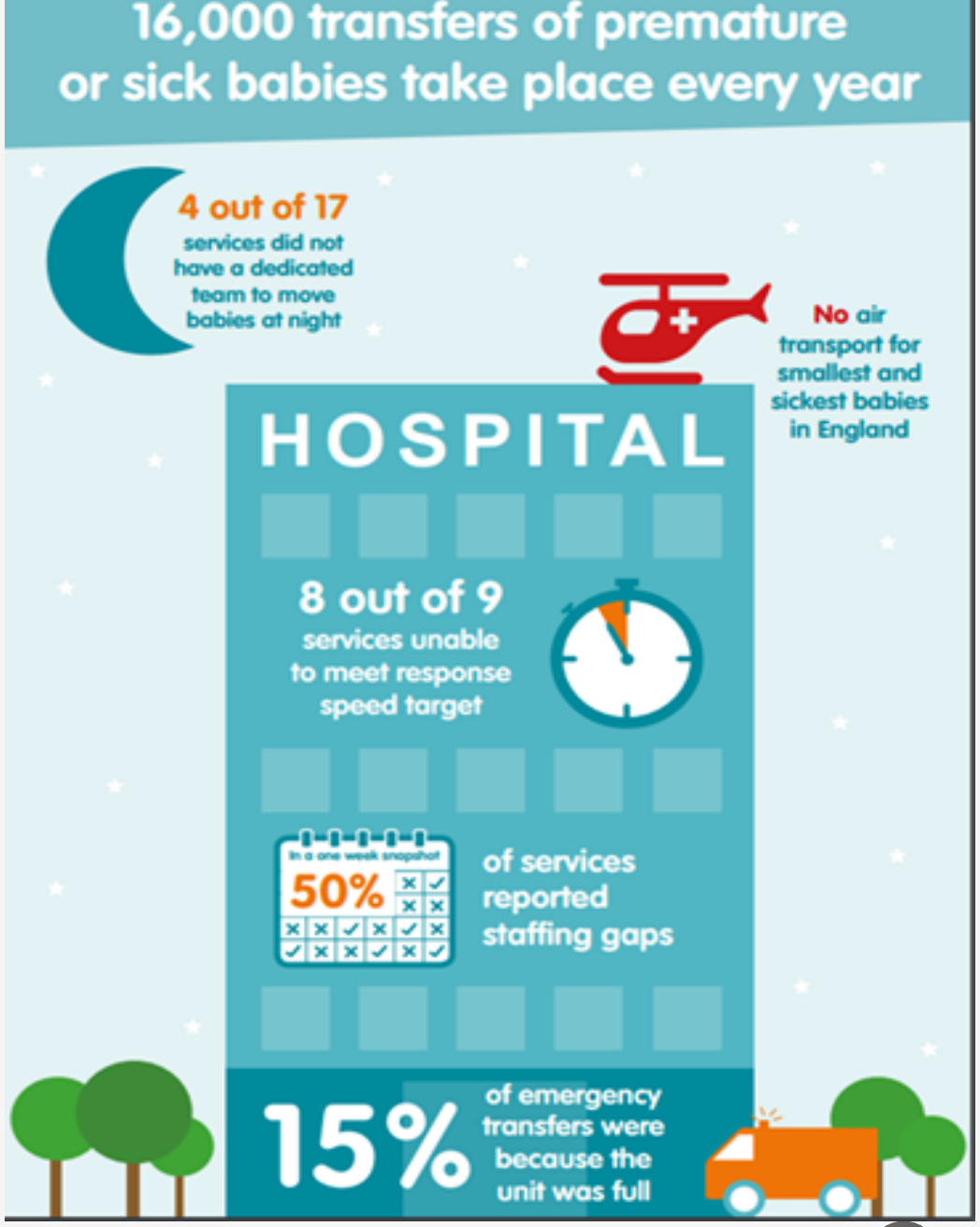
NATIONAL NEONATAL RESEARCH DATABASE (NNRD)

- National database covering neonatal care provided in NHS neonatal units in the UK since 2008[1]
- Hosted at the Neonatal Data Analysis Unit at Imperial College London
- Covers 100% of infants born at 25 to 31+6 weeks' GA[2]
  - 23 weeks' GA 70%, 24 weeks' GA 90%
  - Does not routinely include delivery room deaths and stillborn infants

1. https://www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_neonatal_data_set/national_neonatal_data_set_-_episodic_and_daily_care_fr.asp?shownav=1
2. Battersby et al. PLoS One. 2018 Aug 16;13(8):e0201815

NEONATAL CARE IN THE UK

- Over 160 neonatal units
- Centralisation to level 3 units recommended for <28 week deliveries
- Most regions do not reach the goal of 85% centralisation
  - Early transports are frequent
  - 17 dedicated neonatal transport teams



https://www.bliss.org.uk/research-campaigns/campaigns/services-under-pressure/neonatal-transport

EARLY NEONATAL TRANSFERS IN ENGLAND

Research

Association of early postnatal transfer and birth outside a tertiary hospital with mortality and severe brain injury in extremely preterm infants: observational cohort study with propensity score matching

BMJ 2019 ; 367 doi: https://doi.org/10.1136/bmj.l5678 (Published 16 October 2019)
Cite this as: *BMJ* 2019;367:l5678

MATERIALS AND METHODS

- >18,000 infants born in England in 2008-2015 <28 weeks' GA
- Divided into groups based on place of birth and transfer status at 48h
  - Control: born in level 3 unit, no transfer (N=10,866)
  - Upward transfer: born in level 2 unit, transfer to level 3 unit (N= 2,158)
  - Non-tertiary care: born in level 2 unit, no transfer (N= 2,668)

Helenius et al. *BMJ* 2019;367:l5678

MATERIALS AND METHODS: PROPENSITY SCORE MATCHING

- Logistic regression applied to all background variables
  - Designation into transfer groups as ”outcome variable”
  - Groups can be analysed with similar methods as in RCT
  - NB! Group assignment not random, unmeasured confounding not accounted for!
- Outcomes: mortality before discharge, severe brain injury, survival without severe brain injury

RESULTS

- 64% born in level 3 units, 20% transferred within 48h
- Mortality
  - Upward transfer vs. control: OR 1.22 (95% CI 0.92-1.61)
  - Control vs. non-tertiary care: OR 1.34 (95% CI 1.02-1.77)
  - Upward transfer vs. non-tertiary care: OR 0.91 (95% CI 0.69-1.19)

RESULTS

- Severe brain injury
  - Upward transfer vs. control: OR 2.32 (95% CI 1.78-3.06)
  - Control vs. non-tertiary care: OR 0.95 (95% CI 0.70-1.30)
  - Upward transfer vs. non-tertiary care: OR 2.44 (95% CI 1.89-3.23)

RESULTS

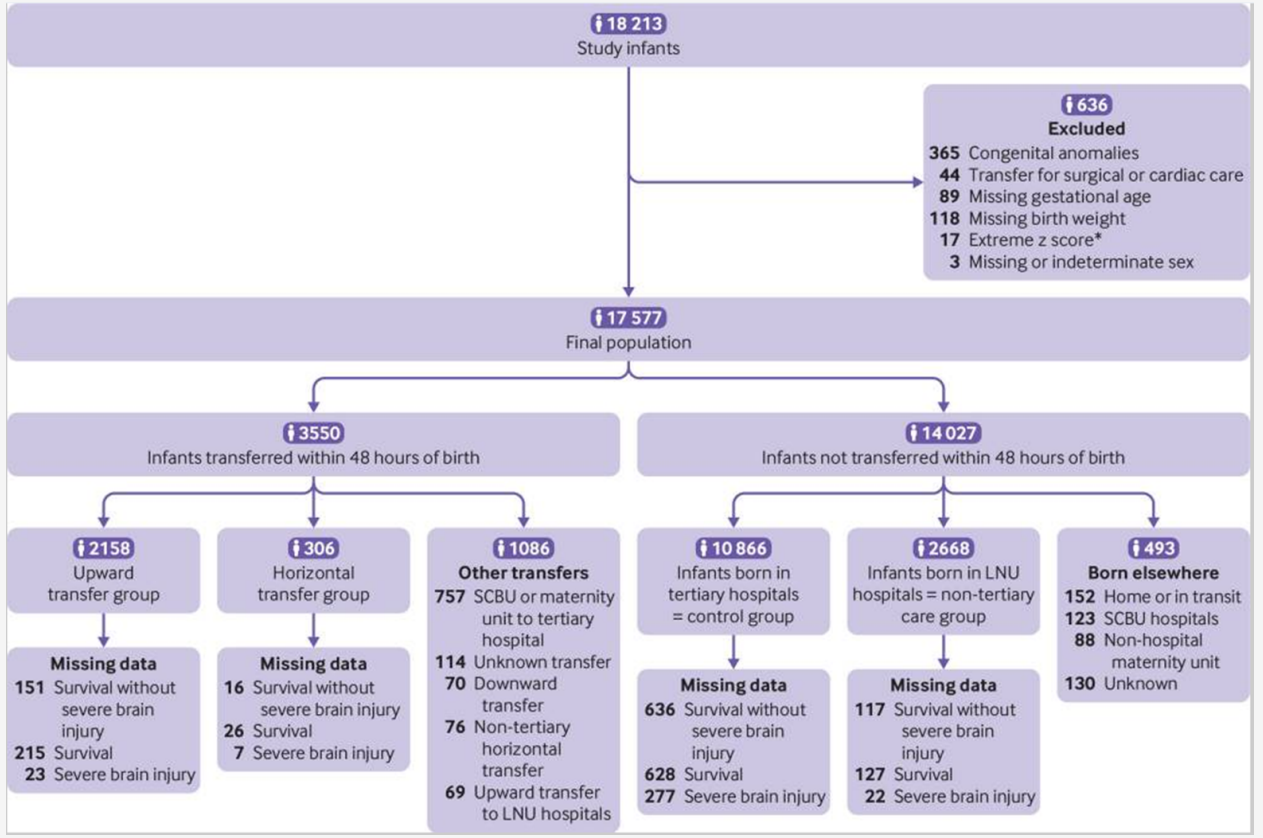
- Survival without severe brain injury
  - Upward transfer vs. control: OR 0.60 (95% CI 0.47-0.76)
  - Control vs. non-tertiary care: OR 1.22 (95% CI 0.95-1.55)
  - Upward transfer vs. non-tertiary care: OR 0.73 (95% CI 0.58-0.92)

CONCLUSION

- In extremely preterm infants,
  - Early postnatal transfer is associated with increased odds of severe brain injury and decreased odds of survival without severe brain injury
  - Birth in non-tertiary units is associated with increased odds of death compared to controls
  - Antenatal transfer is to be preferred for extremely preterm deliveries

Helenius et al. *BMJ* 2019;367:l5678

MATERIALS AND METHODS



Helenius et al. *BMJ* 2019;367:l5678