JAMA Pediatrics

RCT: Noninvasive High-Frequency Oscillatory Ventilation vs Nasal Continuous Positive Airway Pressure vs Nasal Intermittent Positive Pressure Ventilation as Postextubation Support for Preterm Neonates in China

POPULATION

860 Boys, 580 Girls

Intubated neonates born between 25 and 32 weeks and 6 days who were ready for extubation

Mean gestational age at birth, 29.4 weeks

INTERVENTION

1440 Participants randomized and analyzed

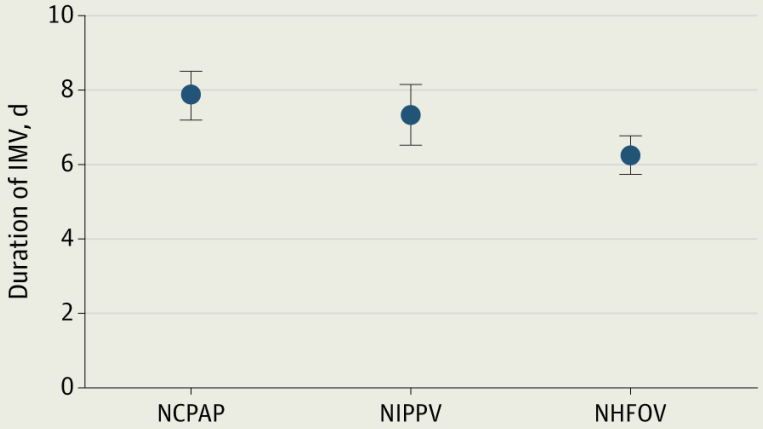
480 NCPAP
Use of nasal continuous positive airway pressure (NCPAP) postextubation

480 NIPPV
Use of noninvasive intermittent positive pressure ventilation (NIPPV) postextubation

480 NHFOV
Use of noninvasive high-frequency oscillatory ventilation (NHFOV) postextubation

FINDINGS

Duration of IMV was slightly but significantly lower with NHFOV than with either NCPAP or NIPPV; there were no significant differences in duration of IMV between NCPAP and NIPPV



Mean between-group differences for duration of IMV:

NCPAP vs NIPPV, 0.44 d (95% CI, -0.7 to 1.6 d)
NCPAP vs NHFOV, 1.5 d (95% CI, 0.3 to 2.7 d)
NIPPV vs NHFOV, 1.2 d (95% CI, 0.01 to 2.3 d)

SETTINGS / LOCATIONS

69 Neonatal intensive care units in China

PRIMARY OUTCOME

Coprimary outcomes were duration (days) of invasive mechanical ventilation (IMV), rate of reintubation, and number of ventilator-free days, defined as the number of neonatal intensive care unit-days without IMV

Zhu X, Qi H, Feng Z, Shi Y, De Luca D; Nasal Oscillation Post-Extubation (NASONE) Study Group. Noninvasive high-frequency oscillatory ventilation vs nasal continuous positive airway pressure vs nasal intermittent positive pressure ventilation as postextubation support for preterm neonates in China: a randomized clinical trial. *JAMA Pediatr*. Published online April 25, 2022. doi:10.1001/jamapediatrics.2022.0710

JAMA

QUESTION In acutely ill children who require noninvasive respiratory support, is first-line use of high-flow nasal cannula therapy (HFNC) noninferior to continuous positive airway pressure (CPAP) for time to liberation from all forms of respiratory support?

CONCLUSION Among acutely ill children clinically assessed to require noninvasive respiratory support in a pediatric critical care unit, HFNC compared with CPAP met the criterion for noninferiority for time to liberation from respiratory support.

POPULATION

347 Male
226 Female

Acutely ill children aged 0 to 15 years who were clinically assessed to require noninvasive respiratory support

Median age: 9 months

LOCATIONS

24 Pediatric critical care units in the United Kingdom

INTERVENTION

600 Patients randomized
573 Patients analyzed

295
HFNC

High-flow nasal cannula therapy, started at a flow rate based on body weight and reduced by 50% for weaning

278
CPAP

Continuous positive airway pressure, started at 7-8 cm H_2O and reduced to 5 cm H_2O for weaning

OUTCOMES

Time from randomization to liberation from respiratory support, defined as the start of a 48-hour period free from all forms of respiratory support

FINDINGS

Median time to liberation

HFNC	CPAP
52.9 hours (95% CI, 46.0 to 60.9 hours)	47.9 hours (95% CI, 40.5 to 55.7 hours)

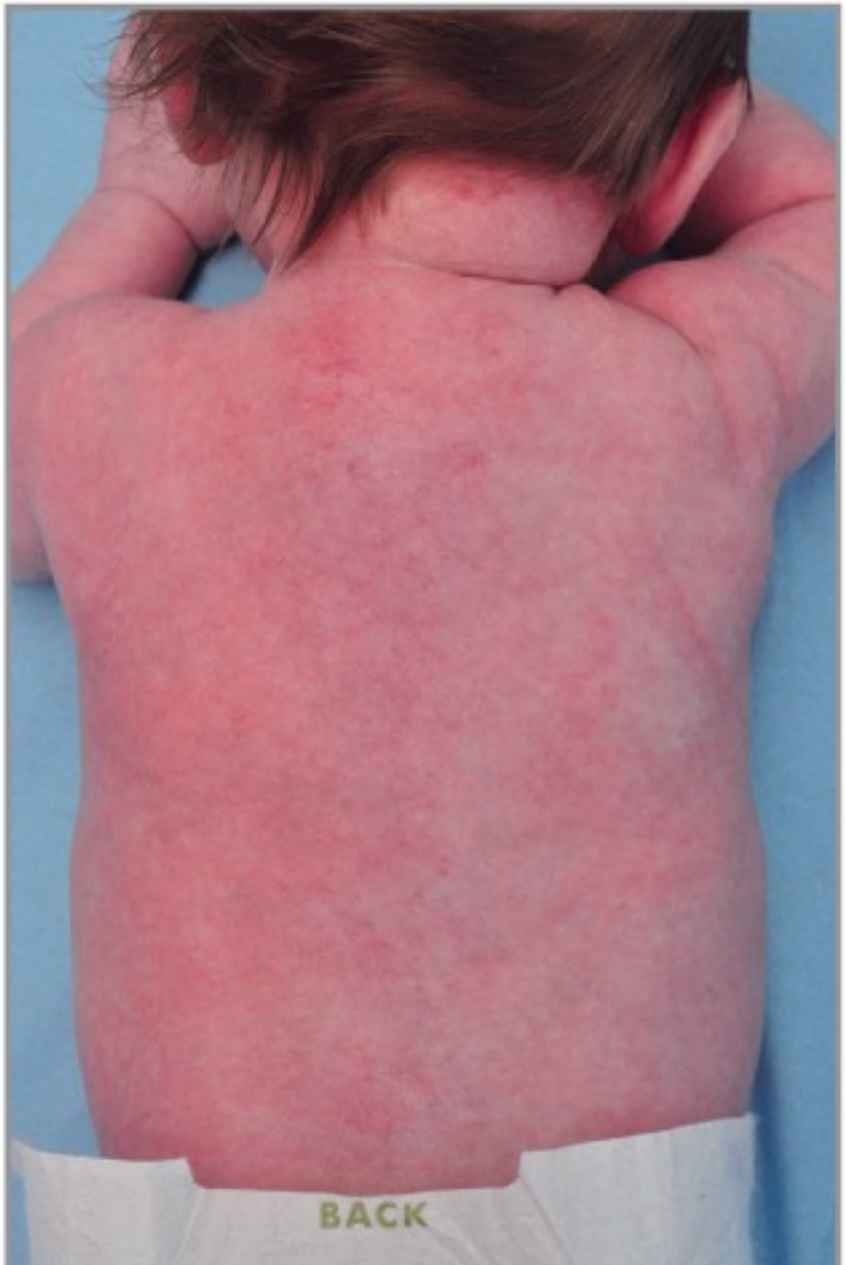
HFNC met the criterion of a noninferiority margin of an adjusted hazard ratio of 0.75 vs CPAP:

Absolute difference, 5.0 hours
(95% CI, -10.1 to 17.4)

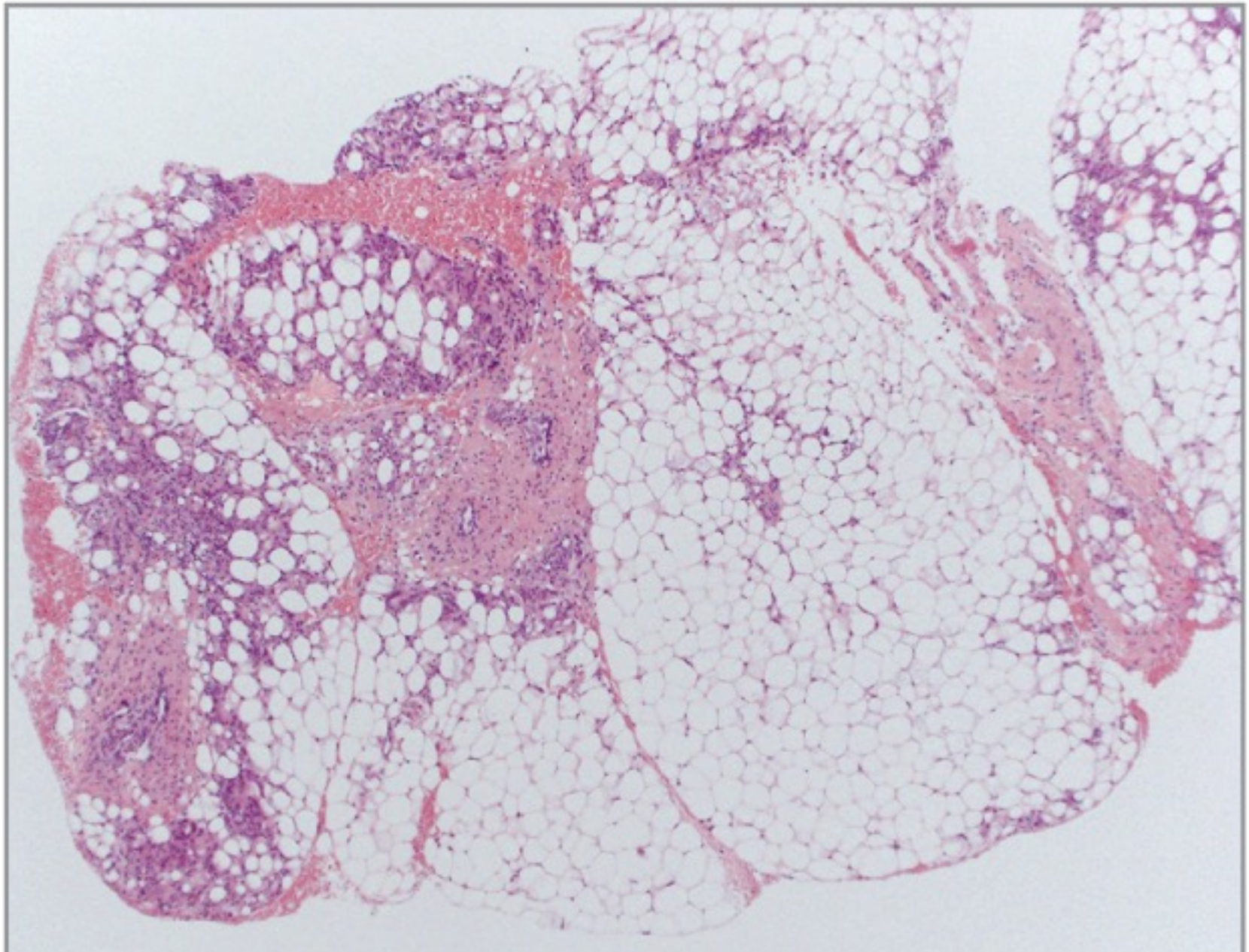
Adjusted hazard ratio, 1.03
(1-sided 97.5% CI, 0.86 to ∞)

Ramnarayan P, Richards-Belle A, Drikite L, et al; FIRST-ABC Step-Up RCT Investigators and the Paediatric Critical Care Society Study Group. Effect of high-flow nasal cannula therapy vs continuous positive airway pressure therapy on liberation from respiratory support in acutely ill children admitted to pediatric critical care units. *JAMA*. Published online June 16, 2022. doi:10.1001/jama.2022.9615

A Clinical image



B Lesional specimen



JAMA Pediatrics

RCT: Efficacy and Safety of Enteral Recombinant Human Insulin in Preterm Infants

POPULATION

171 Males, 132 Females

Preterm infants with a gestational age of 26-32 wk and a birth weight ≥500 g

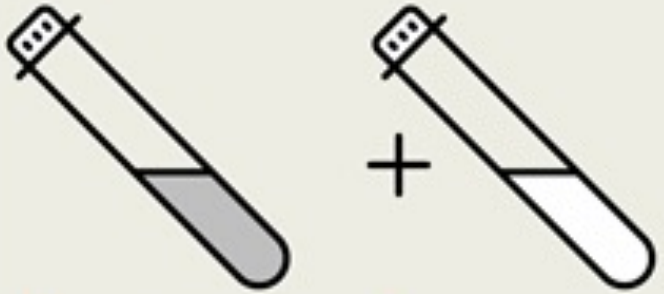
Median age: 4 d

SETTINGS / LOCATIONS

46 Neonatal units in Europe, Israel, and the US

INTERVENTION

303 Preterm infants randomized



110 Low-dose insulin
400 µIU recombinant human (rh) insulin per mL milk for 28 d

95 High-dose insulin
2000 µIU rh insulin per mL milk for 28 d

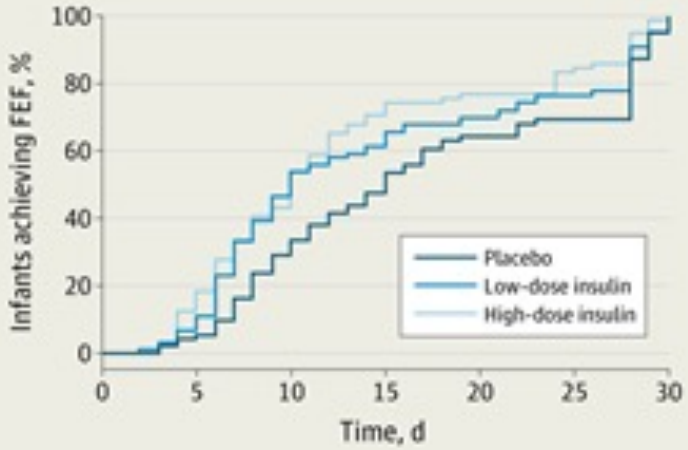
98 Placebo
Milk without supplemental insulin

PRIMARY OUTCOME

Time to achieve full enteral feeding (FEF) defined as an enteral intake of ≥150 mL/kg/d for 3 consecutive days

FINDINGS

Median (IQR) time to FEF was significantly reduced in the low-dose group (10.0 [7.0-21.8] d; *P* = .03) and high-dose group (10 [6.0-15.0] d; *P* = .001) vs the placebo group (14.0 [8.0-28.0] d)



Median (IQR) time to FEF:
low-dose insulin, 10.0 (7.0-21.8) d; *P* = .03
high-dose insulin, 10.0 (6.0-15.0) d; *P* = .001
placebo, 14.0 (8.0-28.0) d

Mank E, Sáenz de Pipaón M, Lapillonne A, et al; FIT-04 Study Group. Efficacy and safety of enteral recombinant human insulin in preterm infants: a randomized clinical trial. *JAMA Pediatr*. Published online February 28, 2022. doi:10.1001/jamapediatrics.2022.0020

Reunión Bibliográfica

- Jama
- NEJM
- BMJ
- Lancet

Alarm Burden in Infants With Bronchopulmonary Dysplasia Monitored With Pulse Oximetry at Home

Heidi M. Herrick, MD, MSCE; Molly Passarella, MS; James Weimer, PhD; Christopher P. Bonafide, MD, MSCE; Sara B. DeMauro, MD, MSC

June 23, 2022

- . Objetivo: evaluar la asociación de límites bajos de saturación de oxígeno (SpO2), retrasos de alarma y tiempos promedio con la incidencia de alarma mediante la simulación de ajustes de umbral
- Datos de un ensayo clínico de monitoreo continuo de SpO2 en el hogar entre RN con BPD en el cual prematuros con DBP moderada a grave son monitoreados con saturometría nocturna desde las 34 a 44 semanas hasta los 6 meses de EGC

Data para contar alarmas de baja SpO2 con:
Límites de 80%, 85% y 90%.
Retraso en alarma de 0, 5, 10, y 15 s
Promedio de 8 y 16 segundos.

Se midió las tendencia lineal en la tasa de alarma por 8 h (alarmas por noche)

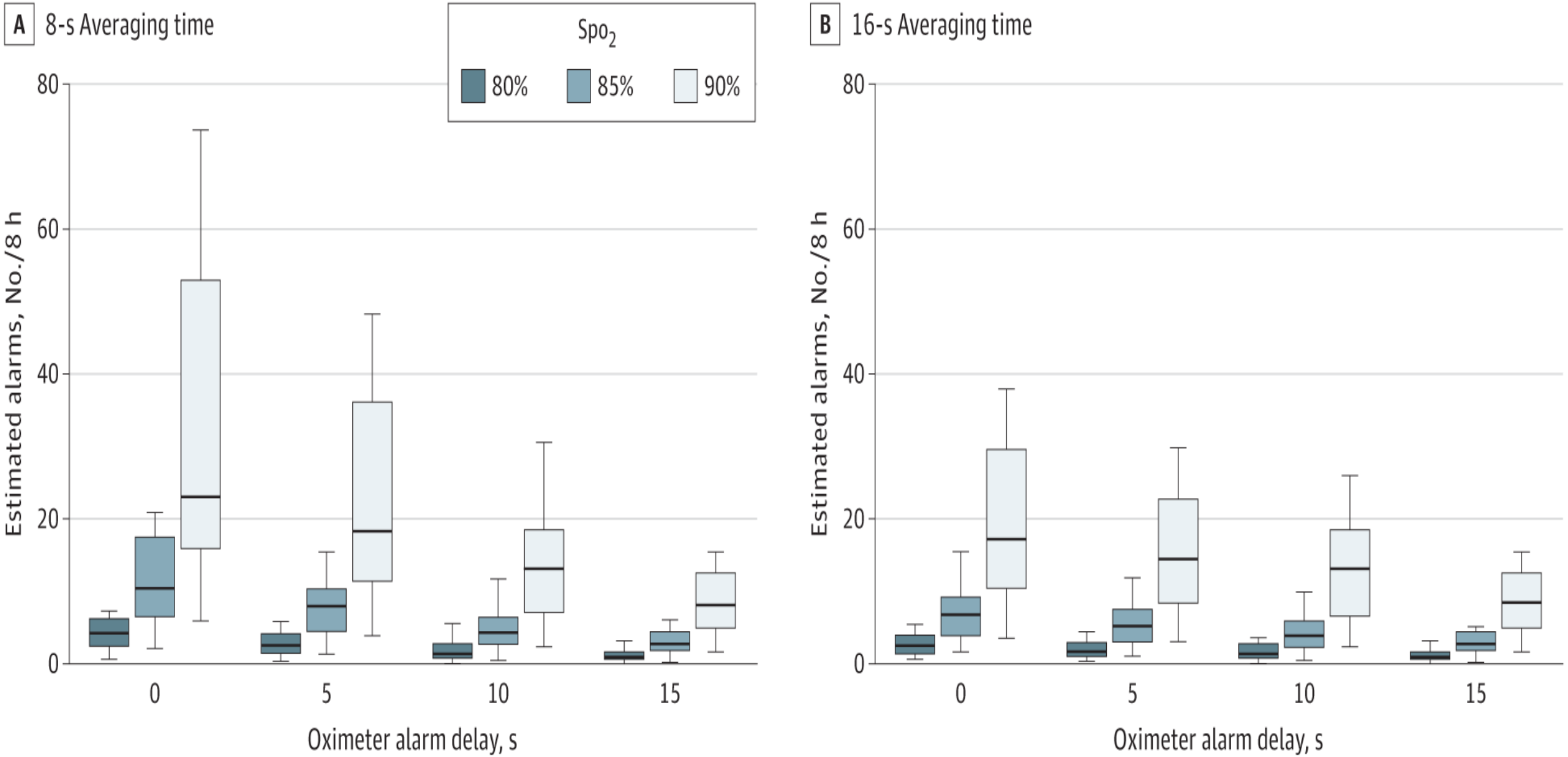
Table. Patient Characteristics

Characteristic	Patients, No. (%) (N = 20)
Birth gestational age, mean (SD), wk	26.1 (1.9)
Severity of BPD[a]	
Moderate	1 (5)
Severe	19 (95)
PMA at hospital discharge, mean (SD), wk	47.4 (5.2)
Respiratory support at hospital discharge	
Nasal cannula	10 (50)
Room air	10 (50)
Length of monitoring, mean (SD), h[b]	114.9 (80.7)

Abbreviations: BPD, bronchopulmonary dysplasia; PMA, postmenstrual age.

[a] BPD severity defined according to 2001 Jobe and Bancalari National Institutes of Health Workshop. Moderate BPD was defined as 28 days of oxygen plus fraction of inspired oxygen of less than 30% at 36 weeks' PMA or discharge; severe, 28 days of oxygen plus fraction of inspired oxygen of 30% or greater and/or positive pressure at 36 weeks' PMA or discharge.

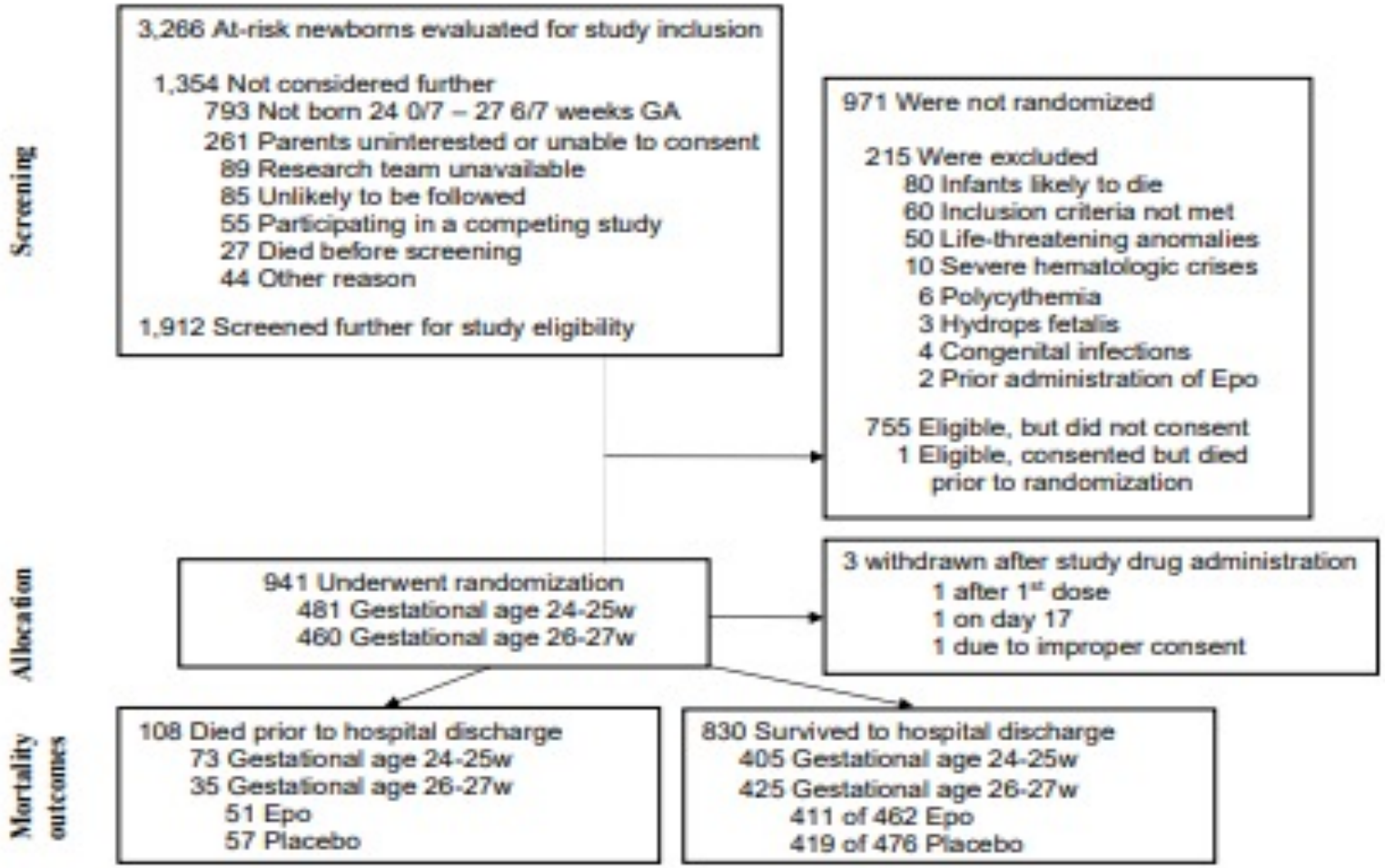
[b] Length of nonzero oxygen saturation monitoring.


A
8-s Averaging time
Spo2
80%
85%
90%
Estimated alarms, No./8 h
0
20
40
60
80
0
5
10
15
Oximeter alarm delay, s
B
16-s Averaging time
Estimated alarms, No./8 h
0
20
40
60
80
0
5
10
15
Oximeter alarm delay, s

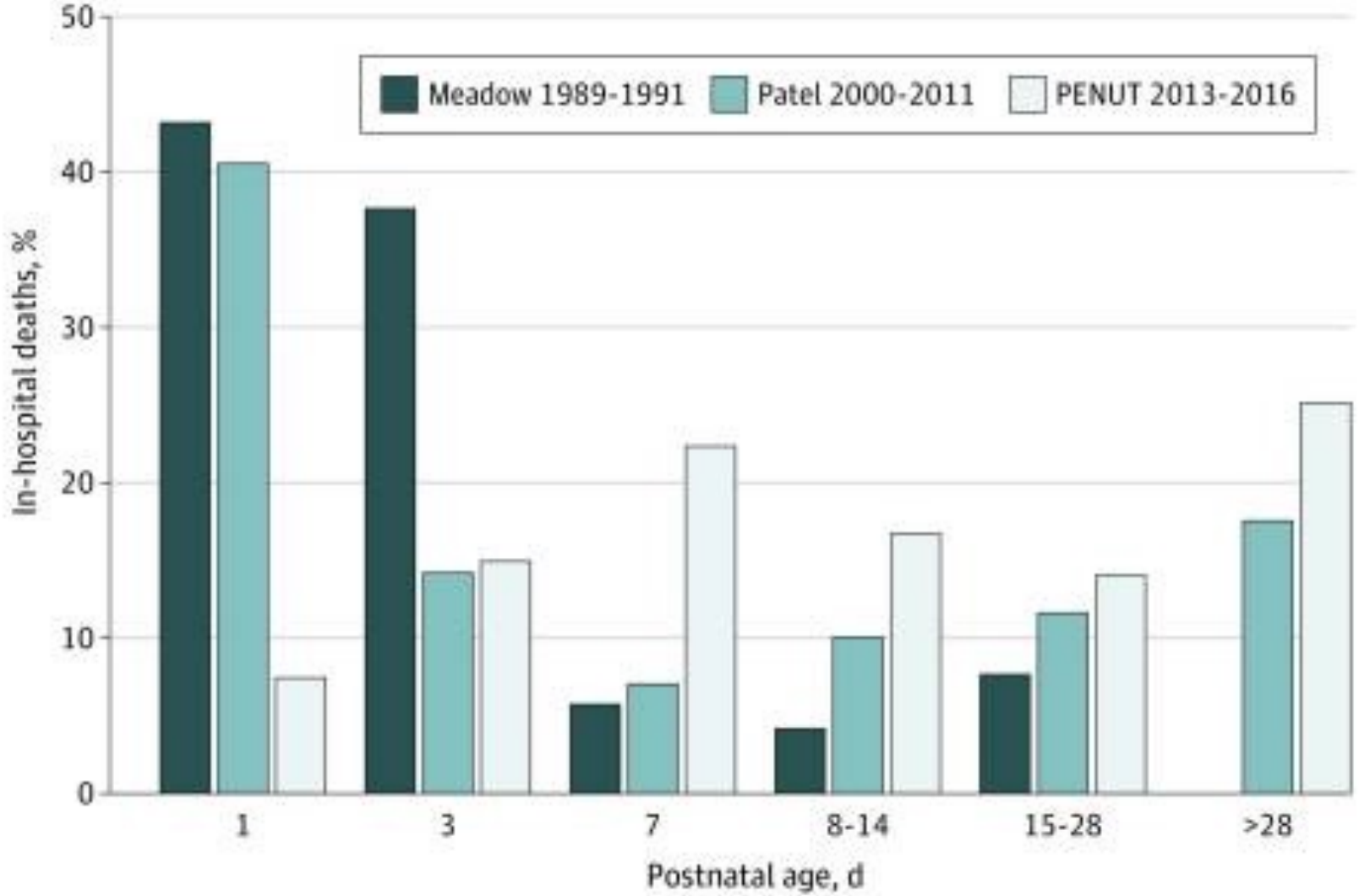
Deaths in a Modern Cohort of Extremely Preterm Infants From the Preterm Erythropoietin Neuroprotection Trial

Sandra E. Juul, MD, PhD; Thomas R. Wood, BM, BCh, PhD; Bryan A. Comstock, MS; Krystle Perez, MD, MPH; Semsa Gogcu, MD, MPH; Mihai Puia-Dumitrescu, MD, MPH; Sara Berkelhamer, MD; Patrick J. Heagerty, PhD; for the PENUT Consortium. February 7, 2022

- Objetivo: Estudiar los factores de riesgo, causas, tiempo y cicunstancias de Muerte en una cohorte de prematuros extremos.
- Revisión retrospectiva de cohortes de RN inscritos en el estudio de neuroprotección con eritropoyetina para prematuros entre el 13 de diciembre de 2013 y el 26 de septiembre de 2016.
- 941 RN. 24 0/7 y 27 6/7.
- 30 unidades de cuidados intensivos neonatales.

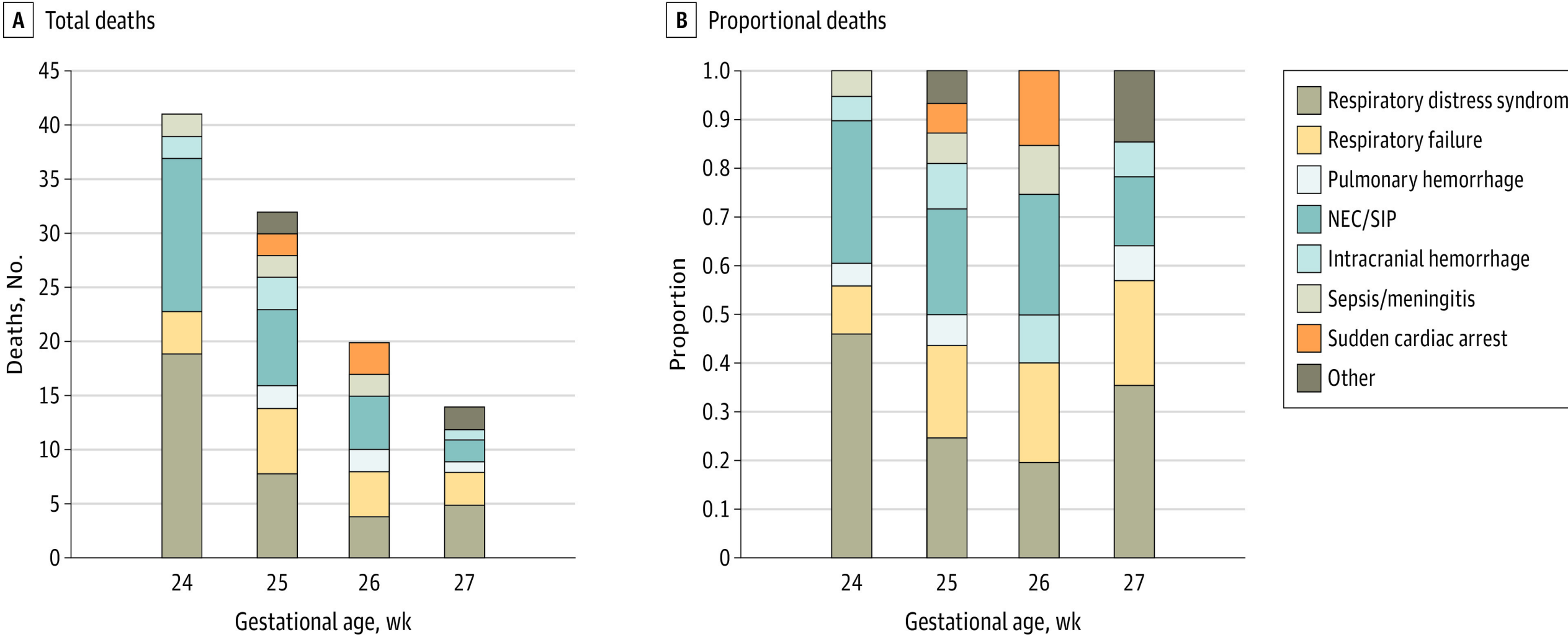


eFigure 1. The CONSORT diagram shows all infants screened, enrolled and randomized to treatment groups in the PENUT Trial, including those who survived or died prior to hospital discharge. Nine children are known to have died following discharge.



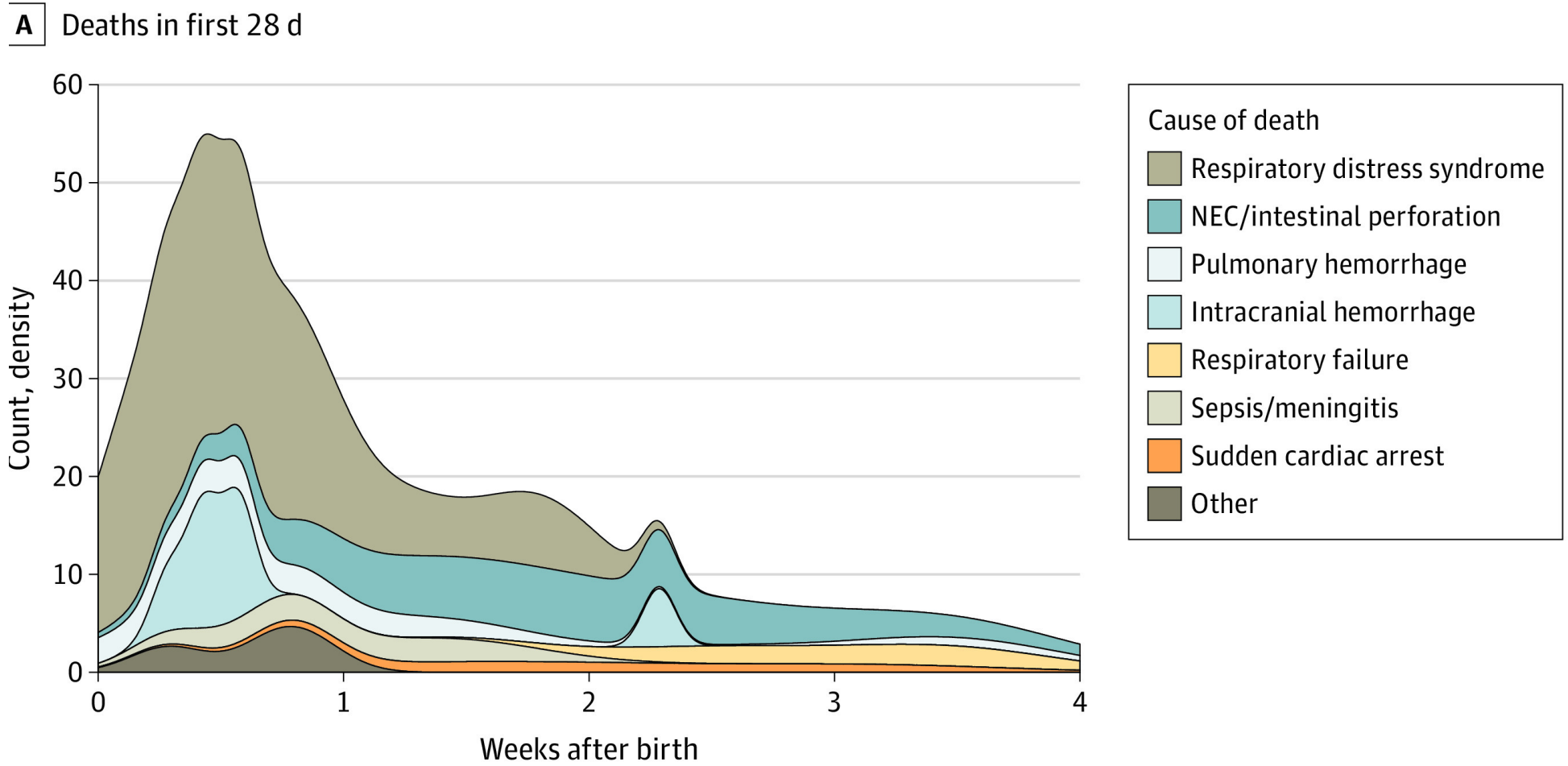
Percentage of Deaths as a Function of Postnatal Age

The percentage of in-hospital deaths is shown by postnatal age for cohorts born 1989-1991 as reported by Meadow et al19 and 2000-2011 as reported by Patel et al,9 compared with the current 2013-2016 cohort from the Preterm Erythropoietin Neuroprotection (PENUT) trial. In the most current cohort, infants survived longer.



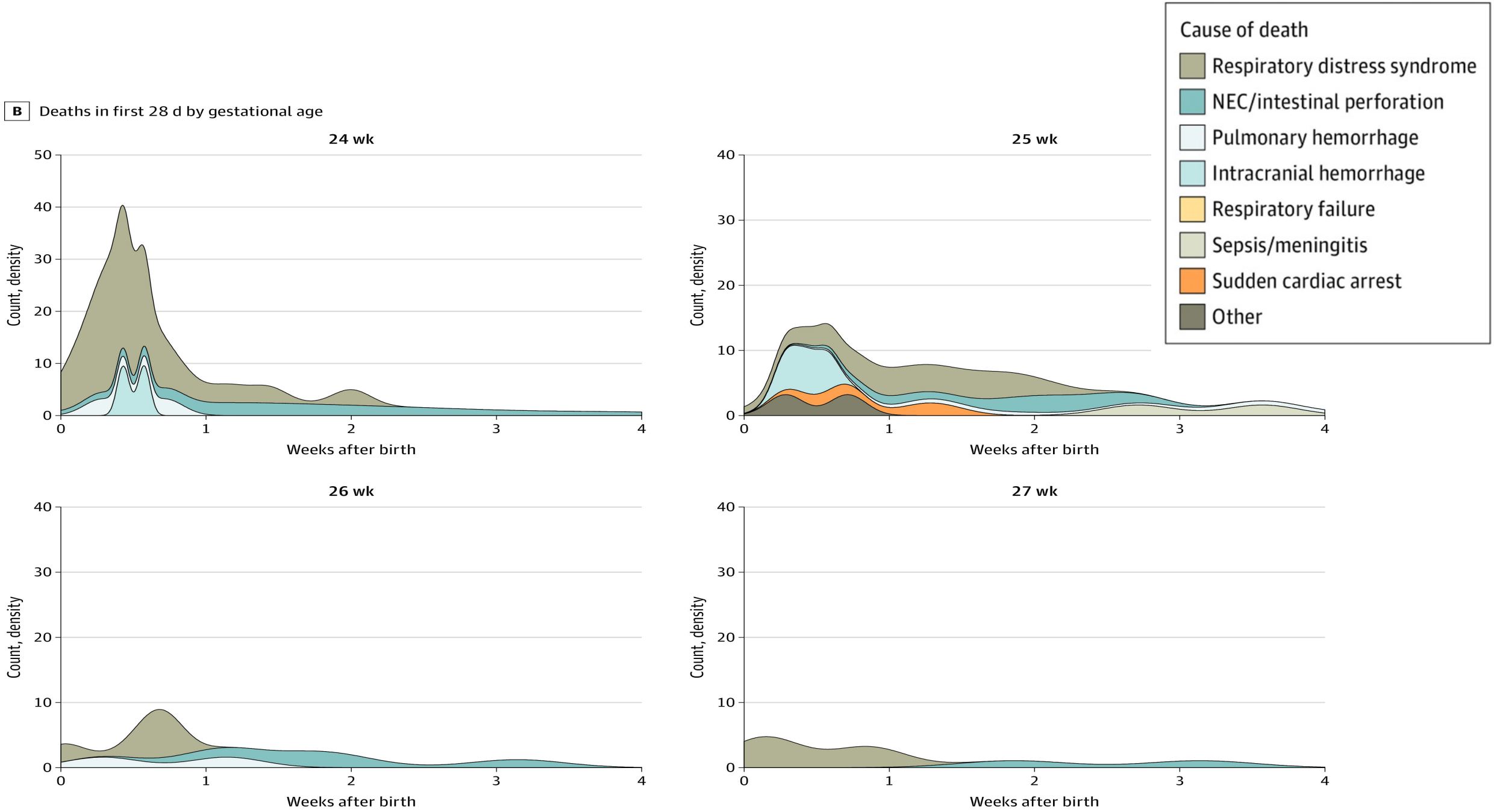
Cause of Death by Gestational Age

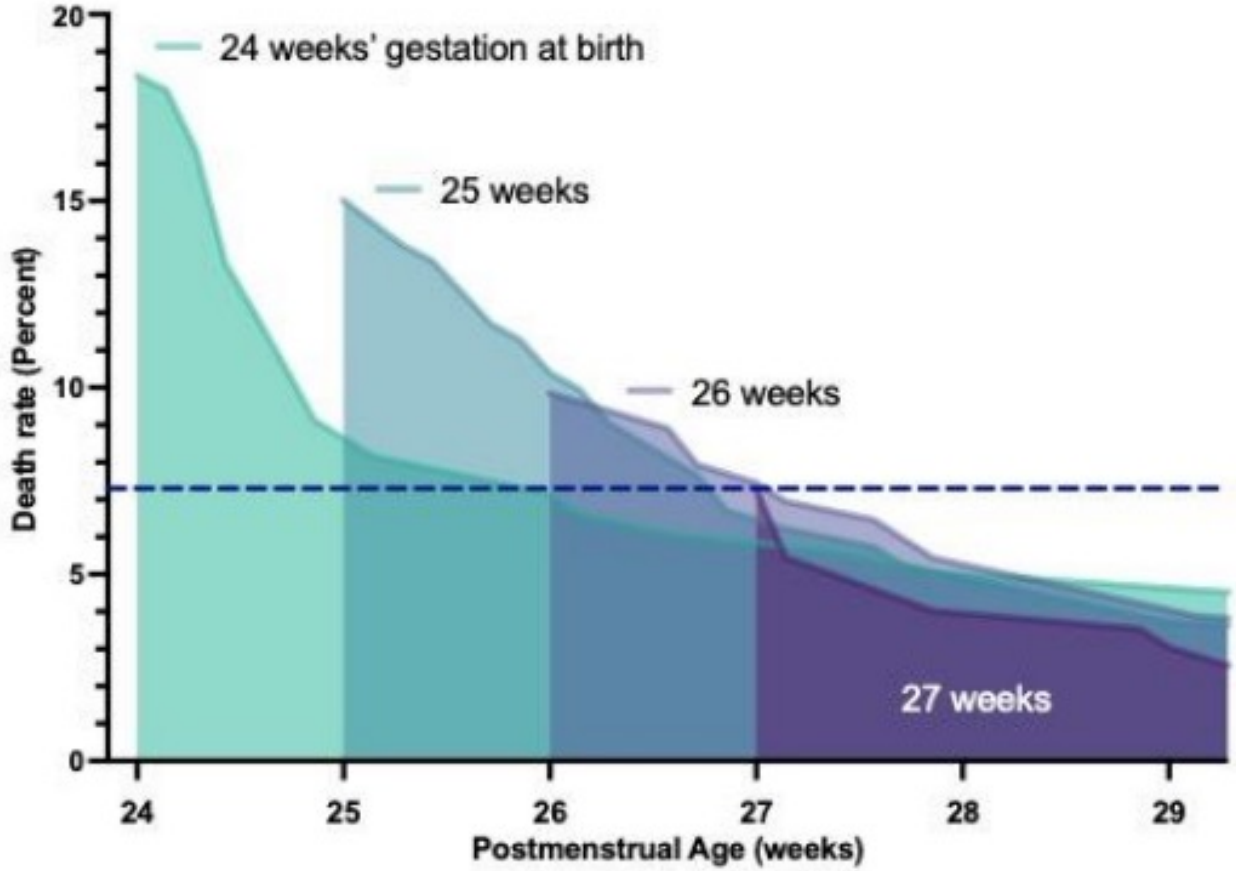
Total deaths (A) and normalized proportion of deaths (B) by gestational age, with proximal cause of death shown. NEC indicates necrotizing enterocolitis; SIP, spontaneous intestinal perforation.



In-Hospital Deaths by Cause in the Neonatal Period Timing and proximal cause of death for all neonatal deaths (first 28 days of life) (A) and separated by week of gestation (B).

The total number of in-hospital neonatal deaths for each cause of death were respiratory distress syndrome, n = 36; necrotizing enterocolitis (NEC)/intestinal perforation, n = 17; pulmonary hemorrhage, n = 7; intracranial hemorrhage, n = 6; respiratory failure, n = 4; sepsis/meningitis, n = 4; sudden cardiac arrest, n = 4; and other, n = 3.


B
Deaths in first 28 d by gestational age
24 wk
25 wk
26 wk
27 wk
Count, density
Weeks after birth
Cause of death
Respiratory distress syndrome
NEC/intestinal perforation
Pulmonary hemorrhage
Intracranial hemorrhage
Respiratory failure
Sepsis/meningitis
Sudden cardiac arrest
Other



eFigure 3:
The rate and timing of in-hospital death for infants born at each week of gestation is shown. The dotted horizontal line shows the risk of death for those infants born at 27 weeks. The point at which each curve crosses the dotted line shows when the risk of death for that group is the same as for infants born at 27 weeks of gestation. For instance, an infant born at 24 weeks' gestation reaches this risk strata after 14 days, while an infant born at 25 weeks reaches this after 10 days, and an infant born at 26 weeks reaches this after 7 days. Thus, both gestational age at birth and postmenstrual age affect the risk of death.

eTable 1. Conditional Risk of Death through Discharge. Conditional risk of death (proportion of infants who die before discharge with 95% CI) at each week of postmenstrual age (PMA), stratified by gestational age (GA) at birth. Each proportion is calculated conditional on infants surviving to that PMA, where: P(death-by-discharge | GA=x, survival to PMA=t).

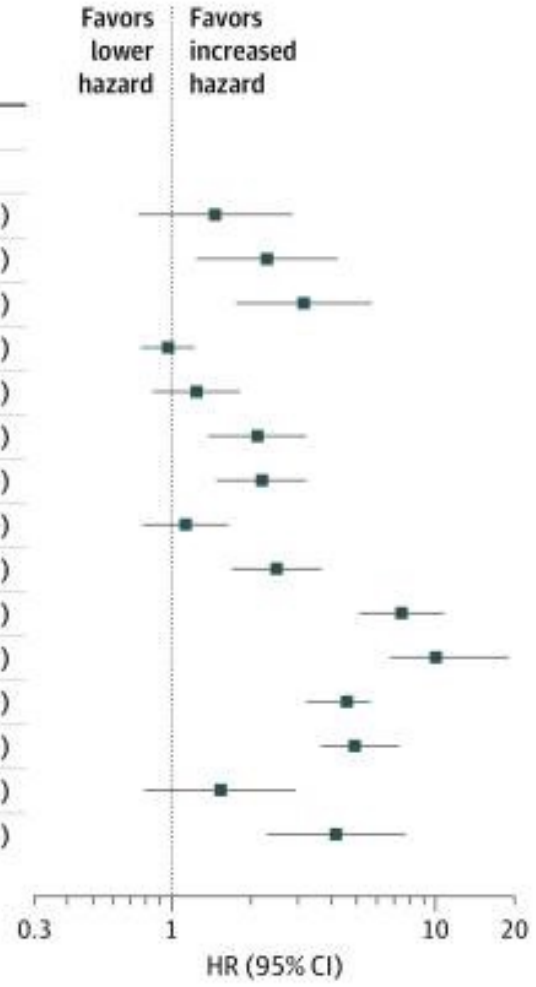
	Conditional Risk of Death through Discharge (95% CI) by Postmenstrual Age					
	24 Weeks	25 Weeks	26 Weeks	27 Weeks	28 Weeks	29 Weeks
24 Weeks GA	0.19 (0.12-0.26)	0.09 (0.04-0.15)	0.08 (0.03-0.13)	0.07 (0.02-0.12)	0.06 (0.01-0.10)	0.06 (0.01-0.10)
25 Weeks GA		0.11 (0.05-0.16)	0.08 (0.03-0.13)	0.04 (0.00-0.07)	0.03 (0.00-0.06)	0.03 (0.00-0.06)
26 Weeks GA			0.08 (0.03-0.14)	0.07 (0.02-0.11)	0.05 (0.01-0.09)	0.05 (0.01-0.09)
27 Weeks GA				0.06 (0.01-0.11)	0.04 (0.00-0.08)	0.04 (0.00-0.08)
p-value*	-	0.27	0.31	0.43	0.43	0.43

*P-value compares a Cox proportional hazards model at that PMA adjusting for treatment group only to a model also including GA at birth, conditional on surviving to that PMA.

eTable2. Withdrawal of Life-Sustaining Care by Demographics			
	Total n (%)	**Died n (%)**	**Died after withdrawal of life-sustaining care n (% of those that died)**
	941	108 (11.5%)	53 (49.1%)
Maternal Data			
Age, mean (SD)	29.0 (6.2)	30.5 (6.5)	29.9 (6.0)
Ethnicity			
Hispanic	200	26 (13%)	11 (42.3%)
Not Hispanic	728	81 (11.1%)	41 (50.6%)
Unknown/Not Reported	12	1 (8.3%)	1 (100%)
Race*			
African American/Black	238	24 (10.1%)	15 (62.5%)
Asian	31	2 (6.5%)	2 (100%)
Native American/Alaskan	16	1 (6.3%)	0 (0%)
Native Hawaiian/Pacific Islander	9	0 (0%)	-
White	614	78 (12.7%)	35 (44.9%)
Unknown/Not Reported	30	3 (10.0%)	2 (66.7%)
Education			
High School or less	307	30 (9.8%)	15 (50.0%)
Some college	284	30 (10.6%)	15 (50.0%)
College degree or greater	234	27 (11.5%)	13 (48.1%)
Not Reported	113	21 (18.6%)	10 (47.6%)

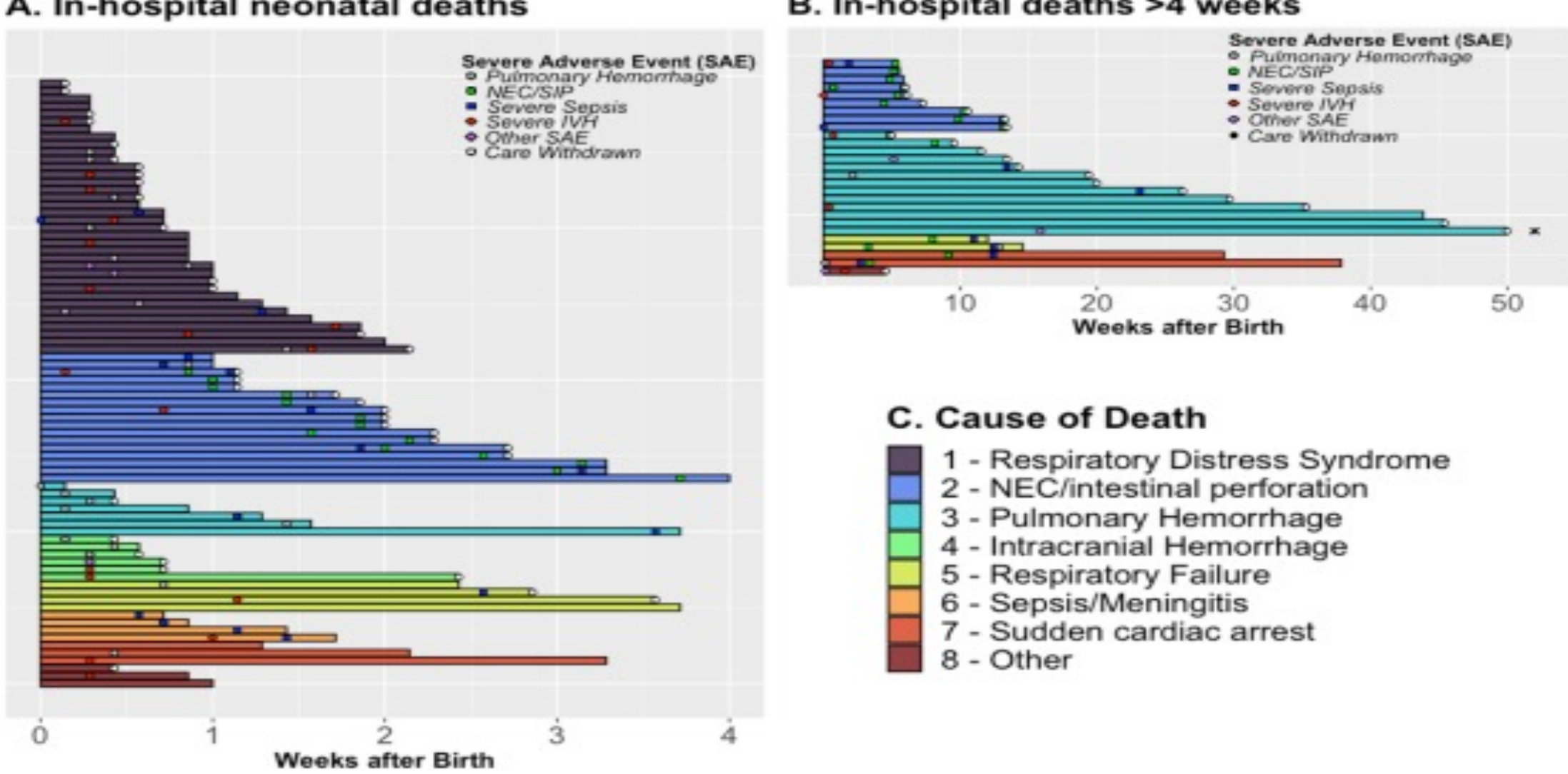
Percentages are row percentages within a given demographic level.

Risk factors	HR (95% CI)
Gestational age, wk	
27	1 [Reference]
26	1.46 (0.75-2.85)
25	2.30 (1.25-4.23)
24	3.17 (1.76-5.71)
Delayed cord clamping	0.97 (0.77-1.22)
Male sex	1.24 (0.85-1.81)
Weight <10th percentile	2.11 (1.38-3.22)
5-min Apgar score <5	2.19 (1.48-3.24)
Epo treatment	1.13 (0.78-1.64)
Sick appearance at birth[a]	2.49 (1.69-3.67)
Grade 2b-3 NEC	7.41 (5.14-10.7)
Pulmonary hemorrhage	10.0 (6.76-18.8)
Severe ICH	4.60 (3.24-5.63)
Severe sepsis	4.93 (3.67-7.21)
SIP	1.53 (0.79-2.94)
Other SAE	4.18 (2.30-7.61)



Infant Factors and Serious Adverse Events (SAEs) Associated With Death
Hazard ratios (HRs) for in-hospital death by infant risk factors and common SAEs. Each factor was considered separately, so the HR for each factor represents the result of a separate Cox proportional hazard model. All models were adjusted for treatment group and gestational age at birth. SAEs were assessed as time-varying covariates for risk of death, with the HR adjudicated from the time the SAE occurred. Epo indicates erythropoietin; ICH, intracerebral hemorrhage; NEC, necrotizing enterocolitis; and SIP, spontaneous intestinal perforation.

A Sick appearance at birth was a subjective assessment by the attending neonatologist.



eFigure 4. Swimmer plots showing timing of in-hospital death and common SAEs, with deaths grouped by cause in the neonatal period (A) and over the entire hospital course (B). One infant who died before discharge at 90 weeks was censored at 50 weeks, denoted by an x. Each horizontal line represents one child, with the SAEs they experienced, the timing of death, and whether care was withdrawn prior to death.

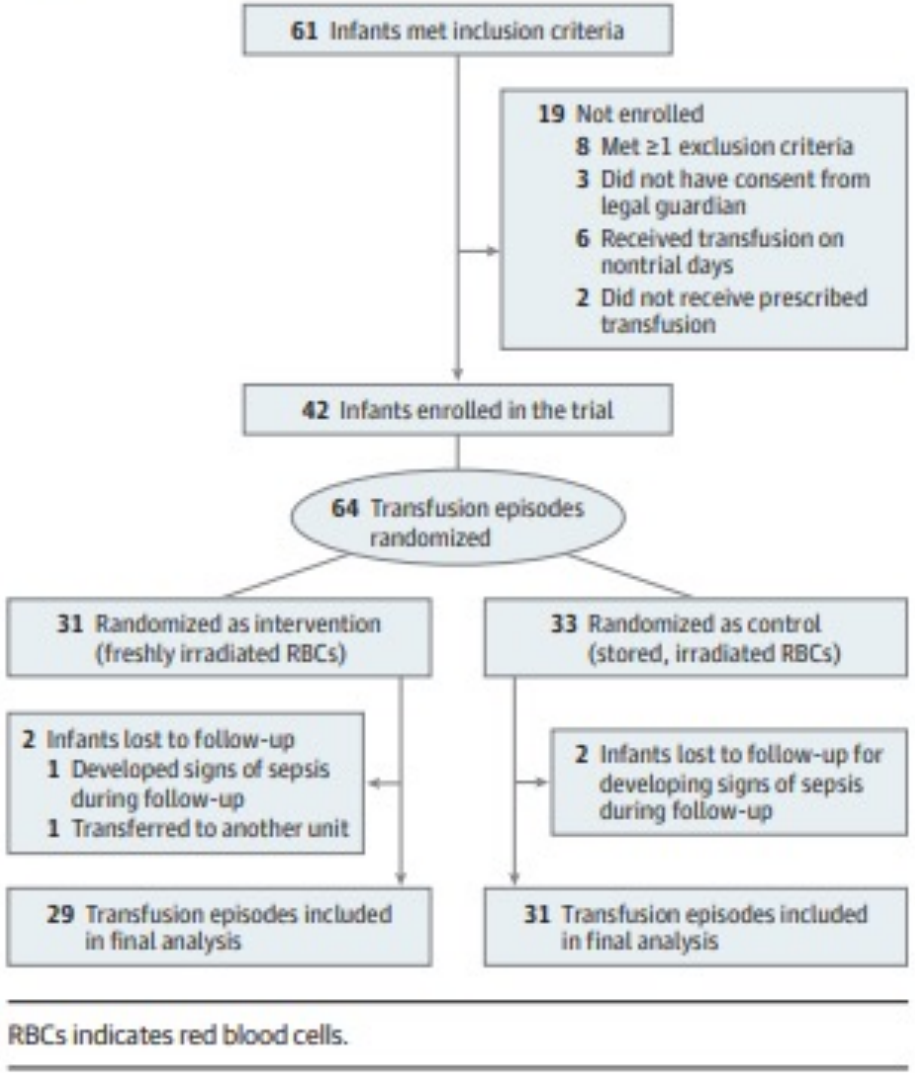
Effects of Freshly Irradiated vs Irradiated and Stored Red Blood Cell Transfusion on Cerebral Oxygenation in Preterm Infants A Randomized Clinical Trial

Maria Saito-Benz, MSc; Karen Bennington, MSc; Clint L. Gray, PhD; William G. Murphy, MD; Peter Flanagan, BMBS; Frederica Steiner, MBChB; Greg Atkinson, PhD; Mary J. Berry, PhD.

AMA Pediatr. 2022;176(5):e220152. doi:10.1001/jamapediatrics.2022.0152 Published online March 28, 2022.

- Objetivo: Evaluar si la transfusion de GR irradiados frescos versus almacenados mejoran la oxigenación cerebral en prematuros con anemia
- Criterios de Inclusión:
- RN < 34 s al nacer
- > 14 días de edad
- Indicación por tratante
- Sin: VMI. Infección, Ductus HS

Figure 1. Flow Diagram of Infants and Transfusion Episodes



RBCs indicates red blood cells.

JAMA Pediatrics

RCT: Effects of Freshly Irradiated vs Irradiated and Stored Red Blood Cell Transfusion on Cerebral Oxygenation in Preterm Infants

POPULATION

29 Boys, 13 Girls

Preterm infants born at <34 wk gestation requiring nonurgent red blood cell transfusion at ≥14 d

Mean corrected postnatal age, 32 wk and 3 d

INTERVENTION

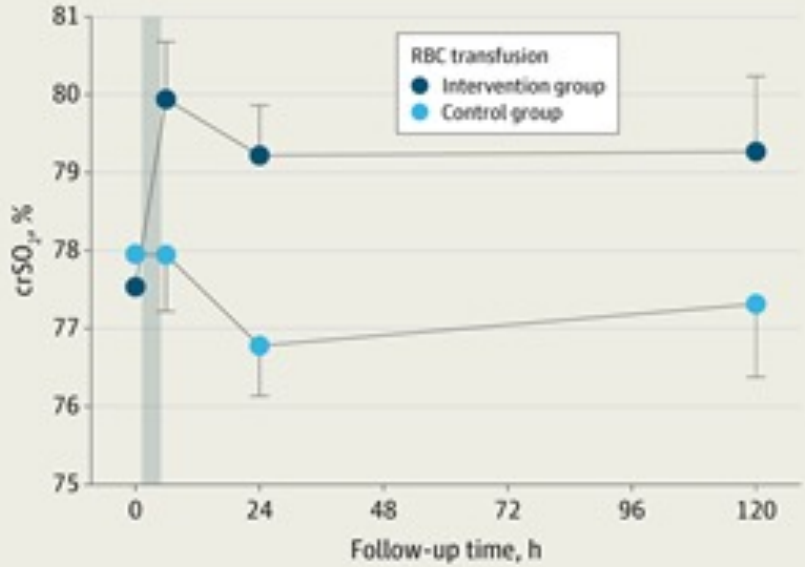
60 Transfusion episodes randomized and analyzed

29 Freshly irradiated (intervention)
Transfusion of red blood cells (RBCs) irradiated on the day of transfusion (15 mL/kg over 3 h)

31 Irradiated and stored (control)
Transfusion of RBCs irradiated and stored per ANZSBT guidelines (15 mL/kg over 3 h)

FINDINGS

The immediate change in mean $crSO_2$ was significantly greater for infants who received freshly irradiated RBCs compared with the control group



Mean change in $crSO_2$ from baseline across all follow-up points for freshly irradiated RBCs vs control, 2.1 (95% CI, 1.6-2.7) percentage points; $P<.0005$

SETTINGS / LOCATIONS

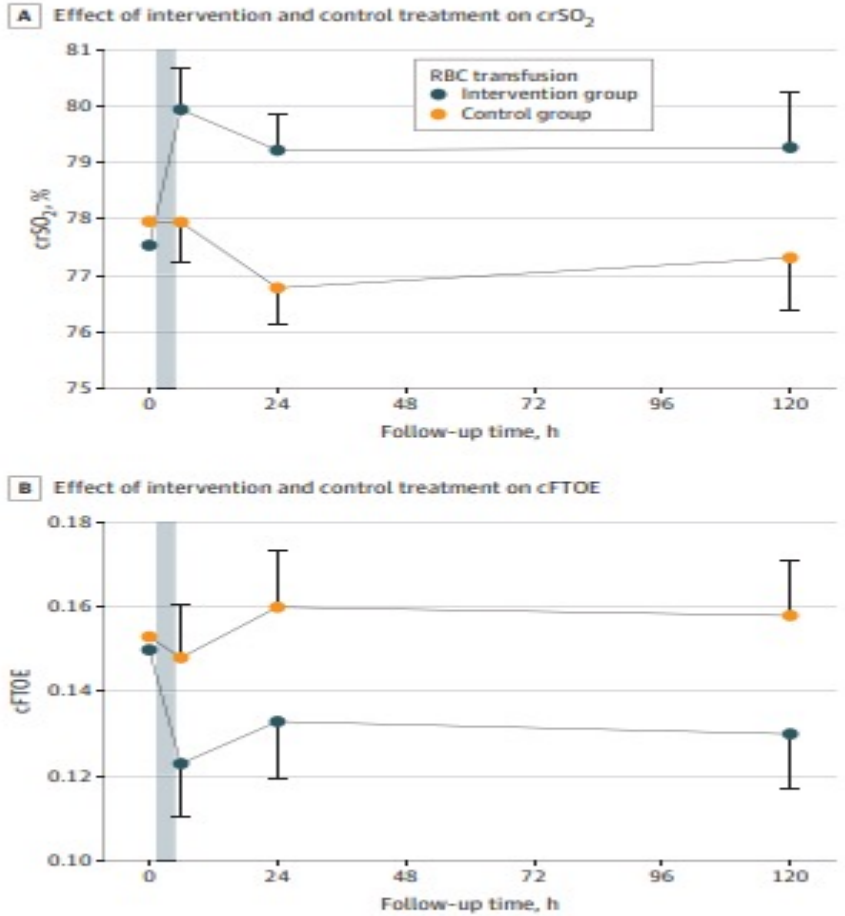
1 Neonatal intensive care unit in Wellington, New Zealand

PRIMARY OUTCOME

Change in cerebral regional oxygenation ($crSO_2$, %) from baseline (immediately before) to immediately after transfusion, adjusted for gestational age at birth and baseline $crSO_2$

Saito-Benz M, Bennington K, Gray CL, et al. Effects of freshly irradiated vs irradiated and stored red blood cell transfusion on cerebral oxygenation in preterm infants: a randomized clinical trial. *JAMA Pediatr*. Published online March 28, 2022. doi:10.1001/jamapediatrics.2022.0152

Figure 2. Effect of Freshly Irradiated Red Blood Cells (RBCs) vs Irradiated and Stored RBCs on Cerebral Regional Oxygen Saturation ($crSO_2$) and Cerebral Fractional Tissue Oxygen Extraction (cFTOE)

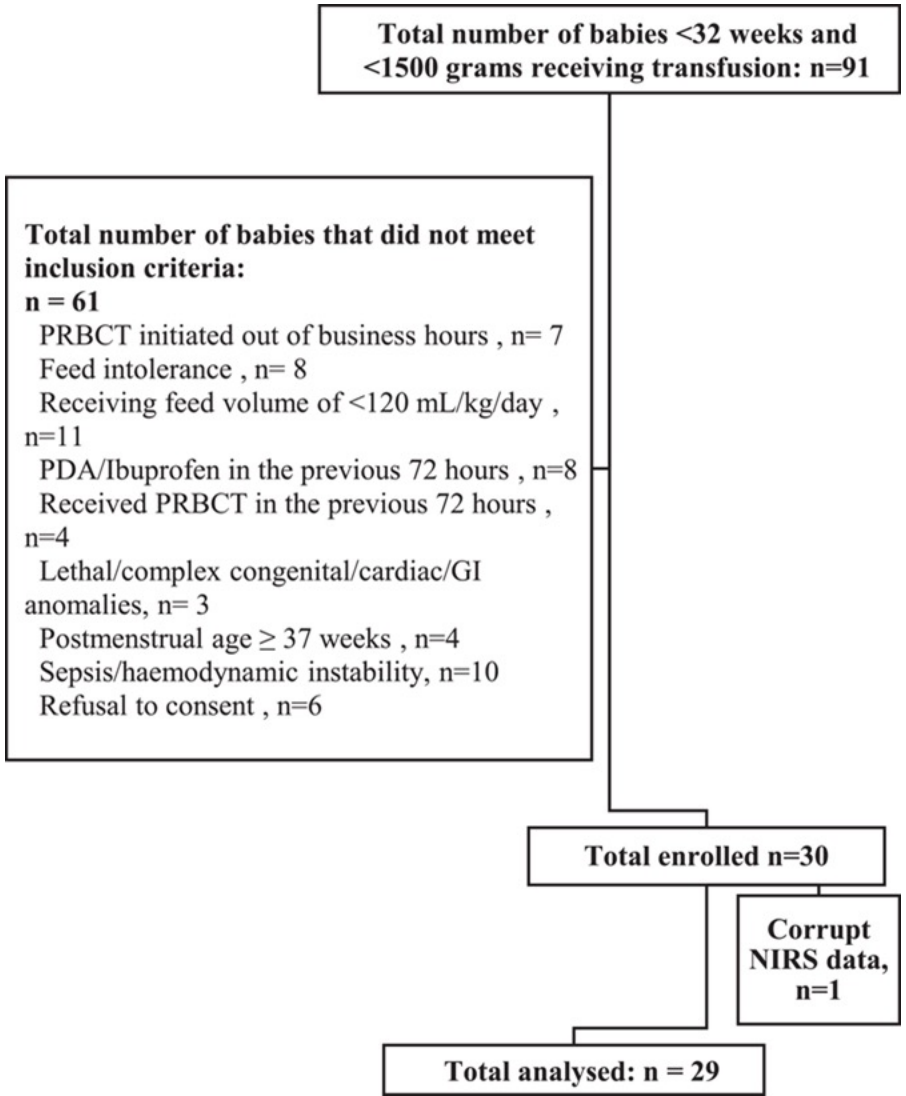


A sustained increase in $crSO_2$ and decrease in cFTOE up to 120 hours (5 days) after transfusion were observed in infants in the intervention group. Negligible changes in $crSO_2$ or cFTOE were observed at any of the time points in infants in the control group. Data are presented as unadjusted means (95% CIs) except for the baseline (0 time point) values, which were used as covariates in the statistical model.

Regional tissue oxygenation and conventional indicators of red blood cell transfusion in anaemic preterm infants

Kiran Kumar Balegar V, Gary KK Low, and Ralph KH Nanan

ww.thelancet.com Vol 46 Month April, 2022



Characteristics	
Gestation, weeks, Median (IQR)	26.4 (25.4 - 28.1)
Birth weight, grams, Median (IQR)	922 (655 - 1064)
Male gender, N. (%)	13 (44.8%)
Female gender, N. (%)	16 (55.2%)
Small for Gestation, N. (%)	6 (20.7%)
Enrolment characteristics	
Postmenstrual age, weeks, Median (IQR)	33.6 (31.7 - 34.9)
Postnatal age, days, Median (IQR)	42 (27 - 58)
Weight, Grams, Median (IQR)	1487 (1110 - 1785)
Breathing support, N. (%)	
None	5 (17.2%)
Continuous positive airway pressure	14 (48.3%)
High flow nasal cannula	8 (27.6%)
Low flow oxygen	2 (6.9%)
Caffeine, N. (%)	25 (86.2%)
Patent ductus arteriosus, N. (%)	0 (0%)
Pre transfusion Hb, (g/L), Median (IQR)	97 (87 - 100)
No (%) of babies who received previous PRBCT	20 (72)
Number of previous PRBCT, Median (IQR)	2 (0 - 5)
pH, Median (IQR)	7.36 (7.34 - 7.37)
PCO_2, Median (IQR)	48 (44 - 50)

***Table 1*: Main clinical characteristics of studied patients (*n* = 29).**
Legends:.
Hb: Haemoglobin; PRBCT: Packed red blood cell transfusion; IQR: Inter quartile range; pH: Potential of Hydrogen; PCO_2: Partial pressure of carbon dioxide.

Transfusión

- Combinación de baja Hb y síntomas:
- Aumento de desaturaciones y bradicardias
- Aumento de requerimientos de oxígeno o apoyo ventilatorio
- Falla para weaning de oxígeno o ventilador
- Mal incremento ponderal
- Umbral: 12 g/dl HB en TN en VMI o inótropos. 8-10 g/dl en RN en VMNI y <8 g/dl en RN sin requerimientos de oxígeno.
- Transfusión: 15 ml/kg en 4 h

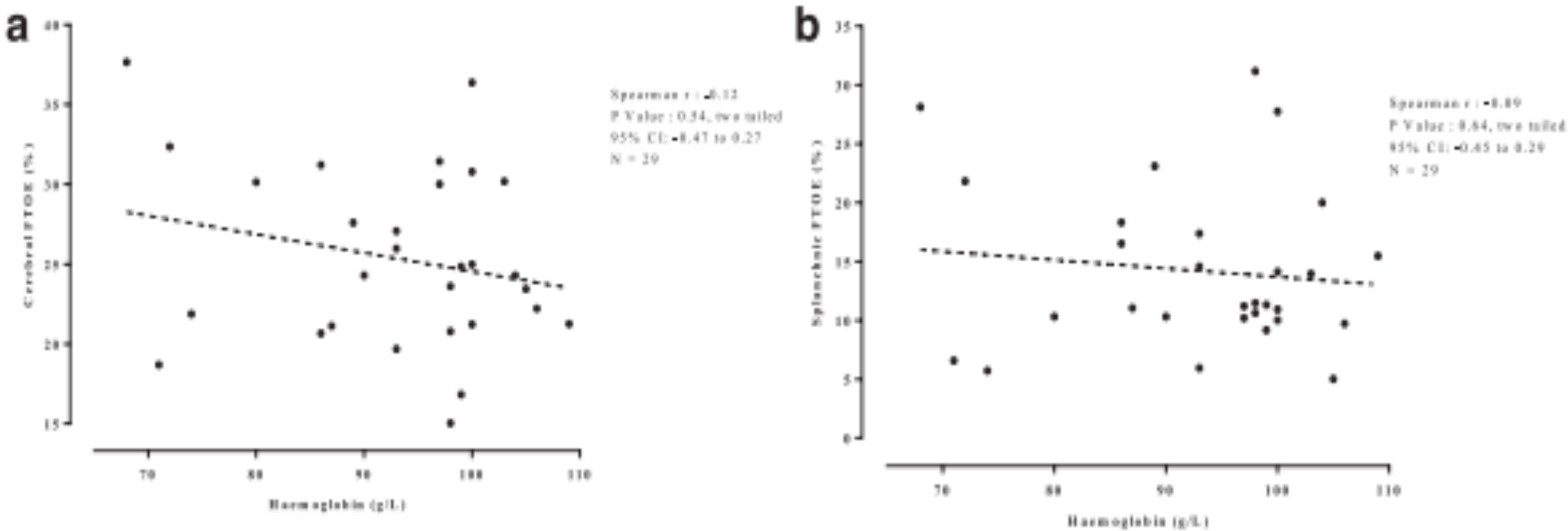


Figure 2. Correlation between cerebral (A) and splanchnic (B) FTOE and haemoglobin

FTOE: Fractional Tissue Oxygen Extraction; n: Number of patients; CI: Confidence interval; r: Correlation coefficient.

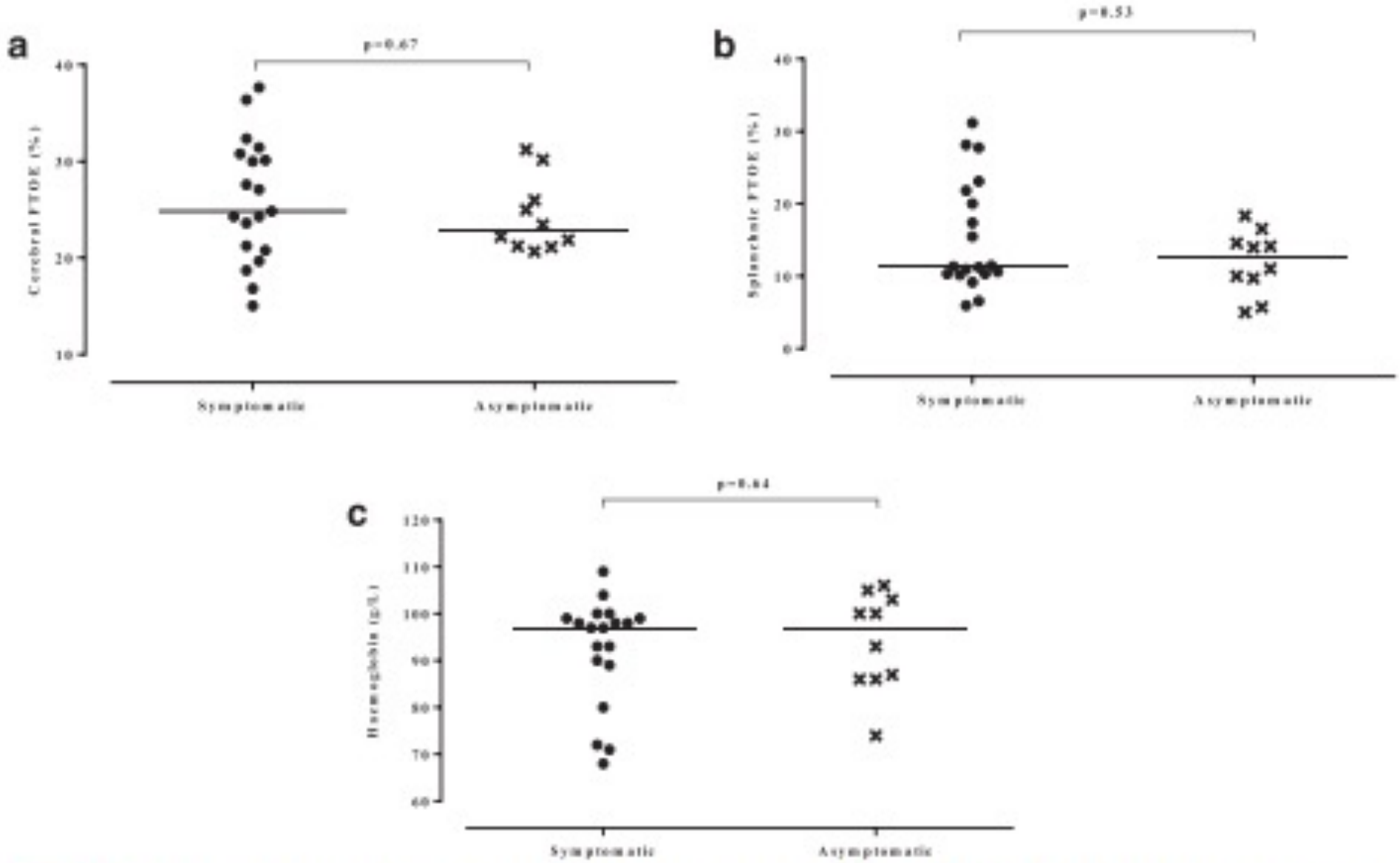


Figure 3. Comparison of cerebral (A) and splanchnic (B) FTOE and comparison of Haemoglobin (C) in infants with symptomatic versus asymptomatic anaemia

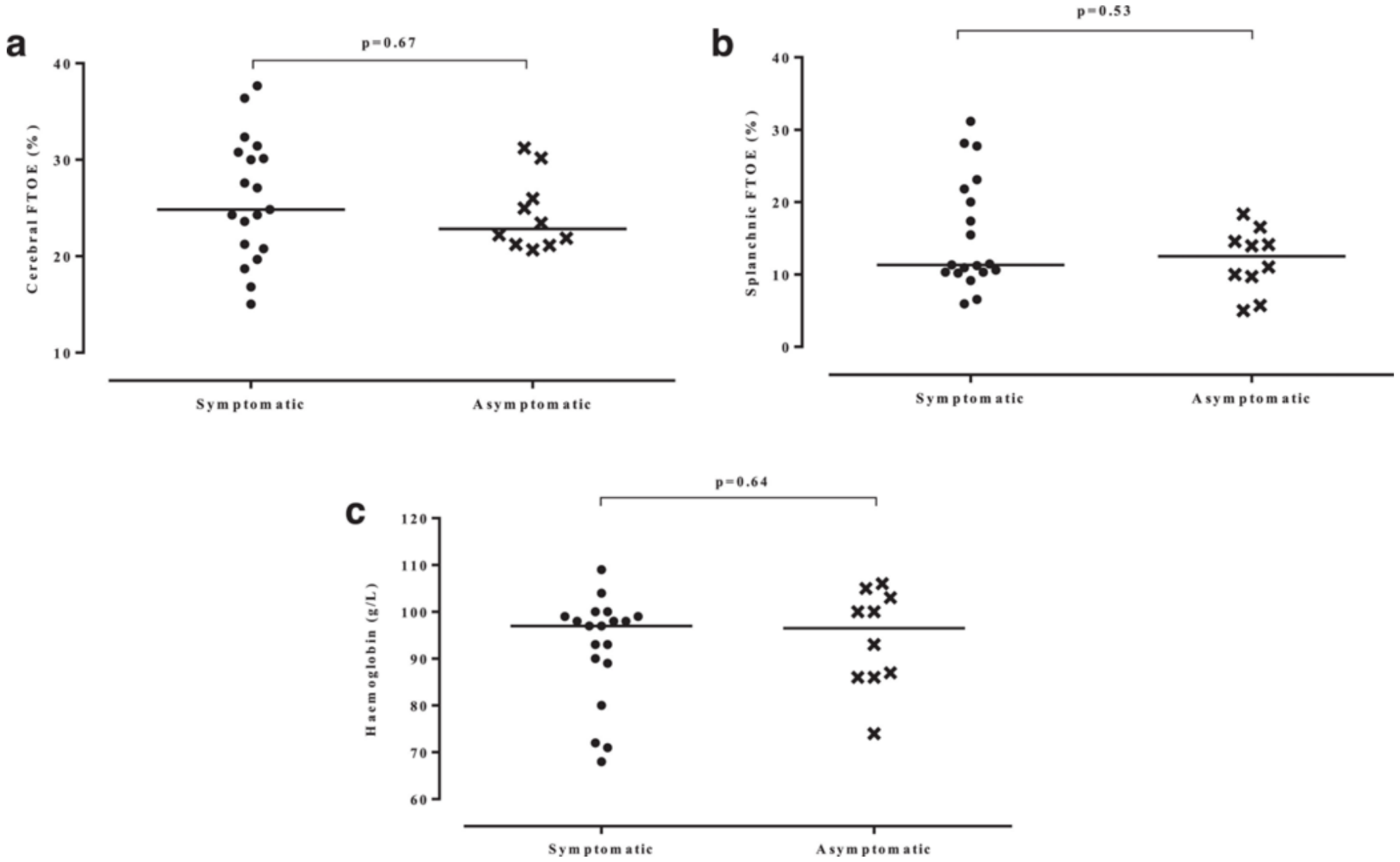
FTOE: Fractional Tissue Oxygen Extraction; Bars represent the median values.

Study type	Bailey et al.[23]	Sandal et al.[22]	Jain et al.[32]	Mintzer et al.[33]	Van Hoften et al.[21]
Nature of the study	Prospective observational cohort study	Case-control study	Prospective observational cohort study	Prospective observational cohort study	Prospective observational cohort study
Number of babies	30	23	30	27	33
Gestation (weeks)	Mean ± SD, 28.4 ± 3	Mean ± SD, 27.7 ± 1.8	Mean ± SD, 26.6 ± 2.03	Mean ± SD, 27 ± 2	Median, (Range), 27.3 (25–34)
Birth Weight (grams)	Mean ± SD, 1115 ± 426	Mean ± SD, 990 ± 285	Mean ± SD, 848 ± 270	Mean ± SD, 966 ± 181	Median, (Range) 1010, (605 - 2080)
Postmenstrual age at enrolment (weeks)	Mean ± SD 32.9 ± 3.4	Not available	Not available	Not available	Median (Range) 30.1 (25.9 - 39.0)
Weight at enrolment / transfusion(gram)	Mean ± SD 1415 ± 456	Mean ± SD 1416 ± 357	Mean ± SD 1008 ± 344	Not available	Not available
Postnatal age at enrolment (days)	Not available	Mean ± SD, 45 ± 14.3	Mean ± SD, 19 ± 12	first 10 days after birth	Median (Range), 17 days (1 - 93)
PRBCT dose	15 mL/kg over 4 h	15 mL/kg over 2–4 h	15 mL/kg over 3 h	Did not involve correlation prior to PRBCT	15 mL/kg over 3 h
Hb (grams/dL) /Hct (%)	(Mean ± SD) Hb 9.3 ± 1.2	(Mean ± SD) Hb 8.7 ± 2.3	(Mean ± SD) Hb 9.8 ± 0.6	(Mean ± SD) Hct 39.7 ± 5.4%	Median (range) Hb 111 (60–128)
NIRS monitoring duration	20 min prior to PRBCT	10 –11 h prior to PRBCT	1 h prior to PRBCT	15 min prior to Hct determination	1 h prior to PRBCT
NIRS frequency	Every 30 s	Every one minute	Not available	Every 6 s	Not available
Correlation of Hb/Hct with cerebral NIRS	No significant correlation with StO_2 ($r = -0.01$, $r^2 = 0$, $n = 30$, $p = 0.98$, two tails)	Weak correlation with FTOE, ($r = -0.24$, $p = 0.041$).	No significant correlation with StO_2 ($R^2 = 0.018$. $p = 0.475$).	Moderate correlation with FTOE (r = - 0.527, 95% CI (0.755 to −0.153) $p = 0.005$.	Significant correlation with StO_2: $r = 0.414$, $p = 0.004$. Significant correlation with FTOE: r = - 0.462; $p = 0.001$
Correlation of Hb/Hct with splanchnic NIRS	No significant correlation with StO_2 ($r = -0.26$, $r^2 = 0.07$, $n = 30$, $p = 0.17$, two tails)	Weak correlation with FTOE ($r = -0.28$, $p = 0.045$)	Not available	Non-significant correlation with FTOE r = - 0.066, 95% CI (- 0.433 to 0.122) p = not significant	Not available
Correlation between NIRS and symptoms	Not available	Not available	Not available	Not available	Not available

***Table 2*: Summary of studies demonstrating association of pre-transfusion Haemoglobin with regional tissue oxygenation.**

Legends.

Hb: Haemoglobin; Hct: Haematocrit; PRBCT: Packed Red Blood Cell Transfusion; NIRS: Near-infrared spectroscopy; FTOE: Fractional tissue oxygen extraction; StO_2: tissue oxygen saturation; SD: standard deviation; r: Correlation coefficient; CI: Confidence interval; g: Grams; kg: Kilo grams; mL: Millilitres.


a
p=0.67
Cerebral FTOE (%)
40
30
20
10
Symptomatic
Asymptomatic
b
p=0.53
Splanchnic FTOE (%)
40
30
20
10
0
Symptomatic
Asymptomatic
c
p=0.64
Haemoglobin (g/L)
120
110
100
90
80
70
60
Symptomatic
Asymptomatic

JAMA Network | Open

RCT: Effect of Point-of-Care Testing for Respiratory Pathogens on Antibiotic Use in Children

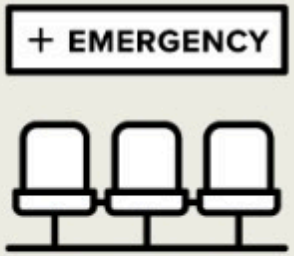
POPULATION

692 Boys, 551 Girls

Children aged 0-17 y with fever and/or any respiratory signs or symptoms

Median age, 3.0 y

SETTINGS / LOCATIONS



1 pediatric emergency department, Oulu, Finland

INTERVENTION

1243 Patients

829 Multiplex polymerase chain reaction (PCR) test
Multiplex PCR point-of-care test for 17 respiratory viruses and 3 bacteria with results in 70 min

414 Routine clinical care
Multiplex PCR testing based on clinical judgment results available next day

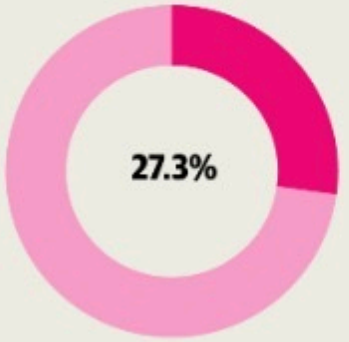
PRIMARY OUTCOME

The proportion of children receiving a prescription for antibiotic therapy

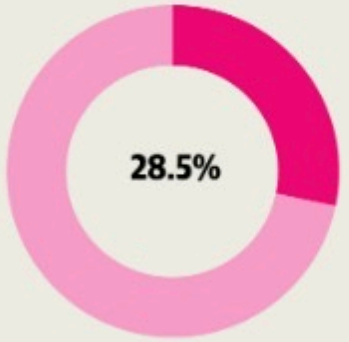
FINDINGS

Antibiotic therapy was started in 226 children (27.3%) in the intervention group and 118 children (28.5%) in the control group. Finding was not statistically significant

Proportion of children receiving antibiotics in the multiplex PCR group



Proportion of children receiving antibiotics in the routine clinical care group



Risk ratio, 0.96; 95% CI, 0.79-1.16

Mattila S, Paalanne N, Honkila M, Pokka T, Tapiainen T. Effect of point-of-care testing for respiratory pathogens on antibiotic use in children: a randomized clinical trial. *JAMA Netw Open*. 2022;5(6):e2216162. doi:10.1001/jamanetworkopen.2022.16162

Efficacy and Safety of Enteral Recombinant Human Insulin in Preterm Infants A Randomized Clinical Trial.

Elise Mank, MD; Miguel Sáenz de Pipaón, MD, PhD; Alexandre Lapillonne, MD, PhD; Virgilio P. Carnielli, MD, PhD; Thibault Senterre, MD, PhD; Raanan Shamir, MD, PhD; Letty van Toledo, MD, PhD; Johannes B. van Goudoever, MD, PhD; for the FIT-04 Study Group

JAMA Pediatr. 2022;176(5):452-460. doi:10.1001/jamapediatrics.2022.0020 Published online February 28, 2022.

Key Points

Question Does the addition of recombinant human (rh) insulin to human milk and preterm formula reduce feeding intolerance in preterm infants?

Findings In this randomized clinical trial that included 303 preterm infants, 2 different rh-insulin dosages significantly reduced the time to full enteral feeding compared with placebo. The percentage of serious adverse events was 15% (16 of 108) in the low-dose group, 13% (11 of 88) in the high-dose group, and 20% (19 of 97) in the placebo group; none of the infants developed serum insulin antibodies.

Meaning These findings support the use of rh insulin as a supplement to human milk and preterm formula.

Table 1. Infant Characteristics[a]

Characteristic	No. (%)		
	Low dose (400 µIU/mL)	High dose (2000 µIU/mL)	Placebo
Total, No.	110	95	98
Gestational age at birth, median (IQR), wk	29.1 (28.1-30.4)	29.0 (27.7-30.5)	28.8 (27.6-30.4)
Birth weight, median (IQR), g	1200 (976-1425)	1250 (1020-1445)	1208 (1021-1430)
Birth weight <1000 g	31 (28)	21 (22)	22 (22)
Head circumference at birth, median (IQR), cm	26.8 (25.0-28.0)	26.5 (25.0-28.0)	27.0 (25.5-28.5)
Infant sex			
Male	65 (59)	52 (55)	54 (55)
Female	45 (41)	43 (45)	44 (45)
Multiple birth	35 (32)	29 (31)	26 (27)
Infant race and ethnicity			
Asian	2 (2)	1 (1)	1 (1)
Black or African American	6 (5)	5 (5)	6 (6)
White	93 (85)	88 (93)	86 (88)
Multiracial[b]	4 (4)	0	3 (3)
Unknown	5 (5)	1 (1)	2 (2)
Apgar score at 5 min, median (IQR)	8.0 (8.0-9.0)	9.0 (8.0-9.0)	8.0 (7.0-9.0)
Cesarean delivery	80 (73)	55 (58)	65 (66)
Antenatal steroids	54 (49)	45 (47)	37 (38)
Age at randomization, median (IQR), d	4 (4-5)	4 (4-5)	4 (3-5)
Age at first enteral feeding, median (IQR), d[c]	2 (1-2)	1 (1-2)	2 (1-2)
Type of nutrition[d]			
Mother's own milk	37 (34)	30 (32)	29 (30)
Donor human milk	2 (2)	3 (3)	4 (4)
Preterm formula	8 (7)	3 (3)	5 (5)
Mixed[e]	61 (55)	56 (59)	60 (61)
Unknown	2 (2)	3 (3)	0
Country			
Europe			
Belgium	14 (13)	5 (5)	8 (8)
Bulgaria	3 (3)	1 (1)	2 (2)
France	4 (4)	10 (11)	12 (12)
Germany	3 (3)	2 (2)	2 (2)
Hungary	7 (6)	6 (6)	5 (5)
Italy	16 (15)	13 (14)	15 (15)
The Netherlands	25 (23)	24 (25)	25 (26)
Spain	17 (15)	20 (21)	11 (11)
UK	5 (5)	3 (3)	5 (5)
Israel	10 (9)	6 (6)	8 (8)
US	6 (5)	5 (5)	5 (5)

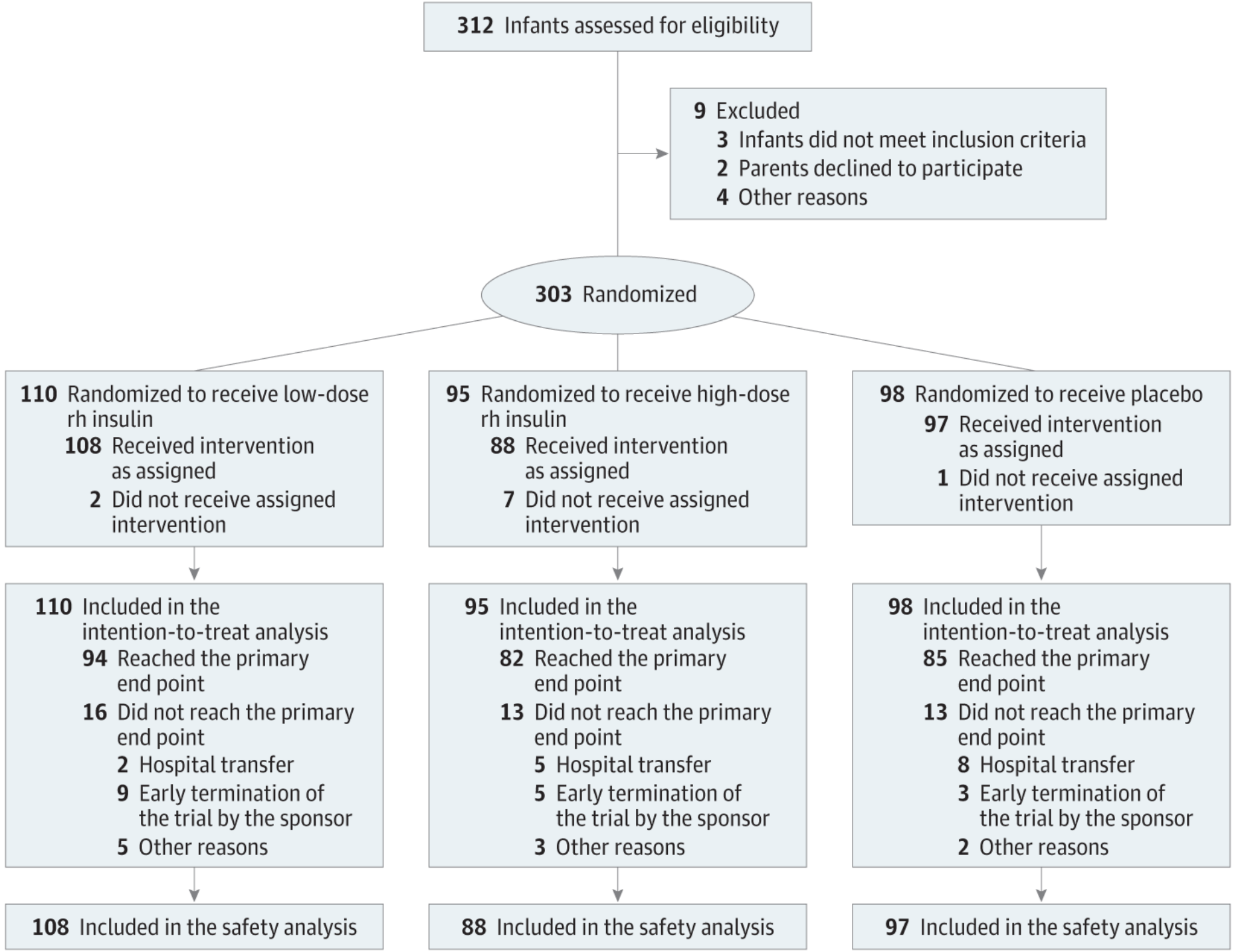
[a] No significant differences were found between the 3 groups in the listed categories.

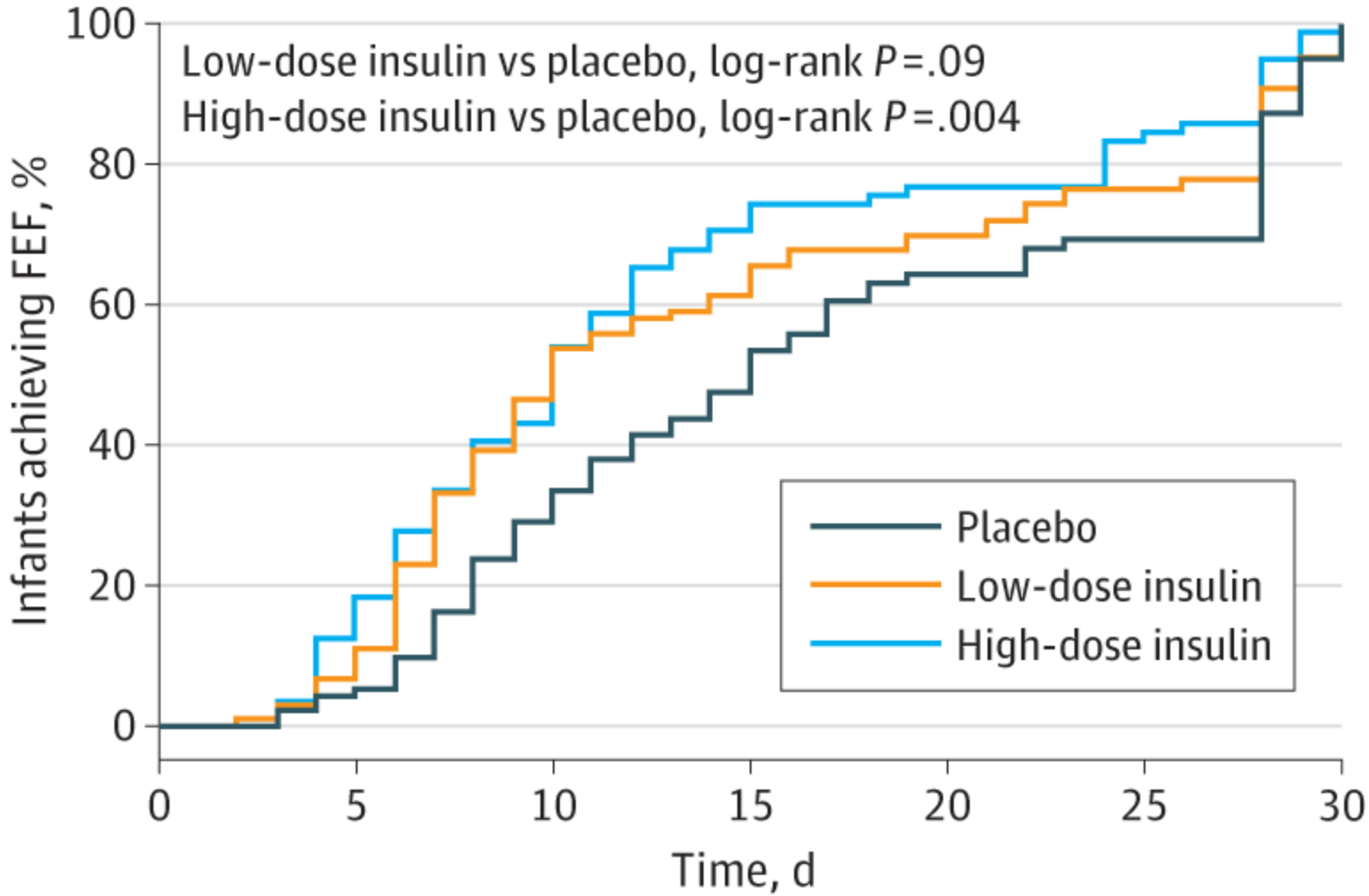
[b] Multiracial indicates that the parents of the infant were each of a different race and ethnicity.

[c] Date of birth was considered as day 1.

[d] Type of nutrition during the intervention period.

[e] Mixed feeding was defined as the total enteral nutrition intake consisting of mother's own milk and donor human milk, donor human milk and preterm formula, or mother's own milk and preterm formula.


312 Infants assessed for eligibility
9 Excluded
3 Infants did not meet inclusion criteria
2 Parents declined to participate
4 Other reasons
303 Randomized
110 Randomized to receive low-dose rh insulin
108 Received intervention as assigned
2 Did not receive assigned intervention
95 Randomized to receive high-dose rh insulin
88 Received intervention as assigned
7 Did not receive assigned intervention
98 Randomized to receive placebo
97 Received intervention as assigned
1 Did not receive assigned intervention
110 Included in the intention-to-treat analysis
94 Reached the primary end point
16 Did not reach the primary end point
2 Hospital transfer
9 Early termination of the trial by the sponsor
5 Other reasons
95 Included in the intention-to-treat analysis
82 Reached the primary end point
13 Did not reach the primary end point
5 Hospital transfer
5 Early termination of the trial by the sponsor
3 Other reasons
98 Included in the intention-to-treat analysis
85 Reached the primary end point
13 Did not reach the primary end point
8 Hospital transfer
3 Early termination of the trial by the sponsor
2 Other reasons
108 Included in the safety analysis
88 Included in the safety analysis
97 Included in the safety analysis



Cumulative No. of infants							
Placebo	0	5	31	48	57	61	85
Low-dose insulin	0	11	53	64	68	74	94
High-dose insulin	0	16	46	62	64	70	82

Table 2. Efficacy Outcomes (Intention to Treat)

Outcome	Recombinant human insulin		Placebo
	Low dose (400-μIU/mL milk)	High dose (2000-μIU/mL milk)	
Primary outcome			
Time to achieve full enteral feeding (≥150 mL/kg/d for 3 consecutive days)			
Total, No.	94	82	85
Median (IQR)	10.0 (7.0 to 21.8)	10.0 (6.0 to 15.0)	14.0 (8.0 to 28.0)
P value[a]	.03	.001	NA
Difference in medians (95% CI)[b]	4.0 (1.0 to 8.0)	4.0 (1.0 to 7.0)	NA
Secondary outcomes			
Infants achieving full enteral feeding (≥150 mL/kg/d for 3 consecutive days)			
Study day 6			
No. (%)	23 (21)	24 (25)	9 (9)
P value[a]	.02	.003	NA
Study day 8			
No. (%)	39 (35)	35 (37)	22 (22)
P value[a]	.04	.03	NA
Study day 10			
No. (%)	53 (48)	46 (48)	31 (32)
P value[a]	.02	.02	NA
Time to achieve an enteral intake of ≥120 mL/kg/d for 3 consecutive days			
No.	95	85	91
Median (IQR), d	6.0 (4.0 to 11.0)	6.0 (4.0 to 11.0)	8.0 (6.0 to 12.0)
P value[a]	.049	.01	NA
Days receiving parenteral nutrition			
No.	101	86	92
Median (IQR), d	6.0 (4.0 to 10.0)	6.0 (3.0 to 10.0)	7.5 (5.0 to 11.0)
P value[a]	.25	.03	NA
Weight gain			
No.	104	91	95
Median (IQR), g/kg/d	17.4 (14.0 to 20.1)	17.2 (15.0 to 19.2)	17.9 (15.2 to 19.6)
P value[a]	.64	.37	NA
Body weight on study day 28			
No.	71	63	70
Median (IQR), g	1740 (1430 to 2150)	1830 (1468 to 2112)	1770 (1566 to 2160)
P value[a]	.99	.31	NA
Body weight *z* score on study day 28			
No.	71	63	70
Median (IQR)	−0.7 (−1.1 to −0.3)	−0.8 (−1.2 to −0.4)	−0.6 (−1.1 to −0.2)
P value[a]	.28	.25	NA
Change in body weight *z* score			
No.	71	63	70
Median (IQR)	−0.1 (−0.3 to 0.2)	−0.1 (−0.4 to 0)	0 (−0.3 to 0.2)
P value[a]	.85	.09	NA
Head circumference			
No.	98	86	88
Median (IQR), cm/wk	0.8 (0.5 to 0.9)	0.8 (0.5 to 0.9)	0.7 (0.5 to 0.9)
P value[a]	.34	.34	NA
Body length			
No.	80	72	76
Median (IQR), cm/wk	1.0 (0.6 to 1.4)	1.0 (0.6 to 1.3)	1.0 (0.5 to 1.4)
P value[a]	.67	.85	NA

Abbreviation: NA, not applicable.

[a] *P* value represents comparison between the active-treatment group and the placebo group.

[b] 95% CI was calculated by bootstrapping as the data were not normally distributed.

Table 3. Safety Outcomes[a]

Outcome	No. (%)		
	Recombinant human insulin		
	Low dose (400-μIU/mL milk)	High dose (2000-μIU/mL milk)	Placebo
Total No. of infants included in safety analysis	108	88	97
Infants with ≥1 SAE	16 (15)	11 (13)	19 (20)
Total No. of reported SAEs	32	18	34
NEC (Bell stage 2 or 3)[b]	7 (6)	4 (5)	10 (10)
Clinical- or culture-proved sepsis	13 (12)	10 (11)	15 (15)
Mortality	5 (5)	1 (1)	4 (4)

Abbreviations: NEC, necrotizing enterocolitis; SAE, serious adverse event.

[a] Reported until discharged to home.

[b] Bell staging criteria, based on clinical and radiographic signs, are used to identify and classify NEC in infants.