



Neonatology



Bronchopulmonary Dysplasia and Risk of Developmental Delay: An EPIPAGE-2 Cohort Study

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Survivors at 2 years eligible for follow-up
(*n* = 3,254)

Parents refused participation (*n* = 155)

Not included :

- severe congenital malformations (*n* = 274)
- neurosensory and motor disabilities at 2 years (*n* = 76)
 - cerebral palsy 2–5
 - deafness
 - blindness

Eligible population
(*n* = 2,749)

Excluded: unknown bronchopulmonary dysplasia status
(*n* = 43)

Analyzed population
(*n* = 2,706)

Lost to follow-up children or missing data on a variable of interest: (*n* = 1,119)

- no response to the doctor or parents questionnaire at 2 years
- unknown neurosensory and motor status at 2 years of age
- unavailable ASQ score at 2 years

ASQ completed at
22–26 months
(*n* = 1,587)



Children included after multiple imputations

Table 1. Results for ASQ at 2 years' corrected age by BPD status

	No-BPD (N = 1,391)	BPD of any grade (N = 196)	p value ^c
ASQ score below threshold ^a , n/N (% ^b)	551/1,391 (39.5)	110/196 (55.3)	<0.001
2 ASQ domains below threshold, n/N (% ^b)	235/1,391 (16.7)	54/196 (27.3)	<0.001
ASQ score below threshold by domain, n/N (% ^b)			
Communication	316/1,391 (22.6)	75/196 (37.9)	<0.001
Fine motor	138/1,391 (9.9)	29/196 (15.3)	0.03
Gross motor	144/1,391 (10.2)	32/196 (15.8)	0.02
Personal-social	230/1,391 (16.3)	45/196 (22.5)	0.04
Problem solving	146/1,391 (10.5)	27/196 (13.7)	0.21
Overall ASQ score <220, n/N (% ^b)	556/1,391 (40.0)	110/196 (58.1)	<0.001
CDI below cutoff, n/N (% ^b)	402/1,303 (30.6)	89/183 (48.1)	<0.001

The information in the table refers to the children without missing data on ASQ. ASQ, Age & Stages Questionnaires; BPD, bronchopulmonary dysplasia; CDI, Communicative Development Inventories. ^a The ASQ score was defined as below threshold if at least one of the domains scored below threshold. Each domain was considered below threshold if it scored below 2 standard deviations from the mean. ^b All percentages were weighted over the recruitment time. ^c χ^2 tests were used for percentages.



Hour-Specific Total Serum Bilirubin Percentiles for Infants Born at 29–35 Weeks' Gestation

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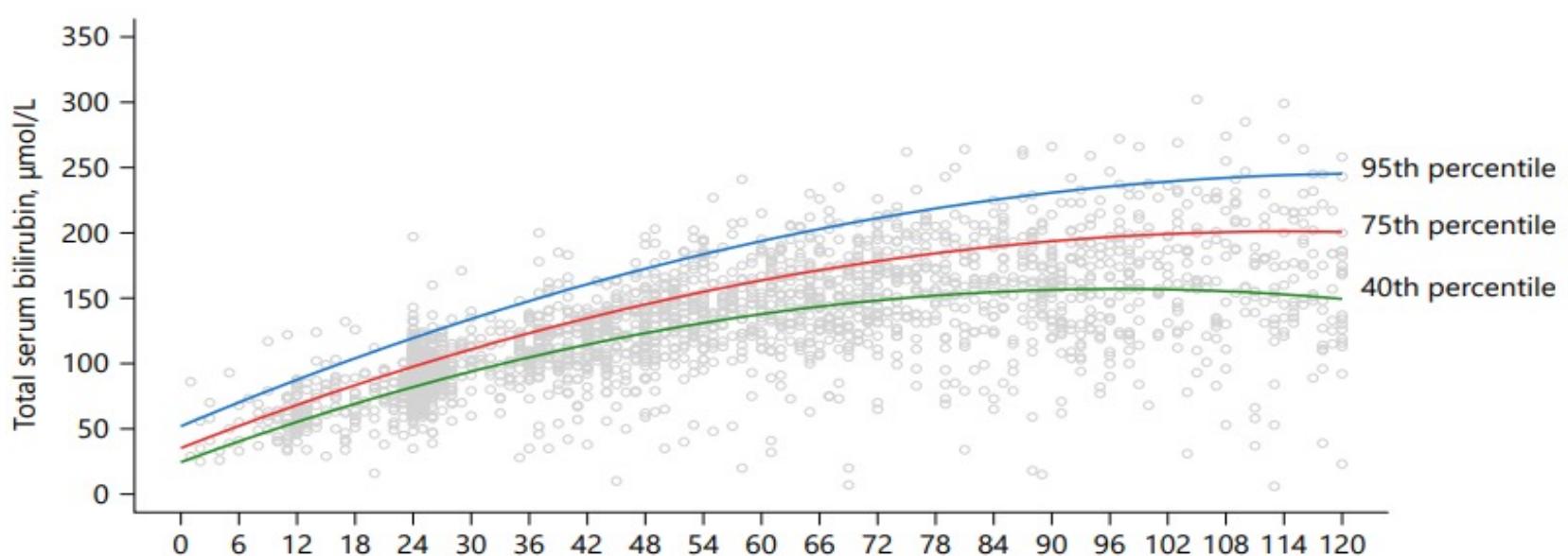
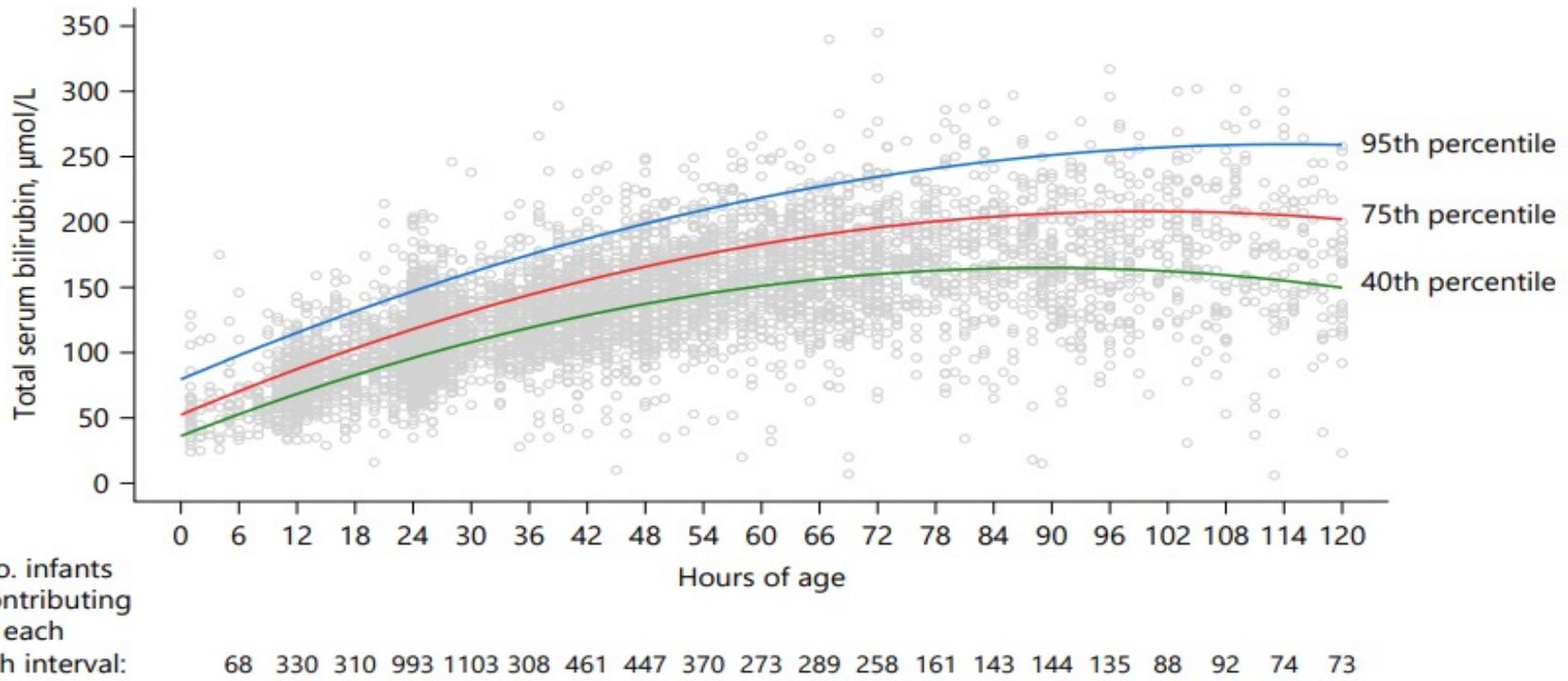
Vibhuti Shah^{d, h, i} Howard Berger^{c, d} Robin Z. Hayeems^{d, j} Michael Sgro^{a, b, h}

for the NeoHBC

Table 1. Neonatal and maternal characteristics of 2,549 preterm infants included in the study by prematurity groups

Characteristic	Overall	By degree of prematurity at birth	
		29 ^{0/7} –32 ^{6/7} weeks	33 ^{0/7} –35 ^{6/7} weeks
Mean (SD) gestational age, weeks	32.6 (1.9)	30.7 (1.1)	34.0 (0.8)
Mean (SD) birthweight, g	1,915.2 (695.3)	1,559.9 (381.8)	2,193.6 (756.1)
Small for gestational age birthweight <10th percentile	471 (18.5)	152 (13.6)	319 (22.3)
Female	1,139 (44.7)	484 (43.2)	655 (45.8)
Mean (SD) maternal age at birth of current infant, ^a y	32.2 (5.8)	31.9 (5.7)	32.5 (5.9)
Mode of delivery			
Caesarean	1,526 (59.9)	691 (61.7)	835 (58.4)
Vaginal	975 (38.2)	409 (36.5)	566 (39.6)
Unknown	48 (1.9)	20 (1.8)	28 (2.0)
Haemolysis			
ABO incompatibility	327 (12.8)	142 (12.7)	185 (12.9)
Feeding			
Enteral only	891 (34.9)	305 (27.2)	586 (41.0)
TPN only	285 (11.2)	137 (12.2)	148 (10.4)
Mixed (enteral and TPN)	1,307 (51.3)	649 (57.9)	658 (46.0)
Unknown	66 (2.6)	29 (2.7)	37 (2.6)
Sepsis with a positive blood or spinal fluid culture	141 (5.5)	73 (6.5)	68 (4.8)
Median (IQR) number of TSB measurements per infant prior to the initiation of phototherapy	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)
Mortality	24 (0.9)	12 (1.1)	12 (0.8)

All data are presented as a number (%) unless otherwise indicated. SD, standard deviation; TPN, total parenteral nutrition. ^aMaternal age missing in <1% of cohort overall and by degree of prematurity.



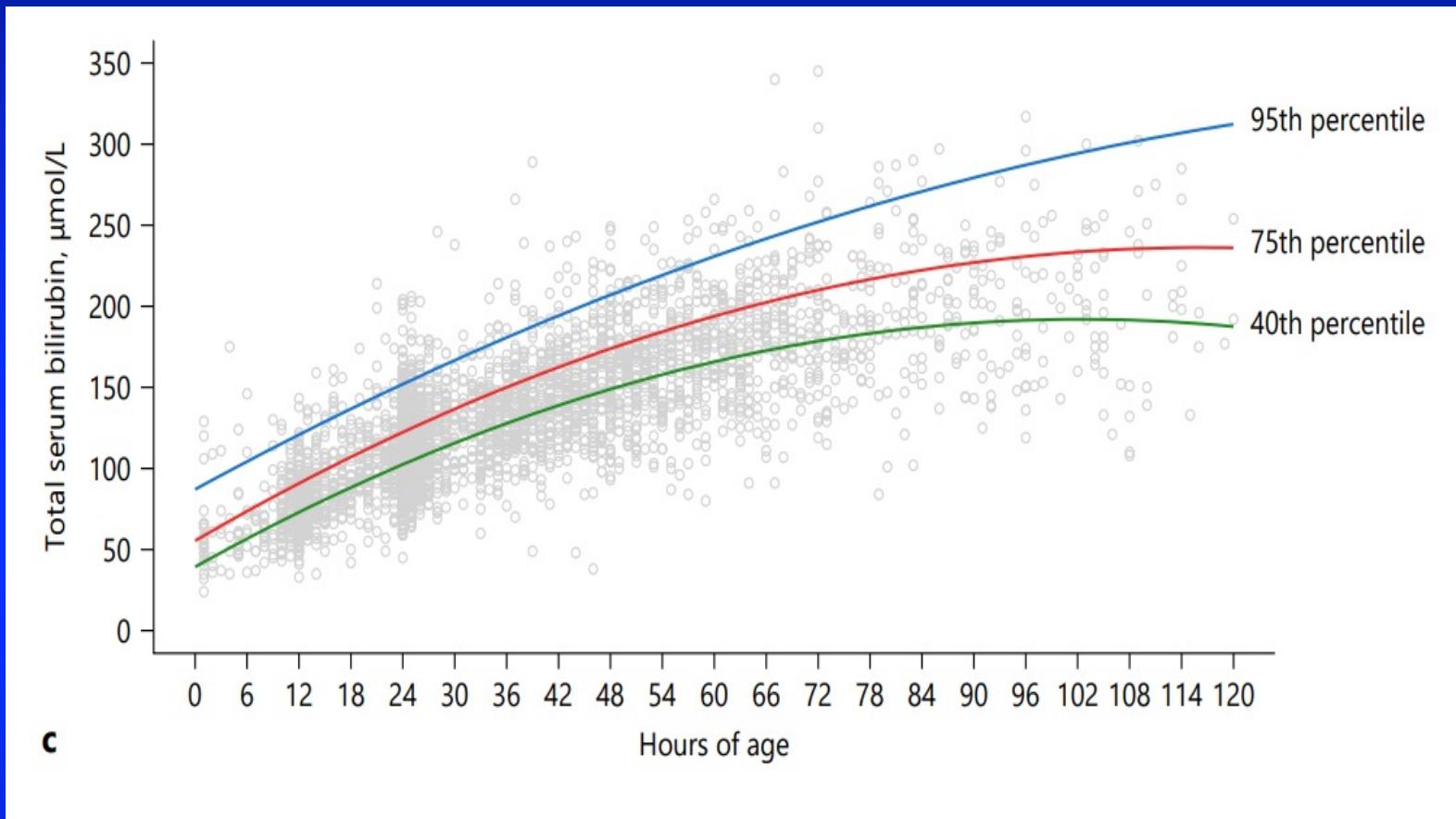


Table 2. Estimated pre-treatment^a TSB percentiles at birth, and the estimated hours of age at peak TSB at the 40th, 75th, and 95th percentiles, by subsequent receipt of phototherapy, and by gestational age

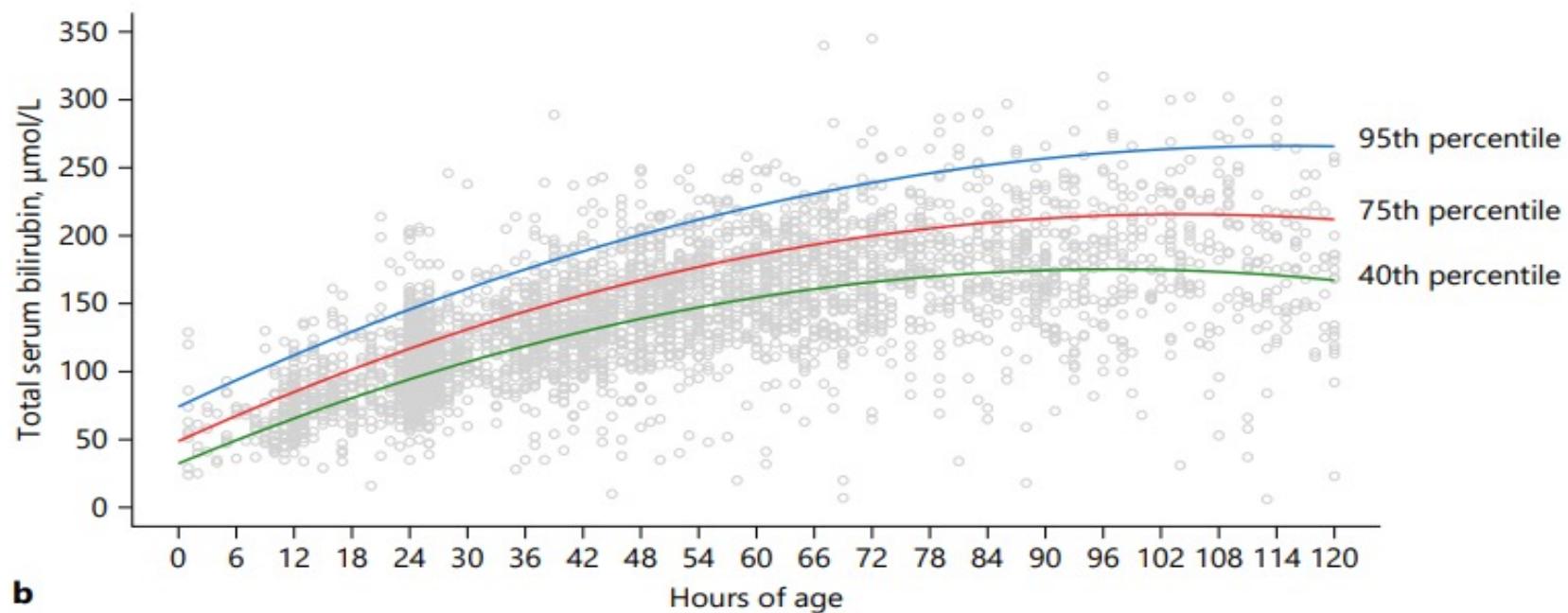
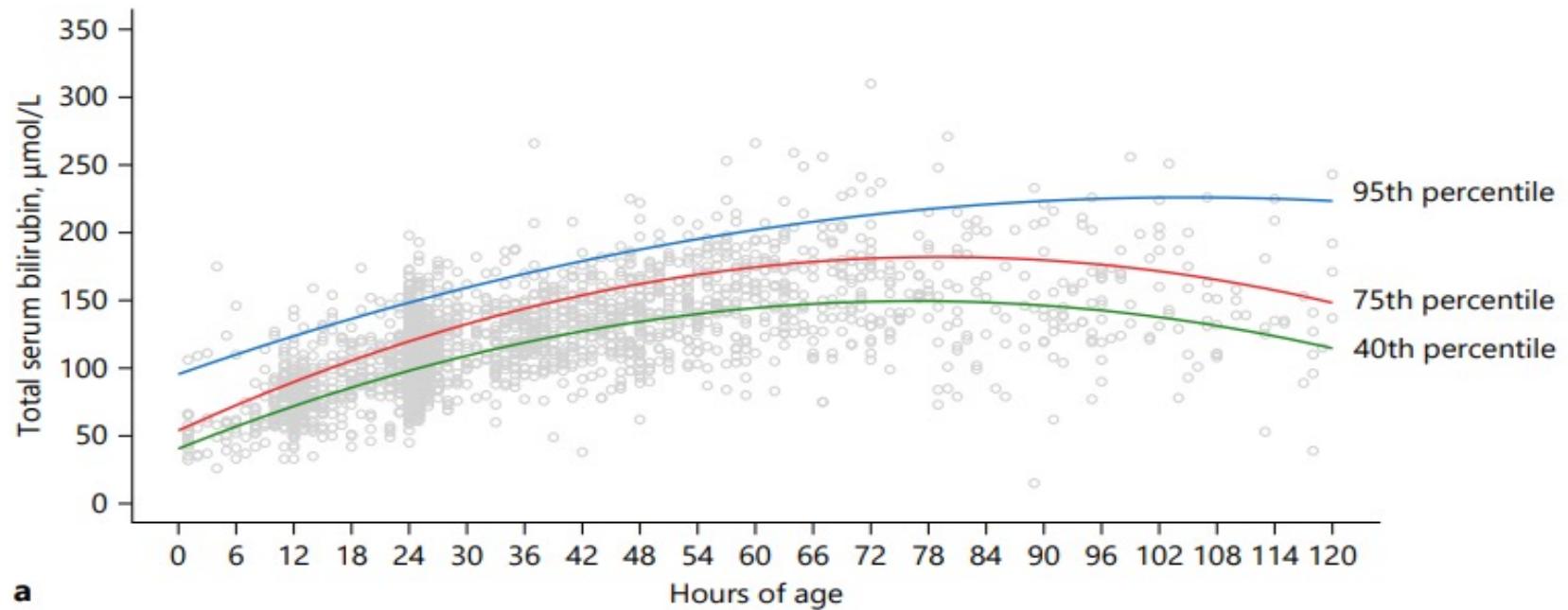
Measure	All infants born at 29–35 weeks' gestation			By subsequent receipt of phototherapy						By gestational age at birth					
				did not subsequently receive phototherapy			prior to the initiation of phototherapy			29–32 weeks' gestation			33–35 weeks' gestation		
	40th	75th	95th	40th	75th	95th	40th	75th	95th	40th	75th	95th	40th	75th	95th
Estimated TSB at birth (95% CI), µmol/L	36.1 (34.3–39.3)	52.3 (49.4–55.1)	79.5 (72.1–89.6)	24.4 (20.4–28.8)	35.3 (31.1–41.5)	52.0 (46.1–62.4)	39.3 (35.9–43.2)	55.4 (52.1–60.2)	87.1 (70.5–102.4)	40.5 (37.0–44.5)	53.9 (49.4–61.0)	95.5 (77.5–105.0)	32.3 (27.6–35.8)	48.7 (43.0–52.3)	74.1 (64.8–83.2)
Estimated rate of rise of TSB at birth (95% CI), µmol/L/h	2.9 (2.7–3.0)	3.1 (3.0–3.3)	3.1 (2.7–3.4)	2.7 (2.5–3.0)	2.9 (2.7–3.1)	3.1 (2.6–3.3)	3.0 (2.8–3.2)	3.1 (2.8–3.3)	2.9 (2.2–3.7)	2.8 (2.6–3.1)	3.2 (2.8–3.5)	2.5 (2.0–3.3)	2.9 (2.8–3.2)	3.2 (3.0–3.4)	3.3 (2.9–3.7)
Estimated change in the rate of rise from birth onwards (95% CI), µmol/L/h ²	-0.016 (-0.017 to -0.015)	-0.015 (-0.017 to -0.014)	-0.014 (-0.017 to -0.009)	-0.014 (-0.016 to -0.012)	-0.013 (-0.015 to -0.011)	-0.012 (-0.014 to -0.008)	-0.014 (-0.017 to -0.012)	-0.013 (-0.016 to -0.010)	-0.009 (-0.017 to -0.003)	-0.018 (-0.021 to -0.016)	-0.020 (-0.023 to -0.015)	-0.012 (-0.019 to -0.007)	-0.015 (-0.018 to -0.014)	-0.015 (-0.018 to -0.014)	-0.014 (-0.018 to -0.011)
Estimated hours of age at the peak of TSB, h	90.6	103.3	110.7	96.4	111.5	>120	107.1	119.2	>120	77.8	80.0	104.2	96.7	106.7	117.8

CI, confidence interval; TSB, total serum bilirubin.^aPresented and referenced as "pretreatment," TSB levels, are TSB levels prior to phototherapy among those administered phototherapy and any TSB level among those not subsequently administered phototherapy.

Table 3. Peak TSB concentration within the first 72 h after birth, as well as the timing of that peak, by neonatal factors

Measure	Overall	By subsequent receipt of phototherapy ^a		By gestational age at birth, weeks ^b			By feeding type among all infants born at 29–35 weeks ^c			By feeding type among infants born at 29–32 weeks ^d			By feeding type among infants born at 33 to 35 weeks ^e			By ABO incompatibility ^f	
		yes	no	29–32	33–35	enteral	TPN	mixed	enteral	TPN	mixed	enteral	TPN	mixed	present	absent	
Mean (SD) peak TSB concentration in the first 72 h of life, µmol/L	142.0 (37.9)	145.7 (37.5)	132.1 (37.2)	133.7 (31.8)	148.5 (41.0)	146.6 (40.6)	134.2 (35.4)	140.8 (36.4)	138.4 (32.9)	128.9 (28.3)	132.7 (32.0)	150.8 (43.5)	139.1 (40.3)	148.8 (38.6)	135.3 (38.2)	143.0 (37.8)	
Mean (SD) time since birth to peak TSB, h	41.7 (17.3)	38.3 (16.6)	50.8 (15.6)	36.3 (16.2)	46.0 (16.9)	44.3 (16.9)	39.1 (17.6)	40.5 (17.3)	37.8 (16.5)	35.0 (16.0)	35.7 (16.2)	47.7 (16.2)	42.9 (18.3)	45.3 (17.1)	37.6 (17.5)	42.3 (17.2)	

SD, standard deviation; TSB, total serum bilirubin; TPN, total parenteral nutrition. ^aMean peak TSB and mean hours of age at the time of peak TSB significantly differed between infants subsequently administered and not administered phototherapy ($p < 0.01$). ^bMean peak TSB and mean hours of age at the time of peak TSB significantly differed between infants born 29–32 weeks' and 33–35 weeks' gestation ($p < 0.01$). ^cMean peak TSB and mean hours of age at the time of peak TSB significantly differed across infants' feeding type among all infants born 29–35 weeks' gestation ($p < 0.01$). ^dMean peak TSB significantly differed across infants' feeding type among infants born 29–32 weeks' gestational age ($p < 0.01$). ^eMean peak total serum bilirubin and mean hours of age at the time of peak total serum bilirubin significantly differed across infant's feeding type among infants born 33–35 weeks' gestational age ($p < 0.01$). ^fMean peak total serum bilirubin and mean hours of age at the time of peak total serum bilirubin significantly differed between infants with and without ABO incompatibility ($p < 0.01$).



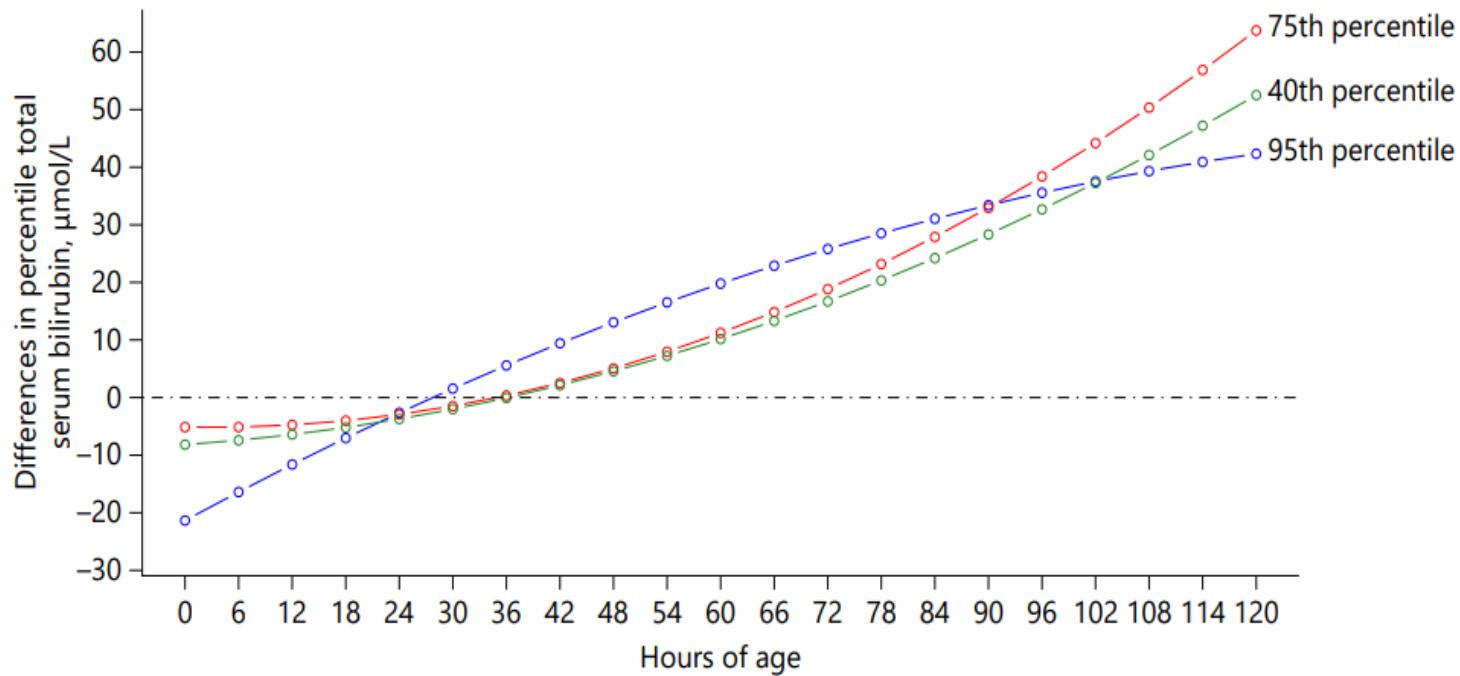


Fig. 3. Pre-treatment TSB percentile net differences between infants born at 33–35 weeks' gestation minus those born at 29–32 weeks' gestation. Pre-treatment TSB levels refer to TSB levels prior to phototherapy among those administered phototherapy and any TSB levels among those not administered phototherapy. To convert mean TSB differences to mg/dL, divide by 17.1. Frames around graphs were removed. TSB, total serum bilirubin.



Prevalence and Infant Mortality of Major Congenital Malformations Stratified by Birthweight

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Table 1. Infants with MCMs by birthweight, numbers, and prevalence (per 10,000 live births, with 95% CIs)

Birthweight	Infants, n				Prevalence			
	<1,500 g	1,500–2,499 g	≥2,500 g	all	<1,500 g	1,500–2,499 g	≥2,500 g	all
All infants	34,401	109,558	2,583,043	2,727,002				
Infants without an MCM	33,417	106,889	2,573,133	2,713,439				
ICD-10								
Any MCM	984	2,669	9,910	13,563	286.04 (268.94, 304.19)	243.62 (234.65, 252.91)	38.37 (37.62, 39.13)	49.74 (48.91, 50.58)
Neural tube defects	41	130	750	921	11.92 (8.79, 16.16)	11.87 (10.00, 14.09)	2.90 (2.70, 3.12)	3.38 (3.17, 3.60)
Encephalocele								
Q01	10	16	119	145	2.91 (1.58, 5.35)	1.46 (0.90, 2.37)	0.46 (0.39, 0.55)	0.53 (0.45, 0.63)
Spina bifida/meningomyelocele								
Q05	31	114	631	776	9.01 (6.35, 12.79)	10.41 (8.66, 12.50)	2.44 (2.26, 2.64)	2.85 (2.65, 3.05)
Severe cardiac malformations	607	1,564	8,145	10,316	176.45 (163.07, 190.91)	142.76 (135.90, 149.95)	31.53 (30.86, 32.22)	37.83 (37.11, 38.57)
Category A (compromised systemic output)	270	559	3,304	4,133	78.49 (69.70, 88.38)	51.02 (46.97, 55.42)	12.79 (12.36, 13.23)	15.16 (14.70, 15.63)
Aortic valve stenosis								
Q23.0	32	71	500	603	9.30 (6.59, 13.13)	6.48 (5.14, 8.17)	1.94 (1.77, 2.11)	2.21 (2.04, 2.40)
Congenital mitral stenosis								
Q23.2	13	42	235	290	3.78 (2.21, 6.47)	3.83 (2.84, 5.18)	0.91 (0.80, 1.03)	1.06 (0.95, 1.19)
Congenital mitral insufficiency								
Q23.3	102	95	489	686	29.65 (24.43, 35.98)	8.67 (7.10, 10.60)	1.89 (1.73, 2.07)	2.52 (2.33, 2.71)
Hypoplastic left-heart syndrome								
Q23.4	33	95	660	788	9.59 (6.83, 13.47)	8.67 (7.10, 10.60)	2.56 (2.37, 2.76)	2.89 (2.70, 3.10)
Coarctation, interrupted aortic arch								
Q25.1	86	242	1,358	1,686	25.00 (20.25, 30.86)	22.09 (19.48, 25.05)	5.26 (4.99, 5.54)	6.18 (5.90, 6.49)
Aortic atresia/hypoplasia								
Q25.2	4	14	62	80	1.16 (0.45, 2.99)	1.28 (0.76, 2.15)	0.24 (0.19, 0.31)	0.29 (0.24, 0.37)
Category B (sustained cyanosis)	173	528	2,876	3,647	50.29 (43.35, 58.34)	48.19 (44.26, 52.47)	11.13 (10.74, 11.55)	13.37 (12.95, 13.81)
Transposition of the great arteries								
Q20.3	30	94	1,006	1,130	8.72 (6.11, 12.45)	8.58 (7.01, 10.50)	3.89 (3.66, 4.14)	4.14 (3.91, 4.39)
Tetralogy of Fallot								
Q21.3	62	187	753	1,002	18.02 (14.06, 23.10)	17.07 (14.79, 19.69)	2.92 (2.71, 3.13)	3.67 (3.45, 3.91)

Table 1 (continued)

Birthweight	Infants, n				Prevalence			
	<1,500 g	1,500–2,499 g	≥2,500 g	all	<1,500 g	1,500–2,499 g	≥2,500 g	all
Pulmonary valve atresia								
Q22.0	24	71	229	394	6.98 (4.69, 10.38)	6.48 (5.14, 8.17)	0.89 (0.78, 1.01)	1.44 (1.31, 1.60)
Tricuspid atresia								
Q22.4	11	31	177	219	3.20 (1.79, 5.73)	2.83 (1.99, 4.02)	0.69 (0.59, 0.79)	0.80 (0.70, 0.92)
Ebstein anomaly								
Q22.5	6	21	108	135	1.74 (0.80, 3.81)	1.92 (1.25, 2.93)	0.42 (0.35, 0.51)	0.50 (0.42, 0.59)
Hypoplastic right-heart syndrome								
Q22.6	13	30	142	185	3.78 (2.21, 6.47)	2.74 (1.92, 3.91)	0.55 (0.47, 0.65)	0.68 (0.59, 0.78)
Pulmonary artery atresia								
Q22.7	18	57	260	335	5.23 (3.31, 8.27)	5.20 (4.02, 6.74)	1.01 (0.89, 1.14)	1.23 (1.10, 1.37)
Total anomalous pulmonary venous return								
Q26.2	9	37	201	247	2.62 (1.38, 4.97)	3.38 (2.45, 4.65)	0.78 (0.68, 0.89)	0.91 (0.80, 1.03)
Category C (congestive heart failure/pulmonary over-circulation)	164	477	1,965	2,606	47.67 (40.93, 55.53)	43.54 (39.81, 47.62)	7.61 (7.28, 7.95)	9.56 (9.18, 9.92)
Truncus arteriosus								
Q20.0	16	31	136	183	4.65 (2.86, 7.55)	2.83 (1.99, 4.02)	0.53 (0.45, 0.62)	0.67 (0.58, 0.78)
Double-outlet right ventricle								
Q20.1	26	119	465	610	7.56 (5.16, 11.07)	10.86 (9.08, 13.00)	1.80 (1.64, 1.97)	2.24 (2.07, 2.42)
Other single ventricle (double-inlet ventricle)								
Q20.4	10	23	188	221	2.91 (1.58, 5.35)	2.10 (1.40, 3.15)	0.73 (0.63, 0.84)	0.81 (0.71, 0.93)
Atrioventricular septal defect								
Q21.2	112	304	1,176	1,592	32.56 (27.07, 39.16)	27.75 (24.80, 31.04)	4.55 (4.30, 4.82)	5.84 (5.56, 6.13)
Multiple cardiac MCMs								
Q21.3	67	275	1,526	1,868	19.48 (15.34, 24.72)	25.10 (22.31, 28.24)	5.91 (5.62, 6.21)	6.85 (6.55, 7.17)
Gastrointestinal and abdominal malformations								
Q23.0, Q23.1	499	1,622	3,165	5,286	145.05 (132.95, 158.24)	148.05 (141.07, 155.37)	12.25 (11.83, 12.69)	19.38 (18.87, 19.91)
Esophageal atresia (±tracheoesophageal fistula)								
Q39.0, Q39.1	96	252	350	698	27.91 (22.86, 34.06)	23.00 (20.33, 26.02)	1.35 (1.22, 1.51)	2.56 (2.38, 2.76)
Duodenal/small-bowel atresia								
Q41	190	363	564	1,117	55.23 (47.93, 63.63)	33.13 (29.90, 36.71)	2.18 (2.01, 2.37)	4.10 (3.86, 4.34)

Table 1 (continued)

Birthweight	Infants, n				Prevalence			
	<1,500 g	1,500–2,499 g	≥2,500 g	all	<1,500 g	1,500–2,499 g	≥2,500 g	all
Anal/rectal atresia Q42	95	277	1,088	1,460	27.62 (22.60, 33.74)	25.28 (22.48, 28.44)	4.21 (3.97, 4.47)	5.35 (5.09, 5.64)
Diaphragmatic hernia Q79.0	35	135	541	711	10.17 (7.32, 14.15)	12.32 (10.41, 14.58)	2.09 (1.93, 2.28)	2.61 (2.42, 2.81)
Omphalocele Q79.2	38	134	381	553	11.05 (8.05, 15.16)	12.23 (10.33, 14.48)	1.48 (1.33, 1.63)	2.03 (1.87, 2.20)
Gastroschisis Q79.3	45	461	241	747	13.08 (9.78, 17.50)	42.08 (38.42, 46.09)	0.93 (0.82, 1.06)	2.74 (2.55, 2.94)
Biliary atresia Q44.2	15	16	134	165	4.36 (2.64, 7.19)	1.46 (0.90, 2.37)	0.52 (0.44, 0.61)	0.61 (0.52, 0.71)
Urethral and urinary bladder malformations	26	75	456	557	7.56 (5.16, 11.07)	6.85 (5.46, 8.58)	1.77 (1.61, 1.94)	2.04 (1.88, 2.22)
Bladder extrophy/epispadias Q64.0 and Q64.1	10	20	93	123	2.91 (1.58, 5.35)	1.83 (1.18, 2.82)	0.36 (0.29, 0.44)	0.45 (0.38, 0.54)
Posterior urethral valve/prune belly syndrome Q64.2 and Q79.4	16	55	363	434	4.65 (2.86, 7.55)	5.02 (3.86, 6.53)	1.41 (1.27, 1.56)	1.59 (1.45, 1.75)
Multiple MCMs	153	540	1,820	2,513	44.48 (37.98, 52.08)	49.29 (45.31, 53.61)	7.05 (6.73, 7.38)	9.22 (8.86, 9.58)

MCM, major congenital malformation; CI, confidence interval.

Table 2. Infant mortality of MCMs in VLBW (<1,500 g) infants, LBW (1,500–2,499 g) infants, and NBW (≥2,500 g) infants

Birthweight	<1,500 g						1,500–2,499 g						≥2,500 g			All		
	died	total	mortality	died	total	mortality	died	total	mortality	died	total	mortality	died	total	mortality			
All infants	4,132	34,401	0.1201				1,430	109,558	0.0131				2,938	2,583,043	0.0011	8,500	2,727,002	0.0031
No MCM	3,852	33,417	0.1153				985	106,889	0.0092				2,084	2,573,133	0.0008	6,921	2,713,439	0.0026
ICD-10			O/E survival rate			95% CI			O/E survival rate			95% CI						
Any MCM	280	984	0.285	0.88	0.86, 0.91		445	2,669	0.167	0.92	0.91, 0.93		854	9,910	0.086	1,579	13,563	0.116
Neural tube defects	24	41	0.585	0.48	0.33, 0.64		20	130	0.153	0.87	0.81, 0.92		14	750	0.019	58	921	0.063
Encephalocele																		
Q01	6	10	0.600	0.49	0.22, 0.81		5	16	0.313	0.76	0.53, 0.91		10	119	0.084	21	145	0.145
Spina bifida/meningomyelocele																		
Q05	18	31	0.581	0.48	0.30, 0.67		15	114	0.132	0.88	0.81, 0.93		4	631	0.006	37	776	0.048
Severe cardiac malformations	220	607	0.362	0.86	0.81, 0.89		434	1,564	0.277	0.87	0.85, 0.88		1,275	8,145	0.157	1,929	10,316	0.187
Category A (compromised systemic output)	90	270	0.333	0.91	0.85, 0.97		158	559	0.283	0.88	0.85, 0.91		582	3,304	0.176	830	4,133	0.201
Aortic valve stenosis																		
Q23.0	8	32	0.250	0.97	0.78, 1.09		19	71	0.268	0.85	0.75, 0.92		65	500	0.130	92	603	0.153
Congenital mitral stenosis																		
Q23.2	8	13	0.615	0.64	0.32, 0.98		19	42	0.452	0.81	0.65, 0.94		74	235	0.315	101	290	0.348
Congenital mitral insufficiency																		
Q23.3	17	102	0.167	1.04	0.97, 1.08		8	95	0.084	1.02	0.97, 1.04		45	489	0.092	70	686	0.102
Hypoplastic left-heart syndrome																		
Q23.4	26	33	0.788	0.38	0.21, 0.64		64	95	0.674	0.52	0.41, 0.65		246	660	0.373	336	788	0.426
Coarctation, interrupted aortic arch																		
Q25.1	29	86	0.337	0.83	0.72, 0.93		41	242	0.169	0.93	0.89, 0.96		138	1,358	0.102	208	1,686	0.123
Aortic atresia/hypoplasia																		
Q25.2	2	4	0.500	0.73	0.26, 1.11		7	14	0.500	0.65	0.41, 0.86		14	62	0.226	23	80	0.288
Category B (sustained cyanosis)	73	173	0.422	0.75	0.67, 0.83		140	528	0.265	0.85	0.82, 0.88		369	2,876	0.128	582	3,647	0.160
Transposition of the great arteries																		
Q20.3	16	30	0.533	0.58	0.38, 0.78		20	94	0.213	0.87	0.79, 0.93		90	1,006	0.089	126	1,130	0.112
Tetralogy of Fallot																		
Q21.3	21	62	0.339	0.79	0.66, 0.90		32	187	0.171	0.89	0.84, 0.92		44	753	0.058	97	1,002	0.097
Pulmonary valve atresia																		
Q22.0	11	24	0.458	0.81	0.57, 1.01		24	71	0.338	0.88	0.79, 0.95		56	229	0.245	91	394	0.231
Tricuspid atresia																		
Q22.4	3	11	0.273	0.95	0.61, 1, 12		7	31	0.226	0.90	0.75, 0.99		24	177	0.136	34	219	0.155
Ebstein anomaly																		
Q22.5	3	6	0.500	0.72	0.30, 1.07		12	21	0.571	0.55	0.35, 0.75		23	108	0.213	38	135	0.281
Hypoplastic right-heart syndrome																		
Q22.6	6	13	0.462	0.74	0.44, 0.99		11	30	0.367	0.78	0.62, 0.90		26	142	0.183	43	185	0.232
Pulmonary artery atresia																		
Q25.5	9	18	0.500	0.69	0.43, 0.93		18	57	0.316	0.85	0.73, 0.93		48	260	0.185	75	335	0.224
Total anomalous pulmonary venous return																		
Q26.2	4	9	0.444	0.88	0.47, 1.19		16	37	0.432	0.81	0.64, 0.93		58	201	0.289	78	247	0.316

Table 2 (continued)

Birthweight and Major Congenital Malformations	Birthweight	<1,500 g					1,500–2,499 g					≥2,500 g			All		
		died	total	mortality			died	total	mortality		died	total	mortality	died	total	mortality	
Category C (congestive heart failure/pulmonary over-circulation)																	
Truncus arteriosus	57	164	0.348	0.88	0.80, 0.95		136	477	0.285	0.86	0.83, 0.89	324	1,965	0.165	517	2,606	0.198
Q20.0	8	16	0.500	0.70	0.43, 0.94		11	31	0.355	0.80	0.64, 0.92	26	136	0.191	45	183	0.246
Double-outlet right ventricle	21	26	0.808	0.27	0.13, 0.51		41	119	0.345	0.82	0.74, 0.88	89	465	0.191	151	610	0.248
Other single ventricle (double-inlet ventricle)	5	10	0.500	0.73	0.38, 1.04		9	23	0.391	0.80	0.58, 0.95	43	188	0.229	57	221	0.258
Atrioventricular septal defect	23	112	0.205	1.05	0.96, 1.10		75	304	0.247	0.88	0.80, 0.89	166	1,176	0.141	264	1,592	0.166
Multiple cardiac MCMs	39	67	0.582	0.61	0.46, 0.76		95	275	0.345	0.85	0.80, 0.89	336	1,526	0.220	470	1,868	0.252
Gastrointestinal and abdominal malformations	135	499	0.271	0.89	0.85, 0.92		206	1,622	0.127	0.95	0.94, 0.95	218	3,165	0.069	559	5,286	0.106
Esophageal atresia (± tracheoesophageal fistula)	28	96	0.292	0.86	0.78, 0.94		41	252	0.163	0.91	0.89, 0.94	26	350	0.074	95	698	0.136
Duodenal/small-bowel atresia	31	190	0.163	0.99	0.94, 1.02		24	363	0.066	0.98	0.97, 0.99	23	564	0.041	78	1,117	0.070
Anal/rectal atresia	22	95	0.232	0.90	0.80, 0.97		42	277	0.152	0.89	0.85, 0.92	36	1,088	0.033	100	1,460	0.068
Diaphragmatic hernia	25	35	0.714	0.40	0.24, 0.61		59	135	0.437	0.70	0.63, 0.78	105	541	0.194	189	711	0.266
Omphalocele	19	38	0.500	0.60	0.43, 0.76		29	134	0.216	0.84	0.78, 0.89	22	381	0.058	70	553	0.127
Gastroschisis	10	45	0.222	0.90	0.76, 1.00		11	461	0.024	1.01	1.01, 1.02	6	241	0.025	27	747	0.036
Biliary atresia	1	15	0.067	1.14	0.92, 1.16		3	16	0.188	0.89	0.66, 0.98	10	134	0.075	14	165	0.085
Urethral and urinary bladder malformations	8	26	0.308	0.80	0.59, 0.95		11	75	0.147	0.88	0.80, 0.94	456	0.024	30	557	0.054	
Bladder extrophy/epispadias	4	10	0.400	0.69	0.38, 0.94		2	20	0.100	0.93	0.76, 0.99	2	93	0.022	8	123	0.065
Posterior urethral valve/prune belly syndrome	4	16	0.250	0.87	0.60, 1.02		9	55	0.164	0.87	0.76, 0.93	9	363	0.025	22	434	0.051
Multiple MCMs	76	153	0.497	0.72	0.63, 0.81		152	540	0.281	0.92	0.89, 0.95	389	1,820	0.214	617	2,513	0.246

Expected survival rates were calculated by multiplying survival rates of VLBW or LBW infants without malformations, respectively, with survival rates of NBW infants with malformations and used to calculate O/E ratios (with 95% CIs). VLBW, very low birthweight; LBW, low birthweight; NBW, normal birthweight; O/E, observed-to-expected ratio; ICD, International Classification of Diseases; CI, confidence interval.

Table 3. General prevalence of major congenital malformations in German, European, and American cohorts (per 10,000 live births, with 95% CIs)

	AOK 2006–2017	EUROCAT (German registries) 2005–2017	EUROCAT (all full registries) 2005–2017	US, NBDPN (European descent) 2010–2014	US, NBDPN (all ethnicities) 2010–2014
N	2,727,002	225,420	9,417,881	~2,345,000	5,186,504
ICD10					
Encephalocele					
Q01	0.53 (0.45, 0.63)	0.47 (0.24, 0.81)	0.34 (0.30, 0.37)	0.77 (0.67, 0.89)	1.03 (0.90, 1.12)
Spina bifida/meningomyelocele					
Q05	2.85 (2.65, 3.05)	2.33 (1.78, 3.00)	1.72 (1.63, 1.80)	3.74 (3.50, 3.99)	3.86 (3.69, 4.03)
Aortic valve stenosis					
Q23.0	2.21 (2.04, 2.40)				
Congenital mitral stenosis or insufficiency					
Q23.2 and Q23.3	3.58 (3.36, 3.81)	4.85 (4.04, 5.78)	1.16 (1.09, 1.23)		
Hypoplastic left-heart syndrome					
Q23.4	2.89 (2.70, 3.10)	1.75 (1.27, 2.34)	1.38 (1.31, 1.46)	2.73 (2.52, 2.95)	2.61 (2.47, 2.75)
Aortic atresia/hypoplasia					
Q25.2	0.29 (0.24, 0.37)	2.29 (1.74, 2.95)	1.25 (1.18, 1.32)		
Coarctation, interrupted aortic arch					
Q25.1	6.18 (5.90, 6.49)	5.55 (4.48, 6.87)	3.92 (3.77, 4.08)	6.79 (6.37, 7.23)	6.17 (5.89, 6.45)
Transposition of the great arteries					
Q20.3	4.14 (3.91, 4.39)	3.26 (2.60, 4.04)	3.02 (2.91, 3.13)	3.82 (3.57, 4.08)	3.80 (3.63, 3.98)
Tetralogy of Fallot					
Q21.3	3.67 (3.45, 3.91)	3.65 (2.95, 4.47)	2.86 (2.75, 2.97)	4.61 (4.34, 4.89)	4.60 (4.42, 4.79)
Pulmonary valve atresia					
Q22.0	1.44 (1.31, 1.60)	0.82 (0.50, 1.25)	0.81 (0.76, 0.87)	1.25 (1.11, 1.40)	1.43 (1.33, 1.54)
Tricuspid atresia					
Q22.4	0.80 (0.70, 0.92)	0.62 (0.35, 1.01)	0.43 (0.39, 0.47)	0.97 (0.84, 1.12)	1.01 (0.92, 1.10)
Ebstein anomaly					
Q22.5	0.50 (0.42, 0.59)	0.54 (0.30, 0.91)	0.38 (0.34, 0.42)	0.82 (0.71, 0.94)	0.79 (0.70, 0.87)
Hypoplastic right-heart syndrome					
Q22.6	0.68 (0.59, 0.78)	0.43 (0.21, 0.76)	0.33 (0.29, 0.37)		
Pulmonary artery atresia					
Q25.5	1.23 (1.10, 1.37)				
Total anomalous pulmonary venous return					
Q26.2	0.91 (0.80, 1.03)	0.78 (0.47, 1.20)	0.63 (0.58, 0.68)	0.95 (0.83, 1.08)	1.39 (1.29, 1.50)
Truncus arteriosus					
Q20.0	0.67 (0.58, 0.78)	0.74 (0.44, 1.15)	0.45 (0.41, 0.50)	0.60 (0.51, 0.71)	0.67 (0.60, 0.74)
Double-outlet right ventricle					
Q20.1	2.24 (2.07, 2.42)	0.97 (0.63, 1.43)	1.05 (0.99, 1.12)	1.56 (1.41, 1.74)	1.69 (1.58, 1.81)
Other single ventricle (double-inlet ventricle)					
Q20.4	0.81 (0.71, 0.93)	0.23 (0.08, 0.51)	0.41 (0.37, 0.46)	0.61 (0.52, 0.73)	0.79 (0.72, 0.88)
Atrioventricular septal defect					
Q21.2	5.84 (5.56, 6.13)	3.26 (2.60, 4.04)	3.15 (3.04, 3.27)	5.62 (5.32, 5.93)	5.37 (5.17, 5.58)
Esophageal atresia (\pm tracheoesophageal fistula)					
Q39.0 and Q39.1	2.56 (2.38, 2.76)	2.25 (1.71, 2.91)	2.28 (2.18, 2.38)	2.77 (2.56, 2.99)	2.37 (2.24, 2.51)
Duodenal/small-bowel atresia					
Q41	4.10 (3.86, 4.34)	2.49 (1.70, 3.55)	2.11 (1.99, 2.25)	3.40 (3.30, 3.60)	3.30 (3.10, 3.40)

Table 3 (continued)

	AOK 2006–2017	EUROCAT (German registries) 2005–2017	EUROCAT (all full registries) 2005–2017	US, NBDPN (European descent) 2010–2014	US, NBDPN (all ethnicities) 2010–2014
Anal/rectal atresia					
Q42	5.35 (5.09, 5.64)	3.69 (2.98, 4.51)	2.54 (2.43, 2.64)	4.39 (4.12, 4.68)	4.57 (4.38, 4.77)
Diaphragmatic hernia					
Q79.0	2.61 (2.42, 2.81)	1.75 (1.27, 2.34)	2.10 (2.01, 2.19)	2.83 (2.62, 3.06)	2.87 (2.72, 3.02)
Omphalocele					
Q79.2	2.03 (1.87, 2.20)	1.16 (0.79, 1.66)	1.21 (1.15, 1.29)	2.47 (2.27, 2.68)	2.45 (2.32, 2.59)
Gastroschisis					
Q79.3	2.74 (2.55, 2.94)	3.22 (2.57, 3.99)	2.32 (2.22, 2.42)	5.20 (4.91, 5.50)	5.39 (5.19, 5.59)
Biliary atresia					
Q44.2	0.61 (0.52, 0.71)	0.43 (0.21, 0.76)	0.33 (0.30, 0.37)	0.70 (0.60, 0.70)	0.50 (0.50–0.60)
Bladder extrophy/epispadia					
Q64.0, Q64.1	0.45 (0.38, 0.54)	0.58 (0.33, 0.96)	0.50 (0.45, 0.54)		
Posterior urethral valve/prune belly					
Q64.2, Q79.4	1.59 (1.45, 1.75)	0.66 (0.38, 1.06)	0.90 (0.84, 0.96)		

AOK, Allgemeine Ortskrankenkasse; EUROCAT, European Surveillance of Congenital Anomalies; US-NBDPN, United States National Birth Defects Prevention Network; ICD, International Classification of Diseases; CI, confidence interval.



The Association between Evidence-Based Healthcare Practices and Outcomes among Preterm Births in China

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investigators

Table 1. Incidence of early death and/or severe brain injury among preterm infants

Gestational age, weeks	N	Early death, n/N (%)	Severe brain injury, n/N (%) ^a	Early death and/or severe brain injury, n/N (%)
24 ⁺⁰ –27 ⁺⁶	911	80/911 (8.8)	157/870 (18.1)	212/911 (23.3)
28 ⁺⁰ –31 ⁺⁶	5,124	91/5,124 (1.8)	359/5,079 (7.1)	430/5,124 (8.4)
All	6,035	171/6,035 (2.8)	516/5,949 (8.7)	642/6,035 (10.6)

^a86/6,035 infants missing neuroimaging results due to early death before they would have been screened.

Table 2. Proportion of infants for each individual healthcare practice

Gestational age, weeks	N	Inborn, n (%)	ACS, n (%)	MgSO ₄ , n (%)	NT, n (%)
24 ⁺⁰ –27 ⁺⁶	911	770 (84.5)	695 (76.3)	456 (50.1)	458 (50.3)
28 ⁺⁰ –31 ⁺⁶	5,124	4,269 (83.3)	4,145 (80.9)	2,638 (51.5)	3,020 (58.9)
All	6,035	5,039 (83.5)	4,840 (80.2)	3,094 (51.3)	3,478 (57.6)

Four Evidence-Based Practices: inborn, born in a tertiary hospital within CHNN; ACS, administration of antenatal corticosteroids for any course; MgSO₄, application of magnesium sulfate before delivery for any reason; NT, maintenance of normal body temperature on admission within (36.0–37.5°C). ACS, antenatal corticosteroids; NT, normothermia.

Infants with GA 24^{+0} – 31^{+6} weeks admitted to CHNN NICUs
within 24 hours of life in 2019
(n = 8,016)

Exclusion:

1. Major Congenital Anomalies (56)
2. Missing information of any one of the four practices (960)
3. Missing information of primary outcome (965)

Study population
(n = 6,035)

Table 3. Characteristics of infants who survived without severe brain injury compared with those who died or developed severe brain injury

Characteristics, n/N (%) ^a	Survival without severe brain injury (N = 5,393)	Early death and/or severe brain injury (N = 642)	p value
Maternal characteristics			
Maternal age, mean (SD), years	31.0 (4.8)	31.1 (4.9)	0.49
Maternal diabetes	989/5,384 (18.4)	80/639 (12.5)	<0.01
Maternal hypertension	1,021/5,386 (19.0)	126/641 (19.7)	0.67
Chorioamnionitis ^b	622/4,136 (15.0)	83/461 (18.0)	0.09
ROM >24 h	1,412/5,304 (26.6)	148/624 (23.7)	0.12
Cesarean section	3,144/5,388 (58.4)	327/639 (51.2)	<0.01
Births, n			
Singleton	3,782/5,393 (70.1)	431/642 (67.1)	
Twins	1,531/5,393 (28.4)	199/642 (31.0)	0.26
Triplets or more	80/5,393 (1.5)	12/642 (1.9)	
Infant characteristics			
Birth weight, mean (SD), g	1,358.1 (308.4)	1,198.9 (332.2)	<0.01
Gestational age, median (IQR), weeks	30.0 (28.7, 31.0)	28.7 (27.1, 30.1)	<0.01
Small for GA, <10th percentile	354/5,393 (6.6)	41/642 (6.4)	0.86
Male	3,012/5,390 (55.9)	390/642 (60.7)	0.02
Apgar score <7 at 5 min	203/5,252 (3.9)	84/621 (13.5)	<0.01

GA, gestational age. ^a All percentages are based on available data. ^b Chorioamnionitis has 24% missing data, while all other variables have less than 3%.

Table 4. The association between the individual practice and the primary outcome of early death or severe brain injury

Exposure	Crude OR (95% CI)		Adjusted OR (95% CI) ^a			
	$24^{+0}-27^{+6}$	$28^{+0}-31^{+6}$	all	$24^{+0}-27^{+6}$	$28^{+0}-31^{+6}$	all
Individual practice						
Inborn	0.76 (0.51, 1.14)	0.84 (0.65, 1.08)	0.83 (0.68, 1.03)	0.89 (0.55, 1.44)	0.90 (0.68, 1.18)	0.91 (0.72, 1.15)
ACS	0.50 (0.36, 0.71)	0.70 (0.55, 0.88)	0.61 (0.50, 0.73)	0.58 (0.39, 0.87)	0.77 (0.60, 1.00)	0.71 (0.57, 0.88)
MgSO ₄	0.78 (0.57, 1.06)	0.83 (0.68, 1.01)	0.81 (0.69, 0.95)	1.09 (0.76, 1.57)	0.94 (0.76, 1.16)	0.97 (0.81, 1.17)
NT	0.75 (0.55, 1.02)	0.88 (0.72, 1.07)	0.79 (0.67, 0.93)	0.76 (0.55, 1.07)	0.97 (0.79, 1.19)	0.91 (0.76, 1.08)

ACS, antenatal corticosteroids; NT, normothermia. ^a Adjusted for gestational age, small for gestational age, sex, Apgar score <7 at 5 min, delivery type, and gestational diabetes.



Intranasal Analgosedation for Infants in the Neonatal Intensive Care Unit: A Systematic Review

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Gestational Age-Dependent Reference Ranges for Albumin Levels in Cord Serum

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GA	N	Albumin levels in umbilical cord serum, g/dL						
		min	5%ile	10%ile	50%ile	90%ile	95%ile	max
22 weeks	9	1.8	1.8	1.8	2.2	2.4	2.4	2.4
23 weeks	22	1.8	1.8	2.0	2.1	2.7	2.8	2.8
24 weeks	48	1.6	1.7	1.8	2.2	2.6	2.8	2.9
25 weeks	44	2.0	2.0	2.1	2.4	2.8	2.9	3.1
26 weeks	51	1.8	1.9	2.0	2.3	2.9	3.0	3.4
27 weeks	54	1.7	1.9	2.0	2.5	2.8	3.1	3.3
28 weeks	74	1.8	1.9	2.0	2.5	2.9	3.0	3.3
29 weeks	80	1.8	2.2	2.2	2.6	3.0	3.1	3.4
30 weeks	80	1.6	2.1	2.3	2.7	3.1	3.2	3.4
31 weeks	101	1.9	2.3	2.3	2.7	3.1	3.2	3.3
32 weeks	133	1.6	2.3	2.4	2.7	3.1	3.2	3.6
33 weeks	157	2.0	2.3	2.5	2.9	3.2	3.3	3.7
34 weeks	246	1.7	2.4	2.6	2.9	3.2	3.3	4.1
35 weeks	232	1.8	2.6	2.6	3.0	3.4	3.5	4.0
36 weeks	281	2.0	2.5	2.7	3.1	3.4	3.4	3.9
37 weeks	422	1.9	2.7	2.8	3.2	3.5	3.6	4.2
38 weeks	299	2.0	2.7	2.9	3.3	3.6	3.8	4.2
39 weeks	278	2.5	2.8	2.9	3.4	3.7	3.8	4.1
40 weeks	227	2.1	2.8	3.0	3.4	3.8	3.8	4.3
41 weeks	79	2.2	2.8	2.9	3.4	3.7	3.8	4.2
Total	2,917	1.6	2.2	2.4	3.0	3.5	3.6	4.3



Mother's Bed Incline and Desaturation Episodes in Healthy Term Newborns during Early Skin-to-Skin Contact: A Multicenter Randomized Controlled Trial

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Multisystemic Inflammatory Syndrome in Neonates: A Systematic Review

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Gestational Age-Dependent Reference Ranges for Albumin Levels in Cord Serum

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