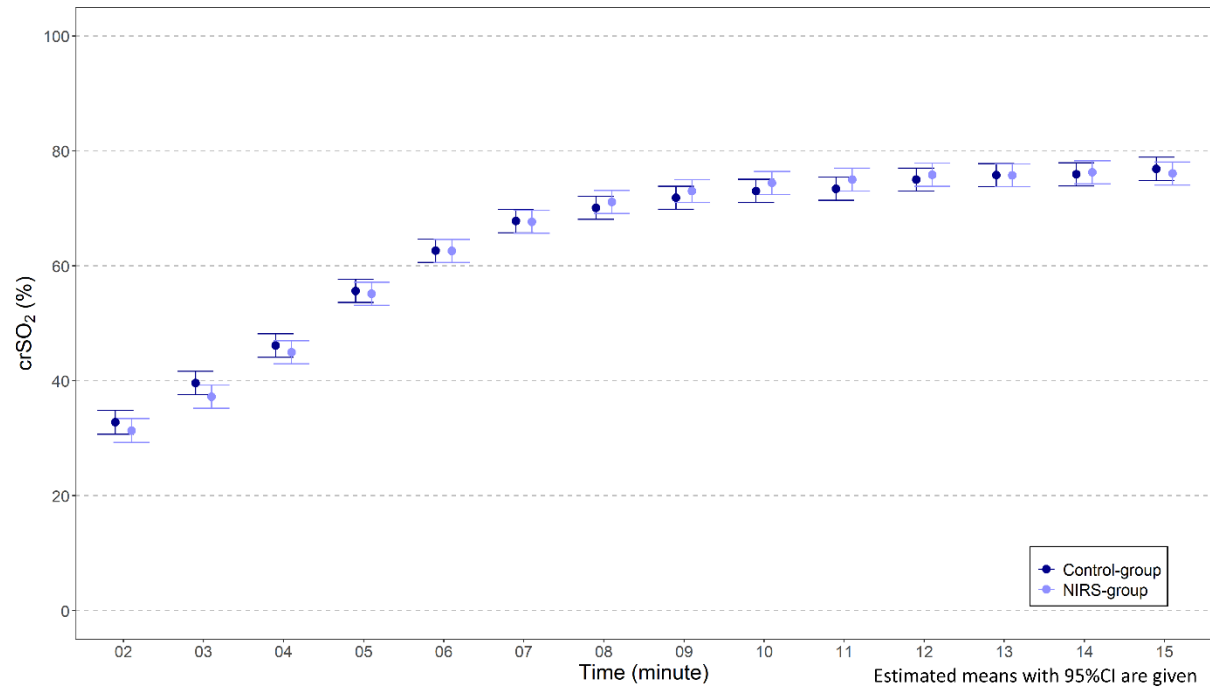


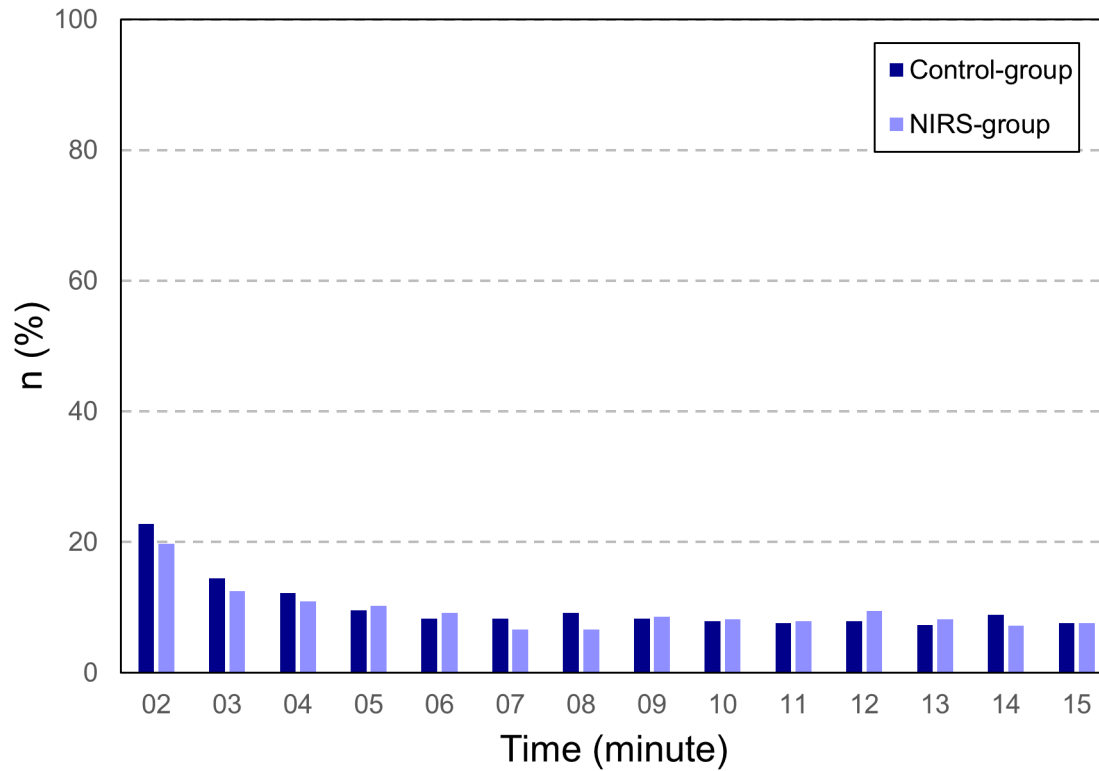
Supplementary Figure S1

Cerebral regional oxygen saturation (crSO₂) during the first 15 minutes after birth in neonates with additional cerebral tissue oxygen saturation monitoring to standard monitoring combined with defined treatment guidelines (NIRS-group) and in neonates with standard monitoring and standard treatment (control-group)



Supplementary Figure S2

Percentage of cerebral regional oxygen saturation (crSO₂) missing values at each minute in neonates with additional cerebral tissue oxygen saturation monitoring to standard monitoring combined with defined treatment guidelines (NIRS-group) and in neonates with standard monitoring and standard treatment (control-group)



Supplementary Table 1

Primary composite outcome measure, primary outcome measures and secondary outcome parameters at term age or before discharge in preterm neonates with gestational age <28weeks and ≥28 weeks

	Gestational age <28weeks				Gestational age ≥28 weeks			
	NIRS group n = 110	Control group n = 118	RR (95% CI)	P-value	NIRS group n = 194	Control group n = 185	RR (95% CI)	P-value
<i>Primary composite outcome</i>								
Survival without cerebral injury*, n (%)	78 (70.9)	78 (66.1)	1.13 (0.83 to 1.52)		174 (89.7)	160 (86.5)	1.17 (0.83 to 1.65)	
<i>Primary outcome measures</i>								
Death and/or cerebral injury*, n (%)	32 (29.1)	40 (33.9)	0.90 (0.69 to 1.17)		20 (10.3)	25 (13.5)	0.86 (0.64 to 1.15)	
Death, n (%)	10 (9.1)	16 (13.6)	0.82 (0.59 to 1.14)		2 (1.0)	0 (0.0)	-	
Intraventricular hemorrhage any grade, n (%)	23 (20.9)	30 (25.4)	0.89 (0.67 to 1.17)		18 (9.3)	25 (13.5)	0.82 (0.62 to 1.08)	
No intraventricular hemorrhage, n (%)	87 (79.1)	88 (74.6)		.69	176 (90.7)	160 (86.5)		.39
Intraventricular hemorrhage I-II, n (%)	14 (12.7)	17 (14.4)			15 (7.7)	22 (11.9)		
Intraventricular hemorrhage III-IV, n (%)	9 (8.2)	13 (11.0)			3 (1.6)	3 (1.6)		
Cystic periventricular leukomalacia any grade, n (%)	6 (5.5)	1 (0.9)	3.7 (0.6 to 22.8)		2 (1.0)	2 (1.1)	0.98 (0.36 to 2.61)	
No cystic periventricular leukomalacia, n (%)	104 (94.6)	117 (99.2)		.10	192 (99.0)	183 (98.9)		.14
Cystic periventricular leukomalacia II, n (%)	3 (2.7)	0 (0.0)			0 (0.0)	2 (1.1)		
Cystic periventricular leukomalacia III, n (%)	3 (2.7)	1 (0.9)			2 (1.0)	0 (0.0)		
<i>Secondary outcome/morbidities</i>								
Respiratory distress syndrome, n (%)	98 (89.1)	104 (88.1)	1.05 (0.71 to 1.53)		150 (77.3)	140 (75.7)	1.05 (0.83 to 1.33)	
No respiratory distress syndrome, n (%)	12 (10.9)	14 (11.9)		.90	44 (22.7)	45 (24.3)		.96
Respiratory distress syndrome not defined, n (%)	10 (9.1)	11 (9.3)			16 (8.3)	17 (9.2)		
Respiratory distress syndrome Grade 1-2, n (%)	58 (52.7)	66 (55.9)			105 (54.1)	97 (52.4)		

Respiratory distress syndrome Grade 3-4, n (%)	30 (27.3)	27 (22.9)		29 (15.0)	26 (14.1)	
Culture proven sepsis, n (%)	48 (43.6)	66 (55.9)	0.79 (0.61 to 1.02)	43 (22.2)	45 (24.3)	0.94 (0.74 to 1.19)
Necrotizing enterocolitis any grade, n (%)	13 (11.8)	11 (9.3)	1.14 (0.73 to 1.80)	4 (2.1)	4 (2.2)	0.98 (0.48 to 1.979)
Bronchopulmonary dysplasia†, n (%)	47 (42.7)	45 (38.1)	1.10 (0.85 to 1.42)	7 (3.6)	12 (6.5)	0.76 (0.53 to 1.09)
Retinopathy of prematurity ≥ Grade 2, n (%)	28 (25.5)	31 (26.3)	0.98 (0.74 to 1.30)	7 (3.6)	2 (1.1)	2.23 (0.65 to 7.59)
Persistent ductus arteriosus with intervention**, n (%)	28 (25.5)	39 (33.1)	0.84 (0.65 to 1.09)	13 (6.7)	15 (8.1)	0.90 (0.63 to 1.30)

* defined as any intraventricular hemorrhage and/or cystic periventricular leukomalacia at term age or before discharge

† defined as oxygen dependency or need of respiratory support at 36 weeks corrected age

** medical and/or surgical intervention

Supplementary Table 2

Primary composite outcome measure, primary outcome measures and secondary outcome parameters at term age or before discharge in neonates delivered by cesarean section and neonates delivered vaginally

	Cesarean section				Vaginal delivery			
	NIRS group n = 253	Control group n = 258	RR (95% CI)	P-value	NIRS group n = 49	Control group n = 43	RR (95% CI)	P-value
<i>Primary composite outcome</i>								
Survival without cerebral injury*, n (%)	213 (84.2)	207 (80.2)	1.05 (0.97 to 1.14)		37 (75.5)	29 (67.4)	1.12 (0.86 to 1.45)	
<i>Primary outcome measures</i>								
Death and/or cerebral injury*, n (%)	40 (15.8)	51 (19.8)	0.80 (0.55 to 1.16)		12 (24.5)	14 (32.6)	0.75 (0.39 to 1.45)	
Death, n (%)	10 (4.0)	12 (4.7)	0.85 (0.97 to 1.05)		2 (4.1)	4 (9.3)	0.44 (0.08 to 2.28)	
Intraventricular hemorrhage any grade, n (%)	32 (12.7)	42 (16.3)	0.78 (0.51 to 1.19)		9 (18.4)	13 (30.2)	0.61 (0.29 to 1.28)	
No intraventricular hemorrhage, n (%)	221 (87.4)	216 (83.7)		.51	40 (81.6)	30 (69.8)		.41
Intraventricular hemorrhage I-II, n (%)	23 (9.1)	30 (11.6)			6 (12.2)	9 (20.9)		
Intraventricular hemorrhage III-IV, n (%)	9 (3.6)	12 (4.7)			3 (6.1)	4 (9.3)		
Cystic periventricular leukomalacia any grade, n (%)	5 (2.0)	2 (0.8)	2.55 (0.50 to 13.0)		3 (6.1)	1 (2.3)	2.63 (0.28 to 24.38)	
No cystic periventricular leukomalacia, n (%)	248 (98.0)	256 (99.2)	-	.15	46 (93.9)	42 (97.7)		.62
Cystic periventricular leukomalacia II, n (%)	0 (0.0)	1 (0.4)			0 (0.0)	0 (0.0)		
Cystic periventricular leukomalacia III, n (%)	5 (2.0)	1 (0.4)			3 (6.1)	1 (2.3)		
<i>Secondary outcome/morbidities</i>								
Respiratory distress syndrome, n (%)	208 (82.2)	206 (79.8)	1.03 (0.95 to 1.12)		39 (79.6)	37 (86.1)	0.93 (0.77 – 1.11)	
No respiratory distress syndrome, n (%)	45 (17.8)	52 (20.2)		.71	10 (20.4)	6 (14.0)		.77
Respiratory distress syndrome not defined, n (%)	18 (7.1)	21 (8.1)			7 (14.3)	6 (14.0)		

Respiratory distress syndrome Grade 1-2, n (%)	139 (54.9)	142 (55.0)		24 (49.0)	21 (48.8)	
Respiratory distress syndrome Grade 3-4, n (%)	51 (20.2)	43 (16.7)		8 (16.3)	10 (23.3)	
Culture proven sepsis, n (%)	78 (30.8)	89 (34.5)	0.89 (0.70 to 1.15)	12 (24.5)	21 (48.8)	0.50 (0.28 to 0.89)
Necrotizing enterocolitis any grade, n (%)	14 (5.5)	10 (3.9)	1.43 (0.65 to 3.15)	3 (6.1)	5 (11.6)	0.52 (0.13 to 2.08)
Bronchopulmonary dysplasia†, n (%)	45 (17.8)	46 (17.8)	1.00 (0.69 to 1.45)	9 (18.4)	10 (23.3)	0.79 (0.35 to 1.76)
Retinopathy of prematurity ≥ Grade 2, n (%)	30 (11.9)	25 (9.7)	1.22 (0.74 to 2.02)	5 (10.2)	8 (18.6)	0.55 (0.19 to 1.55)
Persistent ductus arteriosus with intervention**, n (%)	34 (13.4)	44 (17.1)	0.79 (0.52 to 1.19)	6 (12.2)	10 (23.3)	0.53 (0.21 to 1.33)

* defined as any intraventricular hemorrhage and/or cystic periventricular leukomalacia at term age or before discharge

† defined as oxygen dependency or need of respiratory support at 36 weeks corrected age

** medical and/or surgical intervention

Supplementary Table 3

Arterial oxygen saturation (SpO₂) and fraction of inspired supplemental oxygen (FiO₂) during the first 15 minutes after birth in neonates with additional cerebral tissue oxygen saturation monitoring to standard monitoring combined with defined treatment guidelines (NIRS-group) and in neonates with standard monitoring and standard treatment (control-group)

Minute	SpO ₂		FiO ₂	
	Control Group	NIRS Group	Control Group	NIRS Group
2	56.4 (54.7-58.1)	56.3 (54.6-58.0)	0.33 (0.31-0.35)	0.35 (0.33-0.37)
3	62.2 (60.6-63.8)	61.4 (59.8-63.0)	0.40 (0.38-0.42)	0.41 (0.39-0.43)
4	69.8 (68.2-71.4)	70.1 (68.5-71.6)	0.44 (0.42-0.46)	0.46 (0.44-0.48)
5	78.3 (76.7-79.8)	77.6 (76.1-79.2)	0.44 (0.42-0.46)	0.48 (0.45-0.50)
6	83.6 (82.0-85.2)	82.5 (81.0-84.1)	0.44 (0.42-0.46)	0.47 (0.45-0.49)
7	86.7 (85.1-88.2)	85.9 (84.3-87.4)	0.42 (0.40-0.44)	0.45 (0.42-0.47)
8	88.4 (86.9-90.0)	88.5 (86.9-90.1)	0.39 (0.37-0.41)	0.44 (0.41-0.46)
9	89.2 (87.7-90.8)	89.6 (88.1-91.2)	0.37 (0.35-0.40)	0.42 (0.40-0.44)
10	90.0 (88.5-91.6)	90.3 (88.8-91.9)	0.37 (0.35-0.40)	0.40 (0.38-0.43)
11	90.2 (88.6-91.7)	90.6 (89.0-92.1)	0.36 (0.34-0.39)	0.38 (0.36-0.41)
12	90.7 (89.2-92.3)	90.8 (89.2-92.3)	0.35 (0.33-0.38)	0.37 (0.35-0.39)
13	90.9 (89.3-92.4)	90.9 (89.4-92.5)	0.35 (0.32-0.37)	0.36 (0.34-0.38)
14	91.1 (89.5-92.7)	90.7 (89.1-92.2)	0.33 (0.31-0.36)	0.36 (0.33-0.38)
15	91.9 (90.3-93.5)	90.6 (89.1-92.2)	0.33 (0.31-0.35)	0.35 (0.33-0.37)