

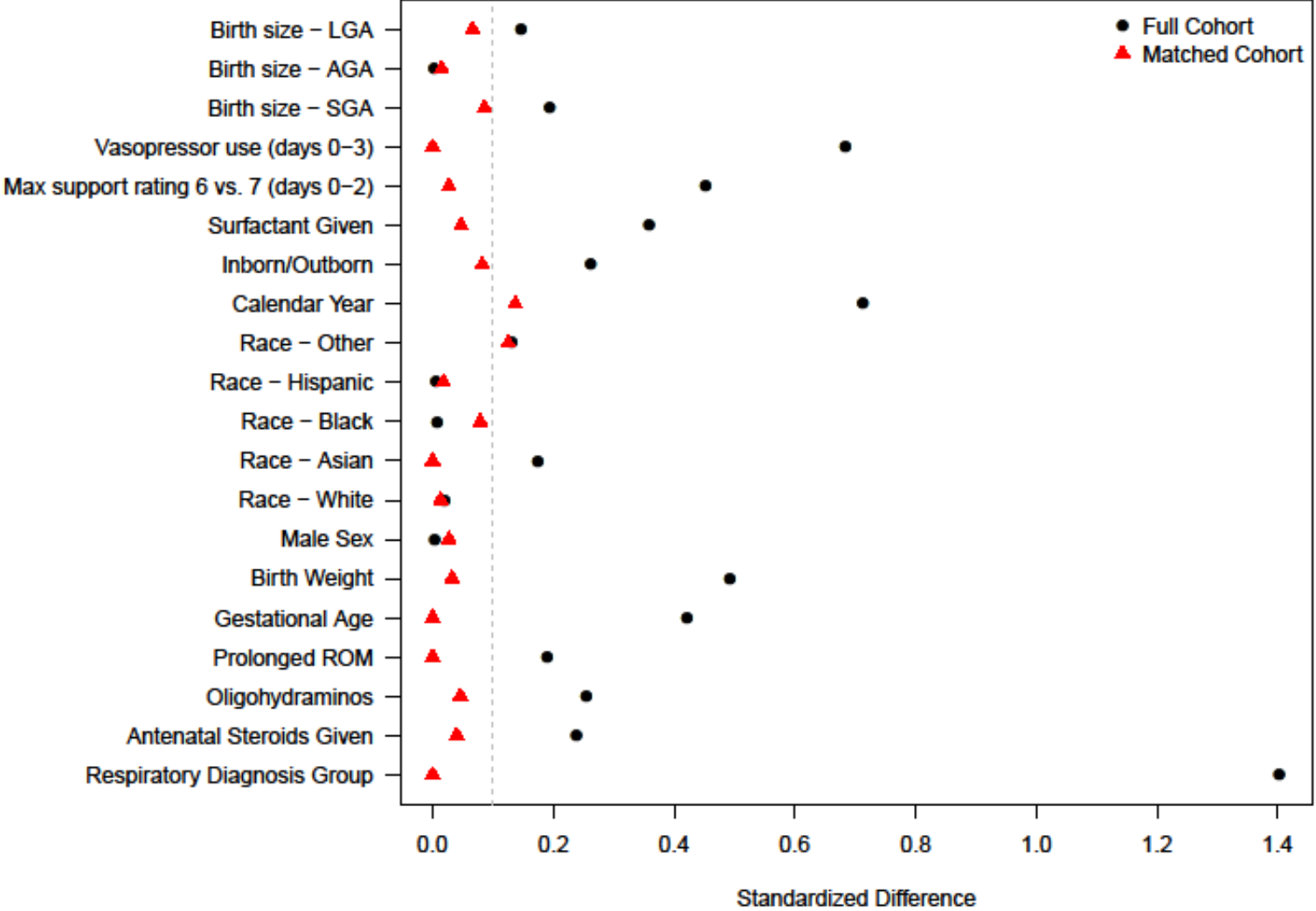
Supplementary Online Content

Ellsworth KR, Ellsworth MA, Weaver AL, Mara KC, Clark RH, Carey WA. Association of early inhaled nitric oxide with the survival of preterm neonates with pulmonary hypoplasia. *JAMA Pediatr*. Published online May 7, 2018. doi:10.1001/jamapediatrics.2018.0761.

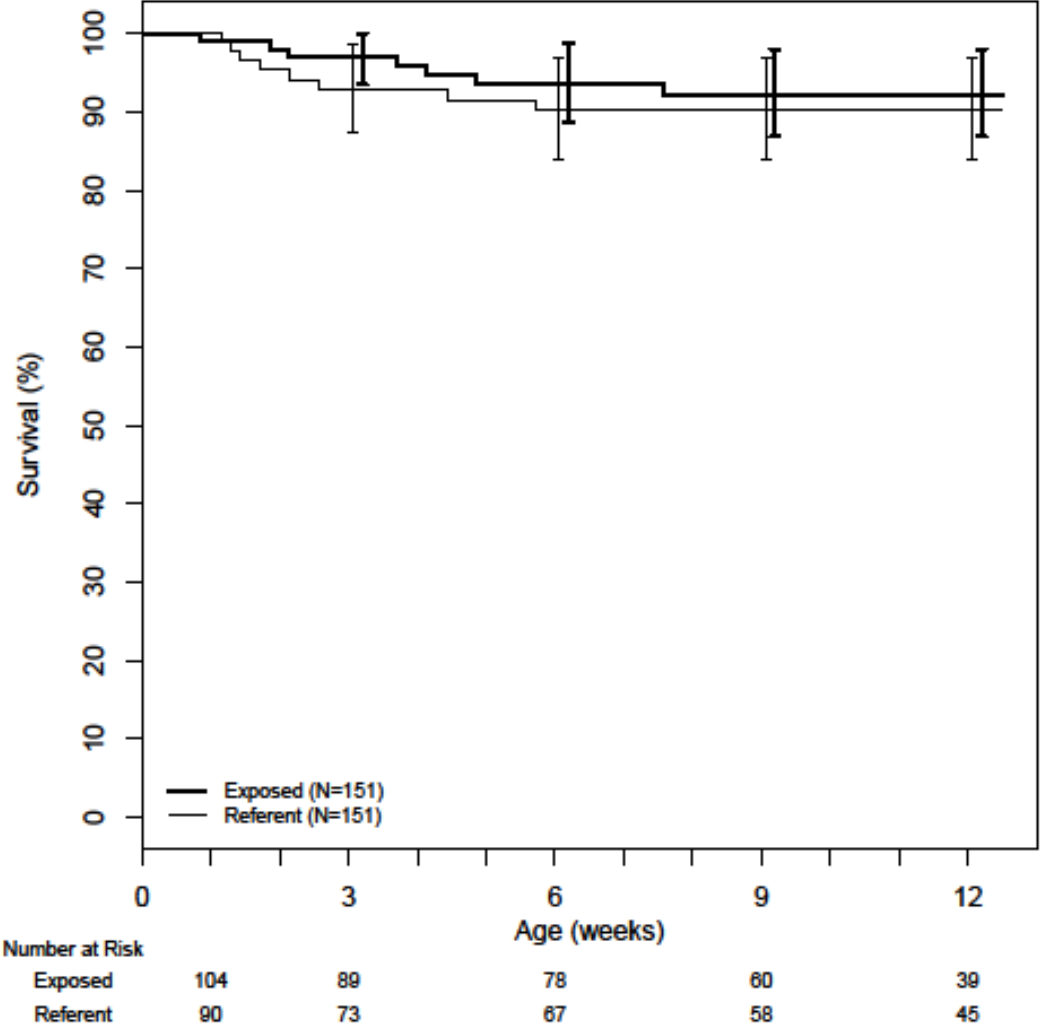
- eFigure 1.** Standardized differences (absolute value) for each covariate used in the derivation of the propensity scores.
- eFigure 2.** NEC-free survival by iNO exposure status of patients in the matched cohort.
- eFigure 3.** Overall survival by iNO exposure status of patients in the matched cohort – sensitivity analysis.
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- eFigure 5.** Overall survival by iNO exposure status of patients in the matched cohort diagnosed with (A) PH+PPHN and (B) PH-PPHN, respectively – sensitivity analysis.
- eTable 1.** Baseline characteristics of the matched cohort stratified by diagnosis.
- eTable 2.** Comparison of secondary outcomes between matched pairs of exposed and referent neonates.

This supplementary material has been provided by the authors to give readers additional information about their work.

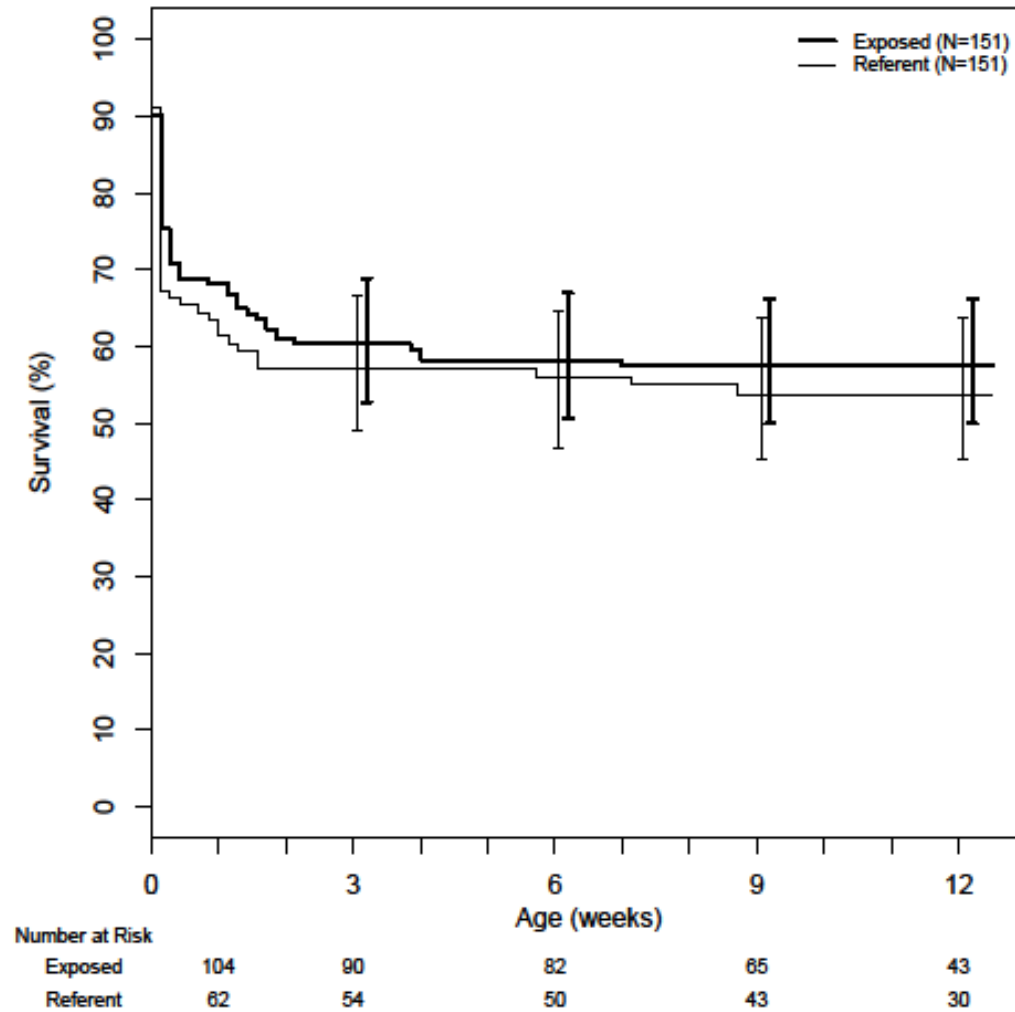
eFigure 1. Standardized differences (absolute value) for each covariate used in the derivation of the propensity scores. In the propensity score-matched cohort, the covariates were more balanced between the two groups with most standardized differences below the 0.10 threshold. AGA, appropriate for gestational age; LGA, large for gestational age; PROM, prolonged rupture of membranes; SGA, small for gestational age.



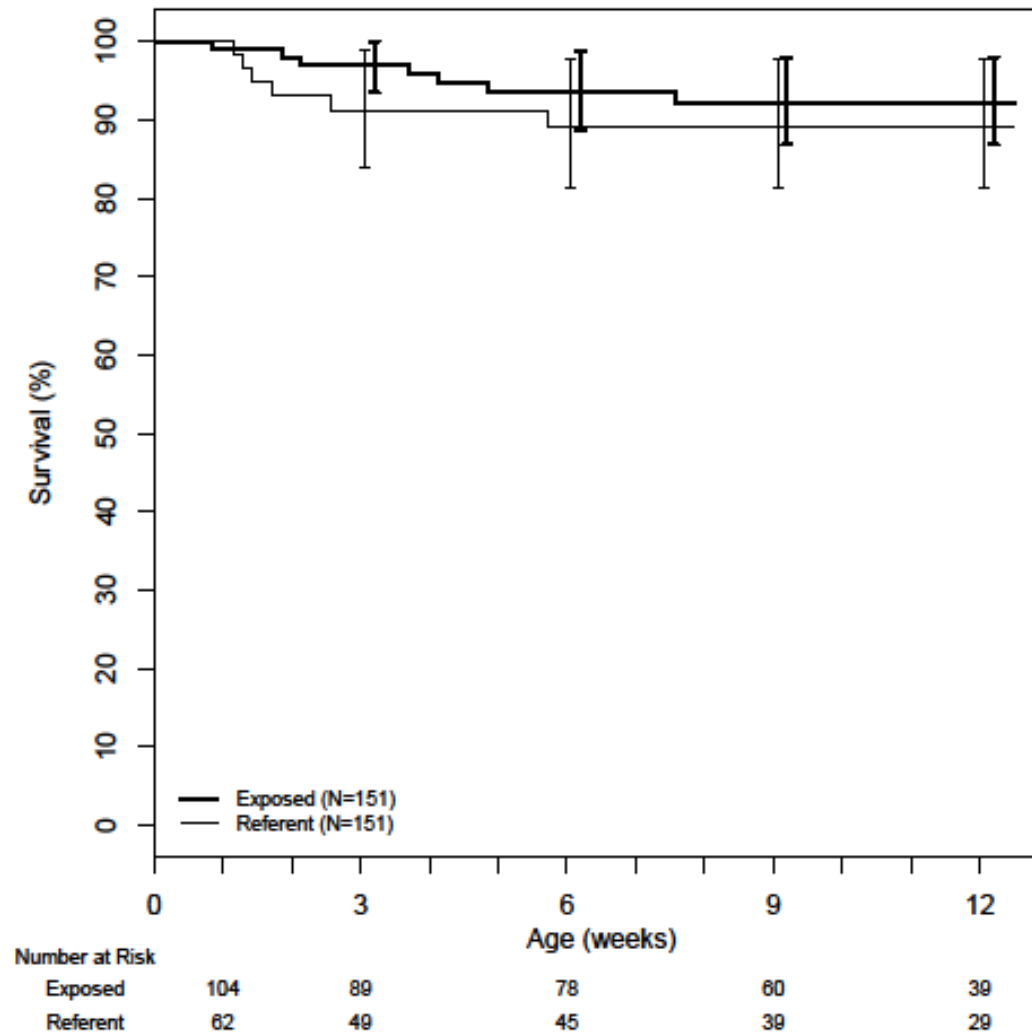
eFigure 2. NEC-free survival by iNO exposure status of patients in the matched cohort. The survival estimates were derived from a Cox model with patients entering the risk set at their respective age at the index date. iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis.



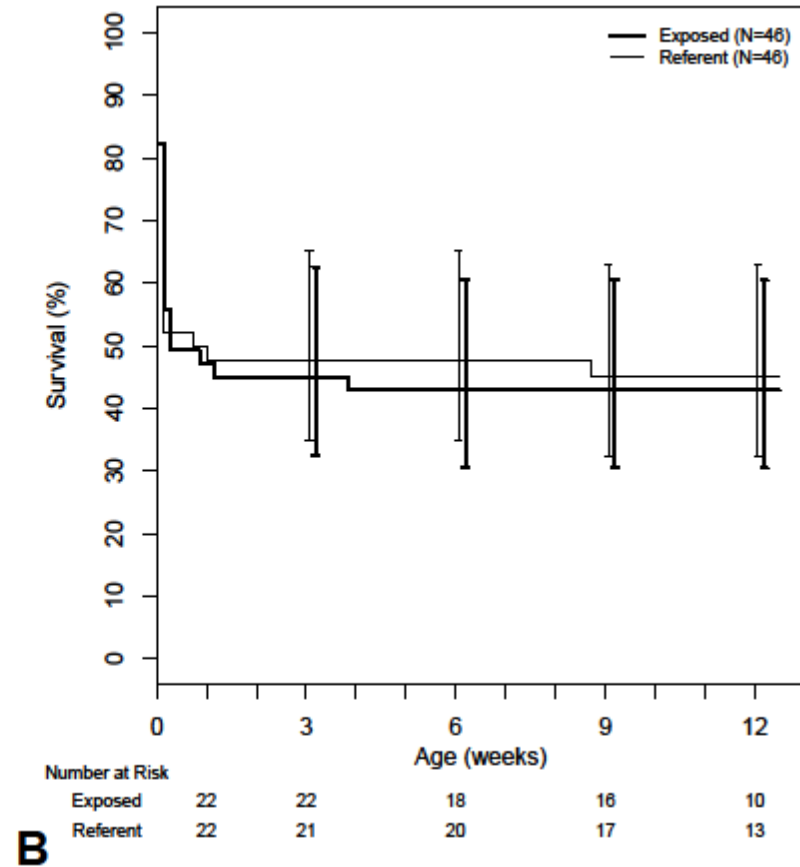
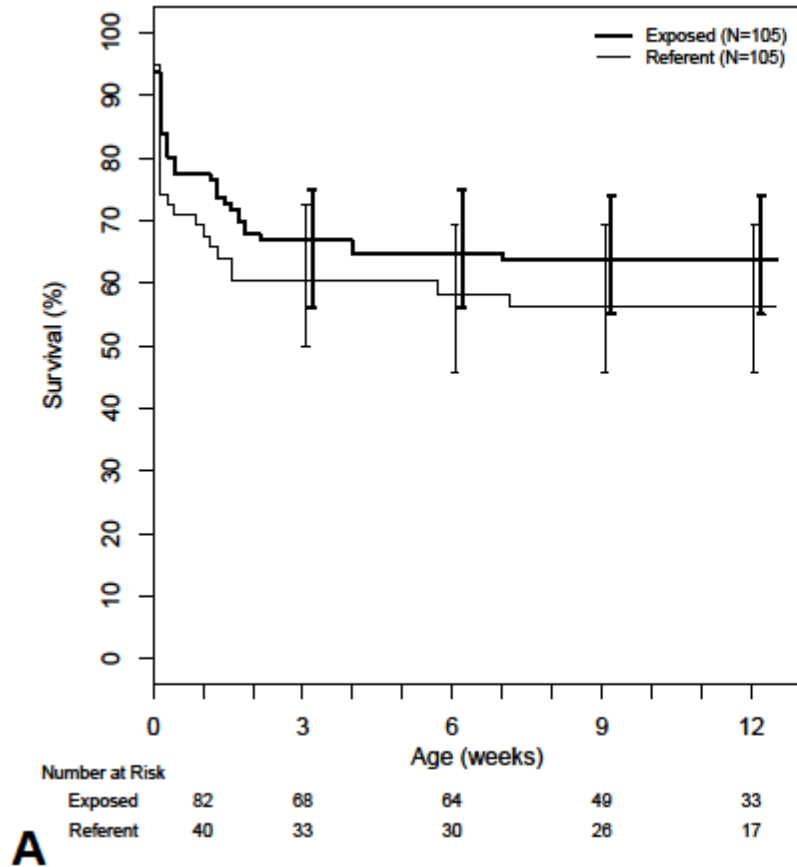
eFigure 3. Overall survival by iNO exposure status of patients in the matched cohort – sensitivity analysis. The survival estimates were derived from a Cox model with patients entering the risk set at their respective age at the index date. iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis.



eFigure 4. NEC-free survival by iNO exposure status of patients in the matched cohort – sensitivity analysis. The survival estimates were derived from a Cox model with patients entering the risk set at their respective age at the index date. iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis.



eFigure 5. Overall survival by iNO exposure status of patients in the matched cohort diagnosed with (A) PH+PPHN and (B) PH-PPHN, respectively – sensitivity analysis. The survival estimates were derived from a Cox model with patients entering the risk set at their respective age at the index date. iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis.



eTable 1. Baseline characteristics of the matched cohort stratified by diagnosis. AGA, appropriate for gestational age; CMV, conventional mechanical ventilation; HFOV, high frequency oscillatory ventilation; iNO, inhaled nitric oxide; LGA, large for gestational age; PH, pulmonary hypoplasia; PPHN, persistent pulmonary hypertension of the newborn; ROM, rupture of membrane; SD, standard deviation; SGA, small for gestational age.

Characteristic	PH+PPHN			PH-PPHN		
	Exposed (N=105)	Referent (N=105)	Standardized difference	Exposed (N=46)	Referent (N=46)	Standardized difference
Maternal Characteristics						
Prolonged ROM	55 (52.4%)	55 (52.4%)	0	22 (47.8%)	22 (47.8%)	0
Oligohydramnios	8 (7.6%)	11 (10.5%)	0.10	5 (10.9%)	4 (8.7%)	0.07
Antenatal steroids given	94 (89.5%)	90 (85.7%)	0.12	37 (80.4%)	43 (93.5%)	0.40
Infant Characteristics						
Gestational age (weeks), mean (SD)	26.9 (1.7)	27.0 (1.5)	0.02	26.2 (1.5)	26.1 (1.6)	0.06
Birth weight (kg), mean (SD)	1.03 (0.30)	1.06 (0.27)	0.10	0.99 (0.29)	0.96 (0.24)	0.12
Birth size assessment						
SGA	9 (8.6%)	6 (5.7%)	0.11	1 (2.2%)	1 (2.2%)	0.13
AGA	75 (71.4%)	77 (73.3%)	0.04	38 (82.6%)	35 (76.1%)	0.17
LGA	21 (20.0%)	22 (21.0%)	0.02	7 (15.2%)	10 (21.7%)	0.12
Sex			0.08			0.09
Female	44 (41.9%)	40 (38.1%)		20 (43.5%)	22 (47.8%)	
Male	61 (58.1%)	65 (61.9%)		26 (56.5%)	24 (52.2%)	
Race						
White	53 (50.5%)	52 (49.5%)	0.02	26 (56.5%)	26 (56.5%)	0
Asian	1 (1.0%)	1 (1.0%)	0	0 (0.0%)	0 (0.0%)	--
Black	22 (21.0%)	25 (23.8%)	0.07	10 (21.7%)	12 (26.1%)	0.10
Hispanic	16 (15.2%)	19 (18.1%)	0.08	9 (19.6%)	7 (15.2%)	0.12
Other	13 (12.4%)	8 (7.6%)	0.16	1 (2.2%)	1 (2.2%)	0
Calendar year (categorized for presentation)						
2000-2004	13 (12.4%)	20 (19.0%)		5 (10.9%)	7 (15.2%)	
2005-2009	35 (33.3%)	38 (36.2%)		16 (34.8%)	13 (28.3%)	
2010-2014	57 (54.3%)	47 (44.8%)		25 (54.3%)	26 (56.5%)	
Inborn/outborn status			0.03			0.19
Inborn	93 (88.6%)	94 (89.5%)		38 (82.6%)	41 (89.1%)	
Outborn	12 (11.4%)	11 (10.5%)		8 (17.4%)	5 (10.9%)	
Surfactant given	97 (92.4%)	93 (88.6%)	0.13	42 (91.3%)	44 (95.7%)	0.18
Maximal respiratory support over days 0-2						
CMV	6 (5.7%)	7 (6.7%)	0.04	3 (6.5%)	3 (6.5%)	0
HFOV	99 (94.3%)	98 (93.3%)		43 (93.5%)	43 (93.5%)	

At least one vasopressor reported on days 0-3	85 (81.0%)	88 (83.8%)	0.08	37 (80.4%)	34 (73.9%)	0.16
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eTable 2. Comparison of secondary outcomes between matched pairs of neonates. CGA, corrected gestational age; CI, confidence interval; CLD, chronic lung disease; iNO, inhaled nitric oxide; OR, odds ratio; PH, pulmonary hypoplasia; PPHN, persistent pulmonary hypertension of the newborn; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.

	PH+PPHN			PH-PPHN		
	Exposed	Referent	OR (95% CI)	Exposed	Referent	OR (95% CI)
ROP Treated						
No. of neonates with ROP evaluated	88	36		20	155	
No. of matched pairs used with ROP evaluated	28	28		16	16	
No	28 (100.0%)	28 (100.0%)		16 (100.0%)	16 (100.0%)	
Yes	0 (0.0%)	0 (0.0%)	-- ^a	0 (0.0%)	0 (0.0%)	-- ^a
CLD						
No. of neonates still in the hospital at CGA ≥36 weeks	77	33		14	129	
No. of matched pairs used that were still in hospital at CGA ≥ 36 weeks	25	25		13	13	
No	9 (36.0%)	5 (20.0%)		2 (15.4%)	4 (30.8%)	
Yes	16 (64.0%)	20 (80.0%)	0.44 (0.12, 1.57) ^b	11 (84.6%)	9 (69.2%)	2.44 (0.36, 16.55)
PVL						
No. of neonates with cranial imaging	120	69		29	224	
No. of matched pairs used with cranial imaging	55	55		25	25	
No	51 (92.7%)	53 (96.4%)		24 (96.0%)	23 (92.0%)	
Yes	4 (7.3%)	2 (3.6%)	2.08 (0.37, 11.85)	1 (4.0%)	2 (8.0%)	0.48 (0.04, 5.65)

^aThe odds ratio was not estimated due to the lack of events in both groups.

^bAdjusted for inborn/outborn status.