

Supplementary Online Content

Gentle JS, Rysavy MA, Li L, et al; National Institute of Child Health and Human Development Neonatal Research Network. Heterogeneity of treatment effects of hydrocortisone by risk of bronchopulmonary dysplasia or death among extremely preterm infants in the National Institute of Child Health and Human Development Neonatal Research Network Trial: a secondary analysis of a randomized clinical trial. *JAMA Netw Open*. 2023;6(5):e2315315. doi:10.1001/jamanetworkopen.2023.15315

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

eTable 1. Demographic and Clinical Characteristics Used for Risk Estimates by Quartile of Baseline Risk for Grades 2 to 3 BPD or Death and Exposure Group

	Quartile 1 18-45%		Quartile 2 46-53%		Quartile 3 54-65%		Quartile 4 66-84%		All	
	HC n=110	Placebo n=89	HC n=89	Placebo n=111	HC n=99	Placebo n=101	HC n=100	Placebo n=100	HC n=398	Placebo n=401
Gestational age (wks) median (IQR)	25 (24-26)	25 (24-26)	25 (24-25)	25 (24-26)	24 (24-26)	25 (24-26)	25 (24-26)	25 (24-26)	25 (24-26)	25 (24-26)
Birth weight (g) median (IQR)	773 (660-860)	848 (720-984)	700 (611-789)	730 (621-790)	665 (580-770)	670 (585-770)	633 (540-710)	630 (520-710)	690 (600-799)	695 (600-810)
Male: n/N (%)	26/110 (24)	32/89 (36)	47/89 (53)	72/111 (65)	55/99 (56)	66/101 (65)	58/100 (58)	65/100 (65)	186/398 (47)	235/401 (59)
Highest FiO ₂ on Day 14: median (IQR)	36 (30-44)	35 (30-41)	46 (38-55)	38 (32-50)	48 (38-62)	48 (36-60)	60 (50-80)	60 (45-76)	46 (35-62)	44 (34-60)
Respiratory support on postnatal day 14:										
Conventional Ventilation	2 (2)	2 (2)	7 (8)	6 (5)	39 (39)	29 (29)	83 (83)	82 (82)	131 (33)	119 (30)
High frequency ventilation	106 (96)	87 (98)	82 (92)	105 (95)	60 (61)	72 (71)	17 (17)	18 (18)	265 (67)	282 (70)
Noninvasive positive pressure ventilation	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (1.8)	2 (2)	2 (2)
Surgical NEC (%)	0 (0)	1 (1)	2 (2)	5 (5)	6 (6)	9 (9)	7 (7)	10 (10)	15 (4)	25 (6)

BPD: bronchopulmonary dysplasia; FiO₂: fraction of inspired oxygen; NEC: necrotizing enterocolitis

eTable 2. Additional Clinical Characteristics by Quartile of Baseline Risk for Grades 2 to 3 BPD or Death

	Quartile 1 18-45%	Quartile 2 46-53%	Quartile 3 54-65%	Quartile 4 66-84%	All
	n=199	n=200	n=200	n=200	n=799
Days of mechanical ventilation ^a : median (IQR)	30 (21-43)	37 (29-51)	42 (30-57)	46 (35-65)	38 (28-54)
Highest FiO ₂ at enrollment: median (IQR)	33 (30-40)	40 (34-48)	50 (40-61)	70 (60-97)	46 (35-61)
Extubation failure ^a : n/N (%)	16 (8)	28 (14)	27 (15)	38 (21)	109 (15)
Open label dexamethasone exposure: n/N (%)	56 (29)	64 (33)	92 (51)	94 (53)	306 (41)
Clinical chorioamnionitis: n/N (%)	36 (18)	43 (22)	29 (15)	22 (11)	130 (16)
Surgical PDA treatment: n/N (%)	30 (15)	40 (20)	27 (14)	27 (14)	124 (16)
Pharmacological PDA treatment: n/N (%)	96 (48)	91 (46)	87 (44)	82 (41)	356 (45)
Early onset sepsis: n/N (%)	2 (1)	2 (1)	7 (4)	3 (2)	14 (2)
Late onset sepsis: n/N (%)	37 (19)	63 (32)	68 (34)	70 (35)	238 (30)

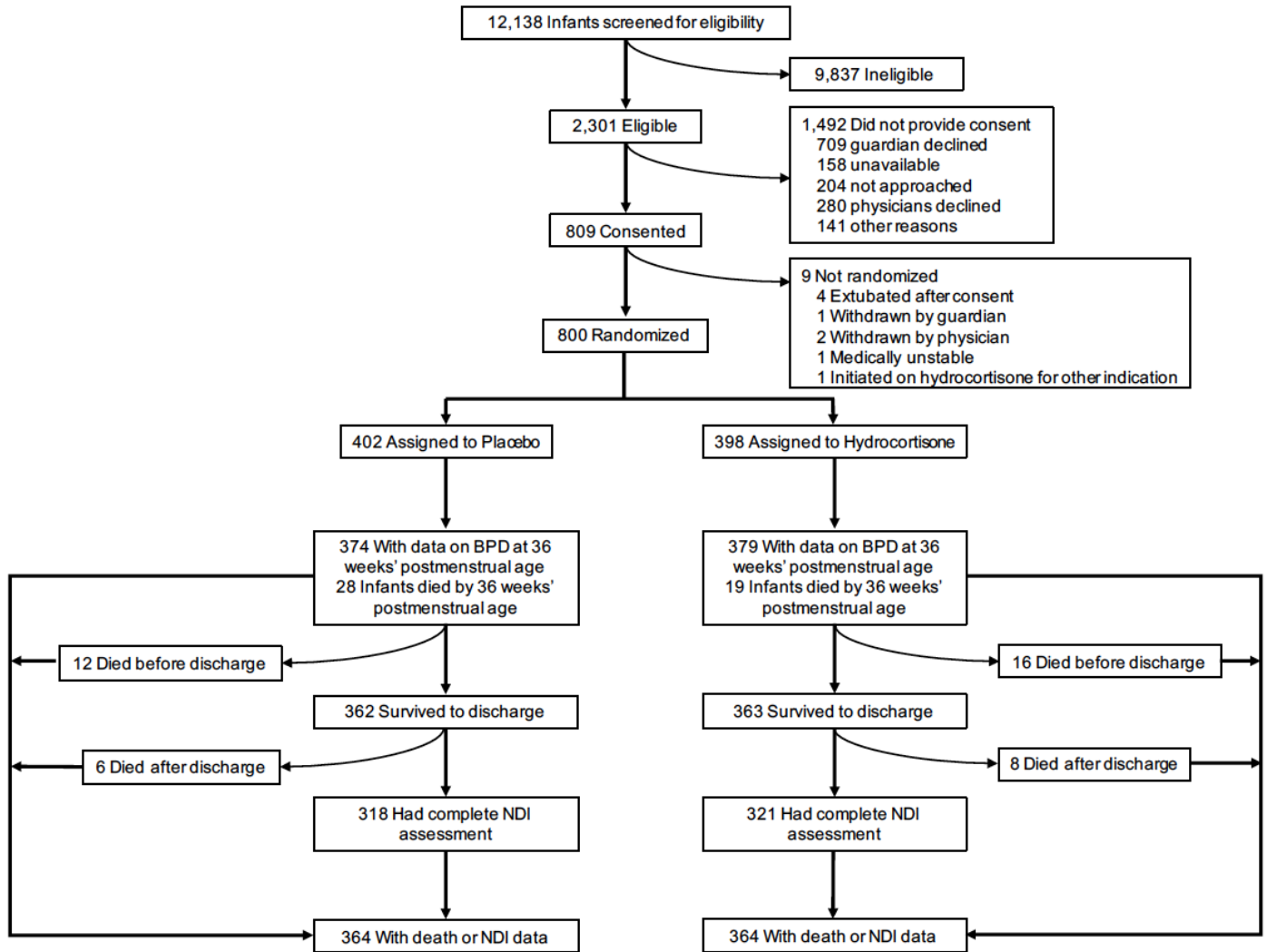
BPD: bronchopulmonary dysplasia; FiO₂: fraction of inspired oxygen; PDA: patent ductus arteriosus

eTable 3. Additional Clinical Characteristics by Quartile of Baseline Risk for Grades 2 to 3 BPD or Death and Exposure Group

	Quartile 1 18-45%		Quartile 2 46-53%		Quartile 3 54-65%		Quartile 4 66-84%		All	
	HC n=110	Placebo n=89	HC n=89	Placebo n=111	HC n=99	Placebo n=101	HC n=100	Placebo n=100	HC n=398	Placebo n=401
Days of mechanical ventilation ^a : median (IQR)	33 (23-46)	29 (20-40)	36 (27-51)	37 (30-51)	40 (27-56)	44.5 (33-58)	43 (31-60)	50 (38-66)	37 (27-54)	40 (30-55)
Highest FiO ₂ at enrollment: median (IQR)	32.5 (30-40)	33 (30-39)	45 (35-50)	39 (34-46)	51 (41-62)	50 (40-60)	73 (59-100)	70 (60-87)	47 (35-63)	45 (35-60)
Extubation failure ^a : n/N (%)	11/109 (10)	5/87 (6)	13/88 (15)	15/108 (14)	13/90 (14)	14/89 (16)	21/91 (23)	17/88 (19)	58/378 (15)	51/372 (14)
Open label dexamethasone exposure: n/N (%)	35/109 (32)	21/87 (24)	27/88 (31)	37/108 (34)	42/90 (47)	50/89 (56)	46/91 (51)	48/88 (55)	150/378 (40)	156/372 (42)
Clinical chorioamnionitis: n/N (%)	24/109 (22)	12/89 (14)	19/89 (21)	24/111 (22)	12/99 (12)	17/100 (17)	10/100 (10)	12/100 (12)	65/397 (16)	65/400 (16)
Surgical PDA treatment: n/N (%)	21/110 (19)	9/89 (10)	22/89 (25)	18/111 (16)	11/99 (11)	16/101 (16)	13/100 (13)	14/100 (14)	67/398 (17)	57/401 (14)
Pharmacological PDA treatment: n/N (%)	58/110 (53)	38/89 (43)	39/89 (44)	52/111 (47)	39/99 (39)	48/101 (48)	37/100 (37)	45/100 (45)	173/398 (44)	183/401 (46)
Early onset sepsis: n/N (%)	2/110 (2)	0/89 (0)	1/89 (1)	1/111 (1)	5/99 (5)	2/101 (2)	1/100 (1)	2/100 (2)	9/398 (2)	5/401(1)
Late onset sepsis: n/N (%)	16/110 (15)	21/89 (24)	30/89 (34)	33/111 (28)	37/99 (37)	31/101 (31)	38/100 (38)	32/100 (32)	121/398 (30)	117/401 (29)

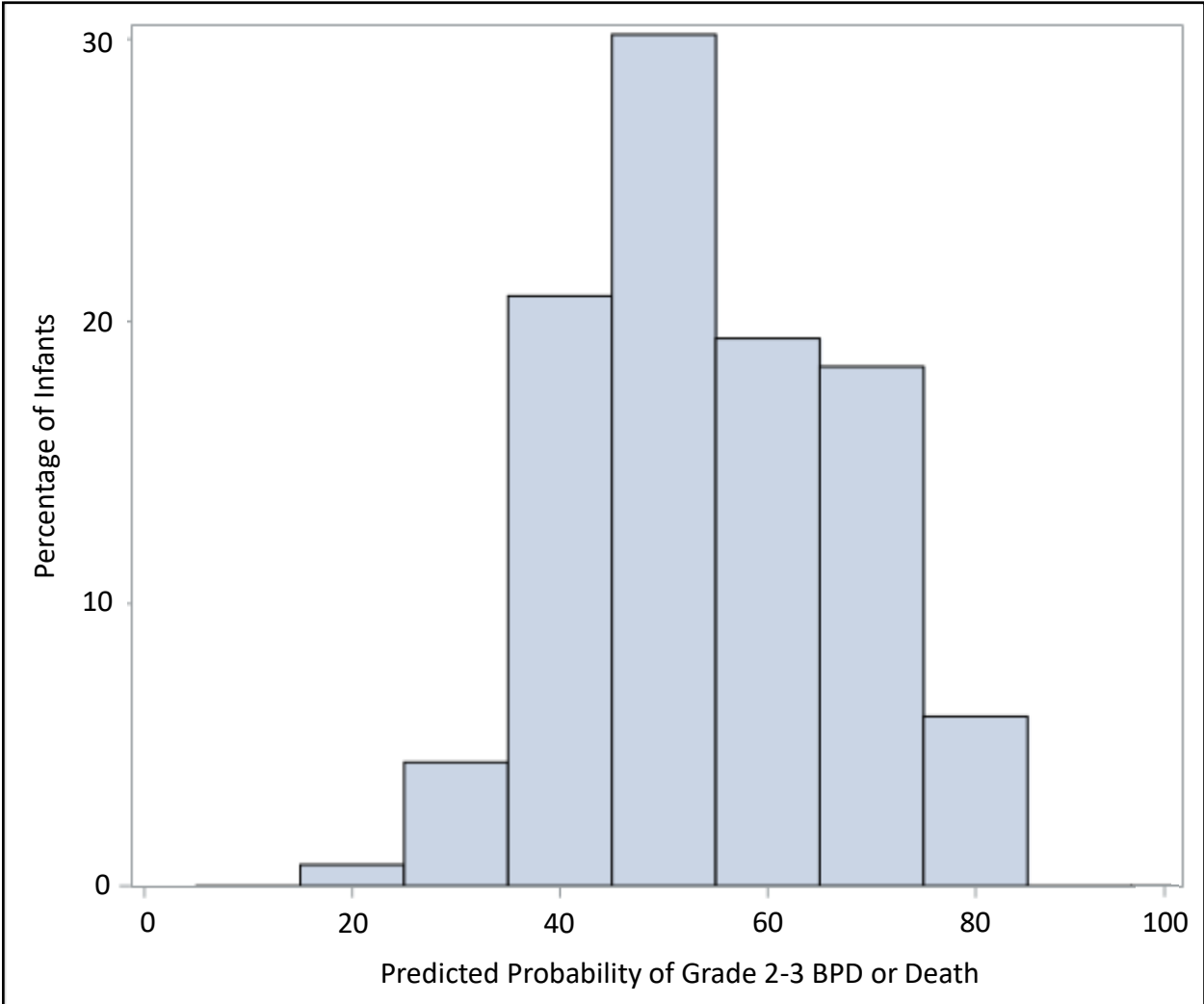
^aAmong surviving infants by 36 weeks' postmenstrual age; PDA: patent ductus arteriosus

eFigure 1. CONSORT Flow Diagram



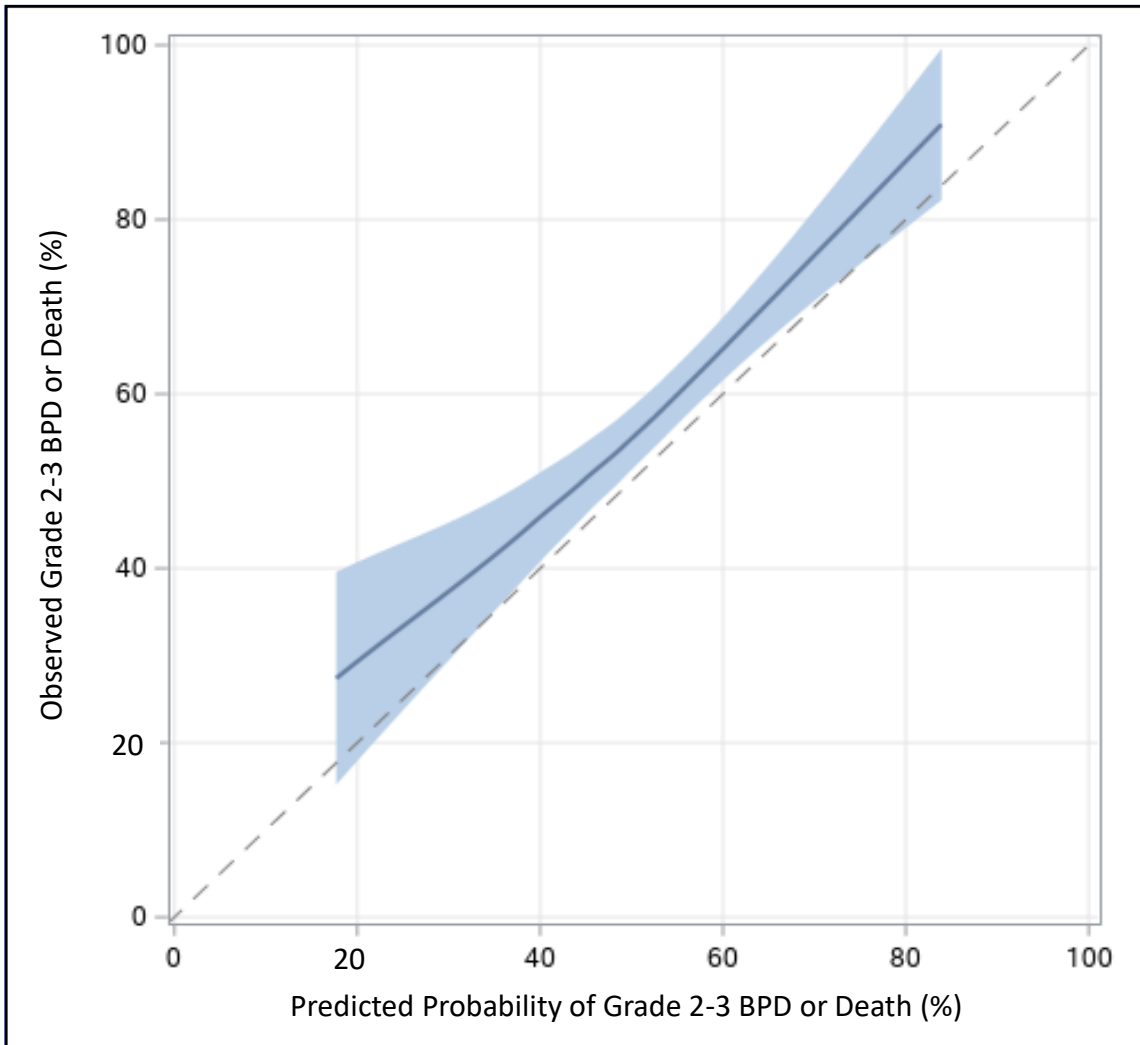
eFigure 1. CONSORT Flow Diagram detailing eligible, consented, and randomized infants followed by infants available for analysis of both safety and efficacy outcomes.

eFigure 2. Distribution of Predicted Probability of Grades 2 to 3 BPD or Death in the Enrolled Population



eFigure 2. Distribution of predicted probability of grade 2-3 BPD or death in the enrolled population. The mean predicted probability was 55% (range 18-84%).

eFigure 3. Calibration Plot of Association of Estimated Probability of Grades 2 to 3 BPD or Death to the Observed Outcome of Grades 2 to 3 BPD or Death



eFigure 3. Calibration plot relating predicted probability of grade 2-3 BPD or death to the observed outcome of grade 2-3 BPD or death. The ratio of observed to expected outcomes was 1.09.