








# Journal of Perinatology



## ARTICLE

# Postnatal maximal weight loss, fluid administration, and outcomes in extremely preterm newborns

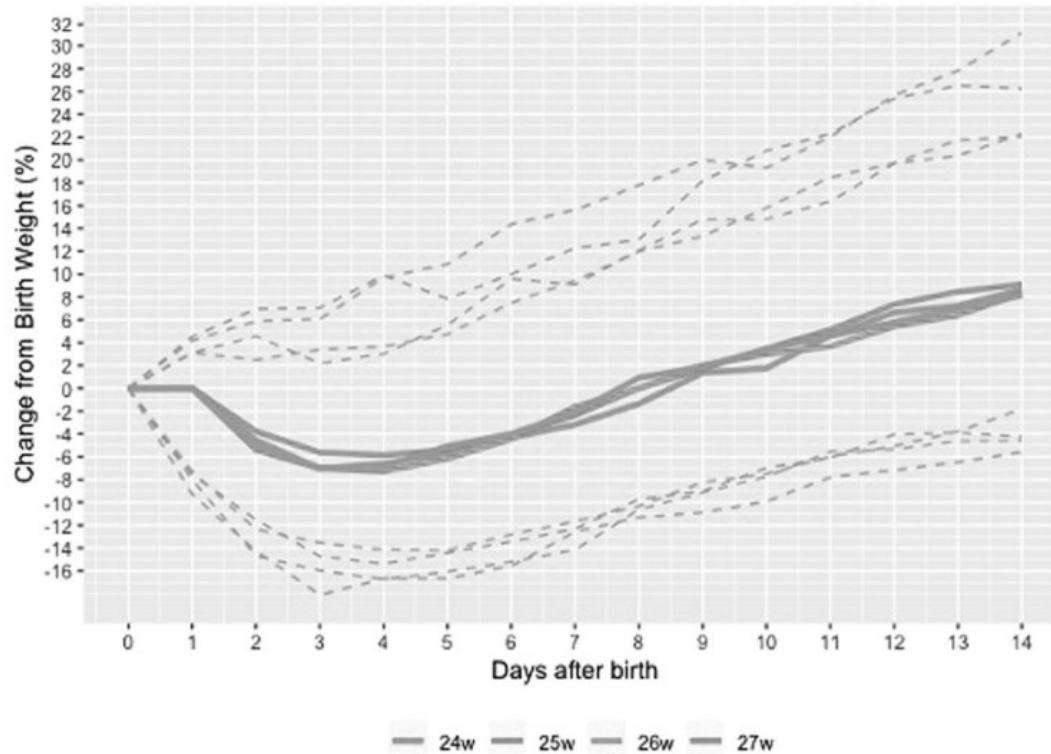
Gregory C. Valentine <sup>1,2,5</sup>✉, Krystle M. Perez<sup>1,5</sup>, Thomas R. Wood <sup>1</sup>, Dennis E. Mayock <sup>1</sup>, Bryan A. Comstock<sup>3</sup>, Mihai Puia-Dumitrescu <sup>1</sup>, Patrick J. Heagerty<sup>3</sup> and Sandra E. Juul <sup>1,4</sup>

**Table 1.** Maternal and infant demographics and factors associated with maximal weight loss category by day 7 in infants surviving for at least 7 days.

Maternal or infant factor	>15% maximum weight loss	15–5% maximum weight loss	<5% maximum weight loss	<i>p</i> value <sup>b</sup>
Total number of infants surviving to day 7	193 (22.9)	457 (54.3)	192 (22.8)	–
Maternal factors				
Maternal age (years)	28.6 (6.3)	29.0 (6.2)	29.6 (6.0)	0.39
Multiple gestation: Yes	59 (27.1)	116 (53.2)	43 (19.7)	0.057
Chorioamnionitis: Yes	20 (18.3)	69 (63.3)	20 (18.3)	0.85
Prenatal steroids				
0 Doses	21 (23.6)	47 (52.8)	21 (23.6)	0.20
1 Dose	38 (23.9)	92 (57.9)	29 (18.2)	
2 Doses	120 (22.9)	281 (53.6)	123 (23.5)	
3+ Doses	14 (20.0)	37 (52.9)	19 (27.1)	
Pregnancy-induced hypertension: Yes	9 (14.0)	30 (46.9)	25 (39.1)	<0.001
Pre-eclampsia: Yes	10 (8.1)	65 (52.8)	48 (39.0)	<0.001
Cesarean delivery: Yes	126 (21.7)	306 (52.7)	149 (25.6)	<0.001
Infant factors				
Gestational age (weeks)	25.3 (1.1)	25.6 (1.1)	25.5 (1.1)	0.22
Birthweight (g)	861 (178)	821 (178)	706 (192)	<0.001
5-minute Apgar (median, IQR)	7 (5–8)	7 (5–8)	7 (5–8)	0.75
10-minute Apgar (median, IQR)	7 (6–8)	7 (6–8)	7 (6–8)	0.76
Gestational age by week <sup>a</sup>				
24 weeks	57 (28.6)	96 (48.2)	46 (23.1)	Reference
25 weeks	47 (21.2)	122 (55.5)	53 (23.9)	0.40
26 weeks	54 (26.5)	104 (51.0)	46 (22.5)	0.90
27 weeks	35 (16.1)	135 (62.2)	47 (21.7)	0.13

Maternal or infant factor	>15% maximum weight loss	15–5% maximum weight loss	<5% maximum weight loss	p value <sup>b</sup>
Sex: female	87 (21.2)	230 (56.0)	94 (22.9)	0.22
Weight <10th percentile (i.e., SGA): Yes	14 (10.9)	49 (38.3)	65 (50.8)	<b>&lt;0.001</b>
Delayed cord clamping: Yes	79 (27.1)	166 (56.8)	47 (16.1)	0.89
Intubation/chest compressions: Yes	166 (24.4)	351 (51.5)	164 (24.1)	0.69
Apgar <5 at 5 mins: Yes	46 (28.6)	79 (49.1)	36 (22.4)	0.61
Postnatal factors in first week				
Day 0 fluid administration (mL/kg) <sup>c</sup>	58.6 (34.1)	54.0 (35.5)	61.1 (36.7)	0.49
Day 1 fluid administration (mL/kg) <sup>c</sup>	109 (33.6)	111 (39.9)	131 (43.8)	<b>&lt;0.001</b>
Average 7-day fluid (mL/kg/day) <sup>d</sup>	129 (18.2)	133 (21.0)	144 (26.5)	<b>&lt;0.001</b>
Treatment group				
Placebo	98 (23.7)	215 (51.9)	101 (24.4)	0.71
Epo	95 (22.2)	242 (56.5)	91 (21.3)	
Benzodiazepines: Yes	57 (23.4)	107 (43.9)	80 (32.8)	0.40
Narcotics: Yes	102 (21.2)	255 (53.0)	124 (25.8)	0.18
Steroids: Yes	17 (20.0)	37 (43.5)	31 (36.5)	0.01
Vasopressors: Yes	23 (15.8)	67 (45.9)	56 (38.4)	<b>&lt;0.001</b>
Spontaneous intestinal perforation: Yes	8 (32.0)	12 (48.0)	5 (20.0)	0.26
Culture positive sepsis: Yes	12 (25.5)	23 (48.9)	12 (25.5)	0.77
Indomethacin use: Yes	67 (20.4)	162 (49.3)	99 (30.2)	0.25

### Percentage Change from Birth Weight by Day



**Fig. 1 Median and 10th–90th percentile weight loss trajectories after birth, depicted and analyzed by gestational age in all  $n = 883$  infants.** All gestational ages had similar weight loss patterns after birth although variation was inversely related to gestational age. Dotted lines represent 10th–90th percentile range.

**Table 2.** Maximal weight loss characteristics for all included infants by gestational age.

Maximal weight loss in first 7 days	Gestational age (weeks)			
	24 (n = 219)	25 (n = 232)	26 (n = 208)	27 (n = 224)
Mean ( $\pm$ SD) <sup>a, b</sup>	11.2 (7.8)	10 (7.1)	10.7 (6.7)	9.4 (5.7)
CoV <sup>a</sup>	69.5	71.0	61.9	58.6
10th-90th Percentile <sup>a</sup>	21.0 to 0.0	18.2 to 0.0	19.0 to 1.8	16.5 to 0.0
Median (IQR) Day of Max Weight Loss	3 (2-5)	3 (2-5)	3 (2-4)	3 (2-4)
Median (IQR) Day for Surpassing Birth Weight	5 (2-9)	4 (1-9)	5 (1-9)	5 (1-9)

CoV Coefficient of variance, IQR Interquartile range, SD Standard deviation.

<sup>a</sup>Data presented as percentiles.

<sup>b</sup>After adjusting for treatment group, each additional completed week of gestation was associated with a 0.55% smaller maximum weight change from birth weight (95% CI 0.14–0.96%,  $p = 0.009$ ).

**Table 3.** Examining MWL categories and odds of in-hospital outcomes of infants surviving at least 7 days including adjustment for TFA.

Event	n/N (%)	Odds Ratio (95%CI)	p value
Death before discharge (N = 838)			
>15% Weight Loss	11/191 (5.8)	Reference	–
5–15% Weight Loss	23/455 (5.1)	0.78 (0.36–1.66)	0.52
<5% Weight Loss	24/192 (12.5)	1.36 (0.59–3.15)	0.47
Any Day 7–9 ICH (N = 817)			
>15% Weight Loss	58/188 (30.8)	Reference	–
5–15% Weight Loss	147/441 (33.3)	1.16 (0.79–1.70)	0.44
<5% Weight Loss	68/188 (36.2)	1.23 (0.77–1.96)	0.39
Severe Day 7–9 ICH (N = 817)			
>15% Weight Loss	21/188 (11.2)	Reference	–
5–15% Weight Loss	44/441 (10.0)	0.92 (0.54–1.57)	0.76
<5% Weight Loss	20/188 (10.6)	0.86 (0.43–1.74)	0.68
NEC (N = 842)			
>15% Weight Loss	17/193 (8.8)	Reference	–
5–15% Weight Loss	21/457 (4.6)	0.49 (0.25–0.98)	<b>0.04</b>
<5% Weight Loss	21/192 (10.9)	1.01 (0.50–2.06)	0.97
Severe BPD (N = 842)			
>15% Weight Loss	124/193 (64.2)	Reference	–
5–15% Weight Loss	271/457 (59.3)	0.88 (0.62–1.25)	0.48
<5% Weight Loss	122/192 (63.5)	0.88 (0.56–1.37)	0.56
PDA requiring surgery (N = 841)			
>15% Weight Loss	23/193 (11.9)	Reference	–
5–15% Weight Loss	56/456 (12.3)	1.03 (0.61–1.75)	0.91
<5% Weight Loss	19/192 (9.9)	6.19 (0.31–1.23)	0.17

All models adjusted for TFA, vasopressor use in first week after birth, weight <10th percentile (SGA), and postnatal steroids in the first week after birth, gestational age, and treatment group.

All data presented as n (%), Mean ± SD unless indicated differently within the table.

BPD Bronchopulmonary dysplasia, ICH Intracranial hemorrhage, PDA Patent ductus arteriosus, SGA Small-for-gestational age, NEC Necrotizing enterocolitis.

Bold values represent statistically significant values.

**Table 4.** Examining TFA categories and odds of in-hospital outcomes of infants surviving at least 7 days including adjustment for MWL.

Event	n/N = (%)	Odds ratio (95% CI)	p value
Death before discharge (N = 838)			
<120 mL/kg birthweight/day fluids	9/229 (3.9)	Reference	–
120–150 mL/kg birthweight/day fluids	30/427 (7.0)	1.40 (0.65–3.01)	0.39
>150 mL/kg birthweight/day fluids	19/182 (10.4)	1.51 (0.61–3.75)	0.37
Any Day 7–9 ICH (N = 817)			
<120 mL/kg birthweight/day fluids	65/226 (28.8)	Reference	–
120–150 mL/kg birthweight/day fluids	136/416 (32.7)	0.99 (0.68–1.45)	0.97
>150 mL/kg birthweight/day fluids	72/175 (41.1)	1.19 (0.73–1.92)	0.49
Severe Day 7–9 ICH (N = 817)			
<120 mL/kg birthweight/day fluids	23/226 (10.2)	Reference	–
120–150 mL/kg birthweight/day fluids	37/416 (8.9)	0.66 (0.37–1.19)	0.17
>150 mL/kg birthweight/day fluids	25/175 (14.3)	0.92 (0.44–1.90)	0.81
NEC (N = 842)			
<120 mL/kg birthweight/day fluids	9/229 (3.9)	Reference	–
120–150 mL/kg birthweight/day fluids	30/427 (7.0)	1.99 (0.89–4.46)	0.10
>150 mL/kg birthweight/day fluids	19/182 (10.4)	3.22 (1.40–7.42)	<b>0.006</b>
Severe BPD (N = 842)			
<120 mL/kg birthweight/day fluids	140/229 (61.1)	Reference	–
120–150 mL/kg birthweight/day fluids	260/430 (60.5)	0.78 (0.55–1.10)	0.16
>150 mL/kg birthweight/day fluids	117/183 (63.9)	0.69 (0.44–1.09)	0.11
PDA requiring surgery (N = 841)			
<120 mL/kg birthweight/day fluids	16/229 (7.0)	Reference	–
120–150 mL/kg birthweight/day fluids	44/430 (10.2)	1.08 (0.58–2.02)	0.8
>150 mL/kg birthweight/day fluids	38/182 (20.9)	2.14 (1.10–4.15)	<b>0.03</b>

All models adjusted for MWL, vasopressor use in first week after birth, weight <10th percentile (SGA), and postnatal steroids in the first week after birth, gestational age, and treatment group.

All data presented as n (%), Mean ± SD unless indicated differently within the table.




BPD Bronchopulmonary dysplasia, ICH Intracranial hemorrhage, PDA Patent ductus arteriosus, SGA Small-for-gestational age, NEC Necrotizing enterocolitis. Bold values represent statistically significant values.





## ARTICLE

# Blood pressure values and hypotension management in extremely preterm infants: a multi-center study

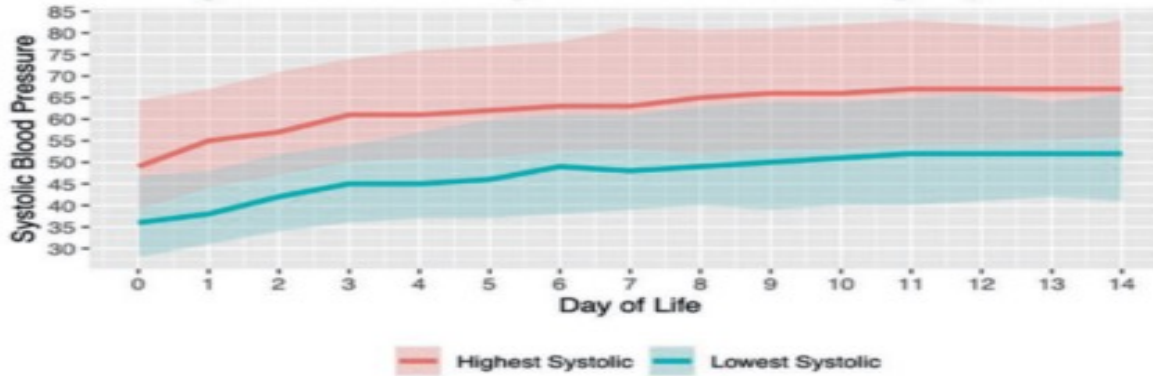
Eric S. Peeples <sup>1,2</sup> , Bryan A. Comstock<sup>3</sup>, Patrick J. Heagerty<sup>3</sup>, Sandra E. Juul <sup>4</sup> and Preterm Erythropoietin Neuroprotection (PENUT) Trial Investigators\*

**Table 1.** Demographic data by treatment with vasoactive infusions (VI) and/or hydrocortisone (HC) within the first 14 days of life.

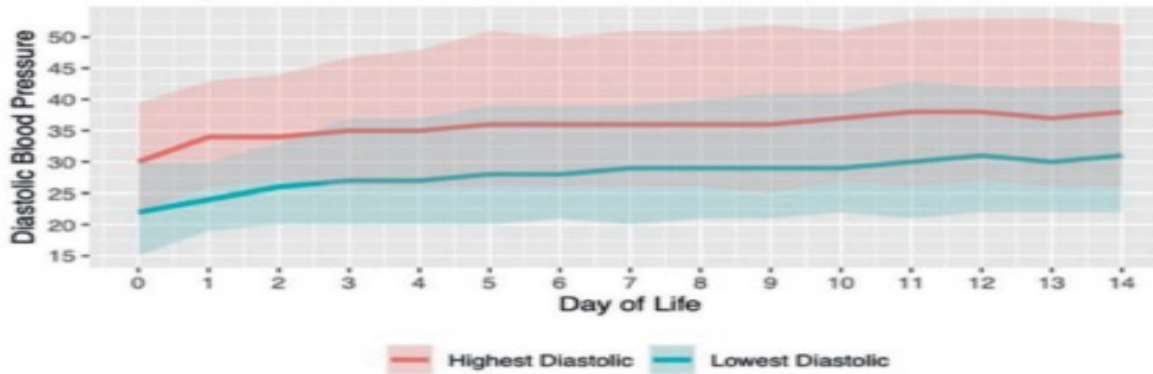
	<b>Neither n = 602</b>	<b>HC only n = 32</b>	<b>VI only n = 185</b>	<b>VI + HC N = 117</b>
Gestational age (GA), mean $\pm$ SD weeks	26.1 $\pm$ 1.2	25.8 $\pm$ 1.0	25.4 $\pm$ 1.1	25.4 $\pm$ 1.0
24 0/7–24 6/7 weeks*	118 (19.6%)	7 (21.9%)	65 (35.1%)	42 (35.9%)
25 0/7–25 6/7 weeks*	124 (20.6%)	12 (37.5%)	68 (36.8%)	41 (35.0%)
26 0/7–26 6/7 weeks*	169 (28.1%)	8 (25.0%)	25 (13.5%)	19 (16.2%)
27 0/7–27 6/7 weeks*	191 (31.7%)	5 (15.6%)	27 (14.6%)	15 (12.8%)
Birth weight, grams*	840 (706, 968)	780 (630, 908)	740 (610, 850)	700 (581, 810)
Weight <10th percentile for GA*	73 (12.1%)	6 (18.8%)	34 (18.4%)	34 (29.1%)
Male	310 (51.5%)	17 (53.1%)	93 (50.3%)	68 (58.1%)
Prenatal magnesium sulfate	498 (82.7%)	26 (81.3%)	132 (71.4%)	93 (79.5%)
Prenatal steroids	547 (90.9%)	30 (93.8%)	160 (86.5%)	105 (89.7%)
Chorioamnionitis	91 (15.1%)	2 (6.3%)	16 (8.6%)	13 (11.1%)
Pregnancy-induced hypertension	117 (19.4%)	7 (21.9%)	40 (21.6%)	29 (24.8%)
Cesarean delivery*	394 (65.4%)	26 (81.3%)	138 (74.6%)	93 (79.5%)
Delayed cord clamping	210 (34.9%)	16 (50.0%)	51 (27.6%)	41 (35.0%)
Apgar score at 5 min*	7 (6, 8)	7 (6, 8)	6 (3, 7)	6 (4, 7)
Received erythropoietin	318 (52.8%)	12 (37.5%)	93 (50.3%)	53 (45.3%)
Fluids day 1 of life, mL/kg *	109 (91, 126)	110 (87, 119)	132 (110, 154)	129 (98, 165)
Fluids day 1–3 of life, mL/kg *	326 (270, 377)	331 (261, 358)	397 (330, 462)	386 (287, 492)
Age at vasopressor initiation, days	–	–	2 (1, 3)	2 (1, 4)
Vasopressor duration, days	–	–	4 (3, 8)	7 (4, 11)
Age at hydrocortisone initiation, days	–	9 (2, 12)	–	4 (2, 10)
Hydrocortisone duration, days	–	20 (7, 36)	–	16 (6, 35)
Death prior to discharge	36 (6.0%)	1 (3.1%)	34 (18.4%)	33 (28.2%)

Continuous variables described as median (interquartile range), binary variables as n (column %), GA as n (row %). Variables with asterisk (\*) were statistically different ( $p < 0.05$ ) between groups.

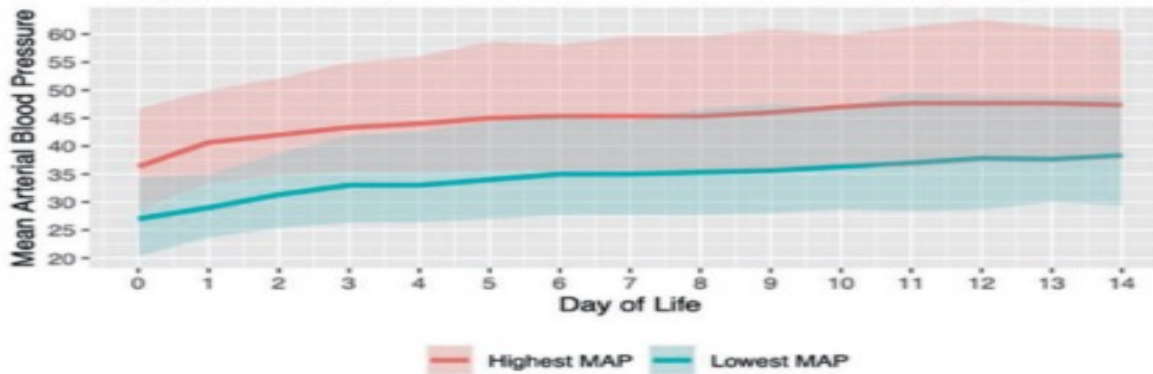
### Highest and Lowest Systolic Blood Pressure by Day of Life

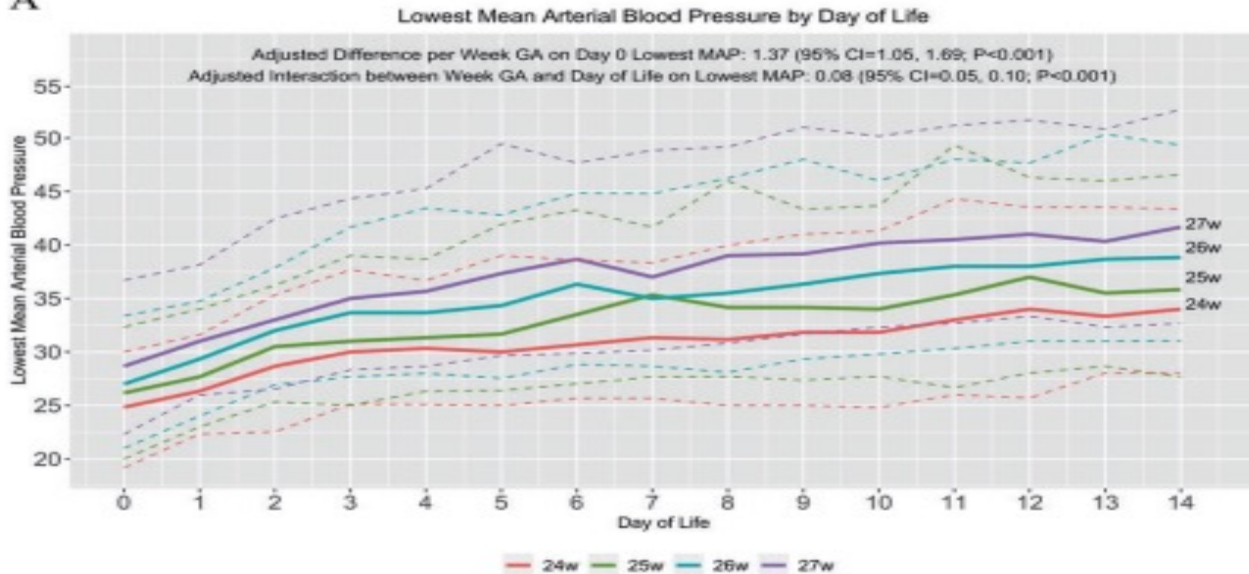
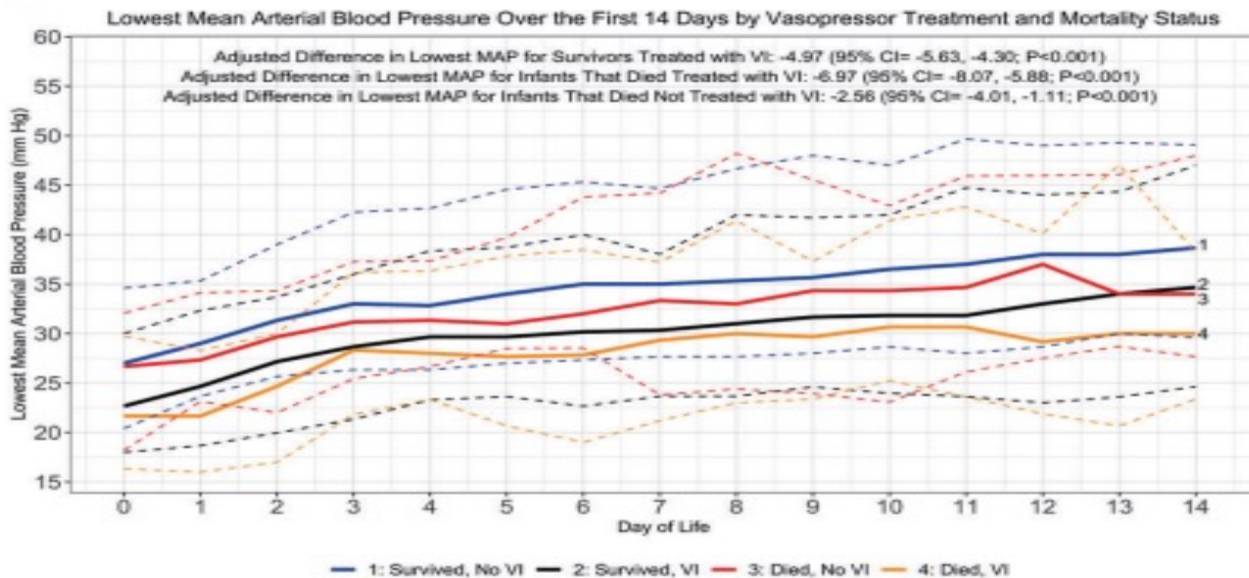


### Highest and Lowest Diastolic Blood Pressure by Day of Life

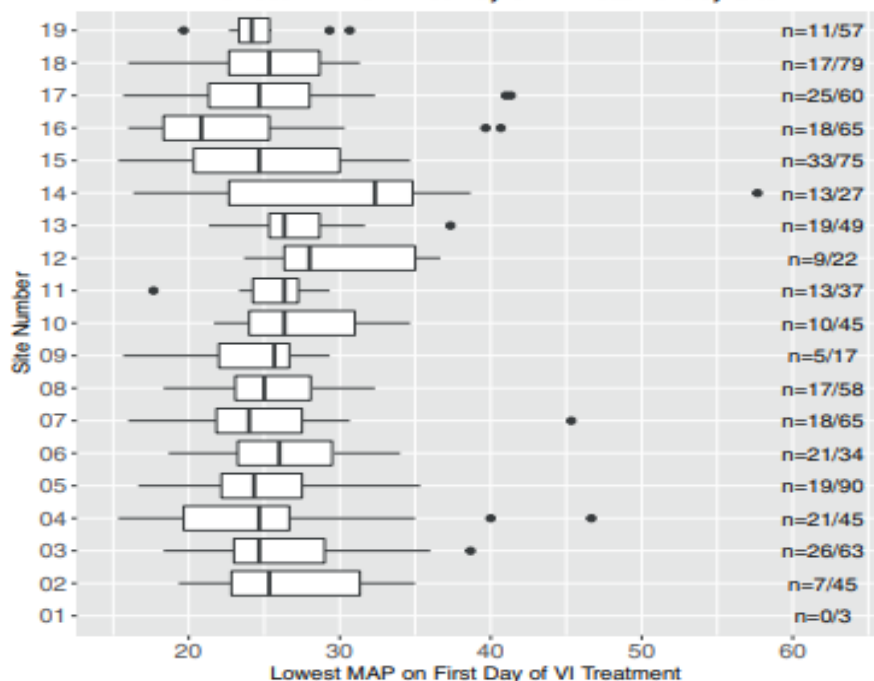


### Highest and Lowest Mean Arterial Blood Pressure by Day of Life

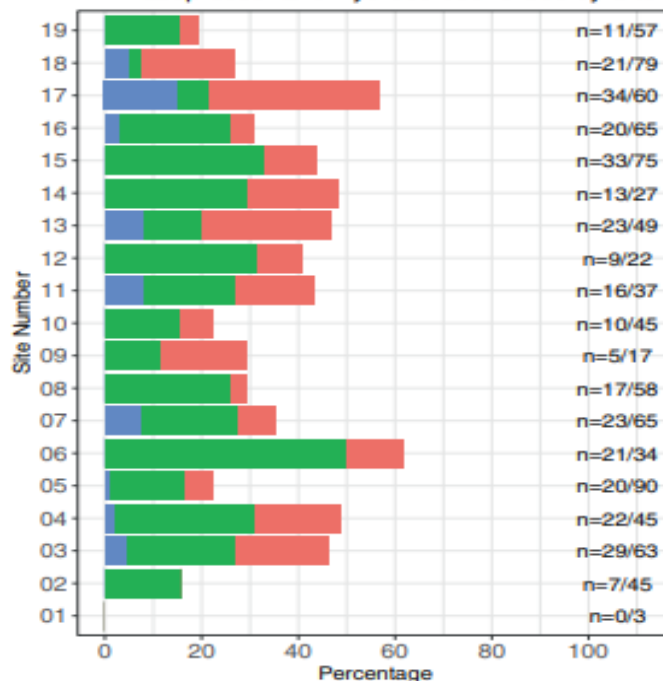


**A****B**

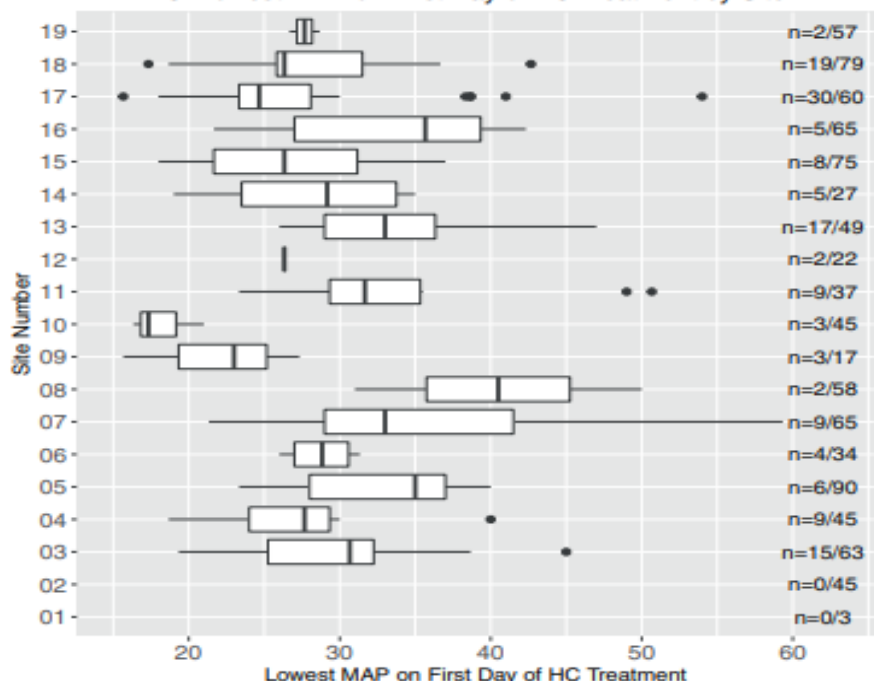
**A: Lowest MAP on First Day of VI Treatment by Site**



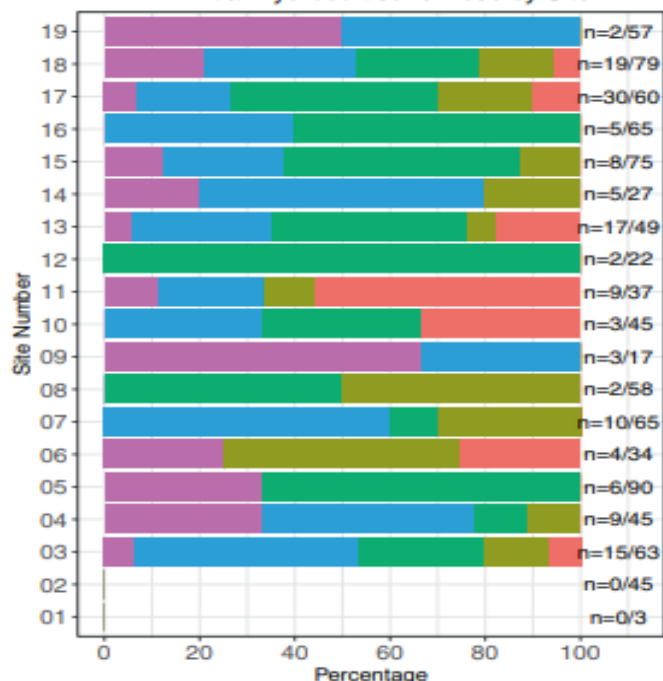
**B: Vasopressor and Hydrocortisone Use by Site**

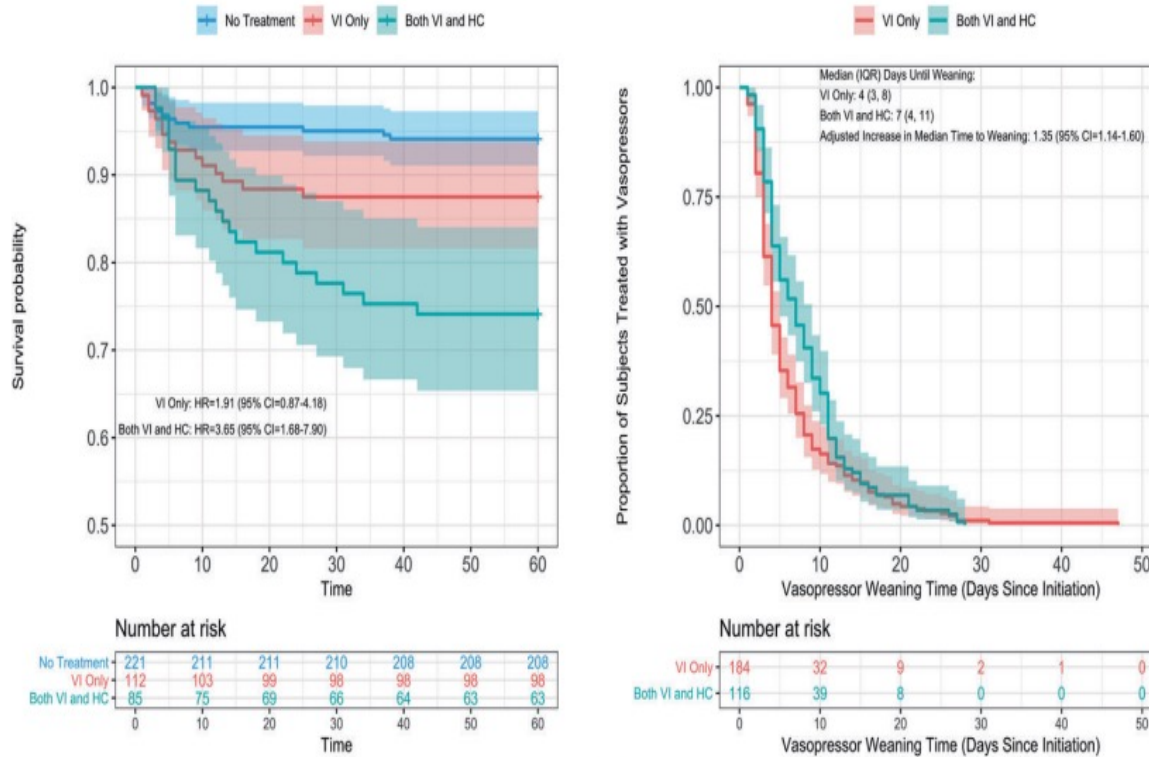


**C: Lowest MAP on First Day of HC Treatment by Site**



**D: Initial Hydrocortisone Dose by Site**








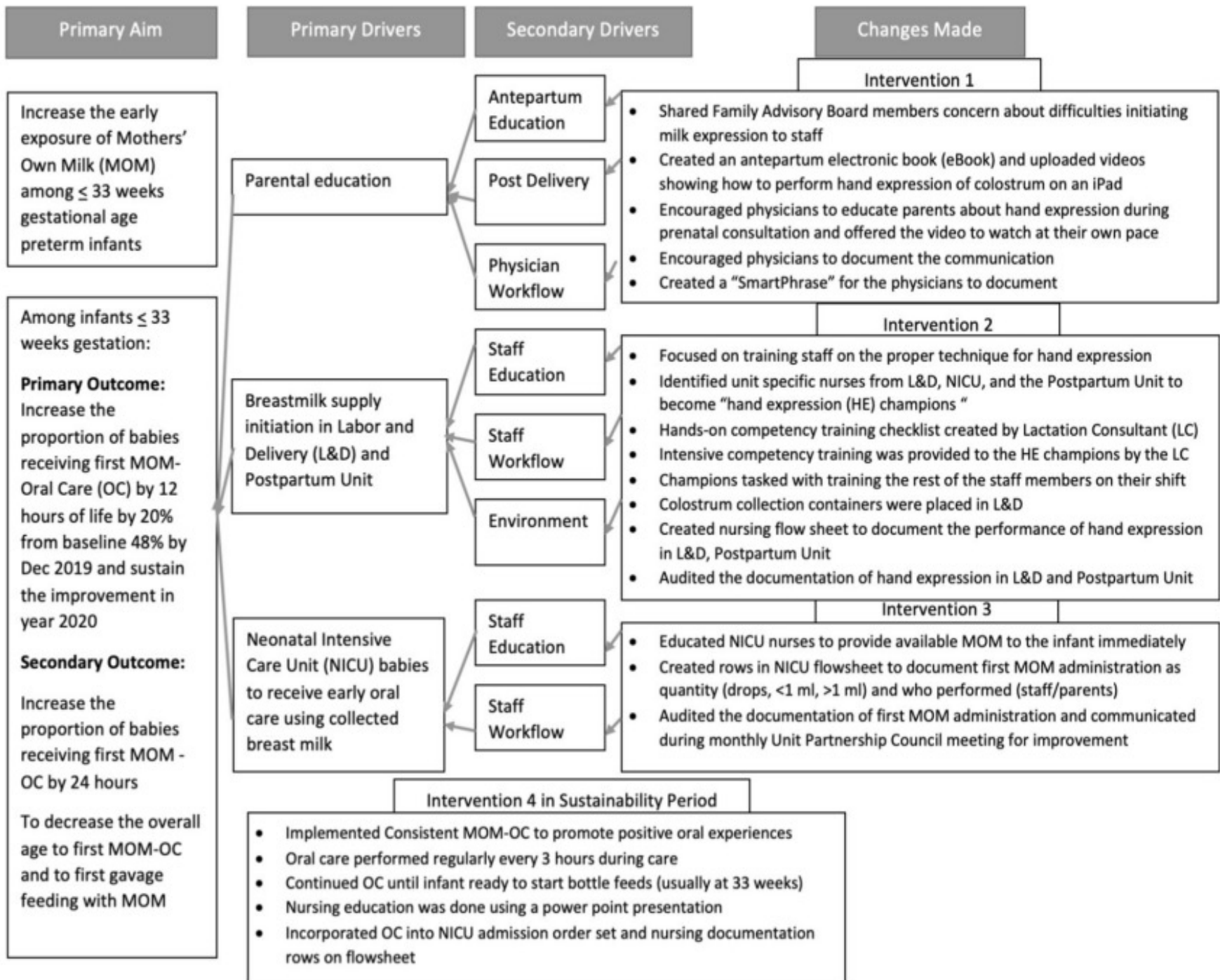
**Fig. 4 Survival and time until weaning off of vasoactive infusions (VI), by treatment group.** Kaplan–Meier curve of (left panel) overall survival among those infants exposed to VI only, VI with hydrocortisone (HC), or no treatment; and (right panel) time-until weaning off of VI between the VI only and VI with HC groups. The HC only group was not included due to sample size.



## QUALITY IMPROVEMENT ARTICLE

# Increasing early exposure to mother's own milk in premature newborns

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**Table 1.** Demographic and Relevant Clinical Variables in three study periods.

		<b>Baseline period Jan 2017–Dec 2017</b>	<b>Implementation period Jan 2018–Dec 2019</b>	<b>Sustainability period Jan 2020–Mar 2021</b>	<b>p value</b>
<i>N</i>		46	66	46	
Maternal age, mean (SD)		33 (5)	33 (5)	33 (5)	0.79
Race <i>N</i> (%)	Asian	30 (64)	34 (52)	29 (63)	0.31
	Black	2 (4)	1 (2)	1 (2)	
	Hispanic/Latino	5 (11)	7 (11)	7 (15)	
	Non-Hispanic White	7 (17)	16 (24)	29 (17)	
	Other	2 (4)	8 (12)	1 (2)	
Marital status <i>N</i> (%)	Married	44 (96)	59 (89)	38 (83)	0.13
Insurance type <i>N</i> (%)	Public	0 (0)	9 (14)	3 (7)	0.026
Mothers language <i>N</i> (%)	English	44 (94)	55 (83)	42 (93)	0.13
	No English	3 (6)	11 (17)	3 (7)	
Prenatal consult <i>N</i> (%)	Yes	37 (80)	50 (76)	39 (85)	0.5
Preeclampsia/hypertension <i>N</i> (%)	Yes	6 (13)	18 (27)	14 (30)	0.11
	No	40 (87)	48 (73)	32 (70)	
Clinical chorioamnionitis <i>N</i> (%)	Yes	14 (30)	2 (3)	7 (15)	<0.001
Maternal diabetes <i>N</i> (%)	Yes	5 (11)	17 (26)	11 (24)	0.14
Complete antenatal steroids <i>N</i> (%)	Yes	35 (77)	59 (89)	32 (70)	0.028
Multiple gestation <i>N</i> (%)	Yes	12 (26)	15 (23)	11 (24)	0.64
Delivery mode <i>N</i> (%)	C-Sec	33 (72)	47 (71)	37 (80)	0.50
General anesthesia <i>N</i> (%)	Yes	5 (11)	6 (9)	2 (4)	0.49
Prior breastfeeding <i>N</i> (%) <sup>a</sup>	Yes	18 (38)	20 (30)	20 (43)	0.002
	No	28 (61)	35 (53)	26 (57)	
Infant sex	Female	22 (48)	31 (47)	26 (57)	0.57
	Male	24 (52)	35 (53)	20 (43)	
Birth weight in grams, mean (SD)		1373 (398)	1462 (434)	1305 (390)	0.13
Gestational age, mean (SD)	Weeks	30 (2.5)	30.9 (2.0)	30.0 (2.3)	0.062
APGAR1, median (IQR)		7 (4, 8)	7 (5, 8)	6 (3, 7)	0.055
APGAR5, median (IQR)		9 (7, 9)	8 (8, 9)	8 (7, 9)	0.35
First skin to skin care, median (IQR)	Hours of life	27 (15, 116)	30 (15, 46)	20 (8, 41)	0.078
Total skin to skin care event, mean (SD)	Hours of life	47 (58)	38 (26)	54 (28)	0.098

<sup>a</sup>Prior breast feeding 11 unknowns in implementation period.

**Table 2.** Primary and secondary outcomes with confidence interval.

	Time to MOM, oral care, (hrs)			Time to MOM, first feeding (hrs)		
	Baseline	Implementation	Sustainability	Baseline	Implementation	Sustainability
<i>N</i>	46	66	46	46	66	46
Mean (SD), hrs	20.6 (25.5)	18.6 (23.6)	12.7 (11.5)	31.7 (16.5)	23.3 (12.6)	24.5 (8.7)
Difference (95% CI) <i>P</i> value	Reference category	-1.9 (-11.3, 7.3) <i>P</i> = 0.67	-7.8 (-15.9, 0.2) <i>p</i> = 0.06	Reference category	-8.4 (-13.3, -3.6) <i>P</i> = 0.001	-7.2 (-12.5, -1.9) <i>P</i> = 0.008
Median, hrs (25th-75th)	13 (7-21)	9 (5-22)	9 (4-19)	28 (20-42)	22 (15-31)	24 (19-31)
Difference (95% CI) <i>P</i> value	Reference category	-3.8 (-7.8, 0.3) <i>P</i> = 0.07	-3.8 (-8.2, 0.7) <i>P</i> = 0.10	Reference category	-6.0 (-11.7, -0.2) <i>P</i> = 0.04	-4.0 (-10.3, 2.3) <i>P</i> = 0.21
MOM Oral Care ≤ 12 h			MOM Oral Care ≤ 24 h			
	Baseline	Implementation	Sustainability	Baseline	Implementation	Sustainability
<i>N</i> (%)	22/46 (47.8%)	40/66 (60.6%)	32/46 (69.6%)	36/46 (78.3%)	51/66 (77.3%)	41/46 (89.1%)
Relative change <sup>a</sup> (95% CI) <i>P</i> value	Reference category	1.27 (0.89, 1.81) <i>P</i> = 0.20	1.45 (1.02, 2.08) <i>P</i> = 0.03	Reference category	0.99 (0.81, 1.21) <i>P</i> = 0.90	1.14 (0.95, 1.37) <i>P</i> = 0.15
Absolute change <sup>b</sup> (95% CI) ( <i>P</i> value)	Reference category	12.8% (-5.9, 31.4) <i>P</i> = 0.18	21.7% (2.1, 41.4) <i>P</i> = 0.03	Reference category	-1.0-16.6, 14.6) <i>P</i> = 0.90	10.9% (-5.1, 25.8) <i>P</i> = 0.16

<sup>a</sup>Relative change = (percent period 2 or 3)/percent period 1.

<sup>b</sup>Absolute change (percent period 2 or 3) – percent period 1.

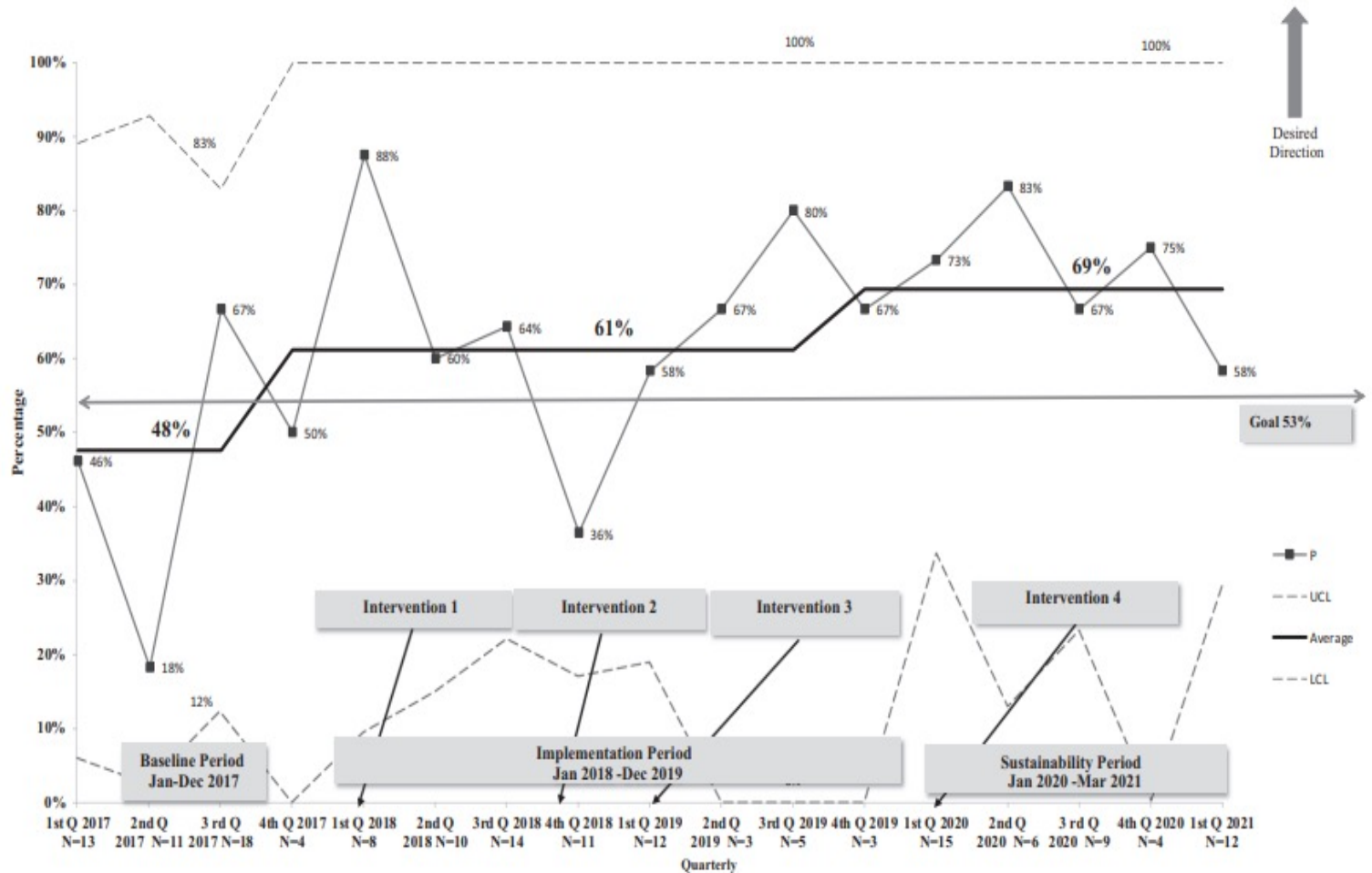
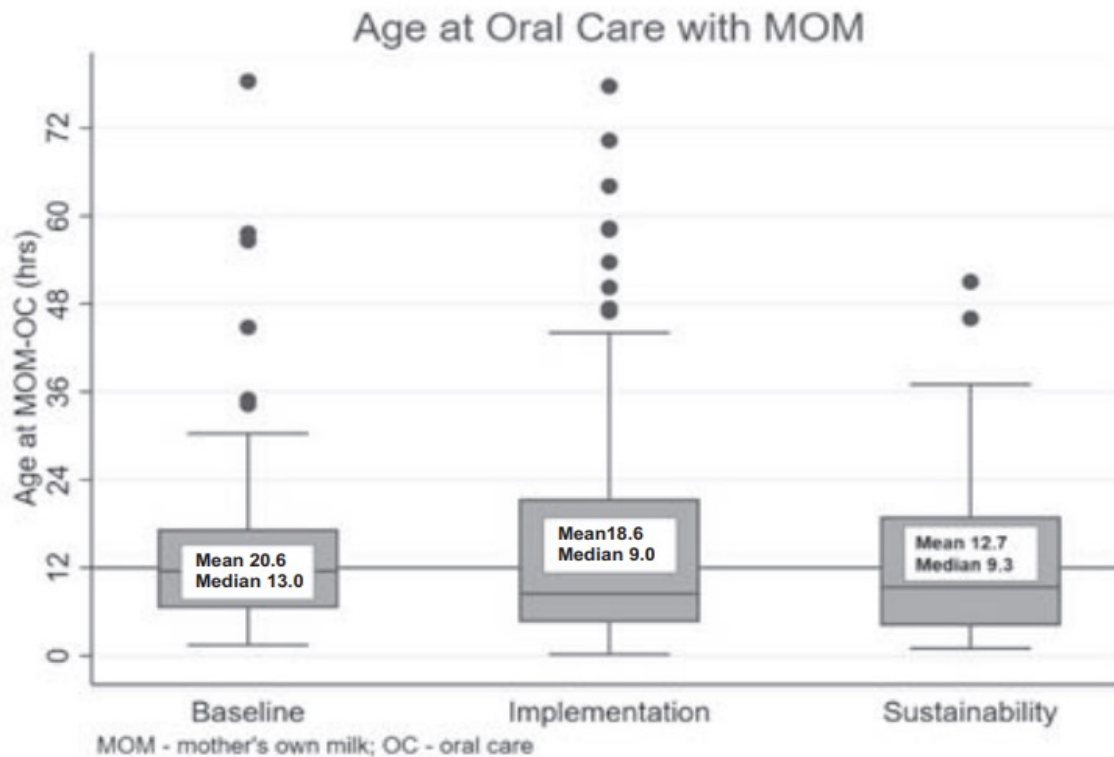


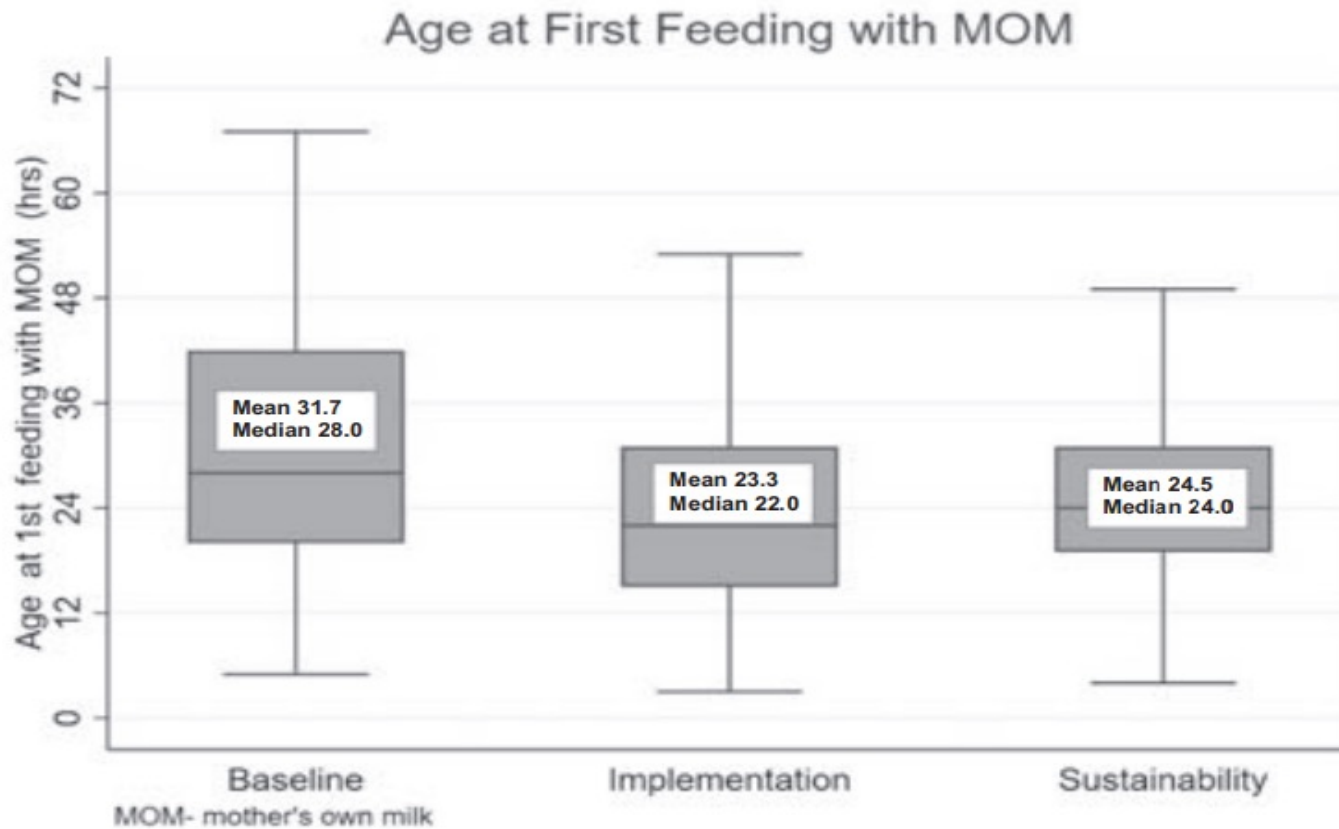
Fig. 2 Primary outcome: proportion of ≤33 weeks infants who received early MOM-OC p chart.

C



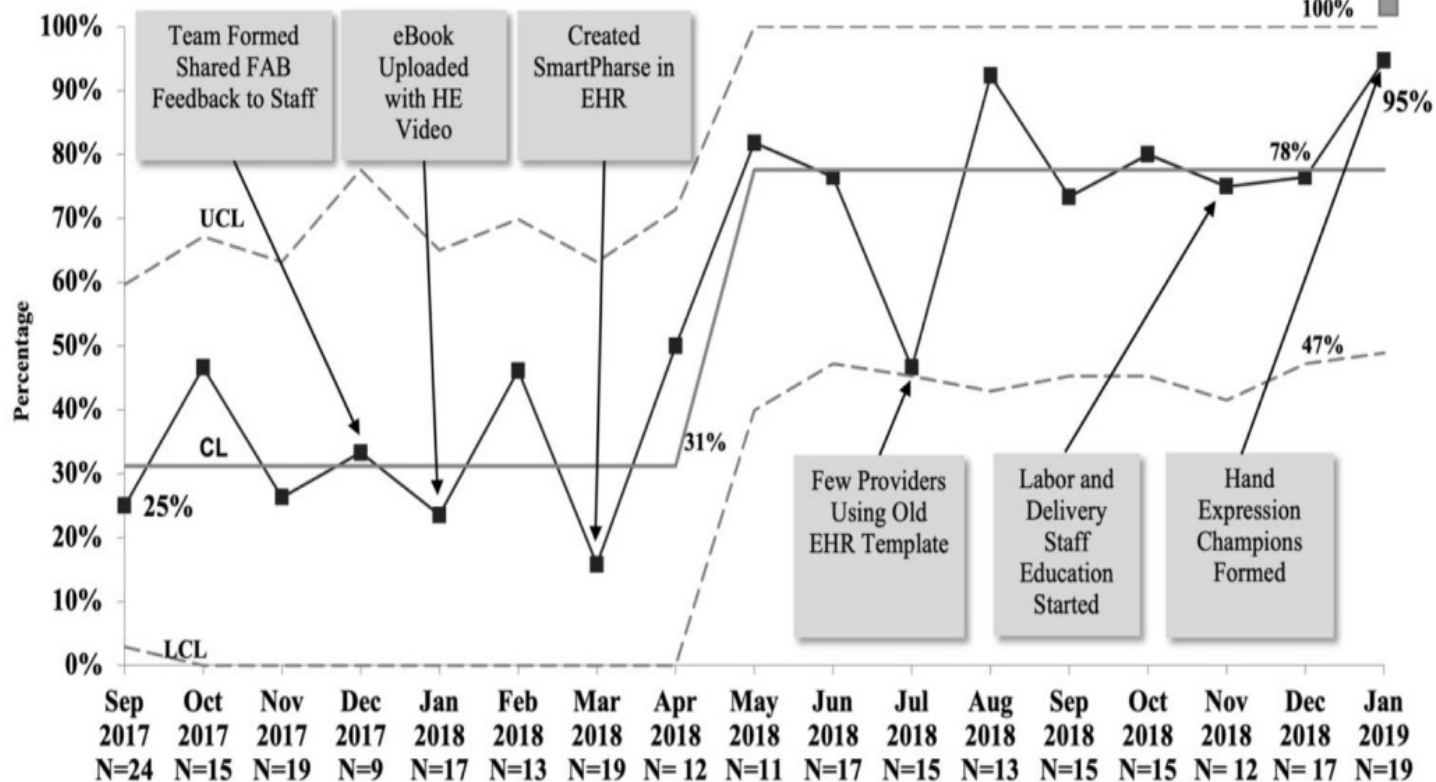
3 outliers with age >80 h was omitted from the graphic to expand the scale: 2 in the baseline and 1 in the implementation period

d



a

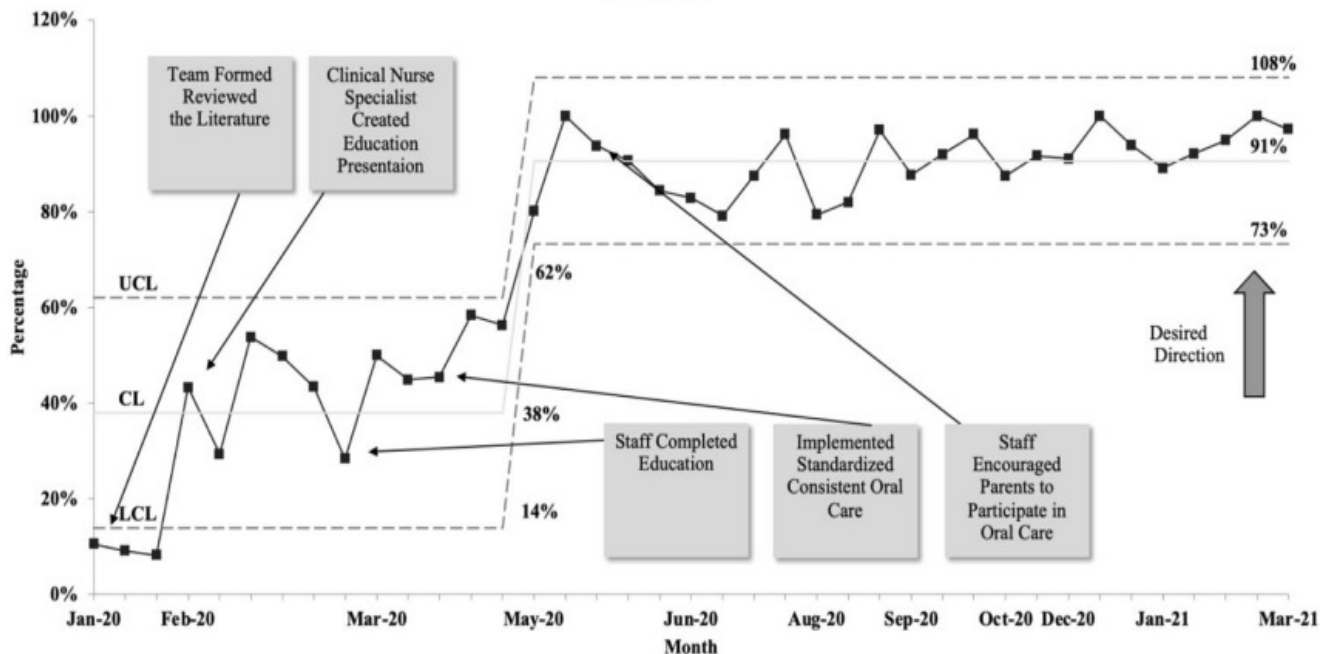
## Proportion Of Admission Notes With Hand Expression Communication Documentation



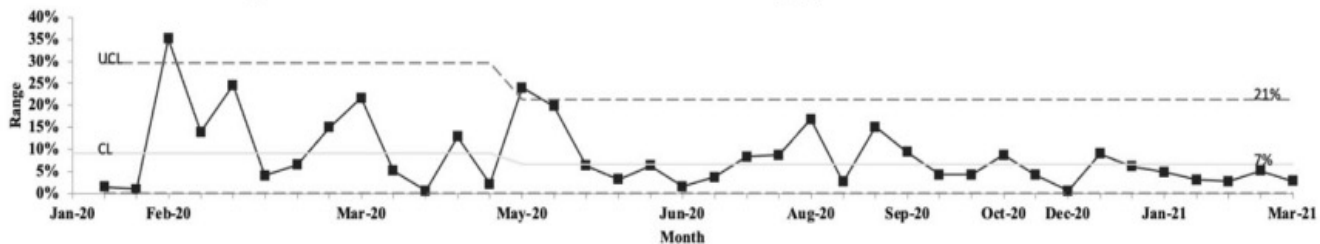
FAB- Family Advisory Board; HE -hand expression; EHR-electronic health record

b

Percentage of Consistent MOM Oral Care Received by  $\leq 33$  Weeks Infants  
X Chart



Percentage of Consistent MOM Oral Care Received by  $\leq 33$  Weeks Infants - mR Chart





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## ARTICLE

# Breast milk vs 24% sucrose for procedural pain relief in preterm neonates: a non-inferiority randomized controlled trial

Pradeep Kumar Velumula <sup>1</sup>✉, Faesal Elbakoush<sup>2,3</sup>, Carl Tabb Il<sup>2,3</sup>, Ahmad Farooqi<sup>4</sup>, Mirjana Lulic-Botica<sup>2,5</sup>, Sanket Jani <sup>2,3,4</sup>,  
Girija Natarajan<sup>2,3,4</sup> and Monika Bajaj <sup>2,3,4</sup>





## ARTICLE




# Implementation and outcomes of a standard dose dextrose gel protocol for management of transient neonatal hypoglycemia

Purnahamsi Desai <sup>1,2</sup>✉, Sourabh Verma <sup>1,2</sup>, Sweta Bhargava <sup>3</sup>, Marissa Rice <sup>4</sup>, Joanna Tracy <sup>2</sup> and Chanda Bradshaw <sup>1,2</sup>




## ARTICLE

# Pulmonary hemorrhage in extremely low birth weight infants: Significance of the size of left to right shunting through a valve incompetent patent foramen ovale




Jaclyn M. Kappico <sup>1</sup>✉, Rowena Cayabyab <sup>1</sup>, Mahmood Ebrahimi<sup>1</sup>, Merujan Y. Uzunyan<sup>2</sup>, Lorayne Barton<sup>1</sup>, Bijan Siassi<sup>1</sup> and Rangasamy Ramanathan <sup>1</sup>



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## ARTICLE

# Antimicrobial utilization in very-low-birth-weight infants: association with probiotic use

Joseph Y. Ting<sup>1,2</sup>, Eugene W. Yoon<sup>3</sup>, Carlos A. Fajardo<sup>4</sup>, Thierry Daboval <sup>5</sup>, Valérie Bertelle<sup>6</sup>, Prakesh S. Shah <sup>3,7</sup>  and Canadian Neonatal Network (CNN) Investigators\*