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Early Life Outcomes in Relation to Social Determinants of Health for Children Born Extremely Preterm

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Abstract

Objective—To characterize the relationships between social determinants of health (SDOH) and outcomes for children born extremely preterm.

Study Design—This is a cohort study of infants born at 22–26 weeks' gestation in NICHD Neonatal Research Network centers (2006–2017) who survived to discharge. Infants

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were classified by three maternal SDOH: education, insurance, and race. Outcomes included postmenstrual age (PMA) at discharge, readmission, neurodevelopmental impairment (NDI), and death post-discharge. Regression analyses adjusted for center, perinatal characteristics, neonatal morbidity, ethnicity, and two SDOH (eg, group comparisons by education adjusted for insurance and race).

Results—Of 7438 children, 5442 (73%) had at least one risk-associated SDOH. PMA at discharge was older (adjusted mean difference 0.37 weeks, 95% confidence interval (CI) 0.06–0.68) and readmission more likely (adjusted odds ratio (aOR) 1.27, 95% CI 1.12–1.43) for infants whose mothers had public/no insurance versus private. Neither PMA at discharge nor readmission varied by education or race. NDI was twice as likely (aOR 2.36, 95% CI 1.86–3.00) and death five times as likely (aOR 5.22, 95% CI 2.54–10.73) for infants with three risk-associated SDOH compared with those with none.

Conclusions—Children born to mothers with public/no insurance were older at discharge and more likely to be readmitted than those born to privately insured mothers. NDI and death post-discharge were more common among children exposed to multiple risk-associated SDOH at birth compared with those not exposed. Addressing disparities due to maternal education, insurance coverage, and systemic racism are potential intervention targets to improve outcomes for children born preterm.

Introduction

Social determinants of health (SDOH) are non-medical factors that influence health outcomes of children even before birth.(1, 2) Maternal SDOH relevant to childhood outcomes for children born preterm include education level,(3, 4) insurance status,(5, 6) and race(7, 8) as a marker of systemic racism. In one longitudinal birth cohort, SDOH accounted for 35% of the total variance in cognition for low birth weight children at 9 years while birth weight and gestational age accounted for only 9% of the variance.(9) In the ELGAN cohort, children whose mothers had low education levels were more likely to score 2 standard deviations below the norm for language, academic achievement, and executive functioning at 10 years.(10) Infant mortality in the United States varies by maternal insurance status with the lowest mortality rate in infants born to mothers with private insurance.(11)To optimize outcomes of children born preterm, it is necessary to identify and address SDOH associated with disadvantage.

Embedded within SDOH are structural determinants of health, such as systemic racism, which adversely impact health through epigenetic activity, psychologic stress, and inequities in education, housing, employment, or income.(12) Perinatal care in the United States is fraught with racism-rooted disparities.(7, 8, 13–15) The infant mortality rate is significantly higher for Black infants than White infants.(16, 17) Perinatal mortality disparities persist for well-educated Black mother-infant dyads compared with White dyads.(18–20) In a secondary analysis of the Assessment of Perinatal EXcellence study, the crude frequency of

adverse perinatal outcomes for term newborns differed by race; however, after adjusting for insurance status, the difference was no longer significant.(21) This highlights the need to consider multiple SDOH concurrently and to account for SDOH in analyses.

There is an opportunity to better understand how SDOH relate to outcomes of children born extremely preterm. The current study characterizes discharge characteristics, readmission occurrence, neurodevelopmental impairment (NDI), and death post-discharge through the lens of three SDOH exposures: race, education level, and insurance status.

Methods

This was a secondary analysis of a prospective cohort of infants born at $22^{0/7}$-$26^{6/7}$ weeks' gestation at NRN centers between January 1, 2006, and December 31, 2017, who survived to discharge. Infants were included if their mothers identified as either Black or White race. Self-reported maternal race was abstracted from the medical record to use as a marker for systemic racism.(19, 22) Infants whose mothers identified as American Indian or Alaskan Native, Asian, Native Hawaiian or Pacific Islander, and more than one race were not included due to constraints related to analyzing race as a binary variable. Follow-up occurred at 18–22 months' corrected age for infants born prior to July 2012 and at 22–26 months' corrected age for those born in July 2012 or later. To reduce loss to follow-up and minimize bias, NRN centers attempted to maintain contact between discharge and the comprehensive neurodevelopmental follow-up at 18–26 months' corrected age. Data collection for the NRN databases was approved by each site's institutional review board, and parental consent was obtained if required by the local institutional review board. Infants who were outborn, died prior to discharge, or who had major congenital anomalies were excluded.

Infants were classified by maternal SDOH at birth as binary variables: education (less than high school graduate or high school graduate), insurance status (public/none or private), and race (Black or White). Less than high school education, public/no insurance, and non-White race were considered SDOH exposures associated with social disadvantage and health disparities, henceforth referred to as risk-associated SDOH. Ethnicity was not analyzed as a separate SDOH due to concern for potential masking of differences given the Hispanic paradox,(23) an epidemiological phenomenon in which individuals of Hispanic ethnicity have better health outcomes than non-Hispanic individuals despite socioeconomic disadvantage in the United States.

Outcome Measures

The primary outcome was PMA at discharge. Secondary outcomes were PMA discharge quartile, discharge with oxygen, readmission, NDI, or death post-discharge. Neurodevelopmental follow-up included the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III), to assess cognitive, language, and motor skills. (24) NDI was defined as any of the following: moderate or severe cerebral palsy, gross motor function classification system level 2 or greater,(25) Bayley-III cognitive composite score <85, bilateral blindness with no or some functional vision, or hearing impairment with or without amplification.

Neonatal morbidities in the NRN databases included intracranial hemorrhage (ICH), periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD) defined as respiratory support at 36 weeks' PMA, BPD severity grade,(26) necrotizing enterocolitis (NEC), and retinopathy of prematurity (ROP). ICH was classified by Papile criteria with severe hemorrhage defined as grade III or IV.(27) For the current study, severe ROP was defined as ROP stage 3 or the presence of plus disease.

Statistical Analyses

Demographic, perinatal, and discharge characteristics and 18–26 months' corrected age outcomes were compared between SDOH groups using chi-square tests for categorical variables and t-tests for continuous variables. Only children with data available for all three SDOH variables analyzed were included. There was no data imputation. Regression analyses were conducted to compare outcomes by individual SDOH factors and the total number of risk-associated SDOH at birth. Generalized linear mixed effect models were used to compute adjusted odds ratios or mean differences of outcomes (as applicable) for each of the individual SDOH factors. Models included center as a random effect and controlled for perinatal characteristics, neonatal morbidity, and maternal ethnicity. The neonatal morbidity variable included sepsis (early- or late-onset), brain injury (ICH grade III/IV or PVL), NEC, and ROP stage 3 or plus disease. Models of Bayley-III language composite scores also controlled for the household's primary language while models of readmission also controlled for corrected age at follow-up. To identify which SDOH was associated with the greatest risk, comparisons by individual SDOH controlled for the two remaining SDOH factors (e.g., comparisons by education level were adjusted for race and insurance status). Finally, we counted the individual SDOH for a total number of SDOH and fit similar generalized mixed effect regression models of outcomes, controlling for perinatal characteristics, neonatal morbidity, and maternal ethnicity. We did not correct for multiple comparisons as many analyses were hypothesis-generating in nature.

Results

Of the 7438 children who met inclusion criteria, 5442 (73%) had at least one SDOH associated with disadvantage (Figure 1; available at www.jpeds.com). Mothers with any risk-associated SDOH were younger at delivery (27 years vs. 30 years, p<0.001), less likely to be married (32% vs. 82%, p<0.001), and less likely to receive antenatal steroids (89% vs. 95%, p<0.001) (Table 1). In addition, mothers with public/no insurance and mothers who identified as Black were more likely to be diagnosed with histological chorioamnionitis (insurance: 59% vs. 54%, p<0.001; race: 61% vs. 54%, p<0.001) but less likely to undergo cesarean section (insurance: 64% vs. 66%, p=0.011; race: 62% vs. 67%, p<0.001) compared with mothers with private insurance and mothers who identified as White. For neonatal morbidities, infants whose mothers had public/no insurance and those who identified as Black had a higher incidence of late-onset sepsis and NEC but a lower incidence of BPD than those without these risk-associated SDOH (Table 1).

PMA at discharge did not vary by SDOH in unadjusted analyses (Table 2; available at www.jpeds.com). In adjusted analyses, infants whose mothers had public/no insurance were

discharged at an older PMA compared with those whose mothers had private insurance (Table 3). There was no difference in PMA at discharge by maternal education level or race. While infants whose mothers had public/no insurance were more likely to be in the highest quartile PMA at discharge, infants whose mothers identified as Black were more likely to be in the lowest quartile PMA at discharge. Following the pattern of BPD, infants whose mothers identified as Black were less likely to be discharged with oxygen compared with infants whose mothers identified as White (aOR 0.77, 95% CI 0.68–0.88) (Figure 2). Growth parameter Z-scores at discharge did not vary by SDOH (Table 3).

The overall follow-up rate for children who survived to discharge was 89% (6620/7438). For children exposed to maternal risk-associated SDOH, the follow-up rate was 88% (4798/5442), while for unexposed children, the follow-rate was higher at 91% (1822/1996, p<0.001). While the follow-up rate varied by maternal insurance status (public/no insurance 88% vs. private insurance 91%, p<0.001), the follow-up rate did not vary by education level (88% vs. 89%, p=0.311) or race (89% vs. 89%, p=0.874).

Readmission prior to follow-up was more common among infants whose mothers had public/no insurance compared with those whose mothers had private insurance (aOR 1.27, 95% CI 1.12–1.43) (Table 3). At follow-up, children exposed to either risk-associated education level or insurance status had lower length and head circumference Z-scores compared with unexposed children (Table 4; available at www.jpeds.com). In contrast, weight and length Z-scores were higher for infants with Black mothers compared with those with White mothers (Table 4; available at www.jpeds.com). Unadjusted analyses identified a higher incidence in NDI (41% vs. 26%, p<0.001) and in death post-discharge (2% vs. 1%, p<0.001) among those with any risk-associated SDOH exposure compared with those with no exposure (Table 4; available at www.jpeds.com). In regression analyses, NDI remained more common among children exposed to each risk-associated SDOH compared with those unexposed (less than high school graduate: aOR 1.20 95% CL 1.03, 1.40; public/no insurance: aOR 1.63 95% CL 1.43, 1.86; Black race: aOR 1.30, 95% CL 1.14, 1.49) (Figure 2). Death post-discharge also remained significantly more common among Black children compared with White children (aOR 2.06, 95% CL 1.29, 3.28).

Thirty percent of the cohort (2233/7438) were exposed to one risk-associated SDOH analyzed, while 35% (2640/7438) were exposed to two risk-associated SDOH analyzed and 8% (569/7438) were affected by all three risk-associated SDOH analyzed. In unadjusted analyses, infants with a greater number of risk-associated SDOH at birth were more likely to be discharged at a PMA in the lowest quartile, less likely to be discharged with supplemental oxygen, and more likely to be readmitted by 18–26 months' corrected age (Table 5; available at www.jpeds.com). In adjusted analyses, the higher likelihood for discharge PMA in the lowest quartile and lower likelihood for discharge with oxygen persisted for those with 2 vs. 0, 3 vs. 0, 2 vs. 1, and 3 vs. 1 riskassociated SDOH while readmission occurred more frequently for those with 1 or 2 risk-associated SDOH vs. 0 risk-associated SDOH (Table 6).

With respect to growth parameters, children with risk-associated SDOH had a greater weight Z-score and a lower head circumference Z-score at follow-up compared with those with no risk-associated SDOH (Table 6). NDI at 18–26 months' corrected age occurred more

frequently with increasing number of risk-associated SDOH for nearly all comparisons. Lastly, death post-discharge was five times as likely for those with 3 vs. 0 risk-associated SDOH (aOR 5.22, 95% CL 2.54, 10.73) and twice as likely for those with 3 vs. 2 risk-associated SDOH (aOR 2.03, 95% CL 1.23, 3.37).

Discussion

Extremely preterm birth is an established risk factor for death and altered neurodevelopment among survivors. Children affected by extremely preterm birth frequently have preexisting risk-associated SDOH relevant to infancy and early childhood outcomes. In the current cohort, PMA at discharge varied by maternal insurance status, such that infants of mothers with public/no insurance had longer hospitalizations than infants of mothers with private insurance. At 18–26 months' corrected age, NDI was more common among children who were exposed to any of the three risk-associated SDOH at birth compared with those without risk-associated SDOH exposure at birth. Death post-discharge was more common among children whose mothers had public/no insurance at birth or identified as Black compared with those whose mothers had private insurance at birth or identified as White. This study identifies children who may benefit from expanded support services at discharge due to their combination of preterm birth and sociodemographic risk.

In the United States, low-income women are less likely to have health insurance prior to pregnancy or may have insufficient coverage.(19) In the current study, there were differences in maternal perinatal care pertinent to children born extremely preterm, including less exposure to antenatal steroids for mothers with risk-associated education level, insurance status, or race as well as less frequent cesarean section for mothers with public/no insurance or non-White race. This is consistent with previously reported discrepancies in perinatal maternal interventions by SDOH. Within the Vermont Oxford Network, the rate of antenatal steroid administration for women threatening preterm delivery differed by race with a higher rate for White women compared with Black women.(7) The rate of cesarean section also was higher for White women than Black women.(15)

Infants born to mothers with risk-associated SDOH had a lower incidence of BPD compared with infants born to mothers without SDOH associated with disadvantage. Previously, a lower incidence of BPD among Black infants compared with White infants was found by the Prematurity and Respiratory Outcome Program investigators.(28) BPD is hindered by being defined pragmatically by a treatment, leaving it susceptible to unconscious bias. Infants with any risk-associated SDOH were less likely to be discharged with oxygen than those without such SDOH. The lower incidence of BPD may have been due to physiological differences, genetic differences,(29–31) or due to more aggressive weaning of respiratory support if discharge on supplemental oxygen seemed infeasible for a given family or home environment.

While growth Z-scores at discharge did not differ by risk-associated SDOH, growth Z-scores at follow-up varied by SDOH. Head circumference Z-score at follow-up decreased with increasing number of risk-associated SDOH, which fits with the pattern observed in Bayley-III measures. In contrast, weight Z-score at follow-up increased with increasing number

of risk-associated SDOH. The latter pattern may reflect early underpinnings for childhood obesity, an epidemic that disproportionately affects those with socioeconomic disadvantage in the United States compared with those with socioeconomic security.(32, 33)

Beyond discharge, there may be discrepancies in high-risk infant follow-up program participation based on SDOH. In the current study, the follow-up rate differed by the presence of any maternal risk-associated SDOH at birth. The follow-up rate was lower for infants whose mothers had public/no insurance at time of birth while the follow-up rate did not differ by maternal education level or race. This differs from a California cohort where maternal identity as Black race was associated with reduced odds of referral to high-risk infant follow-up,(34) reduced odds of first visit attendance,(35) and reduced odds of second visit attendance.(36) Insurance type was associated with high-risk infant follow-up attendance, similar to the current study.(35, 36) While societal challenges of poverty and racism are daunting to address at a local level, there is evidence that programs to support families affected by social disadvantage can improve outcomes.(37–39) For example, in Rhode Island, a multi-disciplinary transition home program equipped with family resource specialists and social workers reduced emergency department visits, readmissions, and Medicaid spending.(40, 41)

Strengths of this study included the multicenter design, large sample size, and comprehensive neurodevelopmental follow-up at 18–26 months' corrected age. This study also had limitations. First, only three SDOH were analyzed, and the SDOH at birth were identified by maternal history and records. Other SDOH variables may affect children born prematurely, including neighborhood of residence,(7) paternal characteristics, economic stability, food insecurity, and household preferred language, and ethnicity. SDOH pertinent to women and children may vary internationally, and the results found in this U.S. cohort may not apply to populations in other countries. We did not analyze ethnicity as an independent SDOH given the epidemiologic paradox affecting those who identify as Hispanic(23) but rather adjusted for ethnicity in the analyses. In one recent prospective cohort study of women, there were no differences in the composite maternal or neonatal adverse outcomes between Hispanic and non-Hispanic women, and neonatal morbidities were similar between ethnic groups.(42) In the Assessment of Perinatal EXcellence study, Hispanic term newborns were less likely to experience adverse perinatal outcomes than non-Hispanic newborns despite a high incidence of public/no insurance among mothers who identified as Hispanic.(21) Differences in preferred language and bilingual or multilingual household status, generational differences, and country of origin may contribute to the inconsistent findings in newborn outcomes in relation to ethnicity. Finally, this was a cohort study with many outcomes analyzed; the hypothesis-generating nature of the analyses merits notation.

Socioeconomic factors, such as maternal education and insurance status, and societal factors, such as systemic racism, are intertwined with the outcomes of children born extremely preterm. The duration of birth hospitalization may be prolonged for children whose mothers have public or no insurance compared with those with private insurance, which carries with it a financial and emotional burden. A comprehensive approach to improving outcomes of children born prematurely must include addressing the health of the mother and the

environment beyond the neonatal intensive care unit and beyond the immediate perinatal period.(43, 44) To drive change for children born extremely preterm, preventive strategies must be broadened from individual-level interventions to incorporate family, system, and society-level interventions.(45)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

aOR	Adjusted odds ratio
Bayley-III	Bayley Scales of Infant and Toddler Development, Third Edition
BPD	Bronchopulmonary dysplasia
ICH	Intracranial hemorrhage
NDI	Neurodevelopmental impairment
NICHD	National Institute of Child Health and Human Development
NEC	Necrotizing enterocolitis
NRN	Neonatal Research Network
PMA	Postmenstrual age
PVL	Periventricular leukomalacia
ROP	Retinopathy of prematurity

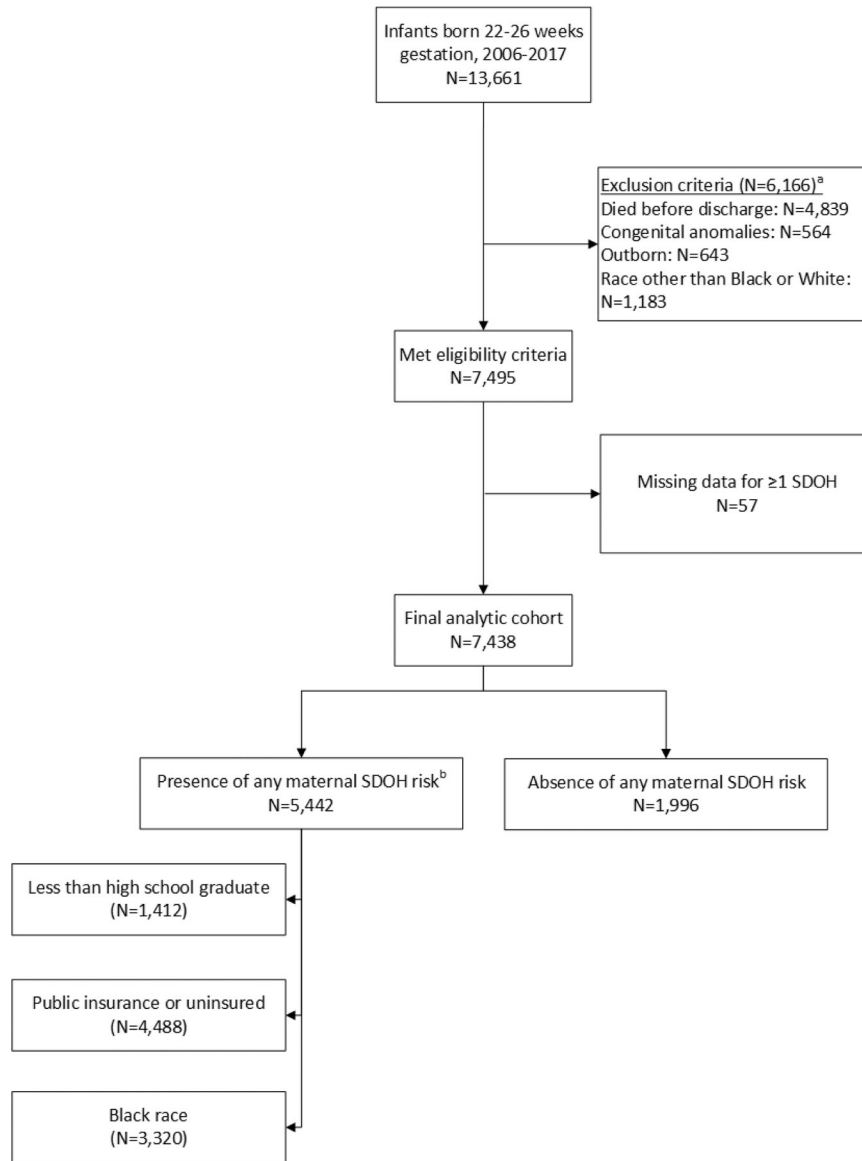| **SDOH**	Social determinants of health

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Figure 1 (Online).

Flow diagram showing subject classification by the presence or absence of maternal social determinants of health associated with risk. a. More than one exclusion criterion may be present. b. SDOH, social determinant(s) of health; more than one risk-associated social determinant of health may be present.
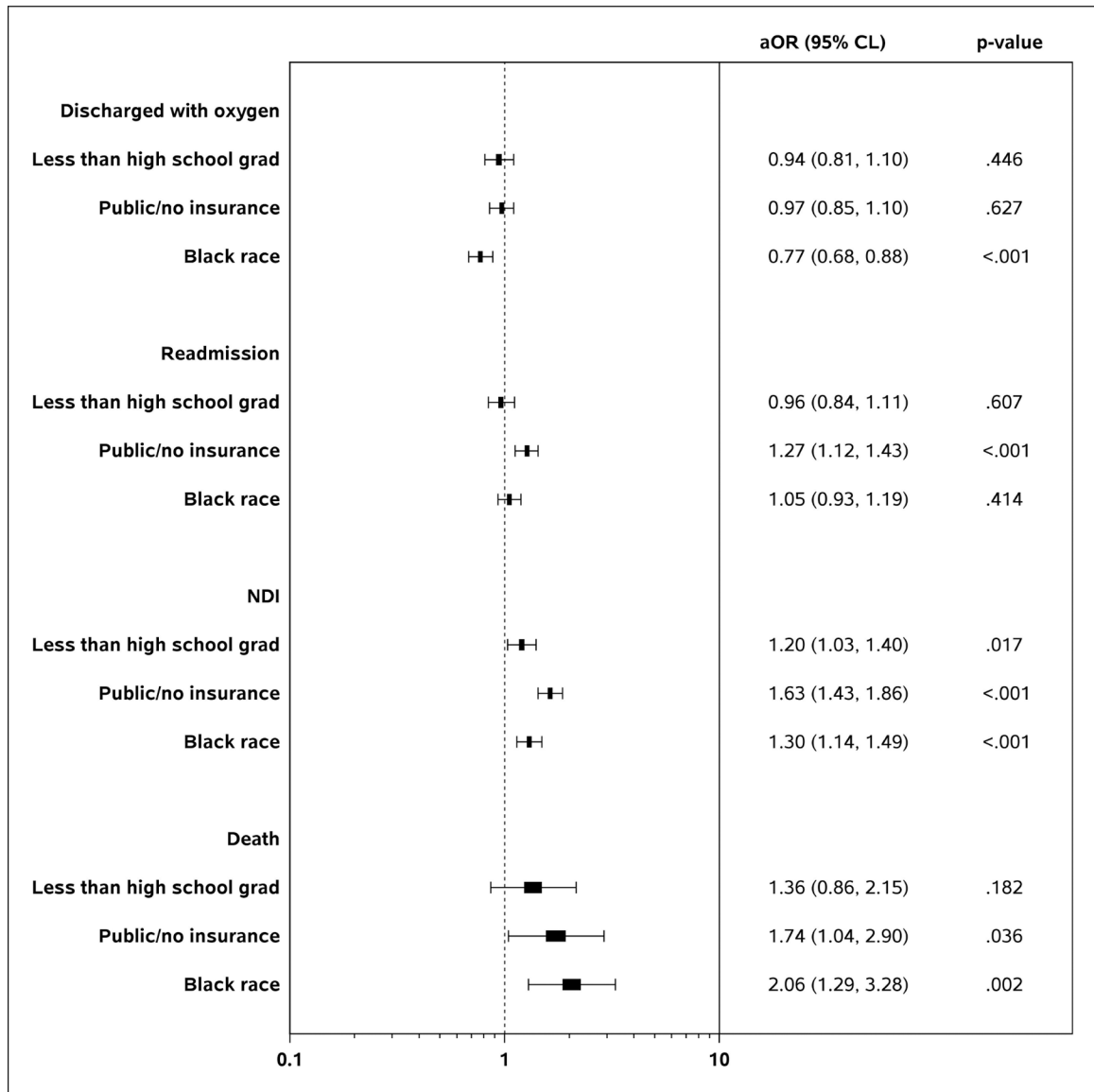
Figure 2.
Forest plots of the regression analyses for highlighted categorical outcomes by social determinants of health at birth.

Table 1.

Maternal and neonatal characteristics and morbidities by social determinants of health at birth

Characteristic†	Education		Insurance		Race		Any SDH Risk Factor	
	<High school grad	High school grad	Public or None	Private	Black	White	Yes	No
Maternal								
Age (years)	24.9 (6.9) ***	28.4 (5.9)	26.2 (6.0) ***	30.2 (5.8)	27.1 (6.2) ***	28.3 (6.3)	26.8 (6.3) ***	30.4 (5.5)
Married	344/1405 (24) ***	2850/5991 (48)	1057/4460 (24) ***	2137/2936 (73)	779/3297 (24) ***	2415/4099 (59)	1546/5405 (29) ***	1648/1991 (83)
Diabetes (insulin-dependent)	59/1411 (4)	262/6024 (4)	197/4486 (4)	124/2949 (4)	159/3319 (5)	162/4116 (4)	247/5439 (5)	74/1996 (4)
Hypertension	296/1411 (21) *	1430/6023 (24)	1017/4487 (23)	709/2947 (24)	890/3319 (27) ***	836/4115 (20)	1286/5440 (24)	440/1994 (22)
Histological chorioamnionitis	699/1237 (57)	3075/5368 (57)	2365/4018 (59) ***	1409/2587 (54)	1818/2960 (61) ***	1956/3645 (54)	2878/4857 (59) ***	896/1748 (51)
Antenatal steroids	1207/1410 (86) ***	5523/6017 (92)	3954/4483 (88) ***	2776/2944 (94)	2953/3314 (89) ***	3777/4113 (92)	4831/5434 (89) ***	1899/1993 (95)
Multiple gestation	246/1412 (17) ***	1598/6026 (27)	890/4488 (20) ***	954/2950 (32)	679/3320 (20) ***	1165/4118 (28)	1082/5442 (20) ***	762/1996 (38)
Cesarean delivery	886/1412 (63)	3926/6024 (65)	2852/4486 (64) *	1960/2950 (66)	2064/3318 (62) ***	2748/4118 (67)	3435/5440 (63) ***	1377/1996 (69)
Neonatal								
Male	693/1412 (49)	3008/6022 (50)	2201/4487 (49)	1500/2947 (51)	1581/3320 (48) **	2120/4114 (52)	2675/5441 (49)	1026/1993 (51)
Gestational age (weeks)	25.0 (1.0)	24.9 (1.0)	24.9 (1.0)	24.9 (1.0)	24.9 (1.1) ***	25.0 (1.0)	24.9 (1.0)	25.0 (1.0)
Birth weight (grams)	769 (157) **	755 (160)	755 (157) *	762 (162)	741 (155) ***	772 (162)	753 (157) ***	770 (164)
Small for gestational age‡	62/1412 (4) *	354/6022 (6)	232/4487 (5) *	184/2947 (6)	192/3320 (6)	224/4114 (5)	291/5441 (5)	125/1993 (6)
Early-onset sepsis	32/1412 (2)	132/6025 (2)	93/4487 (2)	71/2950 (2)	56/3320 (2) **	108/4117 (3)	112/5441 (2)	52/1996 (3)
Late-onset sepsis	446/1411 (32)	1802/6025 (30)	1406/4486 (31) *	842/2950 (29)	1050/3320 (32) *	1198/4116 (29)	1689/5440 (31) *	559/1996 (28)
Grade III/IV intracranial hemorrhage or PVL€	253/1405 (18)	1047/6002 (17)	776/4469 (17)	524/2938 (18)	561/3307 (17)	739/4100 (18)	952/5420 (18)	348/1987 (18)
Bronchopulmonary dysplasia§	809/1403 (58) *	3636/6004 (61)	2612/4471 (58) **	1833/2936 (62)	1775/3301 (54) ***	2670/4106 (65)	3105/5416 (57) ***	1340/1991 (67)
BPD severity¥								

Characteristic†	Education		Insurance		Race		Any SDH Risk Factor	
	<High school grad	High school grad	Public or None	Private	Black	White	Yes	No
No BPD	191/714 (27) *	957/3579 (27)	745/2665 (28)	403/1628 (25)	637/1978 (32) ***	511/2315 (22)	911/3158 (29) ***	237/1135 (21)
Grade 1 BPD	310/714 (43)	1348/3579 (38)	1006/2665 (38)	652/1628 (40)	694/1978 (35)	964/2315 (42)	1182/3158 (37)	476/1135 (42)
Grade 2 BPD	160/714 (22)	923/3579 (26)	666/2665 (25)	417/1628 (26)	442/1978 (22)	641/2315 (28)	766/3158 (24)	317/1135 (28)
Grade 3 BPD	53/714 (7)	351/3579 (10)	248/2665 (9)	156/1628 (10)	205/1978 (10)	199/2315 (9)	299/3158 (10)	105/1135 (9)
Necrotizing enterocolitis	150/1412 (11)	553/6022 (9)	467/4486 (10) **	236/2948 (8)	348/3319 (10) **	355/4115 (9)	555/5440 (10) ***	148/1994 (7)
ROP (any stage)¤	1014/1393 (73)	4347/5952 (73)	3175/4435 (72) **	2186/2910 (75)	2215/3287 (67) ***	3146/4058 (78)	3820/5379 (71) ***	1541/1966 (78)
ROP stage 3 or worse/plus disease	346/1393 (25)	1357/5952 (23)	1020/4435 (23)	683/2910 (23)	641/3287 (20) ***	1062/4058 (26)	1182/5379 (22) ***	521/1966 (27)

*
$P < 0.05$

**
$P < 0.01$

***
$P < 0.001$

†
Values are n/N (%) for categorical variables and mean (SD) for continuous variables.

‡
Small for gestational age defined as <10th percentile based on Alexander growth curves.

€
PVL, periventricular leukomalacia.

§
Bronchopulmonary dysplasia defined as respiratory support at 36 weeks.

¥
BPD, bronchopulmonary dysplasia, severity available for infants born April 1, 2011 or later.

¤
ROP, retinopathy of prematurity.

Table 2 (Online).

Discharge characteristics by social determinants of health at birth

Characteristic[†]	Education		Insurance		Race		Any SDH Risk Factor	
	<High school grad	High school grad	Public or None	Private	Black	White	Yes	No
Discharge								
Postmenstrual age (weeks)	42.0 (5.8)	42.1 (6.1)	42.2 (6.2)	42.0 (5.7)	42.0 (6.5)	42.1 (5.6)	42.1 (6.2)	42.0 (5.5)
Discharged with oxygen	455/1356 (34) ***	2246/5747 (39)	1558/4275 (36) **	1143/2828 (40)	1067/3180 (34) ***	1634/3923 (42)	1864/5193 (36) ***	837/1910 (44)
Weight Z-score[‡]	−0.7 (1.2) *	−0.8 (1.3)	−0.7 (1.2) **	−0.8 (1.3)	−0.9 (1.3) ***	−0.7 (1.2)	−0.8 (1.3)	−0.7 (1.3)
Length Z-score[‡]	−1.8 (1.8) *	−2.0 (1.9)	−2.0 (1.9)	−1.9 (1.8)	−2.1 (2.0) ***	−1.8 (1.8)	−2.0 (1.9) **	−1.8 (1.8)
Head circumference Z-score[‡]	−0.9 (1.7)	−0.9 (1.7)	−0.9 (1.7)	−0.9 (1.7)	−1.0 (1.7) **	−0.9 (1.7)	−0.9 (1.7)	−0.9 (1.7)
Readmission								
Readmission by 18–26 months' corrected	637/1245 (51)	2639/5356 (49)	2075/3919 (53) ***	1201/2682 (45)	1519/2950 (51) **	1757/3651 (48)	2471/4786 (52) ***	805/1815 (44)
Number of readmissions	1.2 (1.9)	1.1 (1.9)	1.3 (2.0) ***	0.9 (1.6)	1.2 (1.8) *	1.1 (1.9)	1.2 (1.9) ***	0.9 (1.7)

*
$P < 0.05$

**
$P < 0.01$

***
$P < 0.001$

[†] Values are n/N (%) for categorical variables and mean (SD) for continuous variables.

[‡] Weight, length, and head circumference Z-scores at discharge are based on INTERGROWTH-21st standards.

Table 3.

Regression analyses of outcomes by social determinants of health at birth

Outcome	Education (<High school grad vs. High school grad)	Insurance (Public/None vs. Private)	Race (Black vs. White)
	aOR or aMD† (95% CL)	aOR or aMD† (95% CL)	aOR or aMD† (95% CL)
Discharge			
Postmenstrual age (weeks)	0.09 (−0.27, 0.45)	0.37 (0.06, 0.68) [*]	−0.28 (−0.60, 0.03)
Postmenstrual age in lowest quartile	0.96 (0.81, 1.12)	0.96 (0.84, 1.10)	1.60 (1.39, 1.85) [***]
Postmenstrual age in highest quartile	1.10 (0.93, 1.29)	1.22 (1.06, 1.41) [**]	0.87 (0.76, 1.01)
Length of hospital stay (days)	0.54 (−1.97, 3.05)	2.74 (0.59, 4.88) [*]	−2.00 (−4.19, 0.20)
Discharged with oxygen	0.94 (0.81, 1.10)	0.97 (0.85, 1.10)	0.77 (0.68, 0.88) [***]
Weight Z-score[‡]	0.04 (−0.03, 0.11)	0.02 (−0.04, 0.09)	0.00 (−0.06, 0.07)
Length Z-score[‡]	0.10 (−0.01, 0.21)	−0.11 (−0.21, −0.02) [*]	−0.08 (−0.18, 0.02)
OFC Z-score[‡]	0.06 (−0.05, 0.16)	−0.07 (−0.16, 0.02)	0.03 (−0.06, 0.13)
Follow-up			
NDI[€]	1.20 (1.03, 1.40) [*]	1.63 (1.43, 1.86) [***]	1.30 (1.14, 1.49) [***]
Death (post-discharge)	1.36 (0.86, 2.15)	1.74 (1.04, 2.90) [*]	2.06 (1.29, 3.28) [**]
Readmission by 18–26 months' corrected age	0.96 (0.84, 1.11)	1.27 (1.12, 1.43) [***]	1.05 (0.93, 1.19)
Bayley-III cognitive composite score	−1.63 (−2.62, −0.64) [**]	−4.07 (−4.91, −3.23) [***]	−2.75 (−3.61, −1.88) [***]
Bayley-III language composite score	−2.16 (−3.30, −1.03) [***]	−4.50 (−5.46, −3.55) [***]	−4.10 (−5.09, −3.12) [***]
Bayley-III motor composite score	−1.49 (−2.68, −0.30) [*]	−3.11 (−4.11, −2.11) [***]	1.19 (0.17, 2.21) [*]
Bayley-III cognitive composite <70	1.11 (0.89, 1.38)	1.31 (1.08, 1.59) [**]	1.02 (0.84, 1.24)
Bayley-III cognitive composite <85	1.21 (1.04, 1.40) [*]	1.69 (1.47, 1.93) [***]	1.37 (1.19, 1.57) [***]
Moderate or severe cerebral palsy	0.95 (0.72, 1.25)	1.03 (0.81, 1.30)	0.93 (0.74, 1.18)
GMFCS level 2[§]	0.96 (0.75, 1.23)	1.06 (0.86, 1.30)	0.76 (0.62, 0.94) [*]
Weight Z-score[¥]	−0.03 (−0.11, 0.04)	−0.07 (−0.13, 0.00) [*]	0.29 (0.22, 0.35) [***]
Length Z-score[¥]	−0.15 (−0.24, −0.06) [**]	−0.15 (−0.22, −0.07) [***]	0.33 (0.25, 0.41) [***]
OFC Z-score[¥]	−0.14 (−0.24, −0.04) [**]	−0.15 (−0.24, −0.06) [**]	0.07 (−0.01, 0.16)

[*]
$P < 0.05$

[**]
$P < 0.01$

[***]
$P < 0.001$

[†]
Adjusted odds ratios (aOR) are calculated for categorical variables and adjusted mean differences (aMD) are calculated for continuous variables. Odds ratios and mean differences are adjusted for the following variables: center, Hispanic origin, maternal age, diabetes (insulin-dependent), hypertension, clinical chorioamnionitis, multiple gestation, Cesarean delivery, birth year, infant sex, gestational age, small-for-gestational age, and neonatal morbidity (sepsis (early or late), IVH grade 3–4/PVL, proven NEC, and ROP stage 3 or greater/plus disease). Comparisons by individual SDH (i.e., less than high school graduate, no or public insurance, non-white race) control for the two remaining SDH factors (e.g., comparisons

by education level were adjusted for race and insurance status). Models of readmission also controlled for corrected age at follow-up. Models of Bayley-III language composite scores also controlled for primary language.

†Weight, length, and head circumference Z-scores at discharge are based on INTERGROWTH-21st standards.

€NDI, neurodevelopmental impairment, defined as any of the following: moderate or severe cerebral palsy, gross motor function classification system level 2 or greater, Bayley-III cognitive composite score <85, bilateral blindness with no or some functional vision, or hearing impairment with or without amplification

§GMFCS, gross motor function classification system.

¥Weight, length, and head circumference Z-scores at follow-up are based on WHO child growth.

Table 4 (Online).

Neurological and sensory outcomes at 18–26 months' corrected age by social determinants of health at birth

Characteristic[†]	Education		Insurance		Race		Any SDH Risk Factor	
	<High school grad	High school grad	Public or None	Private	Black	White	Yes	No
Survival and NDI [‡]								
NDI[‡]	519/1213 (43) ***	1841/5192 (35)	1611/3803 (42) ***	749/2602 (29)	1189/2861 (42) ***	1171/3544 (33)	1904/4643 (41) ***	456/1762 (26)
Death (post-discharge)	34/1410 (2) **	85/6015 (1)	94/4479 (2) ***	25/2946 (1)	79/3314 (2) ***	40/4111 (1)	105/5432 (2) ***	14/1993 (1)
Bayley-III Scales								
Cognitive composite score	84.4 (14.1) ***	87.4 (15.8)	84.6 (14.6) ***	90.2 (16.2)	84.7 (14.7) ***	88.6 (15.9)	84.9 (14.8) ***	91.9 (16.3)
Language composite score	78.7 (15.3) ***	83.5 (17.7)	79.9 (16.1) ***	86.6 (18.3)	80.3 (16.1) ***	84.5 (18.1)	80.2 (16.2) ***	89.0 (18.6)
Motor composite, score€	84.3 (15.9) *	85.7 (16.9)	84.3 (16.5) ***	87.2 (16.9)	85.3 (16.6)	85.6 (16.8)	84.7 (16.6) ***	87.6 (16.9)
Neurological Exam								
Moderate or severe cerebral palsy	86/1239 (7)	400/5308 (8)	295/3898 (8)	191/2649 (7)	224/2935 (8)	262/3612 (7)	367/4758 (8)	119/1789 (7)
Gross motor function level ≥2	112/1237 (9)	523/5303 (10)	382/3892 (10)	253/2648 (10)	274/2931 (9)	361/3609 (10)	470/4750 (10)	165/1790 (9)
Bilateral blindness	13/1239 (1)	78/5308 (1)	47/3896 (1)	44/2651 (2)	31/2934 (1) *	60/3613 (2)	59/4757 (1)	32/1790 (2)
Bilateral hearing impairment	45/1230 (4)	142/5279 (3)	120/3870 (3)	67/2639 (3)	94/2915 (3)	93/3594 (3)	147/4726 (3)	40/1783 (2)
Follow-up Growth								
Weight Z-score§	−0.3 (1.1)	−0.3 (1.1)	−0.3 (1.2)	−0.4 (1.1)	−0.2 (1.2) ***	−0.4 (1.1)	−0.3 (1.2) ***	−0.4 (1.1)
Length Z-score§	−0.9 (1.5) **	−0.8 (1.3)	−0.8 (1.4) *	−0.7 (1.2)	−0.7 (1.4) ***	−0.9 (1.3)	−0.8 (1.4)	−0.8 (1.2)
OFC Z-score§	−0.5 (1.7) ***	−0.3 (1.5)	−0.4 (1.6) ***	−0.2 (1.5)	−0.3 (1.5)	−0.3 (1.6)	−0.4 (1.6) ***	−0.2 (1.5)

*
$P < 0.05$

**
$P < 0.01$

***
$P < 0.001$

[†]
Values are n/N (%) for categorical variables and mean (SD) for continuous variables.

[‡]
NDI, neurodevelopmental impairment, defined as any of the following: moderate or severe cerebral palsy, gross motor function classification system level 2 or greater, Bayley-III cognitive composite score <85, bilateral blindness with no or some functional vision, or hearing impairment with or without amplification

€Bayley-III motor composite score consistently available beginning January 1, 2010.

gWeight, length, and orbitofrontal circumference (OFC) Z-scores at follow-up are based on WHO child growth charts.

Table 5 (Online).

Outcomes by number of risk-associated social determinants of health at birth

	Number of Risk-Associated Social Determinants of Health at Birth				
	0 (N=1996)	1 (N=2233)	2 (N=2640)	3 (N=569)	p-value
Categorical Outcome, n (%)					
Discharge					
Postmenstrual age in lowest quartile	442/1912 (23)	526/2126 (25)	737/2523 (29)	178/549 (32)	<0.001
Postmenstrual age in highest quartile	458/1912 (24)	540/2126 (25)	640/2523 (25)	136/549 (25)	0.686
Discharged with oxygen	837/1910 (44)	820/2124 (39)	872/2520 (35)	172/549 (31)	<0.001
Follow-Up					
NDI[a]	456/1762 (26)	695/1893 (37)	1003/2266 (44)	206/484 (43)	<0.001
Death (post-discharge)	14/1993 (1)	27/2229 (1)	54/2635 (2)	24/568 (4)	<0.001
Readmission by 18–26 months' corrected age	805/1815 (44)	967/1954 (49)	1248/2336 (53)	256/496 (52)	<0.001
Bayley-III cognitive composite <70	161/1755 (9)	251/1886 (13)	309/2258 (14)	57/482 (12)	<0.001
Bayley-III cognitive composite <85	406/1755 (23)	644/1886 (34)	946/2258 (42)	195/482 (40)	<0.001
Moderate or severe cerebral palsy	119/1789 (7)	166/1938 (9)	164/2326 (7)	37/494 (7)	0.127
GMFCS level ≥2[b]	165/1790 (9)	217/1934 (11)	208/2322 (9)	45/494 (9)	0.065
Continuous Outcome, mean (SD)					
Discharge					
Postmenstrual age (weeks)	42.0 (5.5)	42.2 (6.0)	42.1 (6.3)	41.8 (6.3)	0.479
Weight Z-score[c]	−0.7 (1.3)	−0.8 (1.3)	−0.8 (1.2)	−0.8 (1.3)	0.824
Length Z-score[c]	−1.8 (1.8)	−2.0 (1.9)	−2.0 (1.9)	−2.0 (2.0)	0.037
Head circumference Z-score[c]	−0.9 (1.7)	−0.9 (1.8)	−1.0 (1.7)	−0.9 (1.7)	0.190
Follow-up					
Bayley-III cognitive composite score	91.9 (16.3)	86.2 (15.4)	84.0 (14.3)	84.5 (14.3)	<0.001
Bayley-III language composite score	89.0 (18.6)	81.6 (17.0)	79.1 (15.5)	79.9 (15.9)	<0.001
Bayley-III motor composite score[d]	87.5 (16.9)	84.8 (17.0)	84.6 (16.3)	85.0 (16.2)	<0.001
Weight Z-score[e]	−0.4 (1.1)	−0.3 (1.2)	−0.3 (1.2)	−0.3 (1.1)	<0.001

	Number of Risk-Associated Social Determinants of Health at Birth				
	0 (N=1996)	1 (N=2233)	2 (N=2640)	3 (N=569)	p-value
Length Z-score[e]	−0.8 (1.2)	−0.8 (1.4)	−0.7 (1.3)	−0.9 (1.7)	0.227
Head circumference Z-score[e]	−0.2 (1.5)	−0.3 (1.5)	−0.4 (1.6)	−0.4 (1.5)	<0.001

[a] NDI, neurodevelopmental impairment, defined as one or more of the following: moderate or severe cerebral palsy, gross motor function classification system level 2 or greater, Bayley-III cognitive composite score <85, bilateral blindness with no or some functional vision, or hearing impairment with or without amplification.

[b] GMFCS, gross motor function classification system.

[c] Weight, length, and head circumference Z-scores at discharge are based on INTERGROWTH-21st standards.

[d] Bayley-III motor composite score consistently available beginning January 1, 2010.

[e] Weight, length, and head circumference Z-scores at follow-up are based on WHO child growth charts.

Table 6.

Regression analyses of outcomes by number of risk-associated social determinants of health at birth

Outcome	Number of Risk-Associated Social Determinants of Health at Birth					
	1 vs. 0 aOR or aMD† (95% CL)	2 vs. 0 aOR or aMD† (95% CL)	3 vs. 0 aOR or aMD† (95% CL)	2 vs. 1 aOR or aMD† (95% CL)	3 vs. 1 aOR or aMD† (95% CL)	3 vs. 2 aOR or aMD† (95% CL)
Discharge						
Postmenstrual age (PMA, weeks)	0.36 (0.01, 0.72) *	0.21 (−0.15, 0.57)	0.29 (−0.27, 0.85)	−0.15 (−0.48, 0.17)	−0.07 (−0.61, 0.46)	0.08 (−0.43, 0.60)
PMA in lowest quartile	1.03 (0.87, 1.22)	1.34 (1.14, 1.59) ***	1.32 (1.03, 1.69) *	1.30 (1.13, 1.51) ***	1.28 (1.02, 1.62) *	0.98 (0.79, 1.23)
PMA in highest quartile	1.15 (0.98, 1.36)	1.12 (0.95, 1.32)	1.24 (0.96, 1.60)	0.97 (0.84, 1.12)	1.08 (0.85, 1.37)	1.11 (0.88, 1.40)
Length of hospital stay (days)	2.63 (0.16, 5.09) *	1.58 (−0.93, 4.09)	2.00 (−1.91, 5.91)	−1.05 (−3.31, 1.21)	−0.63 (−4.34, 3.08)	0.42 (−3.16, 4.00)
Discharged with oxygen	0.91 (0.78, 1.06)	0.79 (0.68, 0.92) **	0.70 (0.55, 0.90) **	0.87 (0.75, 0.99) *	0.77 (0.62, 0.97) *	0.89 (0.72, 1.11)
Weight Z-score‡	−0.03 (−0.10, 0.04)	0.02 (−0.05, 0.10)	0.06 (−0.05, 0.18)	0.06 (−0.01, 0.12)	0.09 (−0.01, 0.20)	0.04 (−0.06, 0.14)
Length Z-score‡	−0.21 (−0.32, −0.10) ***	−0.15 (−0.27, −0.04) **	−0.16 (−0.34, 0.02)	0.06 (−0.05, 0.16)	0.05 (−0.12, 0.22)	−0.01 (−0.17, 0.15)
OFC Z-score‡	−0.08 (−0.19, 0.03)	−0.06 (−0.17, 0.05)	0.03 (−0.14, 0.20)	0.02 (−0.07, 0.12)	0.11 (−0.05, 0.27)	0.09 (−0.06, 0.24)
Follow-up						
NDI€	1.74 (1.49, 2.03) ***	2.28 (1.95, 2.66) ***	2.36 (1.86, 3.00) ***	1.31 (1.14, 1.50) ***	1.36 (1.09, 1.70) **	1.04 (0.84, 1.28)
Death (postdischarge)	1.65 (0.85, 3.21)	2.57 (1.38, 4.78) **	5.22 (2.54, 10.73) ***	1.55 (0.96, 2.50)	3.16 (1.76, 5.67) ***	2.03 (1.23, 3.37) **
Readmission by 18–26 mo. corrected	1.20 (1.05, 1.38) *	1.34 (1.17, 1.54) ***	1.21 (0.97, 1.50)	1.12 (0.99, 1.27)	1.00 (0.82, 1.24)	0.90 (0.73, 1.10)
Bayley-III cognitive composite score	−5.70 (−6.66, −4.73) ***	−7.48 (−8.46, −6.50) ***	−7.79 (−9.33, −6.26) ***	−1.78 (−2.67, −0.90) ***	−2.10 (−3.56, −0.63) **	−0.31 (−1.72, 1.09)
Bayley-III language composite score	−7.36 (−8.46, −6.27) ***	−9.33 (−10.46, −8.21) ***	−9.70 (−11.44, −7.96) ***	−1.97 (−2.98, −0.96) ***	−2.34 (−4.00, −0.68) **	−0.37 (−1.97, 1.23)
Bayley-III motor composite score§	−3.29 (−4.44, −2.14) ***	−3.05 (−4.21, −1.88) ***	−3.06 (−4.93, −1.18) **	0.25 (−0.81, 1.30)	0.23 (−1.56, 2.02)	−0.01 (−1.73, 1.71)
Bayley-III cognitive composite <70	1.61 (1.28, 2.02) ***	1.56 (1.24, 1.97) ***	1.48 (1.03, 2.11) *	0.97 (0.80, 1.18)	0.92 (0.66, 1.28)	0.94 (0.69, 1.30)
Bayley-III cognitive composite <85	1.82 (1.55, 2.14) ***	2.44 (2.08, 2.87) ***	2.61 (2.05, 3.33) ***	1.34 (1.17, 1.54) ***	1.43 (1.14, 1.79) **	1.07 (0.86, 1.32)

Number of Risk-Associated Social Determinants of Health at Birth

Outcome	1 vs. 0 aOR or aMD† (95% CL)	2 vs. 0 aOR or aMD† (95% CL)	3 vs. 0 aOR or aMD† (95% CL)	2 vs. 1 aOR or aMD† (95% CL)	3 vs. 1 aOR or aMD† (95% CL)	3 vs. 2 aOR or aMD† (95% CL)
Moderate or severe cerebral palsy	1.31 (1.01, 1.70)*	0.97 (0.74, 1.28)	1.10 (0.72, 1.68)	0.74 (0.58, 0.94)*	0.84 (0.57, 1.25)	1.13 (0.77, 1.67)
GMFCS level >2	1.22 (0.97, 1.54)	0.86 (0.67, 1.10)	0.91 (0.62, 1.34)	0.70 (0.57, 0.87)**	0.74 (0.52, 1.07)	1.06 (0.74, 1.51)
Weight Z-score¥	0.09 (0.02, 0.16)*	0.15 (0.07, 0.23)***	0.18 (0.06, 0.30)**	0.06 (−0.01, 0.13)	0.09 (−0.02, 0.20)	0.03 (−0.08, 0.14)
Length Z-score¥	0.01 (−0.08, 0.10)	0.08 (−0.01, 0.17)	−0.03 (−0.17, 0.11)	0.07 (−0.01, 0.15)	−0.04 (−0.17, 0.10)	−0.11 (−0.24, 0.02)
OFC Z-score¥	−0.10 (−0.20, 0.00)	−0.14 (−0.24, −0.04)**	−0.22 (−0.38, −0.06)**	−0.04 (−0.13, 0.05)	−0.12 (−0.28, 0.03)	−0.08 (−0.23, 0.07)

*
$P < 0.05$

**
$P < 0.01$

***
$P < 0.001$

†
Adjusted odds ratios (aOR) calculated for categorical variables and adjusted mean differences (aMD) calculated for continuous variables. Odds ratios and mean differences are adjusted for the following variables: center, maternal age, diabetes (insulin-dependent), hypertension, clinical chorioamnionitis, multiple gestation, Cesarean delivery, birth year, infant sex, gestational age, small-for-gestational age, and neonatal morbidity (sepsis (early or late), ICH grade 3–4/PVL, proven NEC, and ROP stage 3 or greater/plus disease). Analyses of readmission also control for corrected age at follow-up. Models of Bayley-III language composite scores also controlled for primary language. Regression models for comparisons of outcomes by race (non-white vs. white) also control for Hispanic origin.

‡
Weight, length, and head circumference Z-scores at discharge are based on INTERGROWTH-21st standards.

€
NDI, neurodevelopmental impairment, defined as any of the following: moderate or severe cerebral palsy, gross motor function classification system level 2 or greater, Bayley-III cognitive composite score <85, bilateral blindness with no or some functional vision, or hearing impairment with or without amplification

§
The motor domain was administered beginning in January 2010.

¥
Weight, length, and orbitofrontal circumference (OFC) Z-scores at follow-up are based on WHO child growth.