Europe Journal of
Pediatrics & Neonatology

PN Banerjee, et al. (2023): 115-24
Eur J Pedia Neon: EJPN-104

Research Article Open Access

What Is the Impact of Infant Low Birth Weight, Premature Birth and Small for Gestational Age Upon the Association Between Maternal Sensitivity and Cognitive Development?

PN Banerjee, DrPh, Karen McFadden, PhD, Jacqueline D. Shannon, PhD, Leslie L. Davidson, MD, MSc, MRCP (London)

Columbia University, Mailman School of Public Health and bBrooklyn College, Early Childhood Education

***Corresponding author:** PN Banerjee, Columbia University, Mailman School of Public Health and bBrooklyn College, Early Childhood Education. Email: nina.banerjee@gmail.com

Citation: Banerjee PN, McFadden K, Shannon JD, Davidson LL (2023) What Is the Impact of Infant Low Birth Weight, Premature Birth and Small for Gestational Age Upon the Association Between Maternal Sensitivity and Cognitive Development? Eur J Pedia Neon: EJPN-104.

Received Date: January 25, 2023; **Accepted Date:** February 02, 2023; **Published Date:** February 10, 2023

Abstract

Objective- Low birth weight (LBW), a measure of biological vulnerability that includes premature birth and small for gestational age (SGA), has been repeatedly associated with impaired infant cognitive development and reduced maternal sensitivity. However, the research does not reveal whether it is premature birth, SGA or both that drive the association between LBW and maternal sensitivity or cognitive development. This study separated these measures of infant biological vulnerability and controlled for related factors (maternal depression, breastfeeding, demographic covariates) to examine the impact of LBW, premature birth and SGA upon the association between maternal sensitivity and cognitive development.

Methods-The sample included 6,900 infants from the Early Childhood Longitudinal Study-Birth Cohort which utilized birth certificate data as well as assessments (Nursing Child Assessment Teaching Scale (NCATS) for maternal sensitivity and the Bayley Short Form-Research Edition (BSF-R) for infant cognitive development) when infants were 9 months of age. Multiple linear regression was used to examine the impact of LBW, premature birth and SGA upon concurrent measures of maternal sensitivity and infant cognitive development.

Results-Both LBW ($F_{1,6,450}$ =15.33, $p <$ .001) and SGA ($F_{1,6,450}$ = 5.51, $p <$ .001) were associated with maternal sensitivity, however, premature birth had the strongest association ($F_{1,6,450}$ = 29.48, $p <$ .001) with sensitivity. Premature birth also had the strongest negative association with cognitive development ($F_{1,6,450)}$= 390.65, $p <$ .001), in comparison to LBW ($F_{1,6,450)}$= 248.02, $p <$ .001) or SGA ($F_{1,6,450)}$= 14.43, $p <$ .001). In the final regression model, using the strongest measure of biological vulnerability (premature birth), maternal sensitivity (β=.171, p<.001), remained associated with cognitive development (R^2=.05, p<.001), after adjusting for premature birth (β=-.115***), breastfeeding (β=.081***, p<.001), depression (β=-.032**), and demographic covariates.

Conclusion- In this nationally representative sample of 9-month-old infants, maternal sensitivity and breastfeeding remained associated with infant cognitive development, after adjusting for premature birth, maternal depression and demographic covariates. Premature birth, or shorter gestation time, had a stronger negative association with both maternal sensitivity and infant cognitive development in comparison to SGA or LBW. Therefore, insufficient gestational time, rather than adverse uterine environment, had a greater impact on infant cognitive development in this study. The LBW designation combines infants born prematurely with SGA infants, potentially minimizing differences in developmental outcomes of premature and SGA infants.

Funding Source: No external funding was received for this manuscript.

Financial Disclosure: The authors have no financial relationships relevant to this article to disclose.

Conflict of Interest: The authors have no potential conflicts of interest to disclose.

Abbreviations:
Low Birth Weight (LBW)
Very Low Birth Weight (VLBW)
Small for Gestational Age (SGA)
Intrauterine Growth Restriction (IUGR)
Early Childhood Longitudinal Study-Birth Cohort (ECLS-B)
National Center for Educational Statistics (NCES)
Nursing Child Assessment Teaching Scale (NCATS)
Bayley Short Form-Research Edition (BSF-R)
Bayley Scale of Infant Development, II (BSID-II)
Center for Epidemiological Studies' Depression Scale (CES-D)

Contributors' Statement Page
Dr. Nina Banerjee conceptualized and designed the study, drafted the manuscript, and carried out the data analyses.
Drs. Jacqueline D. Shannon, and Karen McFadden obtained the ECLS-B data license to utilize the ECLS-B birth certificate, interview and assessment data, reviewed the data analyses and manuscript, and revised the manuscript.

Dr. Leslie Davidson conceptualized and designed the study, as well as reviewed and revised the manuscript.
All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Introduction

Infancy is a period of rapid growth, when parents must adjust their behaviors daily in response to their infants' growing needs and competencies. It is also a time of unparalleled opportunity for practitioners to support women in their "new" roles as mothers and their relationship with their newborns. Maternal "sensitivity", defined as making accurate inferences about an infant's physical and emotional needs and responding appropriately [1,2], is associated with the infant reaching developmental milestones at an earlier age[3,4]. Maternal sensitivity is associated with an increase in cognitive development at a greater rate in all infants, including biologically vulnerable infants, such as those born low birth weight (LBW) and Small for Gestational Age (SGA) [1,5,6]. The association between maternal sensitivity and infant cognitive development is in line with the "developmental plasticity" theory, which postulates that infant neurological development is malleable, and the infant's brain transforms in response to caregiver and environmental stimuli[7,8].

While maternal sensitivity advances infant's cognitive development, LBW, defined as birth less than 2,500 grams, is considered a risk factor for impaired cognition[9,10]. LBW is a public health problem [9,11] due to its association with numerous adverse cognitive development outcomes[12-14] that can be lifelong[15,16] and include reduced educational attainment[17,18] and diminished occupational success[15,16].

However, LBW is a measure of infant biological vulnerability that conflates premature birth with small for gestational age (SGA). The LBW designation can include 1) infants born prematurely or SGA; 2) infants both premature and SGA; and 3) infants, in rare cases, simply constitutionally small [19]. Although developmental outcomes have been examined in LBW infants using the Early Childhood Longitudinal Study Birth Cohort (ECLS-B) [20-23]. This study, which uses the ECLS-B data at 9-months, extends these findings by separating the infants born prematurely from those who were SGA within the LBW designation, allowing us to disentangle the effects of these two overlapping but distinct biological risks.

In infants born prematurely, gestational weeks is negatively associated with cognitive development [9,24,25]. In contrast, cognitive development for infants born SGA, defined as less than the tenth percentile of birthweight for gestational age, is related to the conditions of the intrauterine environment during gestation[26]. Intrauterine growth restriction (IUGR) commonly leads to infants being born SGA, which is related to structural alterations in the brain[27]. The prognosis for typical cognitive development is more favorable if SGA is related to placental insufficiency or maternal malnutrition rather than infection, genetic or metabolic disorder [16,26]. Unlike infants born prematurely, SGA infants who have had nutritional deficiency in utero may demonstrate rapid "catch up" development if nutritional needs are met after delivery [28]. Therefore, insufficient gestational time (premature birth) and adverse intrauterine conditions (SGA) can lead to entirely different developmental outcomes [24,26,29], a factor minimized by use of the LBW designation, which combines Premature and SGA infants.

Most studies have examined the association between maternal sensitivity and infant cognitive development in normal birth weight samples[2,30,31]. Studies which have utilized LBW samples[12,25,32] have two main limitations. Firstly, since the LBW designation combines infants born prematurely with SGA infants, the question of whether impaired cognitive developmental outcome is associated with insufficient gestational time, adverse intrauterine environment, or other factors remains. Secondly, due to small sample sizes, there has been insufficient power to examine potentially confounding effects of other factors associated with sensitivity, infant cognitive development or both, such as breastfeeding[33], maternal depression[34] or demographic characteristics (e.g., maternal age and education, household income, family structure, and parity) [28,34-36].

Identifying whether the risk for poorer developmental outcomes in LBW infants is centered insufficient gestational time or compromised gestation can aid in individualizing treatment strategies, yet few studies have examined premature and SGA infants separately. Less than 20 studies have used samples of infants born exclusively premature [37-39] and only a handful of studies have used exclusively SGA infants [16,26,40-43]. In these studies, the definitions of premature birth or SGA have varied, challenging cross-study comparison.

Aim

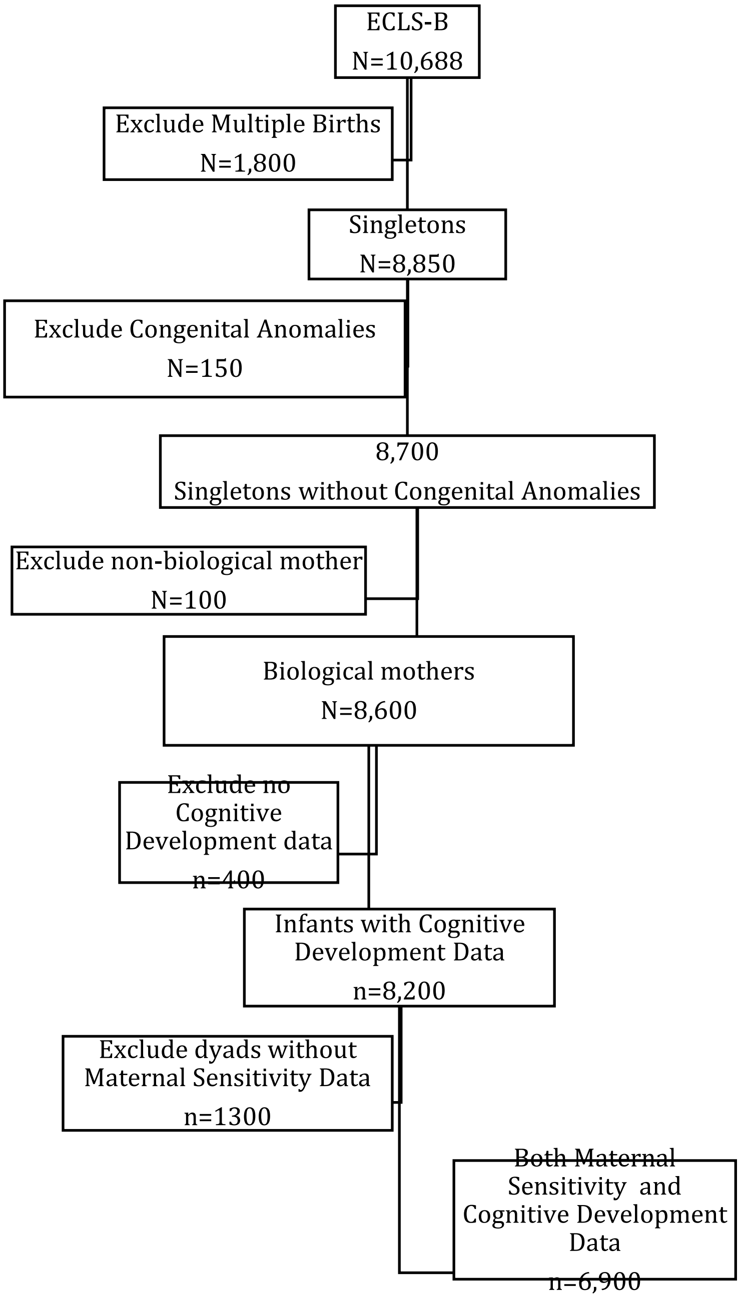
Using a nationally representative population-based sample, this study aimed to examine variation in strength of the association between maternal sensitivity and infant cognition varied by type of biological vulnerability measure used (LBW, premature, or SGA) during infancy. Due to poorer prognoses for cognitive development in premature infants, it was hypothesized that premature birth would have the strongest negative association with both maternal sensitivity and cognitive development, even after controlling for confounding variables (breastfeeding, depressive symptoms and demographics).

Methods

Participants

The Early Childhood Longitudinal Study-Birth Cohort (ECLS-B) is a nationally representative prospective study of factors that influence children's development longitudinally at 9 months, 2 years, preschool, and kindergarten, conducted by the National Center of Educational Statistics (NCES); the present study used the data from the 9-month data collection. The base sample was drawn from approximately 4 million infants born in 2001 and designed to represent the United States population (NCES, 2005a; NCES, 2005b). Over 14,000 infants were sampled, with certain demographic groups (Native Americans, LBW) strategically oversampled, yielding 10,688 participants (after excluding infants with mothers less than age 15, and infants who died or adopted at birth), for a response rate of 76%.

The current study sample used data from Wave 1 (9-month) data of singletons (n=8,850). Multiple births, infants with congenital anomalies, and infants whose primary caregiver was not their biological mother were excluded. The sample was further restricted to infants with both maternal sensitivity and infant cognitive development data, providing a final sample of 6,900 (Figure 1).



At the time of the 9-month interview/infant assessment, infants (51% boys) ranged from 8 to 11-months of age (M = 9.7 months) at assessment. Most mothers (71%) were living in two-parent households. Almost half (42/2%) were first time mothers. They ranged from 15 to 51 years of age and came from diverse racial and ethnic backgrounds: European American (43.9%), Latin American (18.2%), African American (16.5%), and Asian American (13.9%). The majority of mothers graduated from high school/obtained their government equivalency diploma (28.7%) and/or had some college (26.3%), and 25.5% of mothers reported to be below the poverty level.

Procedures

The present study utilized birth certificate data, infant assessments and parent interviews during home visits by trained field researchers who used computer-assisted interview techniques, when infants were approximately 9 months of age (NCES, 2005). The Institutional Review Board considers this study exempt because data collected is part of a publicly available dataset in which data is de-identified and cannot be linked to individuals participating in the study.

Measures

Maternal Sensitivity: The quality of maternal sensitivity was measured from video-taped mother-infant dyadic interactions engaging in a semi-structured teaching task with their infants in the family's home (Ex: pulling a car by a string) as per the Nursing Child Assessment Teaching Scale (NCATS) [76]. The NCATS uses 50 binary items (0 = not observed, 1 = observed) that assess the quality of mother's sensitivity to the child's cues, responsiveness to child's distress, social emotional growth fostering and cognitive growth fostering. NCATS ratings were completed by trained and certified coders blinded to other measures collected on the dyads and checked for quality by University of Washington staff, developers of the NCATS. Raters maintained 85% agreement or greater to meet quality standards. Adequate internal consistency was demonstrated for the NCATS total parent scale for this sample (∞ = .72) and the full ECLS-B sample (∞ = .68 (NCES, 2005a). In this scale, higher scores indicate greater maternal sensitivity.

Infant Cognitive Development: The Bayley Short Form-Research Edition (BSF-R) Mental Scale, developed for use with ECLS-B, was used to measure infant cognitive development (NCES; 2005a, NCES; 2005b). It is a standardized shortened version of the Bayley Scales of Infant Development-Second Edition (BSID-II; Bayley, 1993) and included a core set of 11 items at 9 months that assessed children's cognitive and language ability such as memory, means-end behavior, problem solving, and vocalizations and gestures (Flanagan & West, 2004). Item response theory (IRT) calibration and scoring were used to develop a mental scale score. IRT true-score equating was used to put the ECLS-B results on the same 0- to 178-point scale used by the BSID- 11. The ECLS-B mental scale score is an estimate of the number of items a child would have answered, with a a mean of 100 (SD = 15); scores ranged from 32 to 131). The BSF-R internal consistency reliability coefficient was adequate for this sample (∞=.79). The full sample ∞=.80 (NCES; 2005).

Biological Vulnerability: Biological vulnerability measures of LBW, premature birth and SGA were captured from the birth certificate. Figure 2 shows the overlap between infants born prematurely in normal, LBW, and very low birth weight (VLBW) Categories.

Birthweight. Normal birth weight was defined as 2,500 grams or greater, LBW as 1,500- 2,499 grams, and VLBW as less than 1,500 grams. Birthweight was categorized into 2 categories: normal and LBW. The LBW category includes the VLBW infants.

Premature Birth. was defined as born prior to 37 weeks of gestation, irrespective of birth weight. Data ranged from 0-140 days born prematurely.

SGA. was defined as less than the tenth percentile of birth weight (compared to population distributions of births 2000-2002 Vital Statistics) for gestational age adjusted for plurality, race/ethnicity, and child's sex (also captured from the birth certificate).

Covariates. Several factors associated with sensitivity and development were selected as covariates based on a literature review, including (1) breastfeeding, (2) maternal depression, (3) household income, (4) maternal race/ethnicity, (5) maternal education, (6) family structure, (7) maternal age and (8) parity. All information on the covariates was ascertained from the parent interview.

Breastfeeding. Mothers were asked if they ever breastfed their infant, how long they breastfed and whether they were currently breastfeeding their child. Distribution of data showed mothers largely fell into two groups: those that breastfed for one or more months vs. those that never breastfed. Breastfeeding was categorized as (0) Never Breastfed or breastfed a few days (49.3%) or (1) Breastfed 1 month or longer (50.7%).

Depressive symptoms. A modified version (12 of 20 items from the full version) of the Center for Epidemiological Studies' Depression Scale (CES-D)[44] self-report instrument was used to evaluate depressive symptomology. The CES-D measures absence or presence of negative thoughts, behaviors and feelings in the past 7 days. Some example items: how many days in the past week the respondent had (1) poor appetite, (2) felt bothered or (3) felt lonely. Items were rated using a 4-point Likert scale (0=rarely to 3=all or most days). Mean substitution for missing items were calculated and then mean scores were computed. Higher scores correspond to greater depressive symptomology, and a score over 4 indicates the presence of any depressive symptomology, but not a clinical diagnosis of depression. The scale demonstrated adequate internal consistency for this sample with a coefficient et. of .85.

Demographic variables. Infant data was gathered from infant birth certificates, which provided infant date of birth and gender (1 = boy). During the mother 9-month interview the following information was gathered: Maternal race/ethnicity non-Hispanic White, non-Hispanic Black, Hispanic, Asian, Other), age (15 to 51 years), educational attainment (1= middle school, 2 = some high school, 3 = high school graduate/GED, 4 = some college, 5 = Associate's degree, 6 = college degree/trade, 7 = some graduate, 8 = Master's degree, 9 = doctorate), and parity (1 = 1 target child only, 2 = 2 to 3 children, including target child; 3 = 4 or more children, including target child). Family structure (e.g., two-parent family = 1, single parent = 0),

Data Analyses

Statistical analyses were conducted using SAS 9.4, (SAS Institute, Cary, NC), Jackknife method. Due to ECLS-B's strategic over-sampling and certain exclusions (children born to mothers under age of 15 and adopted at birth), sample and replicate weights provided by the ECLS-B and NCES were used to make sample data representative of the population of biological mothers aged 15 and older, and account for differential selection probabilities and response patterns [75]. The ECLS-B weight of W1C0 (Wave 1; 9-month; Respondent/Child), along with 90 associated replicate weights were used in analyses to adjust standard errors and correct for the oversampling. As per NCES confidentiality requirements for ECLS-B data usage, reported numbers were rounded to the nearest 50.

Results

There was considerable overlap among LBW, premature and SGA infants (Figure 2), however, the study data included 1,050 infants born exclusively prematurely; and 750 infants that were SGA. In a regression model, adjusted for demographic covariates, examining the association between sensitivity (β=.176***, p<.001) and cognitive development including biological vulnerability measures of premature birth (β=--.084***, p<.001), SGA (β=-.032**, p<.01) and a reference category (n=4700), the amount of variance explained was 4% (R^2=.041, p<.001) (Table 1).

Table 1: (Unweighted) Percentage of Premature Birth and SGA in Normal, Low and Very Low Birth Weight Categories.

BIRTH WEIGHT STATUS		Premature Birth	
		% Not Premature	% Premature
Normal Birth Weight	Not SGA	86	7
81%	SGA	7	0
Low Birth Weight	Not SGA	3	38
10%	SGA	45	14
Very Low Birth Weight	Not SGA	0	73
9%	SGA	4	23

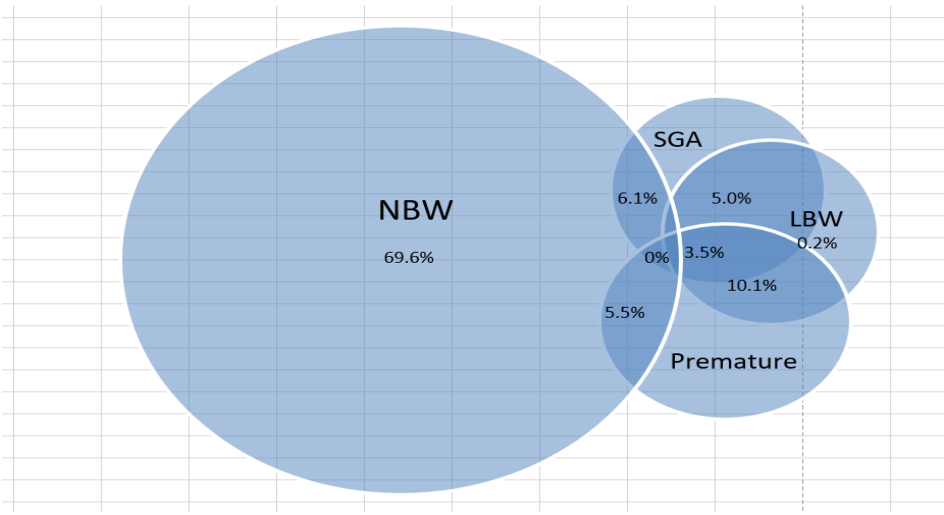


Figure 2: Overlap among the LBW, premature and SGA infants (n=2,050) in whole (unweighted) sample (n=6,750).

While LBW ($F_{1,6,450}$ =15.33, p < .001) and SGA ($F_{1,6,450}$ = 5.51, p < .001) were significantly associated with maternal sensitivity, premature birth ($F_{1,6,450}$ = 29.48, p < .001) had the strongest association with lower sensitivity. LBW ($F_{1,6,450}$)= 248.02, p < .001) and SGA ($F_{1,6,450}$)= 14.43, p < .001) were also significantly associated with cognitive development, but premature birth ($F_{1,6,450}$)= 390.65, p < .001) had the strongest association with lower cognitive development scores (Table 2).

Table 2. *Means, Standard Deviations, and Zero-order Correlations of All Variables of Interest.*

Variables	*Mean (SD)*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*
Maternal Age																				
Maternal Years of Education																				
Household Income																				
Black	.xx (.xx)	**	**		0.03	-0.21 **	-0.30 **	-0.01	-0.21 **	0.03	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06
Latinx		**	*	**	0.33 **	-0.25 **	-0.17 *	-0.27 **	-0.17 *	0.00	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
Asian		**	**	**	0.32 **	-0.07	0.20 **	0.00	0.11	-0.01	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05
White		0.xx **	**	**	-0.62 **	0.45 **	0.25 **	0.36 **	0.26 **	-0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Other			0.x	**	-0.39 **	0.28 **	-0.06	0.15	-0.02	0.06	-0.04	-0.04	-0.04	-0.04	-0.04	-0.04	-0.04	-0.04	-0.04	-0.04
Mother with biological partner				0.00	-0.08	0.37 **	0.39 **	0.26 **	0.31 **	0.08	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
Mother with partner					0.00 **	-0.21 **	-0.04	-0.18 *	-0.03	-0.05	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06	-0.06
Mother without partner																				
Parity								0.00 **	0.59 **	0.18 *	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Maternal Sensitivity																				
Maternal Depressive Symptoms									0.00 **	0.16 *	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
Breastfeeding	.									0.00 **	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
Normal Birth Weight (n=4590)																				
Low Birth Weight (n=?)											x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Small for Gestational Age (n=752)																				
Premature Birth (n=1052)																				

Analyses of mean differences and effect sizes demonstrated mothers of premature infants had lower sensitivity scores (M=33.8, SD =4.54), cohen's d=-.14, than those with SGA infants (M=34.2, SD =4.51), cohen's d=-.02. In addition, infants born prematurely had lower cognitive scores (M=70.84, SD =10.48), cohen's d=-.29; than infants SGA (M =74.45, SD =10.61), cohen's d=-.11.

As hypothesized, premature birth had the strongest negative association with both sensitivity and cognitive development. In subsequent analyses, only the premature birth measure of biological vulnerability was utilized.

In analyses examining the association of breastfeeding, depression, and premature birth with the outcome of maternal sensitivity, while controlling for demographic covariates (Table 3), infant's premature birth was negatively associated with sensitivity (β=-.035, p<.001). The association between maternal depression and sensitivity attenuated once breastfeeding was included in the model (R^2=.10, p<.001).

Table 3. *Means, Standard Deviations, and Zero-order Correlations of All Variables of Interest*

Standardized Beta Coefficient	*β*	*β*	*β*	*β*	*B*	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*B*
Infant sex-male	-.025*	-.026*	-.018	-.027*	-.024*	-.025*	-.022	-.021	-.021	-.019	-.019	-.019	-.019	-.017
Parity			-.019	-.006	-.037**	-.037*	-.030*	-.032	-.032	-.002	-.002	-.002	-.000	.000
Household Income				.244***	198***	.195***	.159***	.159***	.159***	.102***	.103***	.103***	.103**	.101**
Age					.095***	.095***	.089***	.091***	.091***	.037	.039	.039	.032	.035
Race (White Ref)														
Black						-.007	.045***	-.048***	-.048***	-.048***	-.047***	-.046***	-.046***	-.044***
Hispanic							-.137***	-.140***	-.140***	-.117***	-.115***	-.115***	-.116***	-.114***
Asian								-.035**	-.035**	-.044**	-.043***	-.043**	-.042**	-.042**
Other									-.003	-.001	-.001	-.001	.000	.001
Education										.159***	.159***	.159***	.158***	.158***
Family Structure	Reference=Mother with biological father													
Mother w Partner											.029	.029	.029	.031
Mother no Partner												-.002	.001	.000
Maternal Depression														
Depressive Symptomology													-.024~	-.020
Breastfeeding	Reference=Less than 1 month													
Breastfeeding more than 1 month													.007	.007
Premature Birth														-.035**
Model Summary (R^2)	.001***	.002***	.002***	.060***	.066***	.066***	.083***	.084***	.083***	.098***	.098***	.098***	.099***	.100***

Table 3: Factors associated with the outcome of sensitivity.

Standardized Beta Coefficient	*β*	*β*	*β*	*β*	*B*	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*B*
Infant sex-male	-.025*	-.026*	-.018	-.027*	-.024*	-.025*	-.022	-.021	-.021	-.019	-.019	-.019	-.019	-.017
Parity			-.019	-.006	-.037**	-.037*	-.030*	-.032	-.032	-.002	-.002	-.002	-.000	.000
Household Income				.244***	198***	.195***	.159***	.159***	.159***	.102***	.103***	.103***	.103**	.101**
Age					.095***	.095***	.089***	.091***	.091***	.037	.039	.039	.032	.035
Race (White Ref)														
Black						-.007	.045***	-.048***	-.048***	-.048***	-.047***	-.046***	-.046***	-.044***
Hispanic							-.137***	-.140***	-.140***	-.117***	-.115***	-.115***	-.116***	-.114***
Asian								-.035**	-.035**	-.044**	-.043***	-.043**	-.042**	-.042**
Other									-.003	-.001	-.001	-.001	.000	.001
Education										.159***	.159***	.159***	.158***	.158***
Family Structure	Reference=Mother with biological father													
Mother w											.029	.029	.029	.031

Partner														
Mother no Partner												-.002	.001	.000
Maternal Depression														
Depressive Symptomology													-.024~	-.020
Breastfeeding	Reference=Less than 1 month													
Breastfeeding more than 1 month													.007	.007
Premature Birth														-.035**
Model Summary (R^2)	**.001*****	**.002*****	**.002*****	**.060*****	**.066*****	**.066*****	**.083*****	**.084*****	**.083*****	**.098*****	**.098*****	**.098*****	**.099*****	**.100*****

*p < .05; ** p < .01; ***p < .001; ~p<.10

Note: Regression models are weighted with both sample (W1C0) and replicate weights (W1C1-W1C90).

In a final model examining the association between maternal sensitivity with infant cognitive development, (R^2=.05, p<.001), adjusted for premature birth, breastfeeding, maternal depression and demographic covariates, maternal sensitivity (β=.171, p<.001), breastfeeding (β=.081***, p<.001), depression (β=-.032**), and premature birth (β=-.115***) were significantly and independently associated with infant cognitive development (Table 4). The association between sensitivity and cognitive development did not attenuate when breastfeeding, depression or premature birth were included in the model.

Examination of the unstandardized coefficients for maternal sensitivity, breastfeeding and premature birth showed that for every additional point in sensitivity score, the average difference in infant cognitive development score increased by .37 points and by 1.58 points for breastfeeding with all else held constant. For every day premature, cognitive developmental scores decreased by 2.9 points with all else held constant.

Standardized Beta Coefficient	***β***	***β***	***β***	***B***	***β***	***β***	***β***	***β***	***β***	***β***	***β***	***β***
Infant sex (male)	-.033**	-.034**	-.035**	-.037**	-.037**	-.037**	-.034*	-.034*	-.029~	-.030	-.031	-.030 (-1.031, -.108)
Income		.034**	.053**	.043**	.038**	.038**	.044**	.044	.011	.003	-.003	-.010 (-.117, .063)
Age			-.040**	-.039**	-.039**	-.039**	-.040**	-.040**	-.055***	-.059***	-.058***	-.054*** (-.129, -.040)
Race (White=Reference)												
Black				-.008	-.013	-.014	-.022	-.022	-.020	-.018	-.018	-.011 (-1.054, .411)
Hispanic					-.015	-.016	-.017	-.017	.011	.007	-.007	-.004 (-.722, .549)
Asian						-011	-.013	-.013	-.011	-.011	-.010	-.009 (-1.968, .862)
Other							-.007	-.006	-.006	-.006	-.007	-.008 (-1.916, .991)
Years of Education								.029	.008	-.008	-.008	-.007 (-.197, .126)
Sensitivity												
									.182***	.177***	.177***	.171*** (.313, .422)
Depressive Symptoms (No symptoms=Reference)												
Depressive Symptomology										-.037**	-.038**	-.032** (-.099, -.012)
Breastfeeding (Less than 1 month=Reference)												
Breastfeeding more than 1 month											.079***	.081*** (1.135, 2.111)
Premature Birth Days (Greater than 37 weeks =Reference)												
												-.115*** (-.160, -.105)
Model Summary (R^2)	**.001*****	**.002*****	**.003*****	**.003*****	**.003*****	**.003*****	**.003*****	**.003*****	**.033*****	**.033*****	**.039*****	**.052*****

*p < .05; ** p < .01; ***p < .001; ~p<.10

Note: Regression models are weighted with both sample (W1C0) and replicate weights (W1C1-W1C90).

Table 4: Factors associated with the outcome of cognitive Development.

Conclusion

In this study, we investigated how the strength of the association between maternal sensitivity and infant cognitive development at 9-months was affected by three measures of biological vulnerability, while accounting for sociodemographic variables, breastfeeding and maternal depression. The most significant finding was that premature birth, rather than SGA or LBW (a measure of biological vulnerability, which combines infants born prematurely with infants SGA), had the greatest negative association with both sensitivity and cognitive development. Though LBW, SGA, and premature birth are highly correlated and may predict similar cognitive outcomes, results showed that use of LBW as a measure of biological vulnerability may minimize differences between premature and SGA infants.

While premature birth was negatively associated with both sensitivity and cognitive development, it did not explain much variance in either one. This result was unexpected given that an infant born prematurely is more likely to have incomplete development of the amygdala, which develops fully in the third trimester, and is thought to be responsible for homeostatic functions, including biorhythm regulation [45,46].

Although infants born prematurely frequently have poor emotional regulation and is hypothesized to negatively affect maternal sensitivity [47-50], in our study demographic factors explained more (approximately 10%) of the variance in maternal sensitivity. This finding was in line with other studies. A systematic review of mother-infant relationships in infants born prematurely [51] showed that premature birth was not associated with the quality of mother-infant interaction. Five studies showed an equal or higher quality of mother-infant interaction in groups of infants born prematurely compared to full-term infants; the remaining 13 studies showed “negative differences” in maternal interaction between mothers of premature infants in contrast to mothers of full-term infants. However, definitions of sensitivity varied in each of the 18 studies reviewed. The review concluded that infants born prematurely were not at higher risk of poorer dyadic interaction.

Maternal sensitivity, maternal depression, and breastfeeding were identified as factors independently and significantly associated with advanced infant cognitive development in this large, nationally representative study. Interestingly, maternal depression had a negative association with infant cognitive development but was not associated with maternal sensitivity. This lack of association may be related to the small percentage of mothers in the sample who reported experiencing depressive symptomology.

Taken together, sensitivity, breastfeeding, maternal depression, premature birth, and demographic covariates explained 5% of the variance in cognitive development. This finding may seem surprising, but in fact consistent with the concept of extreme malleability in development when infants are less than one year of age. Future studies are planned to examine the impact of biological vulnerability in later waves (e.g., 24, months, 36 months, and kindergarten) of the ECLS-B data.

While the effects of maternal sensitivity are easier to assess in younger infants, cognitive development measured in infancy can vary due to assessment day/time circumstances, even with well-designed instruments, such as the BSF-R. Since assessments conducted when infants are less than one year are not designed to be language-based, some cognitive abilities are not fully captured until the infant is approximately 24 months. The BSID/BSF-R is a global developmental instrument and may not pick up finer deficits or individual differences in cognitive functioning [52-54]. Moreover, the NCATS measure of maternal sensitivity (or any measure of sensitivity) does not account for all dimensions of stimulation the infant may receive from the mother. In this study, only maternal sensitivity was measured, but in many instances, infants receive cognitive stimulation from other household members or childcare providers. Cognitive development in infancy is also explained by genetic and environmental factors not examined in this study.

Our main finding that premature birth, rather than SGA, has a stronger association with impaired cognitive development offers support for the hypothesis that gestational time necessary for the complete development of brain structures in utero, rather than adverse intrauterine environment, accounts for the association between LBW and compromised cognitive development. It is hypothesized that when the prenatal brain is required to develop outside of the womb, the not yet fully developed brain receives sensory stimuli that it is not biologically prepared to receive. The environmental stimuli potentially alters mechanisms of brain functioning such as the myelination process, which protects the neuron and facilitates signal conduction [55]. This, in turn, negatively affects neuronal organization, creating disordered and less efficient nerve networks [56].

The incidence of premature births is approximately 10% in the United States [57-60], and nearly half of these infants demonstrate later cognitive deficits by the age of 8 years, representing a major public health problem [61,62]. Between 2010 and 2012, approximately 9 percent of all births were early elective deliveries [63,64], since not all premature births are due to problematic infant or maternal health. However, the rate of elective preterm cesarean is declining [65] and it is important that parents, health care providers and policy makers to continue to consider the impact of non-medically indicated premature birth upon infant's later cognitive development.

Study Limitations

This study shares many limitations of other studies examining cognitive development in infants, such as visit-day circumstances biasing data measurement. Infants in this cohort were born in 2001 and may not have had the same interventions or hospital practices and nutrition that are currently used in the Neonatal Intensive Care Unit (NICU) today.

Study Strength

The ECLS-B is a large nationally representative one-of-a kind data set for which results can be generalized to the US population. A unique feature of the cohort is the availability of both birthweight and gestational age captured on the birth certificate, allowing premature birth, small for gestational age and low birth weight to be compared. Direct child assessments to measure cognitive development minimize biases related to mother's recall. The use of the validated assessments such as the NCATS, coded by trained third party raters, the BSF-R and the CES-D, are additional strengths of the study.

This investigation is the only one to examine three types of infant biological vulnerability measures in association with maternal sensitivity and cognitive development, and the only to compare infants who are exclusively premature with infants exclusively SGA, while considering breastfeeding, maternal depression multiple demographic covariates.

In this study, premature birth, or insufficient gestational time, rather than compromised gestational time, or adverse intrauterine environment, as experienced infants born SGA, or low birth weight, drove the association between LBW and infant cognition. Maternal sensitivity remained associated with infant cognitive development, after adjusting for premature birth, breastfeeding, maternal depression and demographic covariates in this nationally representative study sample.

Acknowledgements

Thank you to Drs. Deborah Hasin, Katherine Keyes and Ian McKeage for their contributions to this work.

References

1. Bilgin A, Wolke, D. Maternal Sensitivity in Parenting Preterm Children: A Meta-analysis. *Pedatrics.* 2017;136.
2. Shin H, Park YJ, Ryu H, Seomun GA. Maternal sensitivity: a concept analysis. *Journal of advanced nursing.* 2008;64(3):304-314.
3. Bornstein MH, Tamis-Lemonda CS, Hahn CS, Haynes OM. Maternal responsiveness to young children at three ages: longitudinal analysis of a multidimensional, modular, and specific parenting construct. *Developmental psychology.* 2008;44(3):867-874.
4. Tamis-LeMonda CS, Bornstein MH. Maternal responsiveness and early language acquisition. *Advances in child development and behavior.* 2002;29:89-127.
5. Landry SH, Smith KE, Miller-Loncar CL, Swank PR. Predicting cognitive-language and social growth curves from early maternal behaviors in children at varying degrees of biological risk. *Developmental psychology.* 1997;33(6):1040-1053.
6. Smith KE, Landry SH, Swank PR. The role of early maternal responsiveness in supporting school-aged cognitive development for children who vary in birth status. *Pediatrics.* 2006;117(5):1608-1617.
7. Z. Hochberg RF, M. Constancia, M. Fraga, C. Junien, J.-C. Carel, P. Boileau, Y. Le Bouc, C. L. Deal, K. Lillycrop, R. Scharfmann, A. Sheppard, M. Skinner, M. Szyf, R. A. Waterland, D. J. Waxman, E. Whitelaw, K. Ong, and K. Albertsson-Wikland. Child Health, Developmental Plasticity, and Epigenetic Programming. *Endocr Rev.* 2011;32(2):159-224.
8. P Bateson PG, MHanson. The biology of developmental plasticity and the Predictive Adaptive Response hypothesis. *J Physiol.* 2014; 592(Jun 1).
9. Oudgenoeg-Paz O, Mulder H, Jongmans MJ, van der Ham IJM, Van der Stigchel S. The link between motor and cognitive development in children born preterm and/or with low birth weight: A review of current evidence. *Neuroscience and biobehavioral reviews.* 2017;80:382-393.
10. Gu H, Wang, L., Liu, L., Luo, X., Wang, J., Hou, F., Nkomola, P. D., Li, J., Liu, G., Meng, H., Zhang, J., & Song, R. . A gradient relationship between low birth weight and IQ: A meta-analysis. *Scientific reports* 2017;7(18035).
11. Scharf RJ, Rogawski ET, Murray-Kolb LE, et al. Early childhood growth and cognitive outcomes: Findings from the MAL-ED study. *Maternal & child nutrition.* 2018;14(3):e12584.
12. Farajdokht F, Sadigh-Eteghad S, Dehghani R, et al. Very low birth weight is associated with brain structure abnormalities and cognitive function impairments: A systematic review. *Brain and cognition.* 2017;118:80-89.
13. Bhutta AT CM, Casey PH, Cradock MM, Anand KJ. Cognitive and behavioral outcomes of school-aged children who were born preterm: a meta-analysis. *JAMA : the journal of the American Medical Association.* 2002;288(6):728-737.
14. Torche F, Echevarria G. The effect of birthweight on childhood cognitive development in a middle-income country. *International journal of epidemiology.* 2011;40(4):1008-1018.
15. Dobson KG, Ferro MA, Boyle MH, Schmidt LA, Saigal S, Van Lieshout RJ. Socioeconomic Attainment of Extremely Low Birth Weight Survivors: The Role of Early Cognition. *Pediatrics.* 2017;139(3).
16. Yu B, Garcy AM. A longitudinal study of cognitive and educational outcomes of those born small for gestational age. *Acta paediatrica.* 2018;107(1):86-94.
17. Vohr BR, Garcia Coll CT. Neurodevelopmental and school performance of very low-birth-weight infants: a seven-year longitudinal study. *Pediatrics.* 1985;76(3):345-350.
18. Horwood LJ, Mogridge N, Darlow BA. Cognitive, educational, and behavioural outcomes at 7 to 8 years in a national very low birthweight cohort. *Archives of disease in childhood Fetal and neonatal edition.* 1998;79(1):F12-20.
19. Arcangeli T, Thilaganathan B, Hooper R, Khan KS, Bhide A. Neurodevelopmental delay in small babies at term: a systematic review. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 2012;40(3):267-275.

20. Kull MA CR. Early physical health conditions and school readiness skills in a prospective birth cohort of U.S. children. *Social science & medicine.* 2017;142:145-153.
21. Lynch JL GB. Birth weight and Early Cognitive Skills: Can Parenting Offset the Link. *Maternal and child health journal.* 2017;21(1):156-167.
22. Subedi D DM, Scharf RJ. Developmental trajectories in children with prolonged NICU stays. *Archives of disease in childhood.* 2017;102(1):29-34.
23. Stoddard JJ, Miller T. Impact of parental smoking on the prevalence of wheezing respiratory illness in children. *American journal of epidemiology.* 1995;141(2):96-102.
24. Purisch SE, Gyamfi-Bannerman C. Epidemiology of preterm birth. *Seminars in perinatology.* 2017;41(7):387-391.
25. Pascal A, Govaert P, Oostra A, Naulaers G, Ortibus E, Van den Broeck C. Neurodevelopmental outcome in very preterm and very-low-birthweight infants born over the past decade: a meta-analytic review. *Developmental medicine and child neurology.* 2018;60(4):342-355.
26. Stavis RM, B. *Small-for-Gestational-Age (SGA) Infant.* 2017.
27. de Bie HMA OK, Delemarre-van de Waal HA. Brain Development, Intelligence and Cognitive Outcome in Children Born Small for Gestational Age *Hormone research in paediatrics.* 2010;73:6-14.
28. Vaivada TG, MF; Bhutta, ZA. Promoting Early Child Development With Interventions in Health and Nutrition: A Systematic Review. *Pediatrics.* 2017 140(2).
29. Sung IK, Vohr B, Oh W. Growth and neurodevelopmental outcome of very low birth weight infants with intrauterine growth retardation: comparison with control subjects matched by birth weight and gestational age. *The Journal of pediatrics.* 1993;123(4):618-624.
30. Page M, Wilhelm MS, Gamble WC, Card NA. A comparison of maternal sensitivity and verbal stimulation as unique predictors of infant social-emotional and cognitive development. *Infant behavior & development.* 2010;33(1):101-110.
31. Cabrera NJ, Fagan J, Wight V, Schadler C. Influence of mother, father, and child risk on parenting and children's cognitive and social behaviors. *Child development.* 2011;82(6):1985-2005.
32. Linsell L, Malouf R, Morris J, Kurinczuk JJ, Marlow N. Prognostic Factors for Poor Cognitive Development in Children Born Very Preterm or With Very Low Birth Weight: A Systematic Review. *JAMA pediatrics.* 2015;169(12):1162-1172.
33. Gibbs BG, Forste R. Breastfeeding, Parenting, and Early Cognitive Development. *The Journal of pediatrics.* 2013.
34. McManus BM, Poehlmann J. Parent-child interaction, maternal depressive symptoms and preterm infant cognitive function. *Infant behavior & development.* 2012;35(3):489-498.
35. Pope CJ MDDRaT. Breastfeeding and Postpartum Depression: An Overview and Methodological Recommendations for Future Research. *Depression research and treatment.* 2016.
36. Figueiredo B, Canario C, Field T. Breastfeeding is negatively affected by prenatal depression and reduces postpartum depression. *Psychological medicine.* 2013:1-10.
37. McManus BM, Poehlmann J. Maternal depression and perceived social support as predictors of cognitive function trajectories during the first 3 years of life for preterm infants in Wisconsin. *Child: care, health and development.* 2012;38(3):425-434.
38. Glass HC CA, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. *Anesth Analg.* 2015;120(6):1337-1351.
39. Shah PE, Robbins N, Coelho RB, Poehlmann J. The paradox of prematurity: the behavioral vulnerability of late preterm infants and the cognitive susceptibility of very preterm infants at 36 months post-term. *Infant behavior & development.* 2013;36(1):50-62.
40. Oken E, Kleinman KP, Belfort MB, Hammitt JK, Gillman MW. Associations of gestational weight gain with short- and longer-term maternal and child health outcomes. *American journal of epidemiology.* 2009;170(2):173-180.
41. McCowan L HR. Risk factors for small for gestational age infants. *Best practice & research Clinical obstetrics & gynaecology.* 2009;23(6):779-793.
42. Lindström L1 WA, 3, Bergman E1, Lundgren M. Born Small for Gestational Age and Poor School Performance - How Small Is Too Small. *Hormone research in paediatrics.* 2017;88(3-4):215-223.
43. Li X ER, Epstein LH, Shenassa ED, Xie C, Wen X. Parenting and cognitive and psychomotor delay due to small-for-gestational-age birth. *Journal of child psychology and psychiatry, and allied disciplines.* 2017;58(2):169-179.
44. Radloff L. The Center for Epidemiology Study-Depression (CES-D) scale. A self-report depression scale for research in the general population. *Journal of Applied Psychological Measurement.* 1977;1:385-401.
45. Fox NA, Henderson HA, Marshall PJ, Nichols KE, Ghera MM. Behavioral inhibition: linking biology and behavior within a developmental framework. *Annual review of psychology.* 2005;56:235-262.
46. Allen MC. Neurodevelopmental outcomes of preterm infants. *Current opinion in neurology.* 2008;21(2):123-128.
47. Lewis M, Bendersky M. Cognitive and motor differences among low birth weight infants: impact of intraventricular hemorrhage, medical risk, and social class. *Pediatrics.* 1989;83(2):187-192.
48. Landry SH, Schmidt M, Richardson MA. The effects of intraventricular hemorrhage on functional communication skills in preterm toddlers. *Journal of developmental and behavioral pediatrics : JDBP.* 1989;10(6):299-306.
49. Dale PS, Greenberg MT, Crnic KA. The multiple determinants of symbolic development: evidence from preterm children. *New directions for child development.* 1987(36):69-86.
50. Morris BH, Smith KE, Swank PR, Denson SE, Landry SH. Patterns of physical and neurologic development in preterm children. *Journal of perinatology : official journal of the California Perinatal Association.* 2002;22(1):31-36.

51. Korja RL, R; Lehtonen, L. The effects of preterm birth on mother-infant interaction and attachment during the infant's first two years. *Acta obstetricia et gynecologica Scandinavica.* 2012 91(2):164-173.
52. Anderson PJ DLC, Hutchinson E, Roberts G, Doyle LW; Victorian Infant Collaborative Group. Underestimation of developmental delay by the new Bayley-III Scale. *Arch Pediatr Adolesc Med.* 2010;16(4):352-356.
53. Moore TJ, S; Haider, Hennessy, E, & Marlow, N. Relationship between using the Second and Third Editions of the Bayley Scales in Extremely Preterm Children. *The Journal of pediatrics.* 2012;160(8):553.
54. Brito NF, WP, Amso, D; Barr, R; Bell, M; Calkins, S; Flynn, A; Montgomery-Downs, HE; Oakes, LM; Richards, JE; Samuelson, LM; Colombo, J. Beyond the Bayley: Neurocognitive Assessments of Development During Infancy and Toddlerhood. *Developmental neuropsychology.* 2019;44:220.
55. Brumbaugh JE CA, Lee JK, DeVolder IJ, Zimmerman MB, Magnotta VA, Axelson ED, Nopoulos PC. Altered brain function, structure, and developmental trajectory in children born late preterm. *Pediatric research.* 2016;80(2):197-203.
56. Minde K, Goldberg S, Perrotta M, et al. Continuities and discontinuities in the development of 64 very small premature infants to 4 years of age. *Journal of child psychology and psychiatry, and allied disciplines.* 1989;30(3):391-404.
57. WHO MoD, Partnership for Maternal, Newborn & Child Health, Save the Children. Born too soon: the global action report on preterm birth. . 2012.
58. Blencowe H CS, Oestergaard MZ, et al. . National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. . *Lancet 2012.*379: 2162.
59. Martin JA, Kirmeyer S, Osterman M, Shepherd RA. Born a bit too early: recent trends in late preterm births. *NCHS data brief.* 2009(24):1-8.
60. Martin JA HB, Osterman MJ, et al. . Births: Final Data for 2015. In: Rep NV, ed. . https://www.cdc.gov/nchs/data/nvsr/nvsr66/nvsr66_01.pdf 2017.
61. Teitler JO RN, Nepomnyaschy L, Martinson M. . A cross-national comparison of racial and ethnic disparities in low birth weight in the United States and England. . *Pediatrics.* 2007(120): 1182.
62. Behrman RE BA. Preterm Birth, Causes, Consequences, and Prevention, . In: The National Academies Press, ed. Washington, DC 2007.
63. Witt WP WL, Cheng ER, Mandell K, Chatterjee D, Wakeel F, Godecker AL, Zarak D. Determinants of cesarean delivery in the US: a lifecourse approach. *Maternal and child health journal.* 2015; 19(Jan (1)):84-93.
64. Fowler TT SJ, Applegate MS, Griffith K4, Fairbrother GL. Early elective deliveries accounted for nearly 9 percent of births paid for by Medicaid. *Health Aff.* 2014;33(12):2170-2178.
65. Buckles KG, M. Worth the Wait? The Effect of Early Term Birth on Maternal and Infant Health. *J Policy Anal Manage.* 2017;36(4):748-772.