

Supplementary Material

Table S1. Type of variables, models used to predict missing data, and percentages of missing values for each variable included in the imputation model (N=3,150)

Variables	Type of variable	Model used to predict missing data	Percentages of missing values
Perinatal characteristics			
Birth region of the child	Categorical	-	0%
Gestational age	Categorical (4 categories)	-	0%
Maternal age at birth	Continuous	-	0%
Parity	Categorical (3 categories)	Multinomial regression	1.08%
Maternal birth outside France	Categorical (5 categories)	Multinomial regression	1.11%
Maternal level of education	Categorical (4 categories)	Multinomial regression	7.30%
Antenatal steroids	Binary	Logistic regression	3.02%
Multiple pregnancy	Binary	Logistic regression	0.03%
Delivery mode	Categorical (3 categories)	Multinomial regression	1.08%
Sex	Binary	-	0%
Small for gestational age	Binary	-	0%
Extra-uterine growth restriction	Categorical (3 categories)	Multinomial regression	11.27
Postnatal corticosteroids	Binary	Logistic regression	2.60
Inborn	Binary	-	0%
Surfactant	Binary	Logistic regression	0.92%
Hemodynamic disorders	Binary	Logistic regression	1.30%
Necrotizing enterocolitis	Binary	Logistic regression	0.89%
Late-onset sepsis	Binary	Logistic regression	1.27%
Patent ductus arteriosus treatment	Binary	Logistic regression	2.67%
Intraventricular hemorrhage status	Categorical (5 categories)	Multinomial regression	1.30%
BPD	Binary	Logistic regression	0%
Breastmilk at discharge	Categorical (3 categories)	Multinomial regression	6.73%
At 2 years' corrected age			
Cerebral palsy	Categorical (5 categories)	Multinomial regression	16.22%
ASQ Communication score	Continuous	Predictive mean matching	16.86%
ASQ Gross motor score	Continuous	Predictive mean matching	19.02%
ASQ Fine motor score	Continuous	Predictive mean matching	19.71%
ASQ Problem solving	Continuous	Predictive mean matching	21.11%
ASQ Personal social score	Continuous	Predictive mean matching	19.68%
CDI below 28 words	Binary	Logistic regression	22.22%

ASQ=Ages and Stages questionnaire (Squire, 2009); WPPSI-IV=Wechsler Preschool and Primary Scale of Intelligence-Fourth edition (Wechsler, 2014); FSIQ=full-Scale Intelligence quotient; MABC-2=Movement Assessment Battery for Children, Second Edition (Henderson, 2007); SCQ=Social Communication Questionnaire; SDQ=Strengths and Difficulties Questionnaire (Goodman, 1997).

Table S1. Type of variables, models used to predict missing data, and percentages of missing values for each variable included in the imputation model (N=3,150) (continued)

Variables	Type of variable	Model used to predict missing data	Percentages of missing values
At 5-6 years			
Cerebral palsy	Categorical (5 categories)	Multinomial regression	29.24%
Hearing disabilities	Categorical (4 categories)	Multinomial regression	31.08%
Visual disabilities	Categorical (4 categories)	Multinomial regression	38.29%
Total SDQ score	Continuous	Predictive mean matching	38.57%
Total MABC-2 score	Continuous	Predictive mean matching	1.25%
WPPSI-IV FSIQ score	Continuous	Predictive mean matching	38.98%
Epilepsy	Binary	Logistic regression	38.41%
Autism spectrum disorder reported by parents	Binary	Logistic regression	37.21%
SCQ score \geq 90th centile	Binary	Logistic regression	40.89%
Hospitalization in the last 12 months	Binary	Logistic regression	31.87%
Consultation with a pediatric neurologist in the last 12 months	Binary	Logistic regression	33.14%
Consultation with a pediatric pneumologist in the last 12 months	Binary	Logistic regression	45.24%
Complex developmental interventions	Binary	Logistic regression	31.81%
Psychologist or psychiatrist	Binary	Logistic regression	33.71%
Psychomotor therapist	Binary	Logistic regression	33.11%
Speech therapist	Binary	Logistic regression	33.56%
Motor physiotherapist	Binary	Logistic regression	32.60%
Respiratory physiotherapist	Binary	Logistic regression	33.08%
Follow-up in early medico-social action centre	Binary	Logistic regression	35.62%
Type of school: mainstream school without support	Binary	Logistic regression	31.14%

ASQ=Ages and Stages questionnaire (Squire, 2009); WPPSI-IV=Wechsler Preschool and Primary Scale of Intelligence-Fourth edition (Wechsler, 2014); FSIQ=full-Scale Intelligence quotient; MABC-2=Movement Assessment Battery for Children, Second Edition (Henderson, 2007); SCQ=Social Communication Questionnaire; SDQ=Strengths and Difficulties Questionnaire (Goodman, 1997).

Table S2. Comparison of very preterm children with complete assessment at age 5-6 years and those included in the analyses with multiple imputation. (n=3,150)

	Children with complete assessment at age 5-6 years N = 1,914 (60.8%)	Children included in the analyses with multiple imputation N = 1,236 (39.2%)	P-value ^a
Perinatal characteristics			
BPD	248/1,914 (11.8)	146/1,236 (10.5)	0.25
Male, n/N (% ^b)	1,003/1,914 (52.5)	641/1,236 (51.9)	0.76
Gestational age (weeks), n/N (% ^b)			
24-25 ^c	131/1,914 (5.3)	90/1,236 (5.6)	0.32
26-27	386/1,914 (18.5)	222/1,236 (16.4)	
28-29	529/1,914 (28.9)	330/1,236 (27.9)	
30-31	868/1,914 (47.4)	594/1,236 (50.1)	
Small-for-gestational age, n/N (% ^b)	660/1,914 (35.2)	414/1,236 (34.1)	
≥ 1 antenatal steroid course, n/N (% ^b)	1,236/1,850 (68.3)	817/1,205 (59.4)	0.85
Surfactant administration, n/N (% ^b)	1,229/1,901 (63.2)	743/1,220 (59.4)	0.29
Hemodynamic disorders, n/N (% ^b)	466/1,860 (23.9)	306/1,211 (24.0)	0.98
Patent ductus arteriosus treatment, n/N (% ^b)	1,391/1,869 (23.8)	907/1,197 (22.4)	0.37
Necrotizing enterocolitis, n/N (% ^b)	67/1,897 (3.5)	46/1,225 (3.6)	0.83
Intraventricular hemorrhage grade, n/N (% ^b)			
No IVH	1,224/1,888 (65.3)	855/1,221 (70.9)	0.007
Grade 1	359/1,888 (19.1)	182/1,221 (14.8)	
Grade 2	239/1,888 (12.2)	137/1,221 (10.8)	
Grade 3	44/1,888 (2.3)	37/1,221 (2.8)	
Grade 4	22/1,888 (1.1)	10/1,221 (0.8)	
Late-onset sepsis, n/N (% ^b)	430/1,891 (21.4)	244/1,219 (18.9)	0.09
Extra-uterine growth restriction, n/N (% ^b)			
No	842/1,719 (48.5)	555/1,076 (50.7)	0.53
Moderate	438/1,719 (25.3)	259/1,076 (24.2)	
Severe	439/1,719 (26.2)	262/1,076 (25.0)	
Postnatal corticosteroids, n/N (% ^b)	139/1,862 (6.6)	85/1,206 (6.3)	0.70
Maternal sociodemographic characteristics			
Educational level, n/N (% ^b)			
< Secondary school	511/1,857 (27.6)	465/1,063 (43.7)	<0.001
Secondary school	385/1,857 (20.7)	249/1,063 (23.5)	
1 or 2 years post-secondary school	395/1,857 (21.2)	157/1,063 (14.7)	
3 years and more post-secondary school	566/1,857 (30.4)	192/1,057 (18.2)	
Country of birth, n/N (% ^b)			
France	1,523/1,907 (79.9)	851/1,208 (70.6)	<0.001
Other European country	36/1,907 (1.9)	43/1,208 (3.5)	
North Africa country	135/1,907 (7.1)	123/1,208 (10.3)	
Other African country	126/1,907 (6.5)	114/1,208 (9.2)	
Other	87/1,907 (4.6)	77/1,208 (6.4)	

BPD= bronchopulmonary dysplasia; PMA= postmenstrual age

Bronchopulmonary dysplasia was defined with the Jensen et al. 2019 definition. Intraventricular hemorrhage was defined with the Papile classification (Papile, 1978). Necrotizing enterocolitis corresponded to all necrotizing enterocolitis grade ≥ 2 with the Bell classification (Bell, 1978). Patent ductus arteriosus was defined as requiring medical or surgical treatment. Small-for-gestational age was defined as birth weight less than the 10th percentile for gestational age and sex based on French intrauterine growth curves (Ego, 2016).

^a Pearson's chi-squared tests.

^b All percentages were weighted over the recruitment time.

^c Including 5 children born before 24 weeks' gestation, with one survivor at age 5-6 years born at 23 weeks' and 6 days' gestational age.

Table S3. Subgroup analyses: association between bronchopulmonary dysplasia and outcomes for very preterm children born before 29 weeks' gestation alive at age 5-6 years. (n= 1,220)

	Complete-case N= 765		Imputed data N= 1,220	
	BPD N= 199 aOR ^a (95% CI)	P-value ^b	BPD N= 325 aOR ^a (95% CI)	P-value ^b
Neurodevelopmental outcomes				
Overall neurodevelopmental disabilities ^c				
None		0.008	1	<0.001
Mild	1.48 (0.84-2.33)		1.46 (0.98-2.18)	
Moderate	2.94 (1.54-5.59)		2.57 (1.53-4.34)	
Severe	2.41 (1.11-5.21)		2.96 (1.66-3.50)	
Developmental coordination disorders ^d				
Total MABC-2 score \leq 5 th centile ^e	1.86 (0.96-3.60)	0.07	1.99 (1.16-3.41)	0.01
Behavioural difficulties:				
Total SDQ score \geq 90 th centile ^e	1.62 (0.87-3.02)	0.13	1.46 (0.89-2.37)	0.13
Full-scale intelligence quotient ^f				
Total intelligence quotient score (β)	-4.2 (-7.2 to -1.1)	0.008	-5.5 (-8.2 to -2.8)	<0.001
Total intelligence quotient score $<$ -2 SD ($<$ 79) ^e	2.24 (1.22-4.11)	0.009	2.23 (1.48-3.38)	<0.001
Cerebral palsy				
All cerebral palsy	1.42 (0.73-2.75)	0.31	1.60 (0.98-2.61)	0.06
Social interaction disorders				
SCQ score \geq 90 th centile ^e	1.34 (0.80-2.24)	0.27	1.31 (0.87-1.99)	0.20
Healthcare utilisation				
Hospitalisation in the last 12 months	1.52 (0.92-2.49)	0.10	1.48 (0.97-2.26)	0.07
Consultation with a paediatric neurologist in the last 12 months	1.52 (0.83-2.79)	0.18	1.32 (0.81-2.16)	0.27
Consultation with a paediatric pneumologist in the last 12 months	3.22 (1.74-5.97)	<0.001	2.81 (1.70-4.65)	<0.001
Developmental support ^g	1.88 (1.27-2.79)	0.002	1.90 (1.35-2.67)	<0.001

aOR=adjusted odd ratio; β =adjusted regression coefficient for linear models; BPD= Bronchopulmonary dysplasia; CI=confidence interval; GMFCS=Gross Motor Function Classification System; MABC-2=Movement Assessment Battery for Children, 2nd edition; PMA= Postmenstrual age; SCQ=Social Communication Score; SDQ=Strengths and Difficulties Questionnaire

^a Linear models for continuous outcomes, logistic regression models for binomial outcomes, and multinomial regression models for multinomial outcomes. All models were fitted with Generalized Estimating Equations to account for non-independence of outcomes related to multiple births. Reference category for the exposure was children without BPD. The models were multivariable models including the following variables: BPD (4 categories) + gestational age (4 categories) + small-for-gestational-age (binomial) + ≥ 1 antenatal corticosteroids course (binomial) + hemodynamic disorders (binomial) + intraventricular hemorrhage (5 categories) + patent ductus arteriosus (binomial) + necrotizing enterocolitis (binomial) + late-onset sepsis (binomial) + extra-uterine growth restriction (3 categories) + maternal educational level (4 categories) + maternal country of birth (5 categories).

^b Wald-tests.

^c Includes cerebral palsy, vision, hearing, full-scale intelligence quotient, developmental coordination disorders, and behavioural difficulties.

^d Cut-off point of the distribution related to the reference group born at term (37-41 weeks).

^e Among children without cerebral palsy, severe or moderate sensory disabilities, and full-scale intelligence quotient > -2 SD of the distribution related to the reference group born at term.

^f Full-scale intelligence quotients, measured by the Wechsler Preschool and Primary Scale of Intelligence, 4th edition.

^g Developmental support was defined as at least two consultations with a psychologist, psychiatrist, orthoptist, speech therapist, psychomotor therapist, physiotherapist, during the last 12 months or schooling in a special school or follow-up in any type of rehabilitation centre.

Table S4. Sensitivity analyses: association between bronchopulmonary dysplasia using 2001 NICHD definition and outcomes in preterm children alive at age 5-6 years. (n= 3,069)

	Complete-cases N ^a = 1,866				Imputed data N ^a = 3,069			
	Mild BPD N= 316 aOR ^b (95% CI)	Moderate BPD N= 78 aOR ^b (95% CI)	Severe BPD N= 155 aOR ^b (95% CI)	P-value ^c	Mild BPD N= 496 aOR ^b (95% CI)	Moderate BPD N= 119 aOR ^b (95% CI)	Severe BPD N= 247 aOR ^b (95% CI)	P-value ^c
Neurodevelopmental outcomes								
Overall neurodevelopmental disabilities ^d								
<i>None</i>	1	1	1	0.006	1	1	1	0.006
<i>Mild</i>	1.03 (0.72-1.48)	1.13 (0.63-2.01)	1.40 (0.84-2.33)		1.01 (0.75-1.37)	1.18 (0.72-1.95)	1.72 (1.10-2.69)	
<i>Moderate</i>	1.61 (0.89-2.91)	0.97 (0.33-2.88)	4.20 (2.17-8.15)		1.03 (0.65-1.62)	1.26 (0.55-2.86)	2.91 (1.70-4.97)	
<i>Severe</i>	0.93 (0.45-1.91)	1.62 (0.62-4.26)	3.26 (1.39-7.64)		0.90 (0.51-1.57)	1.97 (0.93-4.18)	2.98 (1.57-5.65)	
Developmental coordination disorders ^e								
<i>Total MABC-2 score ≤ 5th centile^f</i>	1.33 (0.76-2.31)	1.68 (0.74-3.80)	1.91 (0.93-3.95)	0.30	1.26 (0.77-2.06)	1.69 (0.82-3.52)	2.17 (1.21-3.89)	0.07
Behavioural difficulties:								
<i>Total SDQ score ≥ 90th centile^f</i>	1.25 (0.73-2.14)	2.08 (0.94-4.60)	1.97 (1.03-3.78)	0.13	1.10 (0.72-1.68)	1.61 (0.85-3.02)	1.80 (1.09-3.00)	0.11
Full-scale intelligence quotient ^g								
Total intelligence quotient score (β)	-0.3 (-2.6 to 1.9)	-1.5 (-5.2 to 2.1)	-4.8 (-8.2 to -1.4)	0.04	0.3 (-1.8 to 2.3)	-3.1 (-6.7 to 0.5)	-5.5 (-8.5 to -2.5)	0.001
<i>Total intelligence quotient score < -2 SD (< 79)^f</i>	1.34 (0.79-2.27)	1.22 (0.56-2.67)	2.97 (1.63-5.40)	0.004	1.06 (0.72-1.56)	1.45 (0.79-2.66)	2.36 (1.53-3.65)	0.001
Cerebral palsy								
<i>All cerebral palsy</i>	1.36 (0.73-2.52)	0.44 (0.12-1.69)	2.05 (1.03-4.08)	0.10	0.96 (0.61-1.52)	1.11 (0.53-2.33)	1.68 (0.98-2.88)	0.18
Social interaction disorders								
<i>SCQ score ≥ 90th centile^f</i>	1.01 (0.65-1.56)	0.97 (0.47-2.02)	1.29 (0.74-2.21)	0.82	1.08 (0.77-1.52)	1.10 (0.62-1.88)	1.37 (0.89-2.11)	0.57
Healthcare utilisation								
Hospitalisation in the last 12 months	0.85 (0.54-1.34)	1.43 (0.72-2.83)	1.55 (0.93-2.58)	0.15	0.92 (0.62-1.36)	1.38 (0.77-2.48)	1.44 (0.91-2.28)	0.21
Consultation with a paediatric neurologist in the last 12 months	0.82 (0.46-1.47)	0.57 (0.19-1.78)	1.53 (0.81-2.90)	0.20	1.00 (0.65-1.55)	1.10 (0.53-2.38)	1.52 (0.90-2.56)	0.40
Consultation with a paediatric pneumologist in the last 12 months	1.19 (0.64-2.23)	2.32 (0.97-5.58)	2.78 (1.44-5.38)	0.01	1.09 (0.68-1.73)	2.31 (1.19-4.49)	2.70 (1.60-4.53)	<0.001
Developmental support ^h	1.17 (0.86-1.60)	1.12 (0.67-1.88)	1.93 (1.25-2.99)	0.03	1.13 (0.88-1.46)	1.39 (0.89-2.17)	1.86 (1.29-2.68)	0.007

aOR=adjusted odd ratio; β=adjusted regression coefficient for linear models; CI=confidence interval; GMFCS=Gross Motor Function Classification System; MABC-2=Movement Assessment Battery for Children, 2nd edition; PMA= Postmenstrual age; SCQ=Social Communication Score; SDQ=Strengths and Difficulties Questionnaire

^a For some children of the study, we did not know whether they were still receiving oxygen at 28 days of life. Therefore, in this sensitivity analysis using the 2001 NICHD definition of BPD, fewer children were included than in the main analysis using the Jensen definition of BPD.

^b Linear models for continuous outcomes, logistic regression models for binomial outcomes, and multinomial regression models for multinomial outcomes. All models were fitted with Generalized Estimating Equations to account for non-independence of outcomes related to multiple births. Reference category for the exposure was children without BPD. The models were multivariable models including the following variables: BPD (4 categories) + gestational age (4 categories) + small-for-gestational-age (binomial) + ≥ 1 antenatal corticosteroids course (binomial) + hemodynamic disorders (binomial) + intraventricular hemorrhage (5 categories) + patent ductus arteriosus (binomial) + necrotizing enterocolitis (binomial) + late-onset sepsis (binomial) + extra-uterine growth restriction (3 categories) + maternal educational level (4 categories) + maternal country of birth (5 categories).

^c Wald-tests.

^d Includes cerebral palsy, vision, hearing, full-scale intelligence quotient, developmental coordination disorders, and behavioural difficulties.

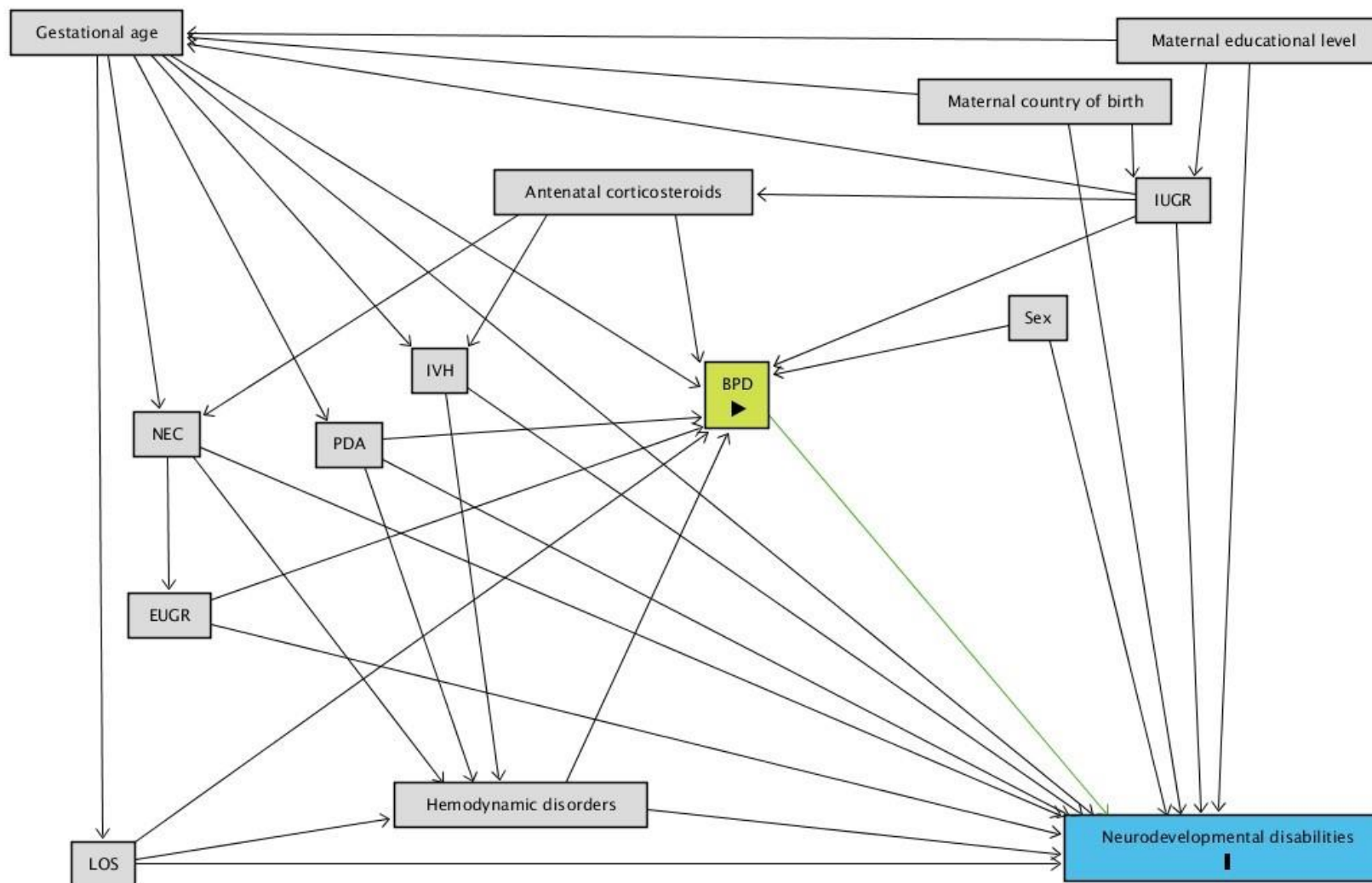
^e Cut-off point of the distribution related to the reference group born at term (37-41 weeks).

^f Among children without cerebral palsy, severe or moderate sensory disabilities, and full-scale intelligence quotient > -2 SD of the distribution related to the reference group born at term.

^g Full-scale intelligence quotients, measured by the Wechsler Preschool and Primary Scale of Intelligence, 4th edition.

^h Developmental support was defined as at least two consultations with a psychologist, psychiatrist, orthoptist, speech therapist, psychomotor therapist, physiotherapist, during the last 12 months or schooling in a special school or follow-up in any type of rehabilitation centre.

Figure S1. Directed acyclic graph of the study



BPD= Bronchopulmonary dysplasia; EUGR= Extraterine growth restriction; IUGR= Intrauterine growth restriction; IVH= Intraventricular hemorrhage; LOS= Late onset sepsis; NEC= Necrotizing enterocolitis; PDA= Patent ductus arteriosus.

Blue box: outcome; Green arrow: causal path; Green box: exposure; Grey boxes: adjusted variables.