Early life predictors of motor, cognitive, and language development: a pooled multi-country analysis

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Background

- More than 250 million under-5 children in LMICs do not attain full development potential.
- Suboptimal development has long term effects on education and income attainment.
- The 2030 Sustainable Development Goals target early childhood development directly.

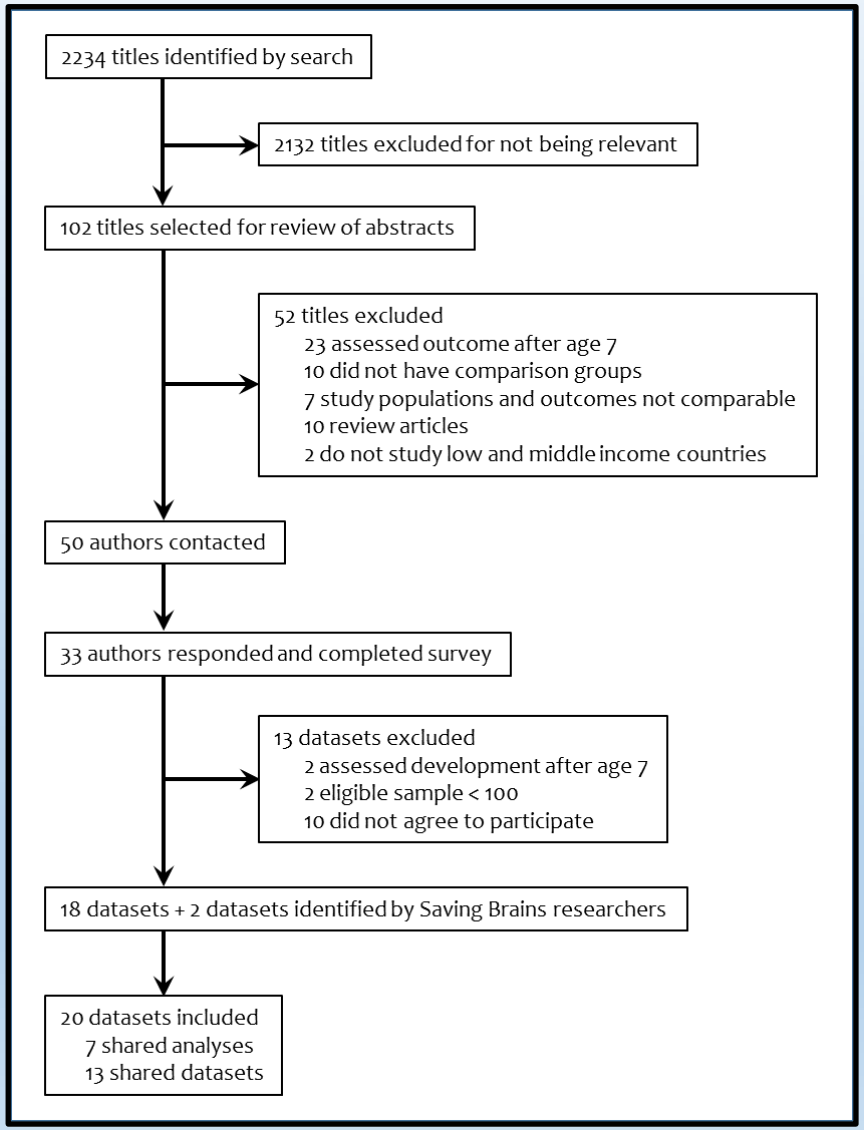
Background

- Exposure to risk and protective factors in 1000 days of life (conception through 24 months of age) is critical for children's development.
- Limited evidence on the role of early life risk factors on child development in LMIC.
- Majority of systematic review of evidence have primarily focused on physical development.

Objective

- To examine the association of early life factors for cognitive, motor and language development among children aged less than 7 years residing in LMICs.

Methods: datasets selection



Methods: the primary inclusion criterion

- Assessment of at least one domain of child development: cognitive, motor, language and socioemotional
- Use of a standard child development assessment instrument
- Development assessment before the age of 7 years
- Collection of at least one early life factor of interest

Methods: early life factors

14 factors included in the analysis.

Parental factors

- father's education
- mother's education
- mother's age
- mother's height
- mother's BMI
- hemoglobin level during pregnancy

Birth spacing, malaria, maternal HIV, iron & zinc supplementation, and stimulation was not available in sufficient number of studies

Child factors

- birth weight
- preterm birth
- small-for-gestational-age (SGA) birth
- exclusive breastfeeding till 6 months of age
- hemoglobin levels in infancy
- access to clean water
- access to sanitation
- diarrhea preceding the 6 months before development assessment

Methods: analyses

- **Individual data set**

- Linear regression models to assess standardized mean differences (SMDs) in cognitive, motor, and language scores
- Adjusted for: child's age and gender, maternal education and a measure of socioeconomic status income or household wealth and intervention assignment if RCT

- **Meta-analysis**

- Estimates from ≥ 4 studies
- Random effects modles using the DerSimonian and Larid method

Results: 20 cohorts, 20379 children

	Study	Year	Setting	Primary study design	Study population	N	Child age in years at assessment (mean ± SD)
Asia							
1	Black	2004	Bangladesh	RCT	cohort	221	1.06±0.03
2	Tofail	2008	Bangladesh	RCT	cohort	2853	0.61±0.02
3	Tofail	2012	Bangladesh	RCT	cohort	249	0.84±0.01
4	Taneja	2005	India	RCT	cohort	571	1.25±0.16
5	Taneja	2015	India	RCT	cohort	422	1.37±0.60
6	Yousafzai	2014	Pakistan	randomized effectiveness trial	cohort	1357	11.6 ±0.83
7	Duazo	2010	Philippines	longitudinal program evaluation	cohort	4904	1.62±0.88
Sub-Saharan Africa							
8	Shapiro	2013	Botswana	RCT	cohort	224	?±?
9	Alemtsehay	2009	Ethiopia	cross-sectional, cohort	cohort	100	61.3±2.95
10	Gladstone	2011	Malawi	cross-sectional, cohort	cohort	840	1.74±0.33
11	McDonald	2013	Tanzania	RCT	cohort	305	1.28±0.04
12	Manji	2014	Tanzania	RCT	cohort	206	0.36±0.19
13	Sudfeld	2015	Tanzania	RCT	cohort	958	2.25±0.52
14	Locks	2016	Tanzania	RCT	cohort	248	1.21±0.03
Latin America							
15	Matijasevich	2010	Brazil	longitudinal cohort	cohort	3868	?±?
16	Santos	2008	Brazil	longitudinal cohort	cohort	365	5.80±3.02
17	Fernald	2011	Ecuador	randomized effectiveness trial	cohort	1265	4.59±0.87
18	Handal	2007	Ecuador	prospective cohort study	cohort	283	2.46±1.46
19	Braun	2012	Mexico	prospective cohort study	cohort	1032	2.02±0.03
Europe							
20	Akman	2004	Turkey	RCT	cohort	108	1.42±0.59

Parental education: positive dose-response relationship with cognitive, motor and language scores

Risk Factor	Cognitive				Motor				Language			
	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)
Mother's education												
No education (<1 years)	15	-0.12 (-0.24, -0.008)	0.05	50.88	18	-0.07 (-0.13, -0.01)	0.03	18.29	5	-0.06 (-0.21, -0.09)	0.49	35.52
Primary (1- <6 years)		Reference				Reference				Reference		
Secondary (6- <10 years)	17	0.14 (0.05, 0.24)	< 0.01	59.70	19	0.12 (0.06, 0.18)	< 0.01	51.80	5	0.13 (0.04, 0.21)	0.04	0.00
Higher (≥10 years)	17	0.36 (0.19, 0.48)	< 0.01	65.81	19	0.26 (0.14, 0.38)	< 0.01	70.64	5	0.21 (0.09, 0.33)	0.03	0.00
Father's education												
No education (<1 years)	13	-0.005 (-0.08, 0.07)	0.91	0.00	17	-0.08 (-0.11, -0.04)	< 0.01	0.00	4	0.02 (-0.15, 0.20)	0.80	30.07
Primary (1- <6 years)		Reference				Reference				Reference		
Secondary (6- <10 years)	15	0.06 (0.015, 0.11)	0.02	0.00	17	0.08 (0.03, 0.13)	< 0.01	30.33	4	0.09 (0.02, 0.16)	0.08	0.00
Higher (≥10 years)	15	0.15 (0.08, 0.21)	< 0.01	0.00	17	0.18 (0.10, 0.26)	< 0.01	42.34	4	0.22 (0.11, 0.32)	0.03	17.98

Maternal age: no association

Risk Factor	Cognitive				Motor				Language			
	No. of studies	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**
Mother's age												
<15 years	5	-0.06 (-0.13, 0.25)	0.57	0.00	5	0.12 (-0.06, 0.30)	0.25	0.00	2	n/a	n/a	n/a
15-<20 years	18	-0.007 (-0.06, 0.05)	0.80	10.74	20	-0.02 (-0.11, 0.08)	0.75	83.67	6	0.01 (-0.09, 0.11)	0.85	37.07
20-34 years		Reference				Reference				Reference		
≥35 years	18	-0.01 (-0.06, 0.04)	0.58	0.00	20	-0.006 (-0.07, 0.05)	0.85	50.13	6	0.02 (-0.05, 0.09)	0.59	0.00

Short maternal stature and low BMI: significantly lower motor scores

Risk Factor	Cognitive				Motor				Language			
	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)
Mother's height												
<145 cm	11	-0.10 (-0.20, -0.004)	0.07	0.00	13	-0.11 (-0.19, -0.03)	0.02	21.52	5	-0.11 (-0.31, 0.09)	0.35	0.00
145 -<150 cm	13	-0.11 (-0.19, -0.02)	0.03	27.19	15	-0.07 (-0.16, 0.03)	0.17	71.10	5	-0.06 (-0.13, 0.06)	0.52	0.00
150- <155 cm	13	-0.09 (-0.14, -0.04)	< 0.01	3.32	15	-0.04 (-0.09, 0.009)	0.14	31.54	5	-0.05 (-0.12, 0.02)	0.22	0.00
>155 cm		Reference				Reference				Reference		
Mother's BMI (kg/m^2)												
<18.5	11	-0.11 (-0.20, -0.02)	0.03	12.73	13	-0.02 (-0.11, 0.07)	0.69	51.40	3	n/a	n/a	n/a
18.5 -<25		Reference				Reference				Reference		
25-<30	12	0.03 (-0.04, 0.09)	0.44	23.37	14	0.04 (-0.03, 0.11)	0.31	64.62	4	-0.04 (-0.21, 0.13)	0.70	61.06
≥30	12	-0.02 (-0.17, 0.14)	0.82	46.31	14	-0.02 (-0.14, 0.10)	0.77	63.68	4	-0.14 (-0.34, 0.06)	0.26	35.98

Maternal hemoglobin: no association

Risk Factor	Cognitive				Motor				Language			
	No. of studies	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**
Mother's hemoglobin level (g/L)												
Normal (≥110 g/L))		Reference				Reference				Reference		
Mild (100-109 g/L)	4	-0.06 (-0.15, 0.03)	0.28	0.00	11	0.06 (0.008, 0.11)	0.04	29.74	1	n/a	n/a	n/a
Moderate (70-99 g/L)	4	-0.06 (-0.19, 0.06)	0.39	0.00	6	-0.01 (-0.06, 0.04)	0.68	16.33	1	n/a	n/a	n/a

Preterm birth: reduced cognitive & motor scores SGA: no effect

Risk Factor	Cognitive				Motor				Language			
	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)	No. of studies	Adjusted[1] effect size (95% CI)	*p*-value	I^2 (%)
Birth weight (g)												
Normal (≥2500 g)		Reference				Reference				Reference		
Low (<2500 g)	14	-0.13 (-0.20, -0.07)	< 0.01	51.04	15	-0.14 (-0.23, -0.06)	< 0.01	66.51	5	-0.11 (-0.22, 0.00)	0.12	74.61
Moderate low (2000-2500 g)	14	-0.07 (-0.12, -0.03)	< 0.01	17.25	15	-0.11 (-0.20, -0.02)	0.03	64.06	5	-0.05 (-0.10, 0.01)	0.20	29.67
Very low (<2000 g)	14	-0.27 (-0.49, -0.07)	0.02	74.01	13	-0.26 (-0.40, -0.12)	< 0.01	74.94	5	-0.28 (-0.60, 0.05)	0.17	81.19
Gestational age (g)[2]												
Term (≥37 weeks)		Reference				Reference				Reference		
Late preterm (34-37 weeks)	8	-0.21 (-0.39, -0.04)	0.04	69.82	8	-0.14 (-0.33, 0.04)	0.17	74.51	5	-0.05 (-0.23, 0.13)	0.64	72.10
Early preterm (<34 weeks)	8	-0.16 (-0.34, 0.31)	0.15	53.56	7	-0.26 (-0.53, 0.006)	0.10	65.06	4	-0.20 (-0.55, 0.15)	0.35	75.49
Size for gestational age[3]												
AGA (≥10 percentile)		Reference				Reference				Reference		
Moderate SGA (3-<10 percentile)	8	-0.05 (-0.11, 0.12)	0.16	0.00	9	-0.01 (-0.10, 0.07)	0.77	36.68	4	-0.06 (-0.18, 0.06)	0.40	29.41
Severe SGA (<3 percentile)	8	-0.09 (-0.24, 0.07)	0.30	72.00	9	0.02 (-0.09, 0.12)	0.78	37.42	4	0.03 (-0.13, 0.19)	0.73	37.75

Anemia in infancy: reduced cognitive and motor scores

Risk Factor	Cognitive				Motor				Language			
	No. of studies	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**
Child hemoglobin level (g/L)												
Normal (≥110 g/L)		Reference				Reference				Reference		
Mild anemia (100-109 g/L)	9	-0.06 (-0.13, 0.01)	0.14	27.74	9	-0.03 (-0.13, 0.07)	0.54	51.25	3	n/a	n/a	n/a
Moderate anemia (70-99 g/L)	9	-0.11 (-0.12, -0.10)	< 0.01	0.00	9	-0.18 (-0.28, -0.09)	< 0.01	49.07	3	n/a	n/a	n/a

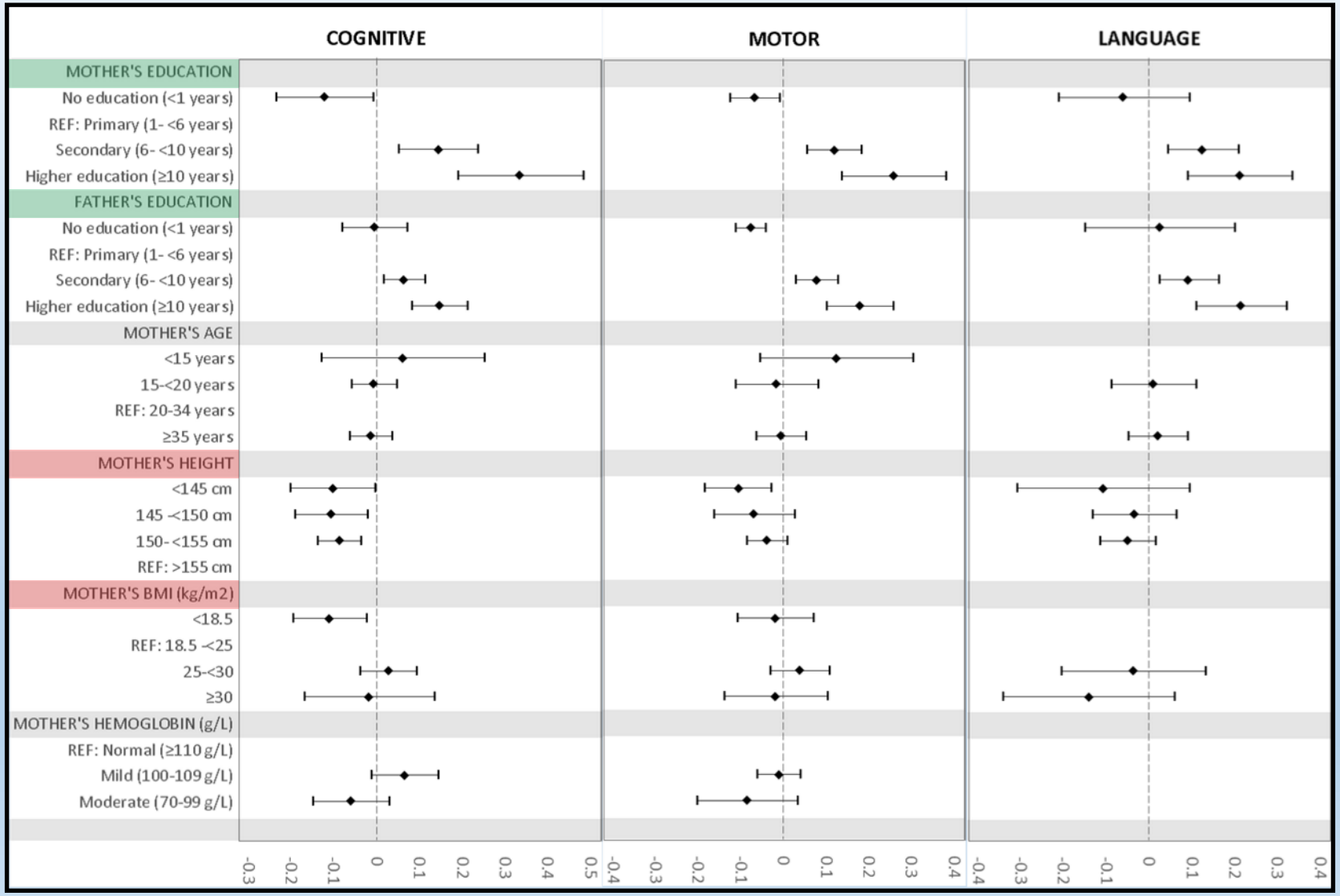
Lack of access to clean water and sanitation: reduced cognitive and motor scores

Risk Factor	Cognitive				Motor				Language			
	No. of studies	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**
Access to clean water												
Yes		Reference				Reference				Reference		
No	8	-0.10 (-0.12, -0.09)	< 0.01	0.00	8	-0.07 (-0.16, 0.01)	0.14	71.09	4	-0.15 (-0.35, -0.05)	0.23	82.55
Access to sanitation												
Yes		Reference				Reference				Reference		
No	8	-0.13 (-0.18, -0.07)	< 0.01	47.51	8	-0.10 (-0.19, -0.01)	0.05	82.82	4	-0.12 (-0.27, 0.03)	0.21	92.48

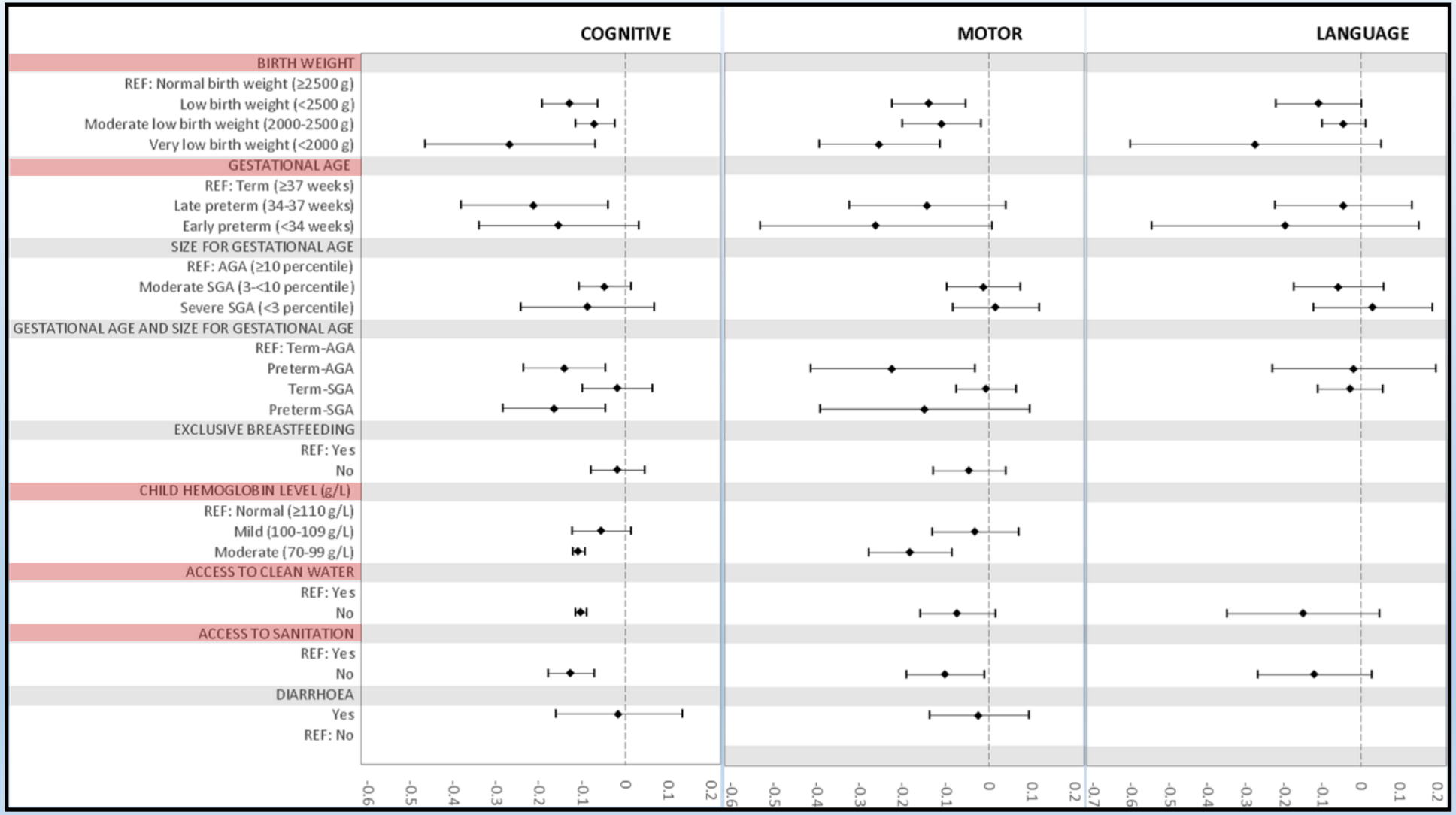
Diarrhea and breastfeeding: no association

Risk Factor	Cognitive				Motor				Language			
	No. of studies	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**	**No. of studies**	**Adjusted[1] effect size (95% CI)**	***p*-value**	**I^2 (%)**
Exclusive breastfeeding												
Yes		Reference				Reference				Reference		
No	4	-0.02 (-0.08, 0.04)	0.60	0.00	4	-0.05 (-0.13, 0.04)	0.36	16.43	?	n/a	n/a	n/a
Diarrhoea												
Yes	5	-0.02 (-0.16, 0.13)	0.84	66.81	5	-0.02 (-0.14, 0.09)	0.71	62.82	2	n/a	n/a	n/a
No		Reference				Reference				Reference		

Summary: Parental factors



Summary: Child factors



Strengths and limitations

- Strengths:
- global coverage of the cohorts
- the large sample size
- uniform classifications of early life exposures and statistical analyses across studies
- Limitations:
- lack of data on child stimulation and education
- observational data, causal relationship cannot be established
- moderate to high level of heterogeneity

Implications

- Differential exposure to risk factors creates large disparities in children's development early in life.
- Intervention targeting these factors during pre-pregnancy through childhood is needed to improve the health and developmental potential of children.

Future research

- Estimate the effects of risk factors that co-occur
- Evaluate effectiveness and delivery strategies for comprehensive intervention packages