

SUPPLEMENT

Table S1. Inflammation-related proteins included in each analysis

	Passed LOD* check	Significant† intervention-mediator results	Significant† mediator-outcome results	Included in the mediation analysis
IL8	√			
VEGFA	√		√	
CD8A	√		√	
MCP-3				
GDNF				
CDCP1	√	√	√	√
CD244	√	√	√	√
IL7	√		√	
OPG	√	√	√	√
LAP TGF-beta-1	√		√	
uPA	√		√	
IL6	√		√	
IL-17C	√		√	
MCP-1	√		√	
IL-17A				
CXCL11	√		√	
AXIN1	√		√	
TRAIL	√		√	
IL-20RA				
CXCL9	√			
CST5	√		√	
IL-2RB				
IL-1 alpha				
OSM	√		√	
IL2				
CXCL1	√		√	
TSLP				
CCL4	√		√	
CD6	√	√	√	√
SCF	√	√	√	√
IL18	√	√	√	√
SLAMF1				
TGF-alpha	√		√	
MCP-4	√		√	
CCL11	√	√	√	√

TNFSF14	√		√	
FGF-23				
IL-10RA				
FGF-5				
MMP-1	√			
LIF-R	√		√	
FGF-21	√		√	
CCL19	√	√	√	√
IL-15RA				
IL-10RB	√	√		
IL-22 RA1				
IL-18R1	√		√	
PD-L1	√		√	
Beta-NGF				
CXCL5	√		√	
TRANCE	√		√	
HGF	√		√	
IL-12B	√		√	
IL-24				
IL13				
ARTN				
MMP-10	√		√	
IL10	√	√	√	√
TNF	√		√	
CCL23	√		√	
CD5	√	√	√	√
CCL3	√		√	
Fit3L	√			
CXCL6	√		√	
CXCL10	√		√	
4E-BP1	√		√	
IL-20				
SIRT2	√		√	
CCL28	√	√	√	√
DNER	√	√	√	√
EN-RAGE	√		√	
CD40	√		√	
IL33				
IFN-gamma	√		√	
FGF-19	√		√	

IL4				
LIF				
NRTN				
MCP-2	√		√	
CASP-8	√		√	
CCL25	√			
CX3CL1	√	√		
TNFRSF9	√	√	√	√
NT-3				
TWEAK	√	√	√	√
CCL20	√			
ST1A1	√		√	
STAMPB	√		√	
IL5				
ADA	√	√	√	√
TNFB	√			
CSF-1	√		√	

* LOD: limit of detection

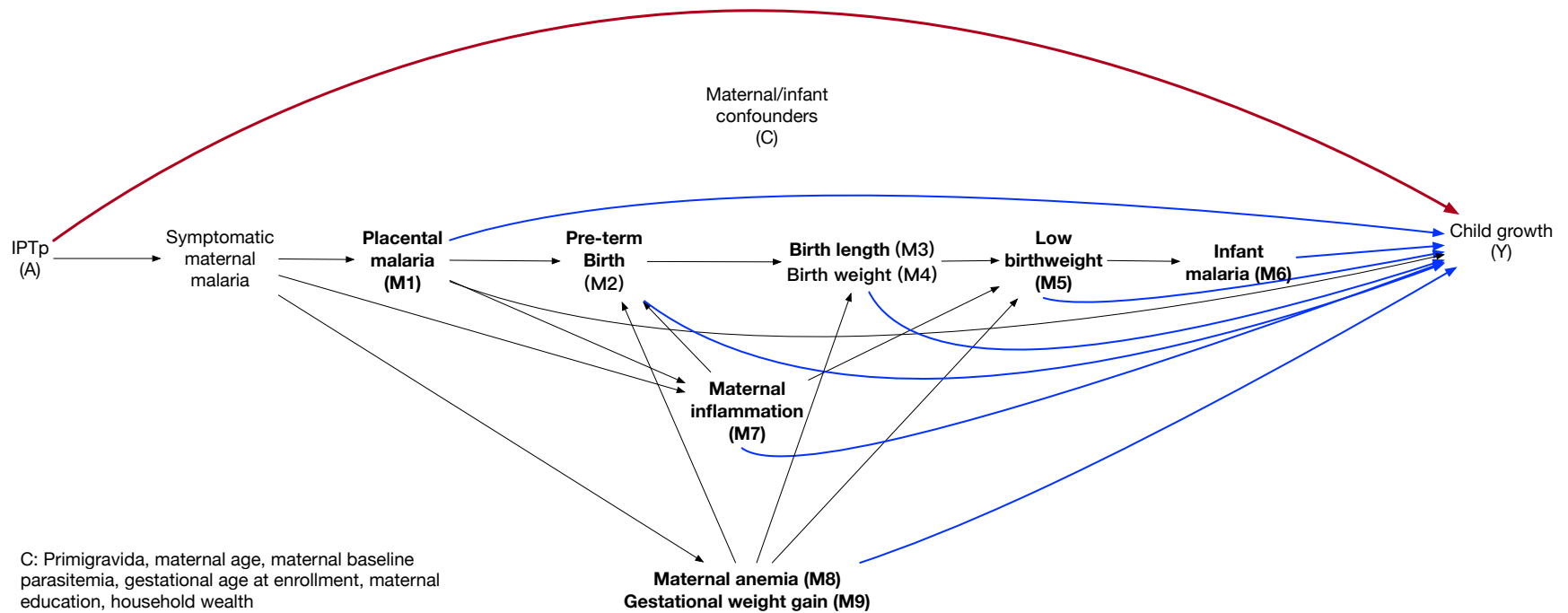
† p-value not accounting for multiple testing < 0.05

Supplement 1. List of deviations from pre-analysis plan

The analysis plan for this study was pre-specified at <https://osf.io/f8wy4/>. We note the following deviations from the plan:

1. We intended to employ principal components analysis and established pathway analysis and term enrichment databases, such as Blood Transcriptional Modules, Gene Ontology, and KEGG, to reduce the dimensionality and identify clusters of Olink inflammation-related biomarkers. However, these approaches did not yield discernible clusters. Therefore, we adhered to parametric regression, t-tests, volcano plots, and forest plots to investigate individual biomarkers. These approaches allowed us to systematically identify and track individual biomarkers demonstrating evidence of associations with the interventions and child growth outcomes for subsequent inclusion in our mediation models.
2. The hypothesized causal pathways of the study as depicted in Figure S1 were sequential. However, due to limitations in available R programming tools, we decided to focus on single-mediator models to examine each intervention-mediator-outcome combination separately.

Figure S1. Directed acyclic graph



Note: all adjusted analyses in this study were controlled for the confounder set C, so for simplicity, the corresponding arrows were omitted.

Figure S2. Flowchart

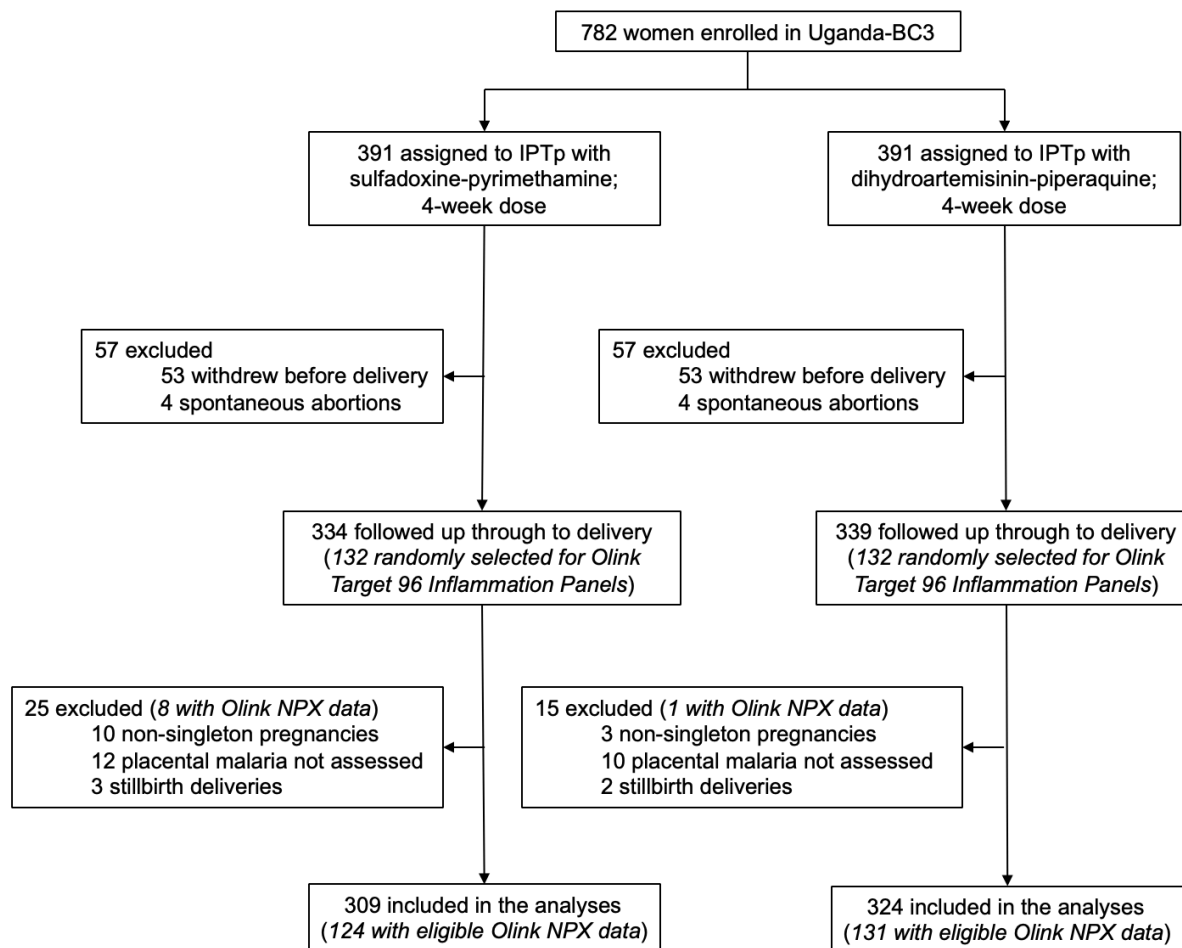


Table S2. Total effect of IPTp-DP vs. IPTp-SP on stunting and wasting incidence

Age category	DP		SP		Unadjusted incidence ratio (95% CI)
	N	Incidence (95% CI)	N	Incidence (95% CI)	
Stunting					
Birth	324	18.2 (14.4, 22.8)	309	14.2 (10.8, 18.6)	1.28 (0.87, 1.89)
1 day-3 months	262	26.0 (21.0, 31.6)	260	20.0 (15.6, 25.3)	1.30 (0.90, 1.86)
>3-6 months	182	10.4 (6.8, 15.7)	197	8.6 (5.5, 13.4)	1.21 (0.63, 2.33)
>6-9 months	160	8.1 (4.8, 13.4)	175	8.6 (5.3, 13.7)	0.95 (0.45, 1.99)
>9-12 months	147	4.8 (2.3, 9.5)	153	2.0 (0.7, 5.6)	2.43 (0.63, 9.39)
Wasting					
Birth	324	2.5 (1.3, 4.8)	309	2.9 (1.5, 5.4)	0.85 (0.33, 2.20)
1 day-3 months	312	12.5 (9.3, 16.6)	295	12.9 (9.5, 17.2)	0.97 (0.62, 1.52)
>3-6 months	259	4.2 (2.4, 7.4)	242	3.3 (1.7, 6.4)	1.28 (0.52, 3.19)
>6-9 months	244	2.5 (1.1, 5.3)	225	2.7 (1.2, 5.7)	0.92 (0.30, 2.86)
>9-12 months	236	2.5 (1.2, 5.4)	211	2.8 (1.3, 6.1)	0.89 (0.29, 2.77)

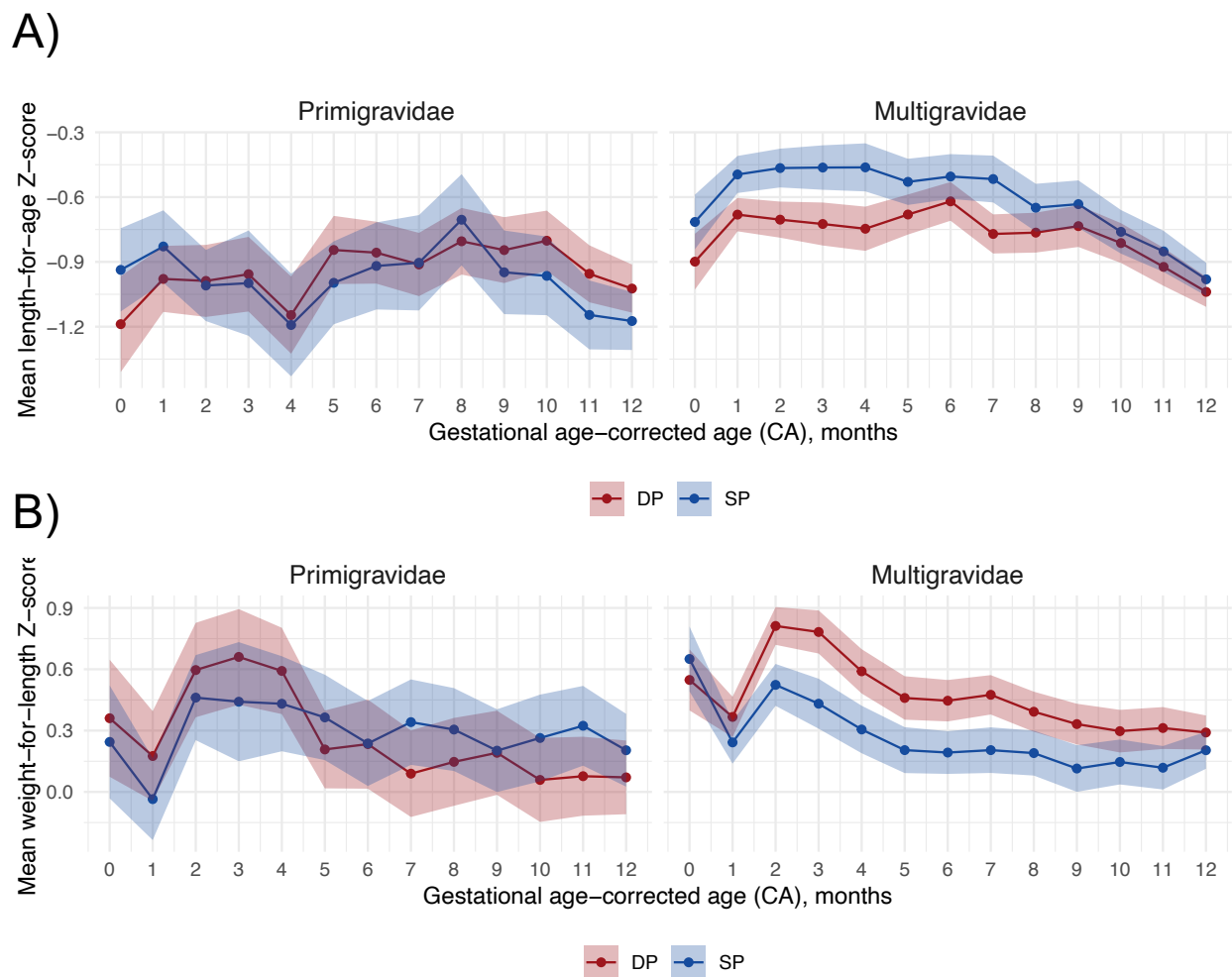


Figure S3 Total effect of IPTp DP vs. SP on mean child growth Z-scores corrected for gestational age by child age and gravidity

Includes 630 children measured from birth to 12 months. Excludes children with negative ages after gestational age correction.

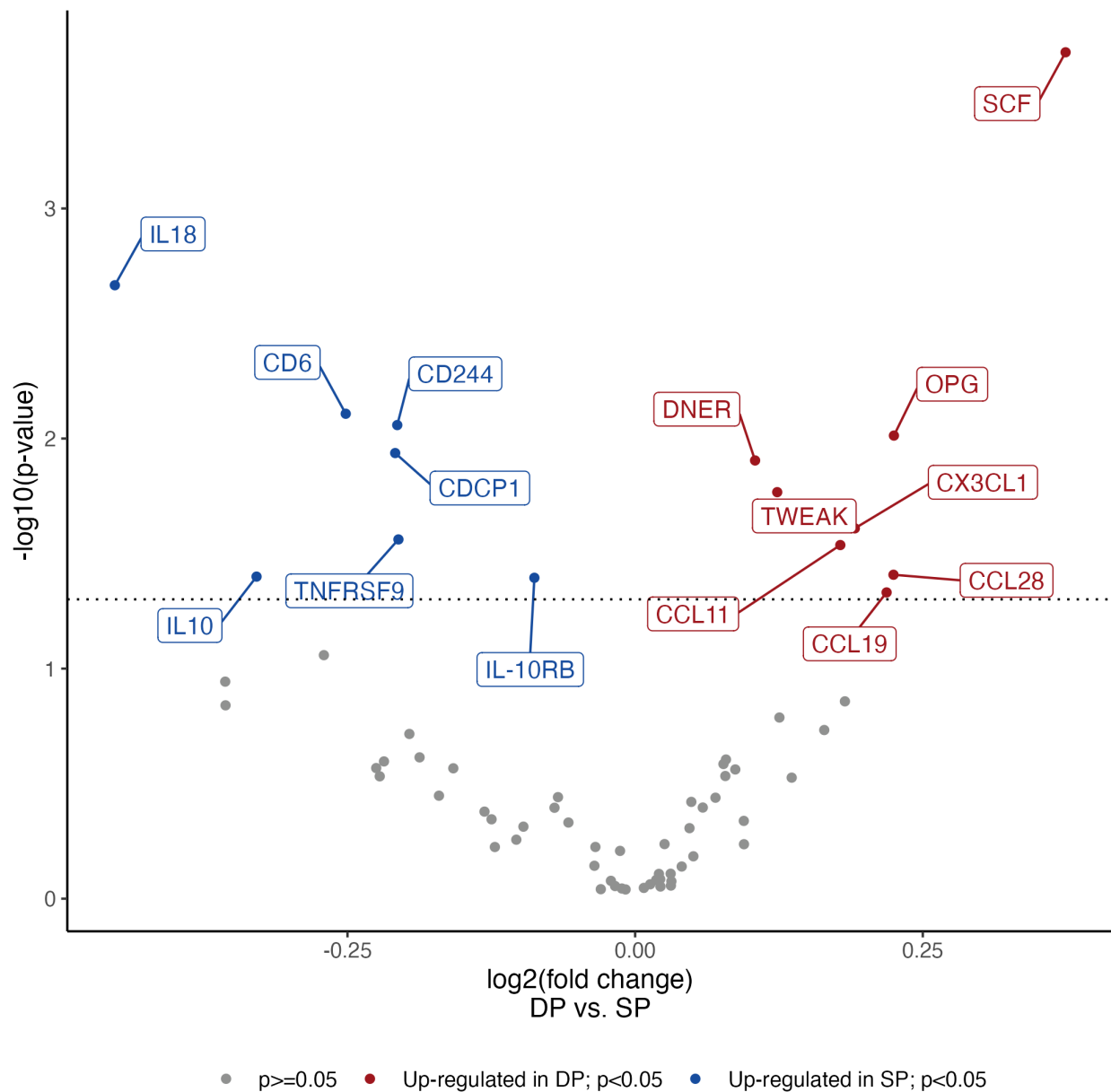


Figure S4. Volcano plot of maternal inflammation-related proteins at delivery by IPTp-DP vs. IPTp-SP among all gravidae

Red points represent proteins upregulated in DP with $p < 0.05$, blue points represent proteins upregulated in SP with $p < 0.05$, and gray points represent non-differentially expressed proteins. Color coding in the plot is based on p-values that were not corrected for multiple testing. After the Benjamini-Hochberg correction (false discovery rate p -value < 0.05), only SCF had a p -value < 0.05 . Among all gravidae, proteins upregulated in SP were IL18, CD6, CD244, CDCP1, TNFRSF9, IL10, and IL-10RB; proteins upregulated in DP were SCF, OPG, DNER, TWEAK, CX3CL1, CCL11, CCL28, and CCL19. Note that among primigravidae (sample size = 51), proteins CD5 and ADA were upregulated in SP, which were not shown on this volcano plot.

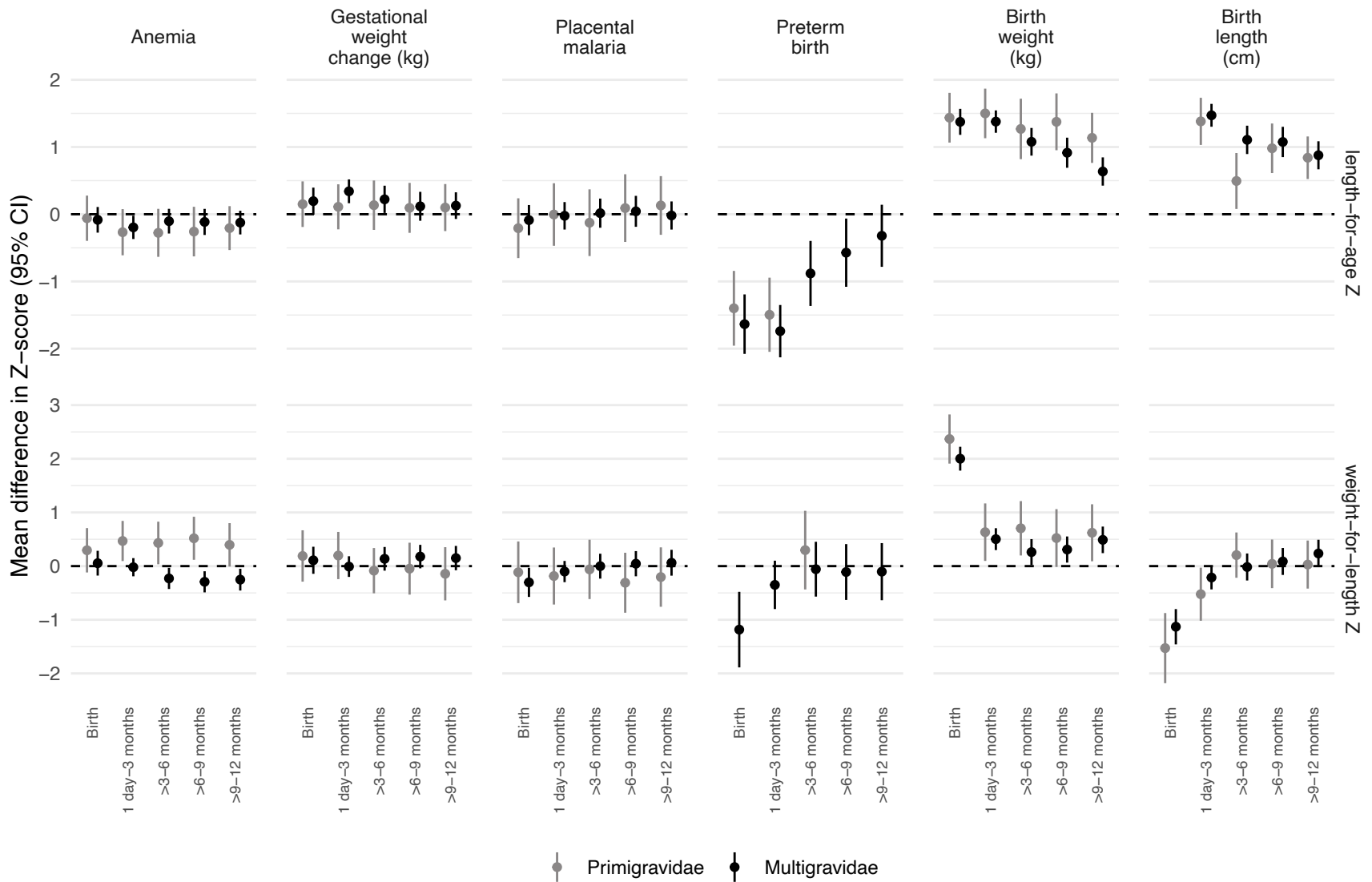


Figure S5. Associations between potential non-inflammation-related mediators and mean child growth Z-scores

Mean differences in Z-scores between each mediator and mean Z-scores adjusted by infant sex, maternal age, maternal baseline parasitemia, gestational age at enrollment, gravidity, maternal education, and household wealth.

Note: Gestational weight change and birth length values have been rescaled (multiplied by a factor of 5) to enhance clarity and visualization on the plot. This adjustment aligns their y-axis range with the other mediators for a more visually coherent presentation.

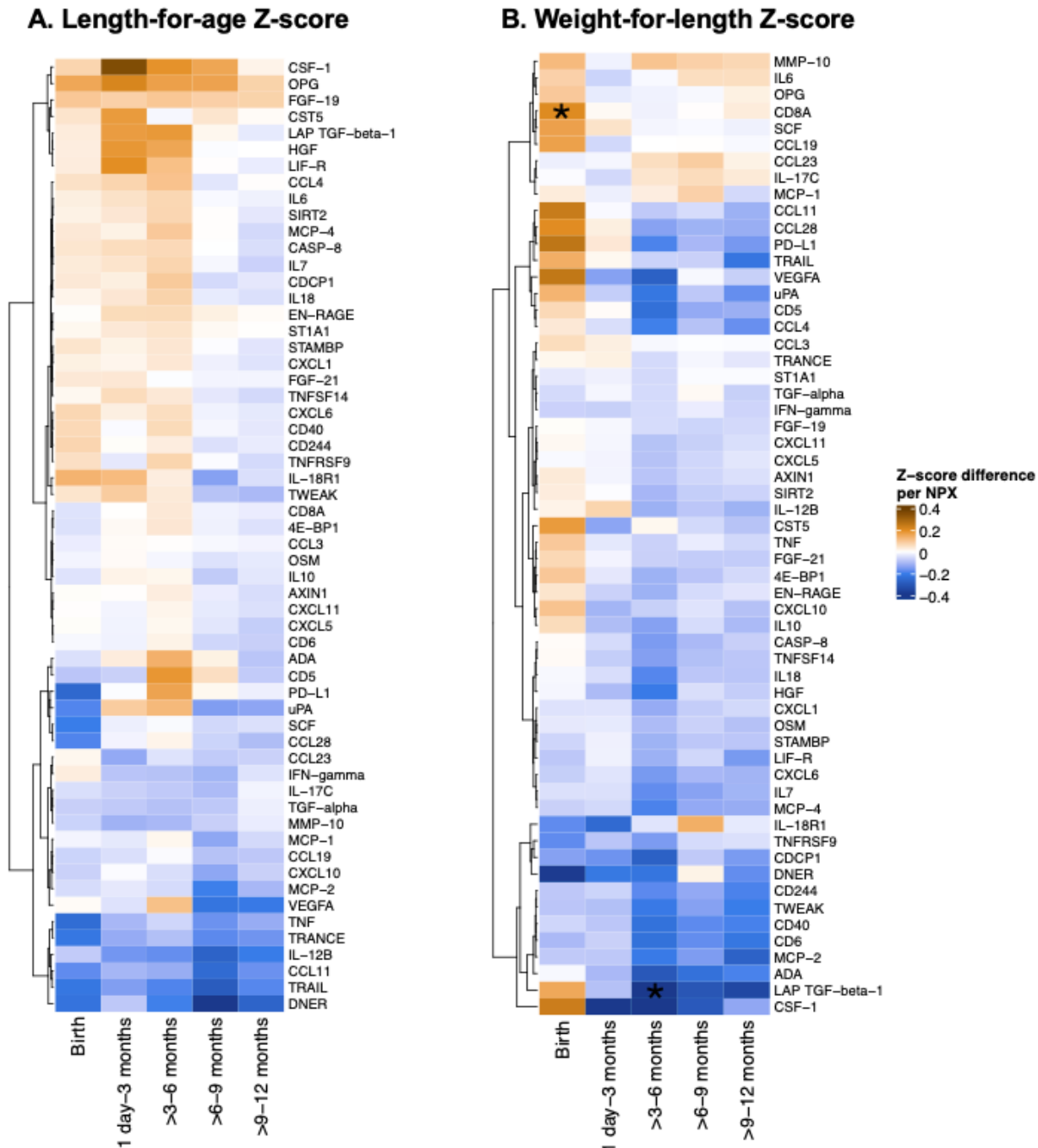


Figure S6 Associations between maternal inflammation-related proteins at delivery and mean child growth Z-scores

Mean Z-score differences per inflammation-related protein NPX were estimated with a model adjusted for infant sex, maternal age, gravidity, maternal baseline parasitemia, gestational age at enrollment, maternal education, household wealth.

*Statistically significant among all gravidae after Benjamini-Hochberg correction (false discovery rate p -value < 0.05).

Table S3. Associations between non-inflammation-related potential mediators and stunting and wasting

	Stunting		Wasting	
	N	Incidence ratio (95% CI)	N	Incidence ratio (95% CI)
Maternal anemia				
Birth	619	1.07 (0.72, 1.58)	619	0.42 (0.14, 1.21)
1 day-3 months	510	1.38 (0.95, 2.00)	593	0.93 (0.59, 1.47)
>3-6 months	374	0.83 (0.41, 1.65)	489	1.48 (0.59, 3.70)
>6-9 months	331	0.97 (0.45, 2.11)	459	1.51 (0.47, 4.91)
>9-12 months	296	0.14 (0.02, 1.11)	437	2.58 (0.74, 9.03)
Gestational weight change (kg)				
Birth	575	0.94 (0.85, 1.03)	575	1.05 (0.84, 1.32)
1 day-3 months	486	0.97 (0.89, 1.05)	552	0.93 (0.84, 1.04)
>3-6 months	361	0.94 (0.81, 1.09)	467	0.99 (0.80, 1.23)
>6-9 months	321	1.06 (0.88, 1.26)	440	0.92 (0.71, 1.19)
>9-12 months	287	0.93 (0.71, 1.21)	419	1.01 (0.78, 1.33)
Placental malaria				
Birth	633	1.38 (0.85, 2.25)	633	1.14 (0.35, 3.7)
1 day-3 months	522	0.94 (0.60, 1.47)	607	0.98 (0.56, 1.73)
>3-6 months	379	1.3 (0.59, 2.86)	501	1.12 (0.35, 3.55)
>6-9 months	335	1.21 (0.51, 2.88)	469	0.81 (0.20, 3.38)
>9-12 months	300	0.22 (0.02, 1.99)	447	1.01 (0.23, 4.39)
Pre-term birth				
Birth	633	3.87 (2.29, 6.52)	633	1.01 (0.13, 7.83)
1 day-3 months	522	2.20 (1.06, 4.56)	607	3.21 (1.71, 6.02)
>3-6 months		--		--
>6-9 months		--	469	2.85 (0.35, 23.39)
>9-12 months		--		--
Birth length (cm)				
Birth	628	0.75 (0.72, 0.79)	628	1.33 (1.16, 1.53)
1 day-3 months	520	0.86 (0.81, 0.91)	605	0.98 (0.88, 1.08)
>3-6 months	378	0.79 (0.67, 0.92)	500	0.91 (0.74, 1.12)
>6-9 months	334	0.79 (0.66, 0.93)	468	1.21 (0.87, 1.68)
>9-12 months	300	1.22 (0.87, 1.71)	446	0.9 (0.72, 1.13)
Birth weight (kg)				
Birth	633	0.17 (0.12, 0.26)	633	0.15 (0.07, 0.36)
1 day-3 months	522	0.33 (0.22, 0.51)	607	0.35 (0.21, 0.57)
>3-6 months	379	0.38 (0.15, 0.97)	501	0.48 (0.13, 1.79)
>6-9 months	335	0.27 (0.09, 0.77)	469	3.30 (0.65, 16.68)
>9-12 months	300	1.54 (0.26, 9.11)	447	0.24 (0.04, 1.38)

Incidence ratios for each potential mediator were adjusted by infant sex, primigravida, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth.

Note: missing values were due to data sparsity.

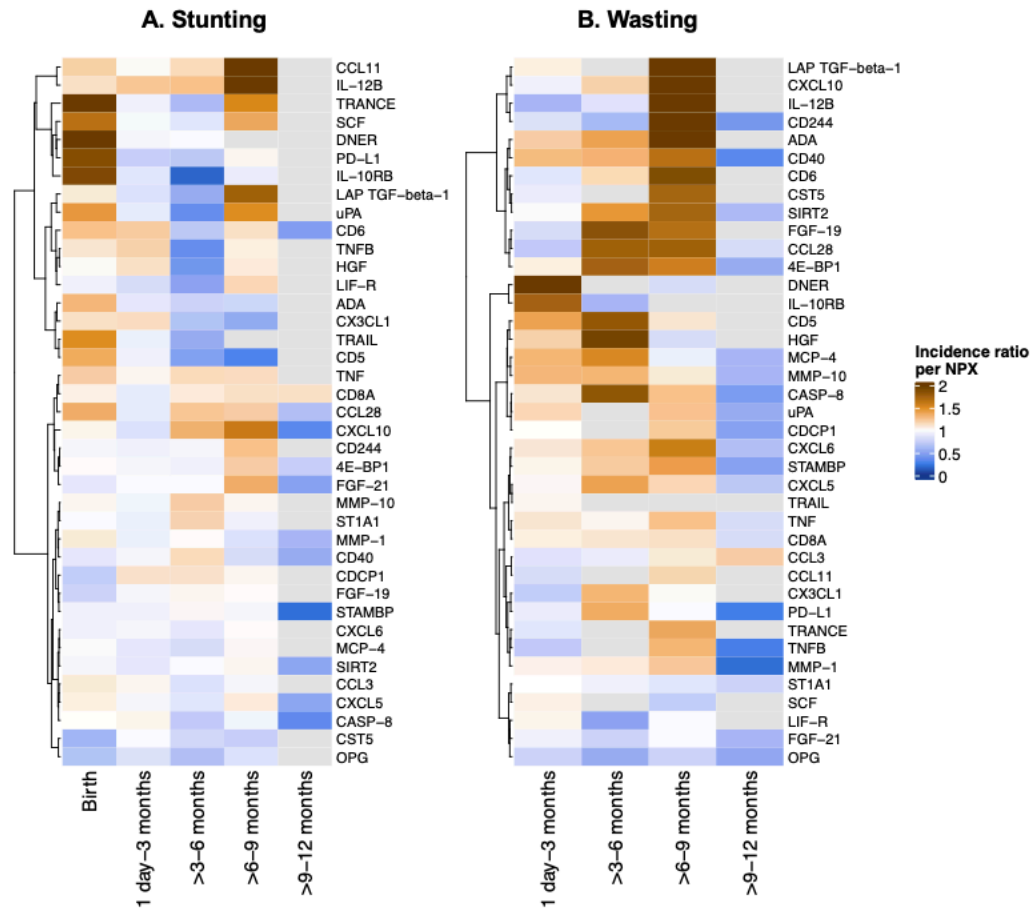
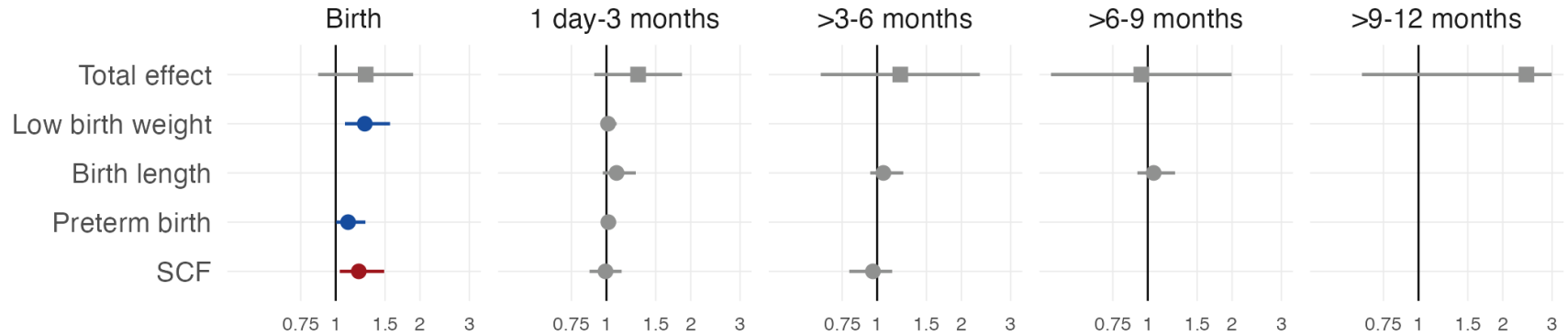


Figure S7 Associations between potential inflammation-related protein mediators and stunting and wasting

Incidence ratios per inflammation-related protein NPX were estimated with a model adjusted by infant sex, primigravida, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. The reference group was SP. Missing point estimates were due to data sparsity and were filled as grey. When there were fewer than 10 incident cases in a certain age group, models were not fit.

A) Stunting



B) Wasting

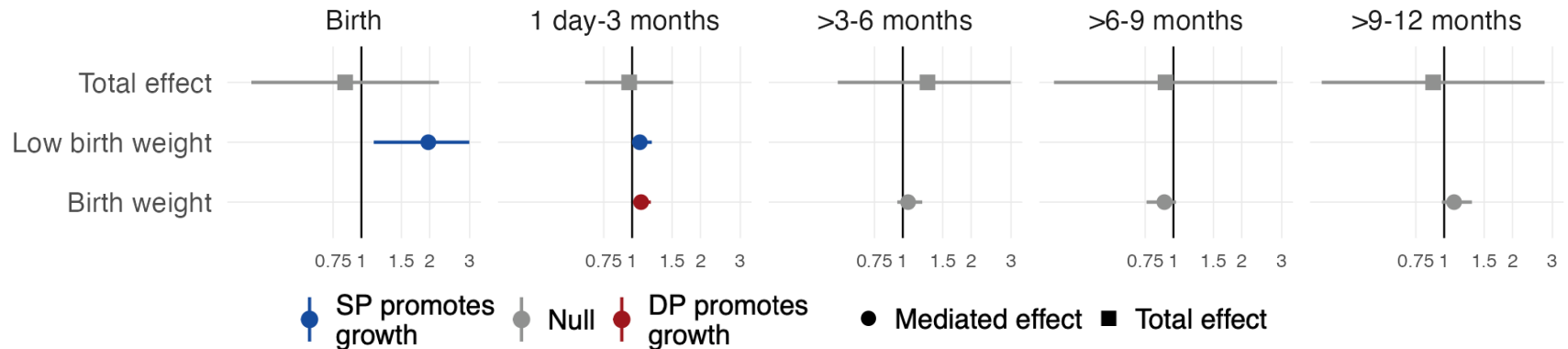


Figure S8. Total effects and mediated effects on incidences of child stunting and wasting

The total effects compare incidence of stunting and wasting between IPTp-DP and IPTp-SP using unadjusted models. The mediated effects were adjusted by infant sex, maternal age, maternal baseline parasitemia, gestational age at enrollment, gravidity, maternal education, and household wealth. The reference group was SP. Note: Missing point estimates were due to data sparsity. When there were fewer than 5 incident cases or 5 observed values of a binary mediator in a certain age group, models were not fit.

Table S4. Mediated effects of IPTp-DP vs. IPTp-SP on Z-scores

	Length-for-age Z		Weight-for-length Z	
	N	Mean difference in Z (95% CI)	N	Mean difference in Z (95% CI)
Maternal anemia				
Birth	608	0.0037 (-0.0077, 0.0225)	582	-0.0028 (-0.0229, 0.0103)
1 day-3 months	593	0.0084 (-0.0116, 0.0357)	581	-0.0025 (-0.0187, 0.0082)
>3-6 months	575	0.0043 (-0.0099, 0.0244)	574	0.0030 (-0.0091, 0.0219)
>6-9 months	559	0.0049 (-0.0099, 0.0256)	558	0.0045 (-0.0095, 0.0264)
>9-12 months	548	0.0049 (-0.0109, 0.0245)	548	0.0039 (-0.0106, 0.0239)
Gestational weight change (kg)				
Birth	567	-0.0007 (-0.0182, 0.0144)	555	-0.0007 (-0.0183, 0.013)
1 day-3 months	552	-0.0036 (-0.0305, 0.0206)	545	-0.0002 (-0.0101, 0.0085)
>3-6 months	541	-0.002 (-0.0264, 0.0186)	538	-0.0006 (-0.0139, 0.0092)
>6-9 months	526	-0.0005 (-0.018, 0.0138)	525	-0.0006 (-0.0177, 0.0137)
>9-12 months	515	0.0004 (-0.0161, 0.0157)	515	0.0002 (-0.0132, 0.0112)
Placental malaria				
Birth	622	0.0358 (-0.0318, 0.1055)	596	0.0903 (-0.002, 0.183)
1 day-3 months	607	0.0049 (-0.0625, 0.0691)	594	0.0414 (-0.0285, 0.1114)
>3-6 months	587	0.0003 (-0.075, 0.0708)	586	0.0057 (-0.0706, 0.0805)
>6-9 months	569	-0.0152 (-0.0897, 0.0545)	568	0.0024 (-0.0727, 0.0782)
>9-12 months	558	-0.0059 (-0.0745, 0.0588)	558	-0.0040 (-0.0778, 0.0691)
Pre-term birth				
Birth	622	0.0098 (-0.0645, 0.0909)	596	0.0087 (-0.0252, 0.0511)
1 day-3 months	607	0.0097 (-0.0695, 0.0916)	594	0.0005 (-0.0143, 0.0161)
>3-6 months	587	0.0134 (-0.024, 0.0656)	586	-0.0013 (-0.0253, 0.0206)
>6-9 months	569	0.0112 (-0.0217, 0.0569)	568	-0.0017 (-0.0229, 0.0147)
>9-12 months	558	0.0087 (-0.0159, 0.0433)	558	-0.0033 (-0.0245, 0.0109)
Birth length (cm)				
Birth	622	-0.2522 (-0.4108, -0.0899)	596	0.0883 (0.0223, 0.1575)
1 day-3 months	605	-0.1235 (-0.2265, -0.0319)	592	0.0231 (0.0026, 0.0551)
>3-6 months	585	-0.0815 (-0.1562, -0.0184)	584	-0.0035 (-0.026, 0.017)
>6-9 months	567	-0.0801 (-0.1586, -0.0099)	566	-0.0050 (-0.0254, 0.0123)
>9-12 months	557	-0.062 (-0.1269, -0.0036)	557	-0.0125 (-0.0384, 0.0027)
Birth weight (kg)				
Birth	622	-0.1115 (-0.2032, -0.023)	596	-0.149 (-0.2817, -0.0167)
1 day-3 months	607	-0.1119 (-0.2058, -0.0207)	594	-0.038 (-0.0786, -0.0045)
>3-6 months	587	-0.0695 (-0.1444, 0.0009)	586	-0.0189 (-0.0499, 0.0037)
>6-9 months	569	-0.0623 (-0.1333, 0.0031)	568	-0.0222 (-0.0541, 0.0005)
>9-12 months	558	-0.0421 (-0.0943, 0.0059)	558	-0.0293 (-0.0707, 0.0036)
CD6				
Birth	255	0.0026 (-0.0485, 0.0519)	245	0.0247 (-0.0221, 0.0853)
1 day-3 months	251	0.0047 (-0.0447, 0.0561)	247	0.0173 (-0.0257, 0.0734)
>3-6 months	255	-0.0056 (-0.0651, 0.049)	255	0.0609 (0.0037, 0.1464)
>6-9 months	255	0.0158 (-0.0361, 0.0765)	254	0.0440 (-0.0056, 0.1172)

>9-12 months	255	0.0183 (-0.0237, 0.0704)	255	0.0575 (0.0032, 0.1392)
CDCP1				
Birth	255	-0.008 (-0.0500, 0.0274)	245	0.0291 (-0.0115, 0.0911)
1 day-3 months	251	-0.0053 (-0.0512, 0.0351)	247	0.0319 (-0.0040, 0.0874)
>3-6 months	255	-0.0196 (-0.0779, 0.0243)	255	0.0584 (0.0056, 0.1341)
>6-9 months	255	0.0111 (-0.032, 0.0643)	254	0.0154 (-0.0227, 0.0643)
>9-12 months	255	0.0071 (-0.0321, 0.0496)	255	0.0316 (-0.0115, 0.0965)
DNER				
Birth	255	-0.0233 (-0.0734, 0.0107)	245	-0.0386 (-0.1157, 0.0088)
1 day-3 months	251	-0.0077 (-0.0532, 0.0312)	247	-0.0200 (-0.0668, 0.0095)
>3-6 months	255	-0.0202 (-0.0785, 0.0234)	255	-0.023 (-0.0805, 0.0173)
>6-9 months	255	-0.0458 (-0.1128, -0.0026)	254	0.0024 (-0.0404, 0.0461)
>9-12 months	255	-0.0277 (-0.0798, 0.0054)	255	-0.0177 (-0.0699, 0.0215)
IL18				
Birth	255	-0.0095 (-0.0678, 0.0465)	245	0.0046 (-0.0630, 0.0784)
1 day-3 months	251	-0.0199 (-0.0822, 0.0362)	247	0.0237 (-0.0248, 0.0838)
>3-6 months	255	-0.0374 (-0.1161, 0.0281)	255	0.0890 (0.0234, 0.1738)
>6-9 months	255	0.0139 (-0.0470, 0.0840)	254	0.0393 (-0.0126, 0.1082)
>9-12 months	255	0.0219 (-0.0291, 0.0792)	255	0.0408 (-0.0076, 0.1038)
OPG				
Birth	255	0.0384 (-0.0049, 0.1003)	245	0.0235 (-0.0239, 0.0839)
1 day-3 months	251	0.0543 (0.0057, 0.1243)	247	-0.0077 (-0.0583, 0.0418)
>3-6 months	255	0.0419 (-0.0025, 0.106)	255	-0.0044 (-0.0573, 0.0497)
>6-9 months	255	0.0408 (-0.0026, 0.1041)	254	-0.0023 (-0.0559, 0.0538)
>9-12 months	255	0.0196 (-0.0228, 0.0747)	255	0.0068 (-0.0395, 0.0594)
SCF				
Birth	255	-0.0706 (-0.1404, -0.0161)	245	0.0592 (-0.0082, 0.1535)
1 day-3 months	251	-0.0071 (-0.0587, 0.0435)	247	0.0166 (-0.0342, 0.0787)
>3-6 months	255	-0.0022 (-0.0658, 0.0646)	255	-0.0043 (-0.0696, 0.0641)
>6-9 months	255	-0.0192 (-0.0874, 0.0463)	254	-0.0023 (-0.0660, 0.0652)
>9-12 months	255	-0.0152 (-0.0689, 0.0361)	255	-0.0063 (-0.0699, 0.0581)

Mediated effects were adjusted for infant sex, primigravida, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Analysis includes all gravidae. The reference group was SP.

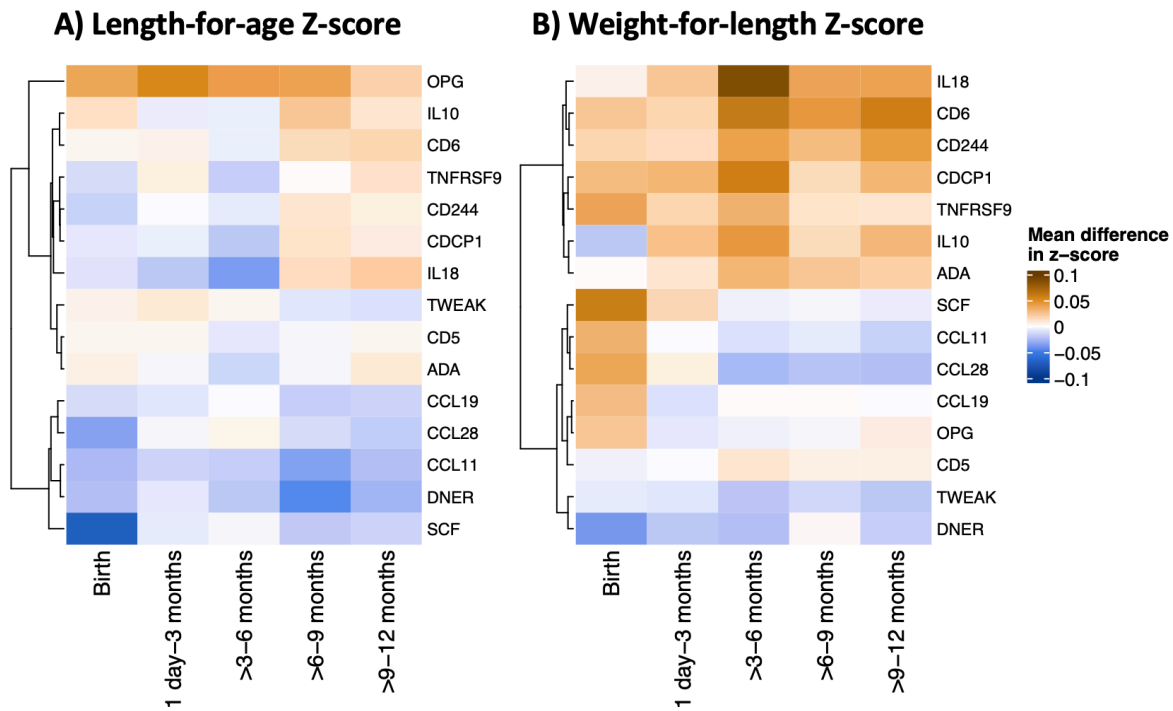


Figure S9 Inflammation-related protein-mediated effects of IPTp-DP vs. IPTp-SP on Z-scores

Mediated effects were adjusted by infant sex, primigravida, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Analysis includes all gravidae. The reference group was SP.

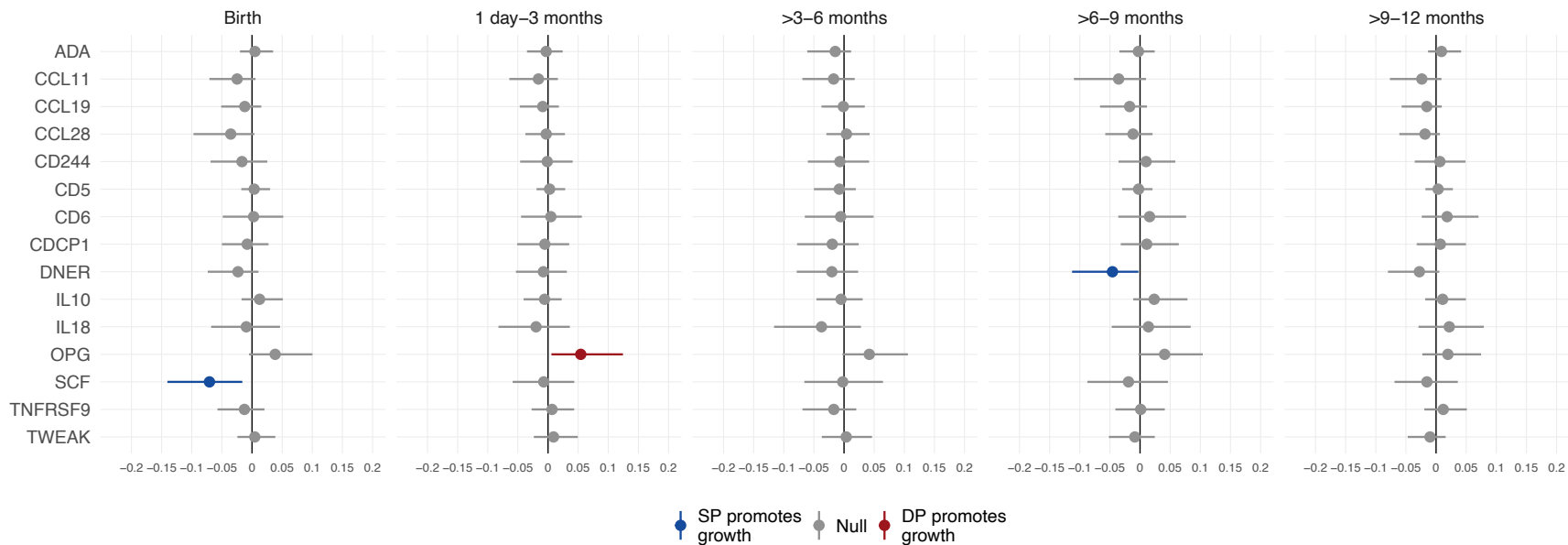


Figure S10 Inflammation-related protein-mediated effects on length-for-age Z

Mediated effects were adjusted for infant sex, maternal age, gravidity, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Analysis includes all gravidae. The reference group was SP.

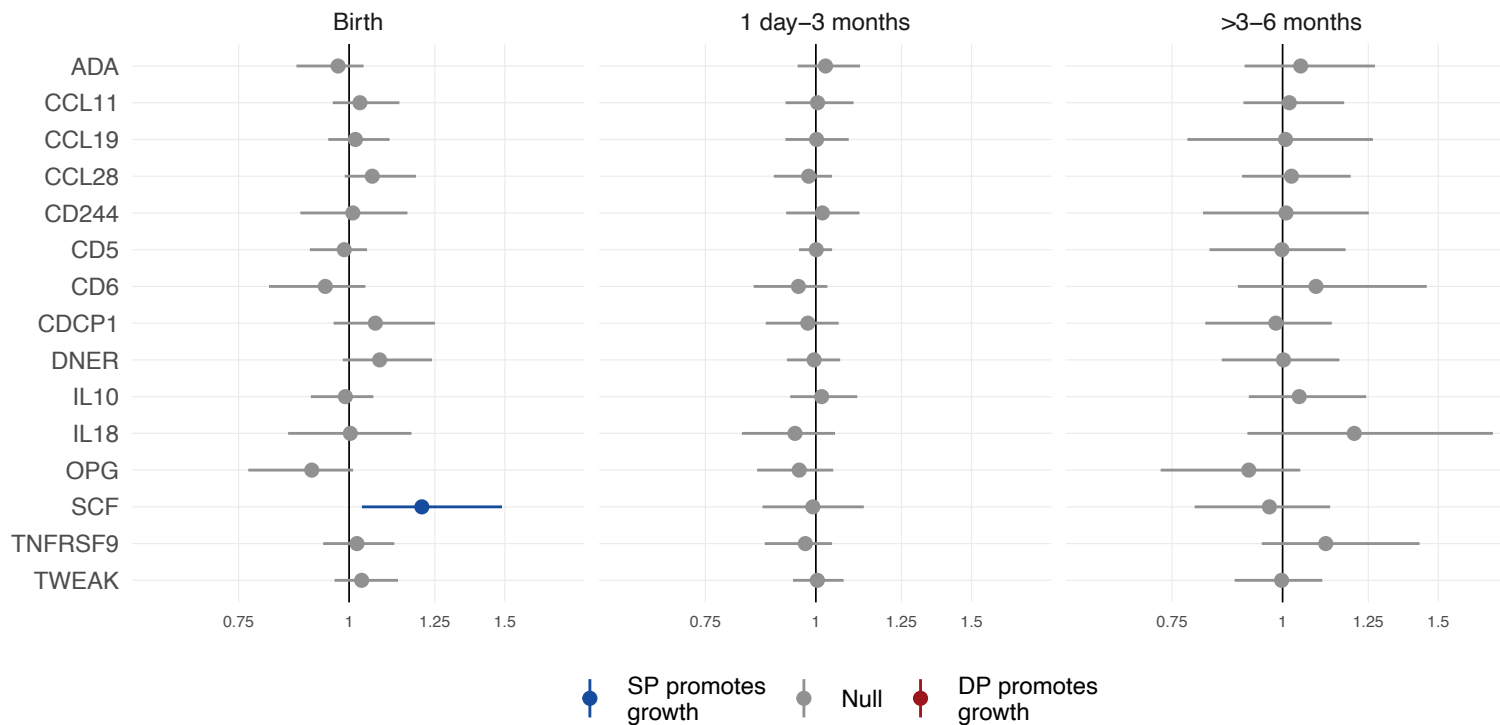


Figure S11 Inflammation-related protein-mediated effects on child stunting

Mediated effects were adjusted by infant sex, gravidity, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Mediation models were only fit from birth through age 6 months due to data sparsity at other ages. Analysis includes all gravidae. The reference group was SP.

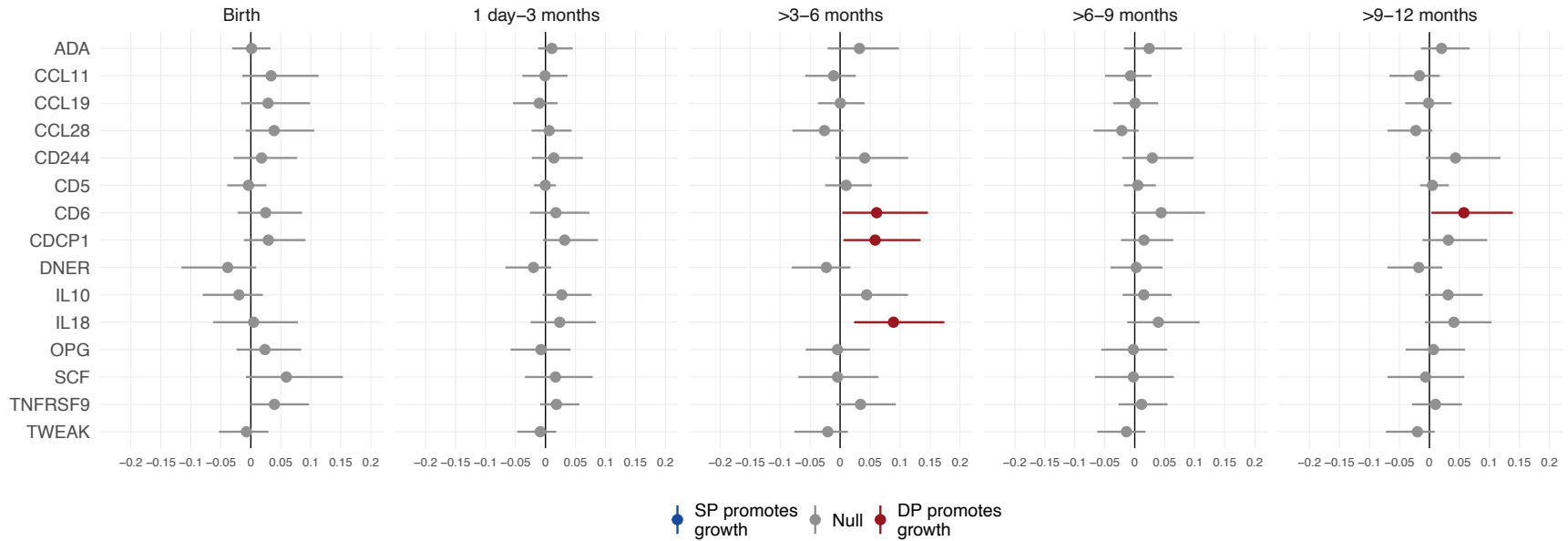


Figure S12 Inflammation-related protein-mediated effects on weight-for-length Z

Mediated effects were adjusted by infant sex, gravidity, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Analysis includes all gravidae. The reference group was SP.

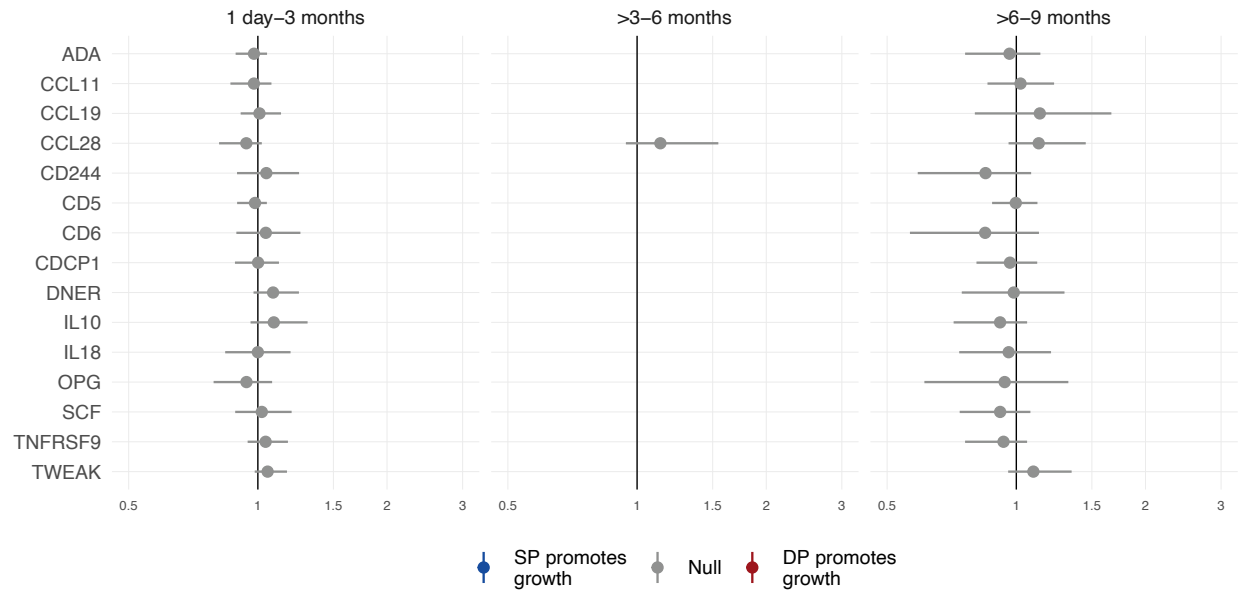


Figure S13 Inflammation-related protein-mediated effects on child wasting

Mediated effects were adjusted by infant sex, gravidity, maternal age, maternal baseline parasitemia, gestational age at enrollment, maternal education, and household wealth. Analysis includes all gravidae. The reference group was SP. Mediation models did not fit at birth or >9-12 months due to data sparsity.