Supplementary information

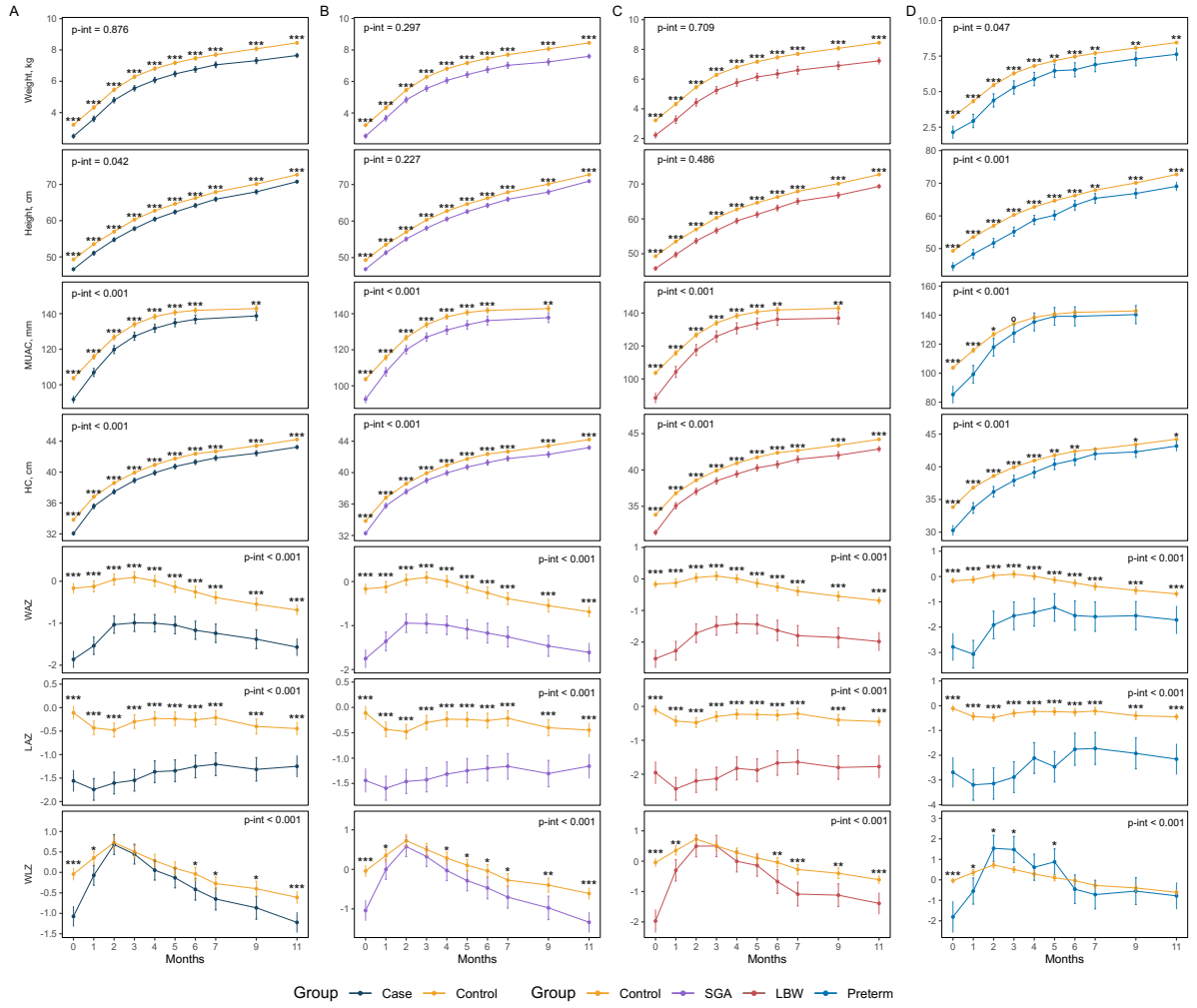

Figure S1. Longitudinal infant anthropometric trajectories in SVN and individual newborn vulnerability sub-phenotypes compared with non-SVN controls.

Estimated mean trajectories with 95% confidence intervals for weight, length, mid-upper arm circumference (MUAC), head circumference (HC), weight-for-age z-score (WAZ), length-for-age z-score (LAZ), and weight-for-length z-score (WLZ) from birth to 11 months. **(A)** SVN cases versus non-SVN controls. **(B)** Small-for-gestational-age (SGA) infants versus non-SVN controls. **(C)** Low-birthweight (LBW) infants versus non-SVN controls. **(D)** Preterm infants versus non-SVN controls. p-int indicates the significance of the group-by-time interaction from linear mixed-effects models. Asterisks indicate cross-sectional case-control differences at individual timepoints after multiple-testing adjustment within each outcome (*** FDR < 0.001, ** FDR < 0.01, * FDR < 0.05, º FDR < 0.1, ~ unadjusted p < 0.05).

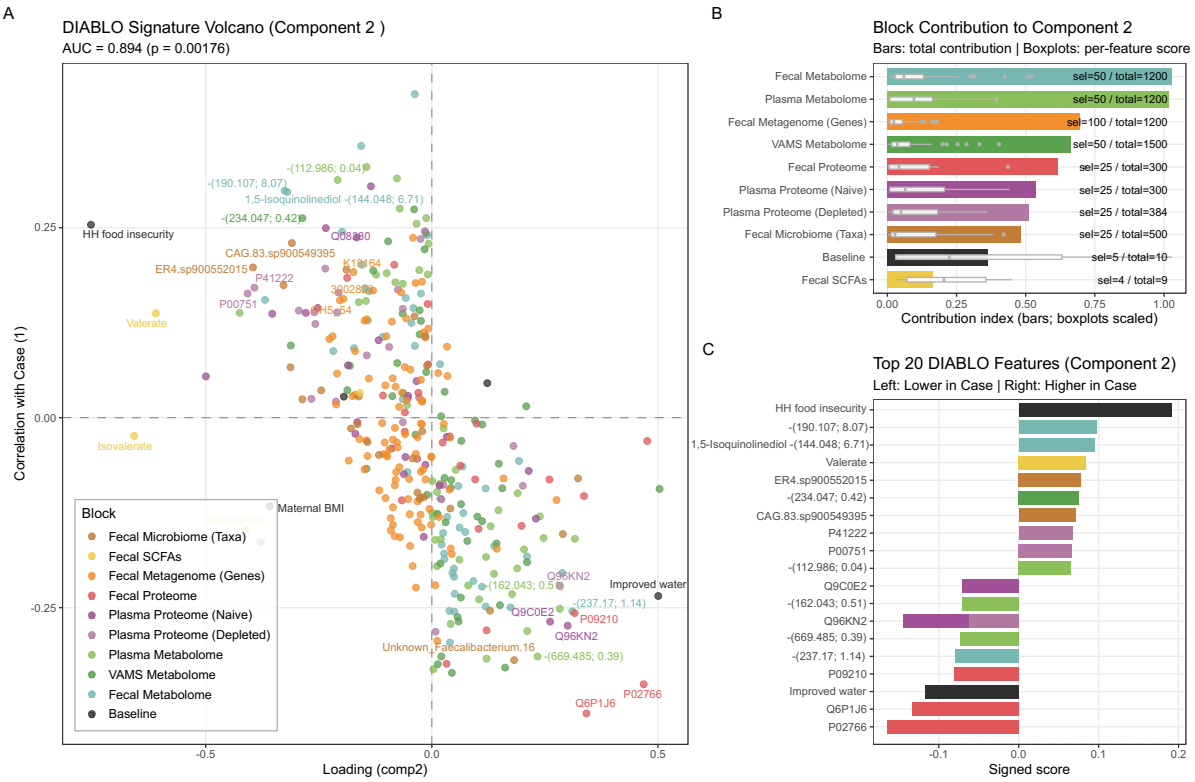

Figure S2. Prenatal maternal multi-omics DIABLO signature associated with SVN at trimester 3, Component 2.
(A) DIABLO signature volcano plot for Component 2 (n = 58), showing feature loading on the x-axis and correlation with SVN status on the y-axis. Positive y-values indicate features relatively higher in SVN cases, whereas negative y-values indicate features relatively lower in cases. Component 2 significantly discriminated SVN cases from controls (AUC = 0.894, p = 0.0018).
(B) Block-level contribution to Component 2. Colored bars indicate the total contribution of each block, calculated as the sum of feature-level scores, and overlaid boxplots show the distribution of per-feature scores within each block. Labels indicate the number of selected features relative to the total number of features entering the DIABLO model in each block. Total features represent the number of variables retained after preprocessing; for high-dimensional blocks, features were capped at a predefined block-specific maximum by retaining the most variable variables based on median absolute deviation.
(C) Top 20 Component 2 features ranked by signed score. Bars extending to the right indicate features relatively higher in SVN cases, whereas bars extending to the left indicate features relatively lower in cases. Untargeted metabolites are labelled in ion mode (m/z; rt) format when no annotation is available. A full feature table is provided in **Supplementary Data 1**.

Figure S3. Supplementary maternal milk, infant gut and maternal gut microbiome and stool biomarker profiles in SVN cases and controls.

(A) Mean genus-level relative abundance profiles in maternal milk, infant gut, and maternal gut across sampled timepoints in SVN cases and controls. Stacked bars show average relative abundance, with low-abundance genera grouped as “Other”.
(B) Shannon diversity in maternal milk, infant gut, and maternal gut by timepoint and SVN status. Points represent individual samples and boxplots summarize the distribution within each group.
(C) Beta-diversity ordinations of maternal milk, infant gut, and maternal gut microbiome profiles at each sampled timepoint. Dashed ellipses indicate group-level dispersion for SVN cases and controls, and p-values indicate the significance of case-control separation at each timepoint.
(D) Differentially abundant microbial taxa in maternal milk, infant gut, and maternal gut comparing SVN cases and controls at each sampled timepoint. Volcano plots show log2 fold change on the x-axis and -log10(FDR) on the y-axis. Labeled points denote selected differentially abundant taxa; grey labels indicate taxa that were no longer significant in sensitivity analyses using ANCOM-BC2 with pseudocount adjustment.
(E) Maternal stool short-chain fatty acid (SCFA) concentrations in SVN cases and controls. Boxplots show total SCFAs and individual SCFAs, with p-values indicating cross-sectional group comparisons.
(F) Maternal stool calprotectin concentrations in SVN cases and controls across timepoints. Boxplots show the distribution within each group, with p-values indicating cross-sectional group comparisons.

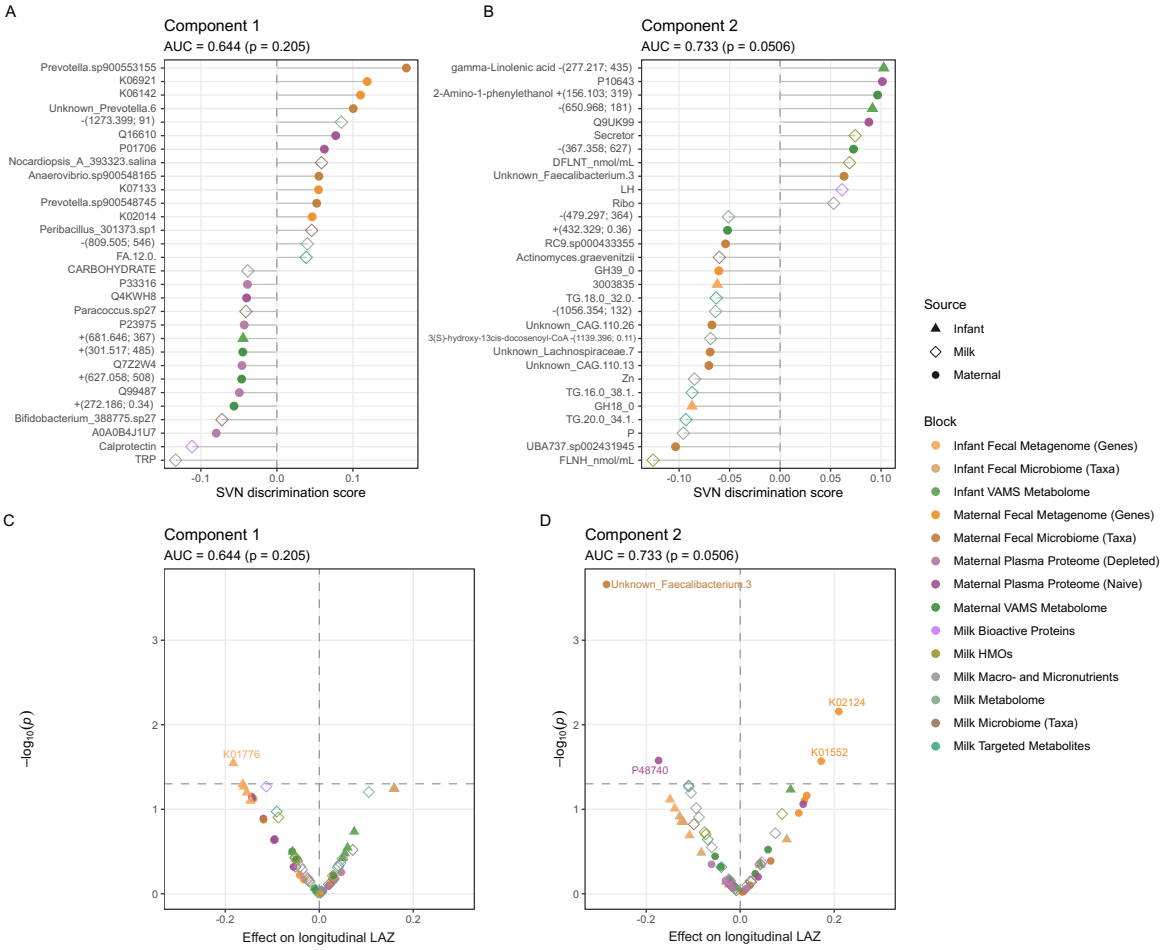

Figure S4. Later postnatal multi-omics features distinguishing SVN and their associations with longitudinal LAZ.

(A,B) Top later postnatal DIABLO features that discriminated SVN cases from controls (n = 43) for Component 1 (A) and Component 2 (B). The x-axis shows the signed SVN discrimination score, with positive values indicating features relatively higher in SVN cases and negative values indicating features relatively lower in cases. Features are colored by data block.

(C,D) Associations of the same component-specific SVN-discriminating features with longitudinal height-for-age z-score (LAZ) in mixed-effects models for Component 1 (C) and Component 2 (D). The x-axis shows the estimated effect of each feature on longitudinal LAZ, and the y-axis shows -log10(p). Positive coefficients indicate association with higher LAZ, whereas negative coefficients indicate association with lower LAZ. Untargeted metabolites are labelled in ion mode (m/z; rt) format when no annotation is available. A full feature table is provided in **Supplementary Data 2.**

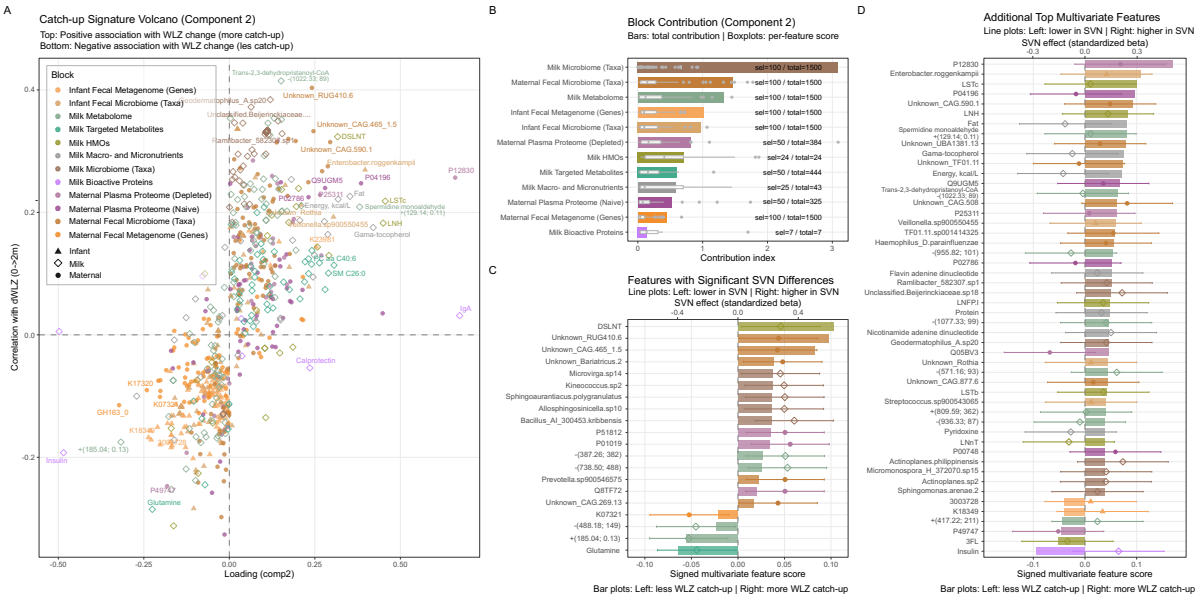

Figure S5. Early-life multi-omics features associated with early WLZ catch-up in SVN infant: Component 2.
(A) Block sPLS volcano plot for Component 2 (n = 78), showing feature loading on the x axis and correlation with change in WLZ form birth to 2 months on the y axis. Positive y-values indicate features positively correlated with early WLZ catch-up, whereas negative y-values indicate features negatively correlated with early WLZ catch-up.
(B) Block-level contribution to Component 2. Colored bars indicate the total contribution of each block, and overlaid boxplots show the distribution of per-feature scores within blocks. Labels indicate the number of selected features relative to the total number of retained features in each block after preprocessing.
(C) Features with significant univariate differences by SVN status in Component 2. Bars represent signed multivariate scores (loading : correlation), with positive values indicating association with greater WLZ catch-up. Points and lines show standardized case-control effect estimates and 95% confidence intervals.
(D) Additional top Component 2 features ranked by signed multivariate feature score, displayed using the same format as panel C. Untargeted metabolites are labelled in ion mode (m/z; rt) format when no annotation is available. A full feature table is provided in **Supplementary Data 3.**

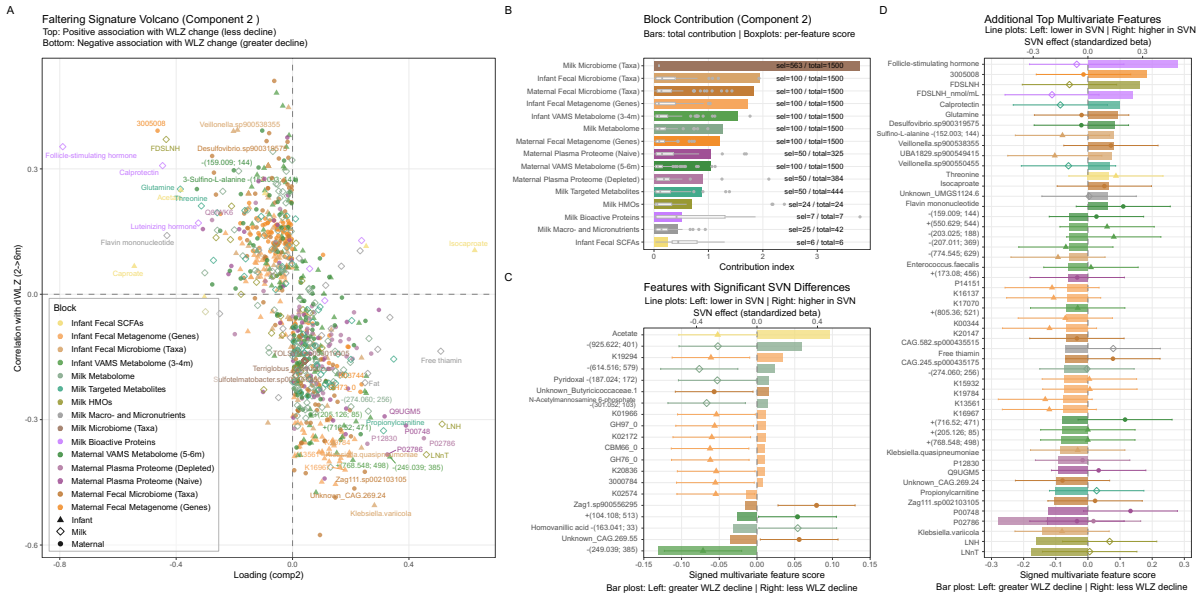

Figure S6. Later postnatal multi-omics features associated with WLZ faltering in SVN infants: Component 2.
(A) Block sPLS volcano plot for Component 2 (n = 43), showing feature loading on the x-axis and correlation with dWLZ_2_6 on the y-axis. Positive y-values indicate features positively correlated with change in WLZ from 2 to 6 months, consistent with less WLZ decline, whereas negative y-values indicate features negatively correlated with change in WLZ, consistent with greater decline.
(B) Block-level contribution to Component 2. Colored bars indicate the total contribution of each block, and overlaid boxplots show the distribution of per-feature scores within blocks. Labels indicate the number of selected features relative to the total number of retained features in each block after preprocessing.
(C) Features with significant univariate differences by SVN status in Component 2. Bars represent signed multivariate scores, with positive values indicating association with less WLZ decline and negative values indicating more WLZ decline. Points and lines indicate standardized case–control effect estimates and 95% confidence intervals.
(D) Additional top Component 2 features ranked by signed multivariate feature score, excluding those shown in panel C, displayed using the same format. Untargeted metabolites are labelled in ion mode (m/z; rt) format when no annotation is available. A full feature table is provided in **Supplementary Data 4.**

Table S1. Baseline maternal, infant, and household characteristics stratified by newborn vulnerability group

Characteristics	MISAME-III	BioSpé substudy					
	Overall (*n* = 1897)	SGA (*n* = 74)	LBW (*n* = 40)	Preterm (*n* = 12)	Case: SVN (*n* = 85)	Control: Healthy (*n* = 209)	*P* value
Health center catchment area, n (%)							0.801
Boni	433 (22.8)	9 (12.2)	4 (10.0)	1 (8.3)	10 (11.8)	36 (17.2)	
Dohoun	200 (10.5)	12 (16.2)	3 (7.5)	0 (0.0)	12 (14.1)	25 (12.0)	
Dougoumato II	346 (18.2)	12 (16.2)	11 (27.5)	2 (16.7)	14 (16.5)	35 (16.7)	
Karaba	193 (10.2)	13 (17.6)	6 (15.0)	2 (16.7)	14 (16.5)	25 (12.0)	
Kari	350 (18.5)	16 (21.6)	9 (22.5)	3 (25.0)	19 (22.4)	47 (22.5)	
Koumbia	375 (19.8)	12 (16.2)	7 (17.5)	4 (33.3)	16 (18.8)	41 (19.6)	
Household level							
Household food insecurity, n (%)	1277 (67.5)	52 (70.3)	23 (57.5)	8 (66.7)	58 (68.2)	120 (57.4)	0.089
Wealth index, 0 to 10 points	4.59 ± 1.76	4.47 ± 1.85	4.42 ± 2.16	4.26 ± 1.39	4.46 ± 1.81	4.82 ± 1.78	0.118
Household size, number	6.26 ± 4.38	6.80 ± 5.58	7.10 ± 6.63	5.17 ± 3.30	6.81 ± 5.60	6.38 ± 4.34	0.484
Number of children under five	1.05 ± 0.98	1.08 ± 1.17	1.10 ± 1.34	0.92 ± 0.90	1.12 ± 1.21	1.09 ± 1.02	0.823
Improved water, n (%)	1193 (62.9)	37 (50.0)	16 (40.0)	6 (50.0)	43 (50.6)	133 (63.6)	0.049
Improved sanitation, n (%)	1135 (59.8)	50 (67.6)	26 (65.0)	6 (50.0)	55 (64.7)	129 (61.7)	0.691
Mother							
Ethnic group, n (%)							0.104
Bwaba	1086 (57.3)	37 (50.0)	21 (52.5)	7 (58.3)	43 (50.6)	125 (59.8)	
Mossi	662 (34.9)	27 (36.5)	11 (27.5)	2 (16.7)	29 (34.1)	65 (31.1)	
Others	148 (7.8)	10 (13.5)	8 (20.0)	3 (25.0)	13 (15.3)	19 (9.1)	
Religion of pregnant woman, n (%)							0.232
Animist	432 (22.8)	9 (12.2)	8 (20.0)	4 (33.3)	13 (15.3)	56 (26.8)	
Muslim	801 (42.2)	35 (47.3)	17 (42.5)	4 (33.3)	39 (45.9)	87 (41.6)	
Catholic	261 (13.8)	9 (12.2)	2 (5.0)	0 (0.0)	9 (10.6)	13 (6.2)	
Protestant	335 (17.7)	18 (24.3)	10 (25.0)	4 (33.3)	21 (24.7)	48 (23.0)	
No religion, no animist	68 (3.6)	3 (4.0)	3 (7.5)	0 (0.0)	3 (3.5)	5 (2.4)	
Primary education and above, n (%)	797 (42.0)	32 (43.3)	21 (52.5)	6 (50.0)	36 (42.4)	97 (46.4)	0.703
Number of jobs, n (%)							0.241
0	1152 (60.7)	48 (64.9)	29 (72.5)	9 (75.0)	57 (67.1)	118 (56.5)	
1	671 (35.4)	24 (32.4)	11 (27.5)	3 (25.0)	26 (30.6)	82 (39.2)	
2 and above	74 (3.9)	2 (2.7)	0 (0.0)	0 (0.0)	2 (2.4)	9 (4.3)	
Parity, n (%)							0.015
0	429 (22.6)	26 (35.1)	19 (47.5)	5 (41.7)	31 (36.5)	43 (20.6)	
1-2	654 (34.5)	22 (29.7)	8 (20.0)	3 (25.0)	25 (29.4)	88 (42.1)	
3 or more	814 (42.9)	26 (35.1)	13 (32.5)	4 (33.3)	29 (34.1)	78 (37.3)	
Age, years	25.0 ± 6.17	23.66 ± 5.47	22.50 ± 5.89	23.17 ± 7.46	23.62 ± 5.76	24.35 ± 5.60	0.318
Weight, kg	58.17 ± 8.67	54.50 ± 7.31	51.99 ± 7.74	52.10 ± 10.66	54.40 ± 7.70	59.53 ± 9.94	< 0.001
Height, cm	162.54 ± 6.03	160.93 ± 6.13	159.15 ± 6.51	159.46 ± 8.37	160.99 ± 6.41	163.01 ± 5.59	0.008
Body mass index, kg/m^2	21.99 ± 2.87	21.03 ± 2.46	20.50 ± 2.54	20.35 ± 2.70	20.96 ± 2.47	22.37 ± 3.31	< 0.001
Mid-upper arm circumference, mm	262.02 ± 26.63	253.56 ± 23.78	248.57 ± 24.32	248.25 ± 24.89	253.21 ± 23.76	264.18 ± 28.21	0.002
Hemoglobin, g/dL	11.34 ± 1.51	11.59 ± 1.59	11.25 ± 1.70	11.15 ± 1.43	11.53 ± 1.56	11.74 ± 1.40	0.249
Gestational weight gain, kg	6.17 ± 3.52	6.20 ± 2.69	5.72 ± 2.41	5.42 ± 1.29	6.08 ± 2.59	6.86 ± 3.87	0.089
Dietary diversity score, 0 to 10 points	3.96 ± 1.61	4.17 ± 1.20	4.04 ± 1.30	3.90 ± 1.47	4.11 ± 1.25	4.04 ± 1.33	0.680
BEP intervention, n (%)							0.792
Fully control	489 (25.8)	18 (24.3)	13 (32.5)	4 (33.3)	21 (24.7)	57 (27.3)	
Postnatal intervention	471 (24.8)	24 (32.4)	13 (32.5)	4 (33.3)	28 (32.9)	57 (27.3)	
Prenatal intervention	462 (24.4)	16 (21.6)	6 (15.0)	1 (8.3)	18 (21.2)	44 (21.1)	
Pre- and Postnatal intervention	475 (25.0)	16 (21.6)	8 (20.0)	3 (25.0)	18 (21.2)	51 (24.4)	
Infant							
Sex, male, n (%)	862 (49.6)	37 (50.0)	16 (41.0)	6 (50.0)	42 (50.0)	101 (48.3)	0.798
Born in lean season, n (%)	527 (31.8)	28 (37.8)	6 (15.8)	0 (0.0)	28 (33.7)	88 (42.1)	0.233
Birth weight, kg	3.01 ± 0.44	2.53 ± 0.27	2.22 ± 0.24	2.14 ± 0.33	2.49 ± 0.31	3.22 ± 0.31	< 0.001
Birth length, cm	48.29 ± 2.19	46.81 ± 1.76	45.79 ± 1.99	44.49 ± 1.87	46.59 ± 1.88	49.30 ± 1.69	< 0.001
Birth head circumference, cm	3.42 ± 1.58	32.28 ± 1.29	31.38 ± 1.36	30.28 ± 0.91	32.06 ± 1.39	33.84 ± 1.24	< 0.001
Birth mid-upper arm circumference, mm	100.76 ± 8.29	92.57 ± 6.80	88.47 ± 7.65	85.27 ± 5.16	91.74 ± 7.07	103.66 ± 6.77	< 0.001
Gestational age at birth, weeks	39.91 ± 1.75	39.80 ± 1.28	38.07 ± 2.36	34.77 ± 1.59	39.19 ± 2.16	40.07 ± 1.11	< 0.001
Exclusively breastfeeding duration, months	5.61 ± 1.67	5.77 ± 1.02	5.66 ± 1.25	5.69 ± 1.30	5.75 ± 1.06	5.81 ± 1.00	0.670
Hemoglobin level at 6 months, g/dL	10.41 ± 1.36	10.18 ± 1.22	9.86 ± 1.22	9.93 ± 1.20	10.17 ± 1.22	10.38 ± 1.24	0.256
Morbidity at 6 months, times	6.40 ± 1.77	6.05 ± 1.02	6.08 ± 0.85	6.45 ± 0.52	6.08 ± 0.98	6.13 ± 0.90	0.680

P value comparing Case and Control

There is overlap in n among SGA, LBW, and preterm, totalling to the 85 in the Case: SVN group.

Data are presented as n (%) for categorical variables and mean ± sd for continuous variables.

Comparisons were performed using Fisher's exact test for categorical variables and linear regression for continuous variables.

Supplementary Data 1. DIABLO multi-omics signature for SVN at trimester 3

Supplementary Data 2. Postnatal multi-omics features associated with SVN status and longitudinal child growth

Supplementary Data 3. Early postnatal multi-omics fratures associated with early WLZ catch-up in SVN infant

Supplementary Data 4. Later postnatal multi-omics features associated with WLZ faltering in SVN infants