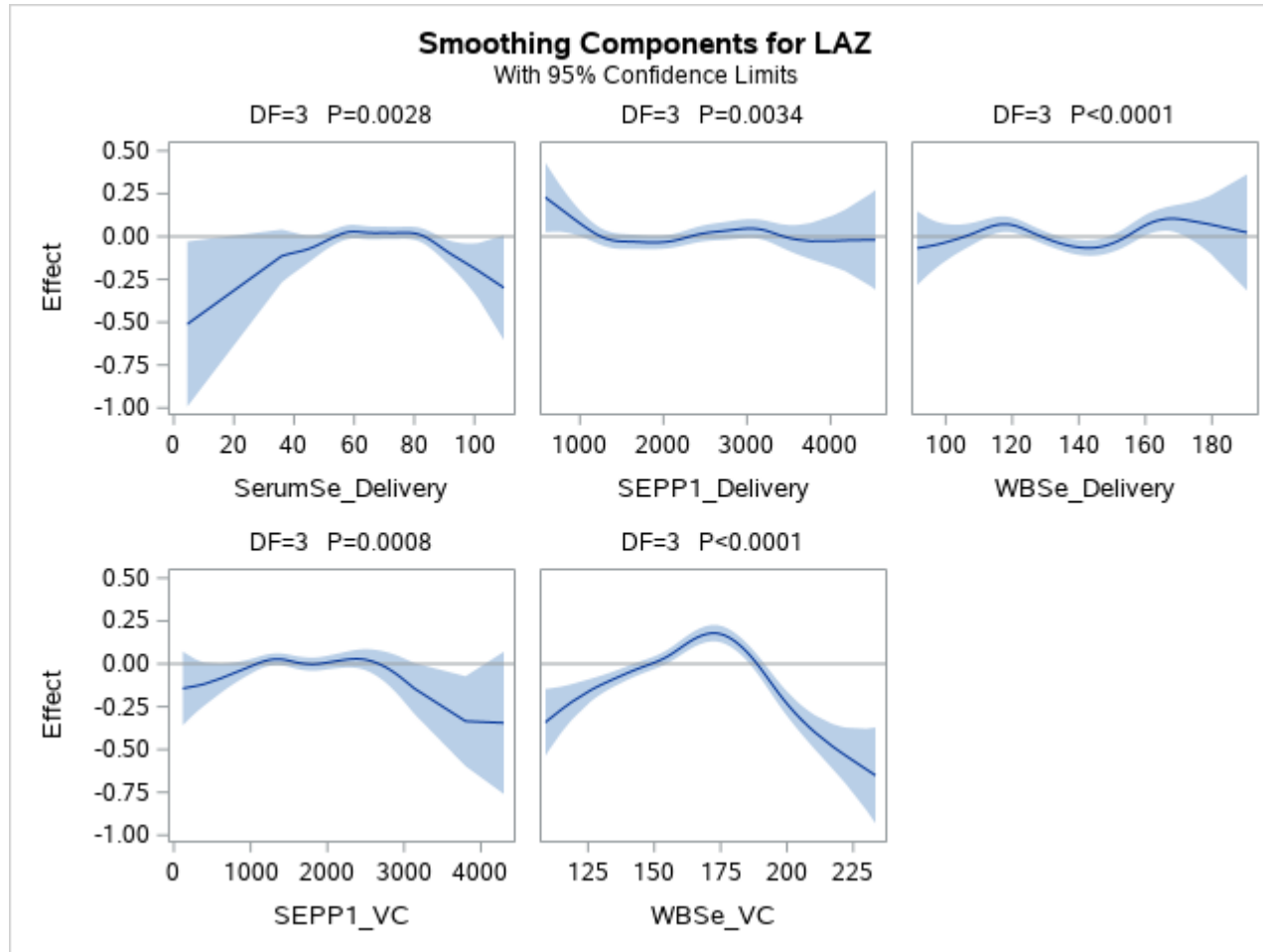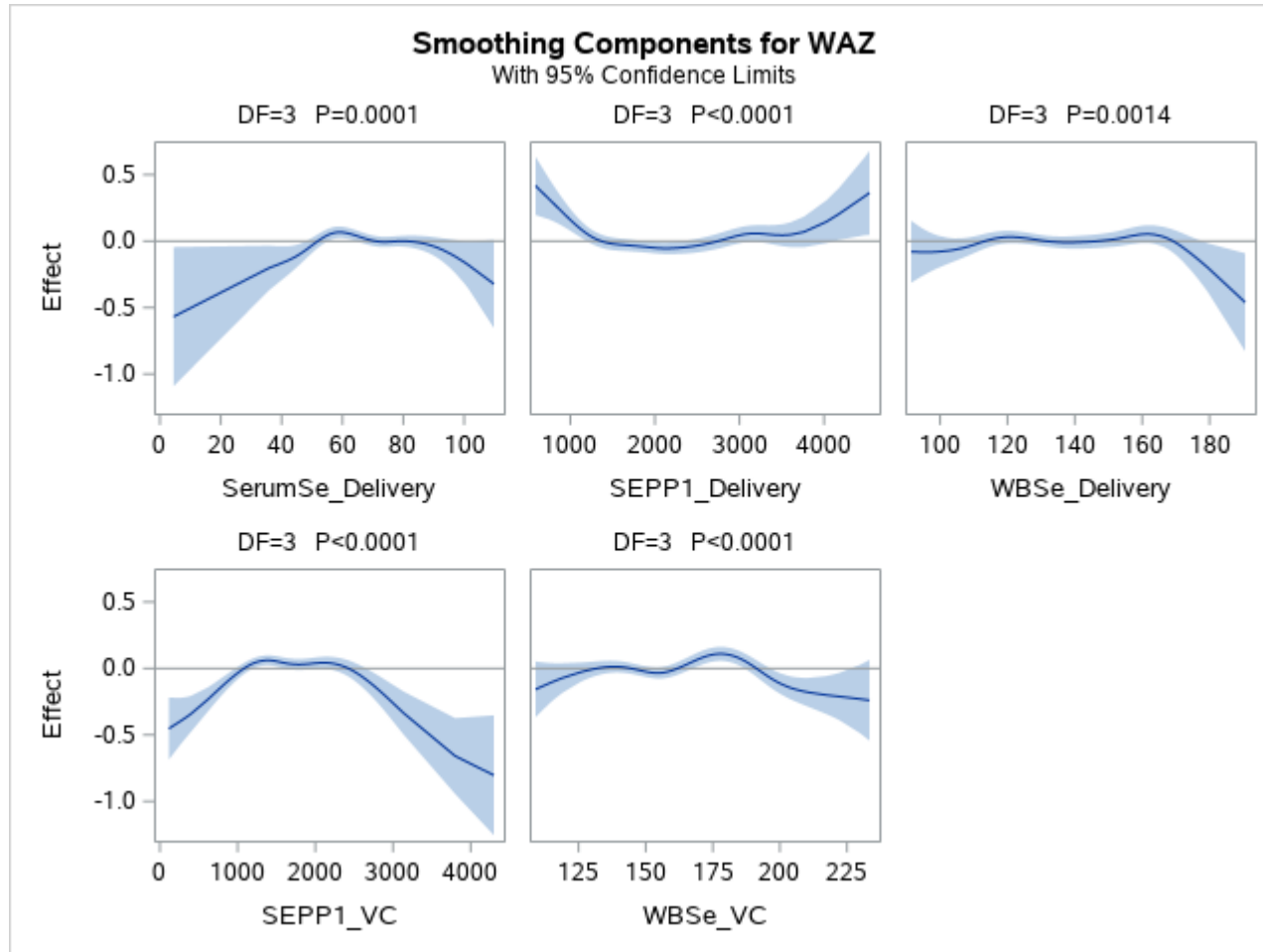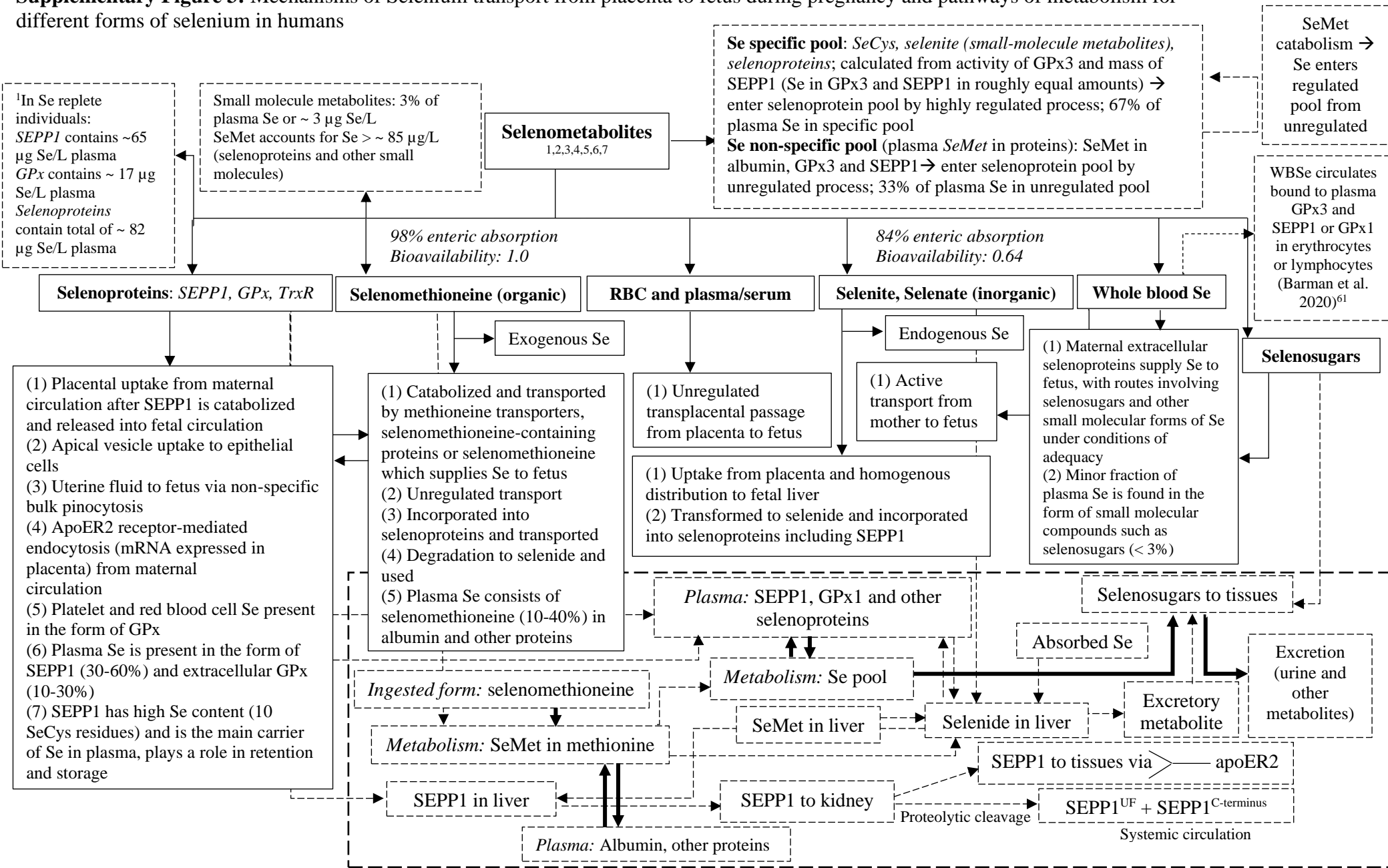**Supplementary Figure 1:** General additive models for associations between length-for-age z-scores and selenium biomarkers at delivery and in venous cord blood

Supplementary Figure 2: General additive models for associations between weight-for-age z-scores and selenium biomarkers at delivery and in venous cord blood

Supplementary Figure 3: Mechanisms of Selenium transport from placenta to fetus during pregnancy and pathways of metabolism for different forms of selenium in humans

SeMet catabolism → Se enters regulated pool from unregulated

Se specific pool: *SeCys, selenite (small-molecule metabolites), selenoproteins*; calculated from activity of GPx3 and mass of SEPP1 (Se in GPx3 and SEPP1 in roughly equal amounts) → enter selenoprotein pool by highly regulated process; 67% of plasma Se in specific pool

Se non-specific pool (plasma *SeMet* in proteins): SeMet in albumin, GPx3 and SEPP1 → enter selenoprotein pool by unregulated process; 33% of plasma Se in unregulated pool

[1]In Se replete individuals:
SEPP1 contains ~65 µg Se/L plasma
GPx contains ~ 17 µg Se/L plasma
Selenoproteins contain total of ~ 82 µg Se/L plasma

Small molecule metabolites: 3% of plasma Se or ~ 3 µg Se/L
SeMet accounts for Se > ~ 85 µg/L (selenoproteins and other small molecules)

Selenometabolites
1,2,3,4,5,6,7

WBSe circulates bound to plasma GPx3 and SEPP1 or GPx1 in erythrocytes or lymphocytes (Barman et al. 2020)[61]

98% enteric absorption
Bioavailability: 1.0

84% enteric absorption
Bioavailability: 0.64

Selenoproteins: *SEPP1, GPx, TrxR*

Selenomethioneine (organic)

RBC and plasma/serum

Selenite, Selenate (inorganic)

Whole blood Se

Exogenous Se

Endogenous Se

Selenosugars

(1) Placental uptake from maternal circulation after SEPP1 is catabolized and released into fetal circulation
(2) Apical vesicle uptake to epithelial cells
(3) Uterine fluid to fetus via non-specific bulk pinocytosis
(4) ApoER2 receptor-mediated endocytosis (mRNA expressed in placenta) from maternal circulation
(5) Platelet and red blood cell Se present in the form of GPx
(6) Plasma Se is present in the form of SEPP1 (30-60%) and extracellular GPx (10-30%)
(7) SEPP1 has high Se content (10 SeCys residues) and is the main carrier of Se in plasma, plays a role in retention and storage

(1) Catabolized and transported by methioneine transporters, selenomethioneine-containing proteins or selenomethioneine which supplies Se to fetus
(2) Unregulated transport
(3) Incorporated into selenoproteins and transported
(4) Degradation to selenide and used
(5) Plasma Se consists of selenomethioneine (10-40%) in albumin and other proteins

(1) Unregulated transplacental passage from placenta to fetus

(1) Active transport from mother to fetus

(1) Maternal extracellular selenoproteins supply Se to fetus, with routes involving selenosugars and other small molecular forms of Se under conditions of adequacy
(2) Minor fraction of plasma Se is found in the form of small molecular compounds such as selenosugars (< 3%)

(1) Uptake from placenta and homogenous distribution to fetal liver
(2) Transformed to selenide and incorporated into selenoproteins including SEPP1

Plasma: SEPP1, GPx1 and other selenoproteins

Selenosugars to tissues

Absorbed Se

Ingested form: selenomethioneine

Metabolism: Se pool

SeMet in liver

Selenide in liver

Excretion (urine and other metabolites)

Metabolism: SeMet in methionine

Excretory metabolite

SEPP1 to tissues via ⟩ —— apoER2

SEPP1 in liver

SEPP1 to kidney

SEPP1[UF] + SEPP1[C-terminus]

Plasma: Albumin, other proteins

Proteolytic cleavage

Systemic circulation

——— Placental transport of selenometabolites in humans during pregnancy
- - - - - Selenium metabolism and transport in the body (not exclusive to pregnancy) across assorted selenometabolites (adapted from Burk et al., 2015)[45]
▬▬▬ Ingested Se and plasma forms of Se (SeMet in Met pool metabolized via trans-sulfuration pathway and SeCys *β-lysase* → metabolically active Se in the Se pool)
Selenosugar (1β-methylseleno-*N*-acetyl-D-galactosamine) is filtered into urine by the kidney, it does not accumulate in plasma

Adapted from: Burk et al., (2013)[62]; Chen et al., (2014)[63]; Santos et al., (2017)[64]; Anan et al., (2008)[65]; Al-Saleh et al., (2015)[66]; Burk et al., (2015)[45]; EFSA (2014)[8]; Burk et al., (2006)[67]

Supplementary Table 1: Selenoprotein concentrations in mid-gestation and delivery specimens in the growth study

Biomarkers	Maternal mid-gestation (17-24 weeks)		Maternal delivery	
	GPx	TrxR	GPx	TrxR
N[1]	*201*	*201*	*145*	*144*
Selenium biomarker concentration (µg/L), median (IQR)	135.3 (32.3)	4.8 (2.8)	138.3 (36.8)	7.3 (8.1)
Gestational age at birth (in weeks), median (IQR)	-	-	38.9 (1.9)	38.9 (1.9)
Birth weight (g), mean (SD)	-	-	2647.5 (470.0)	2653.8 (481.3)

[1]Sample sizes exclude observations where measures of selenoprotein & birth weight are not available

Supplementary Table 2: Linear associations between selenoproteins – GPx and TrxR and birth weight

Outcome	Se Biomarker	Timepoint	N	Unadjusted β (95% CI)	p-value	N	Adjusted β[2] (95% CI)	p-value	N	Adjusted β[2] (95% CI)	p-value
										Cotinine Sensitivity Analysis	
Birth weight[1]	GPx	Mid-gestation	145	1.1 (-0.2, 2.3)	0.09	**140**	**1.3 (0.1, 2.5)**	**0.04**	88	1.0 (-0.7, 2.6)	0.2
		Delivery	145	-0.7 (-1.8, 0.4)	0.2	**141**	**-1.1 (-2.1, -0.07)**	**0.04**	90	-0.6 (-2.0, 0.8)	0.4
	TrxR	Mid-gestation	145	4.6 (-8.2, 17.5)	0.5	140	10.6 (-1.6, 22.8)	0.09	88	15.6 (-3.4, 34.6)	0.1
		Delivery	144	-0.1 (-6.9, 6.7)	0.9	140	0.09 (-7.0, 7.1)	0.9	89	1.6 (-7.5, 10.6)	0.7

[1]No scaling applied to GPx and TrxR biomarkers

[2]Models adjusted for infant sex, gestational age at birth, season of birth, maternal age, maternal education, maternal height, maternal BMI, gravidity, vitamin D treatment group, delivery CRP, asset index quintiles, daily protein intake (kg), smoking and tobacco use during pregnancy, cotinine included in sensitivity analysis

Supplementary Table 3: Linear regression sensitivity analyses for associations between maternal delivery and venous cord Selenium biomarkers and growth outcomes adjusting for urinary cotinine

Outcome	Se Biomarker[1]	Timepoint	N	Adjusted β[2,3] (95% CI)	p-value
			Cotinine Sensitivity Analysis		
	WBSe Del	Birth	**307**	**-30 (-50.1, -9.8)**	**0.004**
	WBSe VC	Birth	**247**	**-27.2 (-44.4, -10.0)**	**0.002**
Birth weight	Serum Se Del	Birth	280	-27.7 (-58.3, 2.8)	0.08
	SEPP1 Del	Birth	294	4.2 (-48.2, 56.6)	0.9
	SEPP1 VC	Birth	**249**	**79.0 (9.5, 148.4)**	**0.03**
		Birth	303	-0.06 (-0.1, 0.007)	0.08
LAZ	WBSe Del	12-months	366	-0.04 (-0.09, 0.02)	0.2
		24-months	335	-0.01 (-0.07, 0.04)	0.2
		Birth	**246**	**-0.08 (-0.1, -0.02)**	**0.006**
LAZ	WBSe VC	12-months	**258**	**-0.06 (-0.1, -0.008)**	**0.02**
		24-months	238	-0.04 (-0.09, 0.02)	0.2
		Birth	277	-0.07 (-0.2, 0.04)	0.2
LAZ	Serum Se Del	12-months	332	-0.05 (-0.1, 0.03)	0.2
		24-months	303	-0.05 (-0.1, 0.03)	0.3
		Birth	291	0.02 (-0.2, 0.2)	0.8
LAZ	SEPP1 Del	12-months	345	-0.006 (-0.1, 0.1)	0.9
		24-months	318	-0.04 (-0.2, 0.9)	0.6
		Birth	**247**	**0.3 (0.05, 0.5)**	**0.02**
LAZ	SEPP1 VC	12-months	260	-0.02 (-0.2, 0.2)	0.8
		24-months	241	0.06 (-0.2, 0.3)	0.6
		Birth	**307**	**-0.07 (-0.1, -0.02)**	**0.004**
WAZ	WBSe Del	12-months	**366**	**-0.06 (-0.1, 0.001)**	**0.05**
		24-months	335	-0.01 (-0.08, 0.05)	0.7
		Birth	**247**	**-0.07 (-0.1, -0.03)**	**0.002**
WAZ	WBSe VC	12-months	**258**	**-0.06 (-0.1, -0.008)**	**0.03**
		24-months	238	-0.03 (-0.09, 0.03)	0.3
WAZ	Serum Se Del	Birth	280	-0.07 (-0.1, 0.008)	0.08

		12-months	332	-0.06 (-0.1, 0.03)	0.2
		24-months	303	-0.04 (-0.1, 0.06)	0.4
WAZ	SEPP1 Del	Birth	294	0.01 (-0.1, 0.1)	0.9
		12-months	345	-0.06 (-0.2, 0.08)	0.4
		24-months	318	-0.1 (-0.3, 0.06)	0.2
WAZ	SEPP1 VC	Birth	**527**	**0.2 (0.07, 0.3)**	**0.003**
		12-months	260	-0.1 (-0.3, 0.1)	0.4
		24-months	241	-0.04 (-0.3, 0.2)	0.8
WFL	WBSe Del	Birth	269	-0.04 (-0.1, 0.03)	0.2
		12-months	366	-0.05 (-0.1, 0.005)	0.07
		24-months	335	-0.01 (-0.08, 0.06)	0.8
WFL	WBSe VC	Birth	219	-0.05 (-0.1, 0.01)	0.1
		12-months	258	-0.05 (-0.1, 0.009)	0.1
		24-months	238	-0.02 (-0.08, 0.05)	0.6
WFL	Serum Se	Birth	247	-0.01 (-0.1, 0.09)	0.8
		12-months	332	-0.05 (-0.1, 0.04)	0.3
		24-months	303	-0.02 (-0.1, 0.08)	0.7
WFL	SEPP1 Del	Birth	260	0.06 (-0.1, 0.2)	0.5
		12-months	345	-0.07 (-0.2, 0.07)	0.3
		24-months	318	-0.1 (-0.3, 0.05)	0.2
WFL	SEPP1 VC	Birth	218	0.04 (-0.2, 0.3)	0.7
		12-months	260	-0.1 (-0.4, 0.1)	0.3
		24-months	241	-0.09 (-0.4, 0.2)	0.5
HCAZ	WBSe Del	Birth	306	-0.05 (-0.1, 0.01)	0.1
		12-months	363	-0.03 (-0.08, 0.03)	0.3
		24-months	333	-0.0005 (-0.06, 0.06)	0.9
HCAZ	WBSe VC	Birth	247	-0.02 (-0.08, 0.03)	0.4
		12-months	256	-0.02 (-0.07, 0.03)	0.4
		24-months	238	-0.01 (-0.06, 0.03)	0.6
HCAZ	Serum Se Del	Birth	279	-0.08 (-0.2, 0.01)	0.08
		12-months	329	0.02 (-0.07, 0.1)	0.7
		24-months	302	-0.00002 (-0.9, 0.09)	0.9
HCAZ	SEPP1 Del	Birth	293	-0.1 (-0.3, 0.04)	0.1

		12-months	342	-0.06 (-0.2, 0.07)	0.4
		24-months	**317**	**-0.2 (-0.3, -0.02)**	**0.03**
HCAZ	SEPP1 VC	Birth	249	0.04 (-0.2, 0.3)	0.7
		12-months	257	-0.1 (-0.3, 0.1)	0.4
		24-months	241	-0.2 (-0.4, 0.007)	0.06

[1]Whole blood selenium (WBSe) scaled to represent the change in anthropometric outcome for every 10 µg/L increase in WBSe

[1]Serum selenium scaled to represent the change in anthropometric outcome for every 10 µg/L increase in serum Se

[1]SEPP1 scaled to represent the change in anthropometric outcome for every 1000 µg/L increase in SEPP1

[2]Models adjusted for infant sex, gestational age at birth, season of birth, maternal age, maternal education, maternal height, maternal BMI, gravidity, vitamin D treatment group, delivery CRP, asset index quintiles, daily protein intake (kg), smoking and tobacco use during pregnancy and urinary cotinine in sensitivity analysis

[3]No multi-collinearity problem was detected in models – assessment was conducted after generating directed acyclic graphs (DAG) based on conceptual frameworks developed *a priori*

Supplementary Table 4: Modified Poisson Regression sensitivity analyses for associations between maternal delivery and venous cord Selenium biomarker and birth outcomes adjusting for cotinine analysis

Outcome	Se Biomarker	Timepoint	N	Adjusted Risk Ratio (95% CI)	p-value
			Cotinine Sensitivity Analysis		
Small-for-gestational age (SGA)	WBSe Del	Delivery	307	1.06 (0.96, 1.2)	0.3
	WBSe VC	Venous Cord	247	1.10 (1.0, 1.2)	0.02
	Serum Se Del	Delivery	280	1.11 (0.96, 1.3)	0.2
	SEPP1 Del	Delivery	294	0.98 (0.75, 1.3)	0.9
	SEPP1 VC	Venous Cord	249	0.8 (0.6, 1.2)	0.3
Low birth weight (LBW)	WBSe Del	Delivery	307	1.15 (1.0, 1.3)	0.03
	WBSe VC	Venous Cord	247	1.12 (1.0, 1.2)	0.06
	Serum Se Del	Delivery	280	1.18 (0.97, 1.4)	0.1
	SEPP1 Del	Delivery	294	1.12 (0.78, 1.6)	0.5
	SEPP1 VC	Venous Cord	249	0.9 (0.6, 1.5)	0.8
Preterm birth (PTB)	WBSe Del	Delivery	308	1.42 (0.9, 2.1)	0.08
	WBSe VC	Venous Cord	248	0.99 (0.7, 1.5)	0.9
	Serum Se Del	Delivery	281	1.65 (0.96, 2.8)	0.07
	SEPP1 Del	Delivery	295	1.64 (0.63, 4.3)	0.3
	SEPP1 VC	Venous Cord	250	1.4 (0.3, 7.3)	0.7

[1]Whole blood selenium (WBSe) scaled to represent the change in anthropometric outcome for every 10 µg/L increase in WBSe

[1]Serum selenium scaled to represent the change in anthropometric outcome for every 10 µg/L increase in serum Se

[1]SEPP1 scaled to represent the change in anthropometric outcome for every 1000 µg/L increase in SEPP1

[2]Models adjusted for infant sex, gestational age at birth, season of birth, maternal age, maternal education, maternal height, maternal BMI, gravidity, vitamin D treatment group, delivery CRP, asset index quintiles, daily protein intake (kg), smoking and tobacco use during pregnancy and urinary cotinine in sensitivity analysis

[3]No multi-collinearity problem was detected in models – assessment was conducted after generating directed acyclic graphs (DAG) based on conceptual frameworks developed *a priori*