Supplementary Table S1 The 18 food groups on the maternal food frequency questionnaire and their associated loadings for the top principal component (PC1, explained 17.5% of variance)

17.5% of variance)	
Food or food group	Loading values
Deep fried foods	0.38
Processed meats	0.36
Baked products	0.24
Beef, pork, or lamb as the main dish	0.24
Margarine	0.21
Whole milk dairy foods	0.15
Added salt	0.14
Pasta, rice, or noodles	0.09
Whole eggs	0.06
Citrus fruits	-0.004
Fish or seafood	-0.02
Other fruits such as apples or pears	-0.21
Broccoli, cauliflower, cabbage, or Brussels sprouts	-0.22
Low-fat milk products	-0.26
Other vegetables such as peas or corn	-0.28
Whole grain foods	-0.28
Carrots	-0.29
Dark green leafy vegetables	-0.33

Supplementar	Supplementary Table S2 Assay parameters for C-reactive protein protein and interleukin-8 plasma measurements	eactive protein protein and	l interleukin-8 plasma ı	neasurements			
Biomarker	Assay manufacturer and principle	Assay linearity range	Assay LLD	Samples in % >LLD	Sample dilution	Samples range (min-max)	(%) CA
C-Reactive protein ^a	Meso Scale Discovery Electrochemiluminescence	200,000–2.6 pg/mL	1.49 pg/mL	100%	500x, 2,500x	0.1414–99.71 mg/L	5.036
Interleukin-8	Immunoassay	592–0.146 pg/mL	0.0308 pg/mL	100%	2x, 50x	0.5–13,301 pg/mL	86.9

Abbreviations: CV, coefficient of variation; LLD, lower limit of detection.

This assay was calibrated against the National Institute for Biological Standards and Control (NIBSC) World Health Organization standard 85/506. 1 mg/L in this assay = 9641U of 86/506.

Supplementary Table S3 Clinical characteristics of 36 patients with preterm births

Gestational	Spontaneous	Birth	Potential	Other
age at birth	or induced	mode	contributory	distinguishing
(wk)	labor		factors	characteristics
36.3	Induction	Vaginal	Oligohydramnios	
36.3	Induction		Cligoriyaramilloo	Cholestasis of
30.3	mauction	Vaginal		
				pregnancy,
				perinatal antibiotics
35.3	Induction	Vaginal	Preeclampsia	IUGR/SGA,
				perinatal antibiotics
34.8	Induction	Vaginal	PPROM	
36.0	Induction	Vaginal		Perinatal antibiotics
36.7	Induction	Vaginal		Perinatal antibiotics
			D 1 :	
36.3	Induction	Vaginal	Preeclampsia	Perinatal antibiotics
31.0	Induction	C- section	Preeclampsia	Prolapsed cord, perinatal
				antibiotics
35.3	Induction	C-	Preeclampsia	Perinatal antibiotics
		section		
36.9	Induction	Vaginal		lugr/sga
			Duandamania	
36.4	Induction	Vaginal	Preeclampsia	Perinatal antibiotics
36.4	No labor (C-	C-	Oligohydramnios	SGA, perinatal
	section)	section		antibiotics
36.9	Spontaneous	Vaginal		
26.7	Spontaneous	Vaginal		Perinatal
		J 3		antibiotics
36.4	Spontaneous	Vaginal		
33.9	Spontaneous	Vaginal	PPROM	Perinatal antibiotics
			PPROW	
36.3	Spontaneous	Vaginal		Hematuria,
				possible bladder
				stone
36.6	Spontaneous	Vaginal		Gestational
	· ·			diabetes
36.3	Spontaneous	Vaginal	PPROM	
34.7	Spontaneous	C-	PPROM	Non-reassuring
04.7	Opontaneous	section	T T T T T T T T T T T T T T T T T T T	tracings, single
		Section		
				umbilical artery,
				perinatal antibiotics
36.6	Spontaneous	Vaginal		
36.6	Spontaneous	Vaginal	PPROM	
36.3	Spontaneous	Vaginal		Gestational
	· ·			diabetes
36.3	Spontaneous	Vaginal	PPROM	Perinatal antibiotics
36.3	Spontaneous	C-	TTTOM	Gestational
30.3	Sportaneous	section		diabetes
00.0	0			
36.3	Spontaneous	Vaginal		Gestational
				diabetes
36.9	Spontaneous	Vaginal		Perinatal antibiotics
36.3	Spontaneous	Vaginal		Perinatal antibiotics
35.6	Spontaneous	Vaginal		Perinatal antibiotics
36.0	Spontaneous	Vaginal		Tight cord around
50.0		- agiilai		neck
32.9	Spontaneous	Vaginal		Perinatal
32.9	Spontaneous	vagilial		
20.0	On an tarr	Marin I		antibiotics
32.0	Spontaneous	Vaginal		
35.6	Spontaneous	Vaginal	PPROM	Prolonged rupture
				of membranes,
				chorioamnionitis,
				perinatal antibiotics
36.6	Spontaneous	Vaginal		Nuchal cord
36.7	Spontaneous	Vaginal	PPROM	Perinatal antibiotics
				Perinatal antibiotics
33.6	Spontaneous	Vaginal	PPROM,	rematal antibiotics
			preeclampsia	

Abbreviations: IUGR/SGA, intrauterine growth restriction/small for gestational age; PPROM, preterm premature rupture of membranes. Notes: Legend: preeclampsia (green), spontaneous preterm births (blue), and induced or no labor births without preeclampsia (yellow). Patients who had preeclampsia are shown with green background; those with induced delivery are shown with yellow background and those with spontaneous preterm delivery and no preeclampsia are shown with blue background. Bolded patients had a second sample collection on or after the day of delivery and were excluded in the sensitivity analysis.

Total <i>n</i> = 816	Included (n = 528)	Excluded ($n = 288$)	<i>p</i> -Value
	Number (%)	Number (%)	
Maternal race/ethnicity			
Black			0.83
Hispanic	23 (4.4)	16 (5.6)	
Non-Hispanic	199 (37.7)	116 (40.3)	
Other			
Hispanic	47 (8.9)	27 (9.4)	
Non-Hispanic	39 (7.4)	21 (7.3)	
White			
Hispanic	73 (13.8)	40 (13.9)	
Non-Hispanic	147 (27.8)	68 (23.6)	
Study site			
Boston	156 (29.5)	86 (29.9)	0.33
San Diego	188 (35.6)	89 (30.9)	
St. Louis	184 (34.8)	113 (39.2)	
Treatment arm: high-dose prenatal vitamin D (4,400 IU/d)	252 (47.7)	156 (54.2)	0.09
Maternal age \geq 35 y	42 (8.0)	19 (6.6)	0.57
	Mean (SD)	Mean (SD)	<i>p</i> -Value
Living children (total no.)	0.86 (1.0)	0.94 (1.1)	0.29
Gravidity (total no.)	2.4 (1.6)	2.4 (1.5)	0.97
Prior premature births (total no.)	0.09 (0.3)	0.14 (0.5)	0.14
Third trimester biomarker sampling time (weeks' gestation)	34.06 (1.7)	33.74 (1.7)	0.01

Abbreviations: IU, international units; SD, standard deviation.

Note: *p*-Values are for *t*-tests for continuous variables and Chi-square tests for categorical variables.

Total <i>n</i> = 528	Preterm birth $(n=36)$	Term birth (<i>n</i> = 492)	<i>p</i> -Value
	Number (%)	Number (%)	
Maternal race/ethnicity			
Black			
Hispanic	0 (0.0)	23 (4.7)	
Non-Hispanic	18 (50.0)	181 (36.8)	
Other			
Hispanic	2 (5.6)	45 (9.1)	0.47
Non-Hispanic	3 (8.3)	36 (7.3)	
White			
Hispanic	3 (8.3)	70 (14.2)	
Non-Hispanic	10 (27.8)	137 (27.8)	
Maternal education: less than college	22 (61.1)	312 (63.4)	0.92
Study site			
Boston	4 (11.1)	152 (30.9)	0.01^{a}
San Diego	12 (33.3)	176 (35.8)	
St. Louis	20 (55.6)	164 (33.3)	
Treatment arm: high-dose prenatal vitamin D (4,400 IU/d)	20 (55.6)	232 (47.2)	0.42
Birth mode: C-section	5 (13.9)	141 (28.7)	0.09
Perinatal antibiotics	22 (61.1)	193 (39.2)	0.02^{a}
Any smoke exposure during pregnancy	8 (22.9)	87 (17.9)	0.61
Gestational diabetes	5 (13.9)	29 (5.9)	0.13
Maternal age \geq 35 y	6 (16.7)	36 (7.3)	0.09
	Mean (SD)	Mean (SD)	<i>p</i> -Value
Living children (total no.)	1.03 (1.4)	0.85 (1.0)	0.44
Gravidity (total no.)	2.56 (1.7)	2.4 (1.6)	0.65
Prior premature births (total no.)	0.20 (0.4)	0.09 (0.3)	0.12
Unhealthy diet by PCA	-0.43 (2.0)	0.01 (1.8)	0.22
Frequency of uncontrolled asthma in pregnancy	0.25 (0.40)	0.09 (0.20)	0.24
Prepregnancy BMI	27.1 (6.0)	28.4 (8.0)	0.24
BMI change over pregnancy	4.7 (2.7)	5.0 (3.8)	0.63
Vitamin D level (first trimester)	21.6 (11.6)	23.6 (9.8)	0.33
Vitamin D level (third trimester)	29.8 (16.2)	32.1 (13.9)	0.40
Third trimester sampling time (weeks' gestation)	33.37 (1.55)	33.77 (1.74)	0.34

Abbreviations: BMI, body mass index; IU, international units; PCA, principal component analysis (unhealthy diet high in red meat, processed meats, baked goods, and deep-fried foods)

Note: Missingness: prepregnancy BMI (n = 77), BMI change over pregnancy (n = 98), unhealthy diet and red meat consumption by PCA (n = 3), vitamin D level in third trimester (n = 2), and smoke exposure during pregnancy (n = 6).

Note: p-Values are for t-tests for continuous variables and chi-square tests for categorical variables.

^aDenotes *p*-value less than predefined level of significance, α < 0.05.

	Crude results		Adjusted results			
	OR (95% CI)	<i>p</i> -Value	OR (95% CI)	<i>p</i> -Value		
First-trimester log CRP						
All preterm births included ($n = 36$)	0.87 (0.66, 1.19)	0.38	0.95 (0.66, 1.38)	0.78		
Excluding preeclampsia ($n = 30$)	0.87 (0.64, 1.21)	0.40	0.98 (0.67, 1.46)	0.94		
Only spontaneous preterm birth $(n=22)$	0.95 (0.67, 1.38)	0.78	1.02 (0.67, 1.58)	0.93		
Third-trimester log CRP						
All preterm births included ($n = 36$)	1.14 (0.82, 1.6)	0.46	1.49 (1.02, 2.23)	0.04^{a}		
Excluding preeclampsia ($n = 30$)	1.15 (0.80, 1.67)	0.45	1.58 (1.05, 2.44)	0.03^{a}		
Only spontaneous preterm birth $(n = 22)$	1.65 (1.07, 2.59)	0.03 ^a	2.05 (1.28, 3.39)	< 0.001		
CRP increase						
All preterm births included ($n = 36$)	1.69 (0.80, 3.64)	0.17	3.06 (1.31,7.55)	0.01 ^a		
Excluding preeclampsia ($n = 30$)	1.54 (0.68, 3.55)	0.30	2.77 (1.11, 7.26)	0.03^{a}		
Only spontaneous preterm birth $(n=22)$	3.59 (1.40, 10.1)	0.01 ^a	5.90 (2.07, 19.7)	0.002 ^a		
First-trimester log IL-8						
All preterm births included ($n = 36$)	1.08 (0.84, 1.32)	0.48	1.06 (0.77, 1.38)	0.66		
Excluding preeclampsia $(n=30)$	1.13 (0.89, 1.38)	0.26	1.11 (0.79, 1.43)	0.51		
Only spontaneous preterm birth $(n=22)$	0.90 (0.57, 1.22)	0.58	0.96 (0.61, 1.34)	0.84		
Third-trimester log IL-8						
All preterm births included ($n = 36$)	1.17 (0.89, 1.48)	0.20	1.20 (0.90, 1.54)	0.18		
Excluding preeclampsia ($n = 30$)	1.11 (0.78, 1.43)	0.50	1.13 (0.79, 1.51)	0.46		
Only spontaneous preterm birth $(n = 22)$	1.23 (0.90, 1.57)	0.13	1.22 (0.89, 1.62)	0.17		
IL-8 increase						
All preterm births included ($n = 36$)	1.94 (0.94, 4.14)	0.1	1.74 (0.77, 4.07)	0.19		
Excluding preeclampsia ($n = 30$)	1.59 (0.72, 3.59)	0.25	1.21 (0.50, 2.98)	0.67		
Only spontaneous preterm birth $(n=22)$	1.84 (0.77, 4.60)	0.18	1.63 (0.63, 4.50)	0.32		

Abbreviations: CI, confidence interval; CRP, Greactive protein; IL-8, interleukin-8; OR, odds ratio. Note: Results are from univariate and multivariate logistic regression analyses.

Supplementary Table 57 CRP and IL-8 as nonsignificant mediators in the association between prepregnancy BMI or smoke exposure and preterm birth								
Independent variable	Mediator	Direct effect on preterm birth ^a	Indirect effect on preterm birth ^b	Proportion mediated ^c				
Prepregnancy BMI	First trimester CRP	-0.02 (-0.08, 0.04) p = 0.60	-0.003 (-0.03, 0.03) p = 0.78	0.10 (-4.5, 4.6) p=0.85				
Prepregnancy BMI	Third Trimester CRP	-0.04 (-0.10, 0.02) p = 0.17	0.02 (-0.002, 0.04) $p = 0.05^{d}$	-0.45 (-8.0, 9.3) p = 0.52				
Prepregnancy BMI Third Trimester IL-8 Smoke exposure First trimester CRP Smoke exposure Third Trimester CRP Smoke exposure First trimester IL-8		-0.02 (-0.07, 0.03) p = 0.47	-0.0004 (-0.004, 0.0) p = 0.77	0.002 (-0.33, 0.47) p = 0.91				
		-0.02 (-0.08, 0.03) p = 0.36	0.002 (-0.001, 0.01) p = 0.28	-0.03 (-0.99, 0.99) p = 0.60				
		0.001 (-0.06, 0.08) p = 0.98	-0.001 (-0.06, 0.00) p = 0.77	0.003 (-0.61, 0.89) p = 0.91				
		-0.002 (-0.06, 0.08) p = 0.91	0.001 (-0.06, 0.01) p = 0.77	0.001 (-1.00, 0.97) p = 0.97				
		-0.002 (-0.06, 0.08) p = 0.93	0.001 (-0.003, 0.01) p = 0.68	0.0001 (-0.85, 1.10) p = 0.97				
Smoke exposure	Third Trimester IL-8	-0.0002 (-0.06, 0.08) p = 0.88	0.001 (-0.002 , 0.01) p = 0.53	-0.0004 (-0.81, 0.99) p = 0.99				

Abbreviations: BMI, body mass index; CRP, C-reactive protein; IL-8, interleukin-8

^cProportion mediated = proportion of the effect of an independent variable on the outcome through the mediator (indirect effect/total effect), reported as the proportion (95% confidence interval) and associated *p*-value.

Supplementary Table S8 Biomarker measurements for patients who had samples collected on or after the day of o								
Timepoint of second sample collection	Gestational age at delivery (wk)	First CRP measurement (mg/L)	Second CRP measurement (mg/L)	First IL-8 measurement (pg/mL)	Second IL-8 measurement (pg/mL)			
Day of delivery	26.7	0.65	3.4	3.0	3.4			
Day of delivery	31.0	11.6	5.5	2.6	2.6			
1-d after delivery	32.0	2.2	99.7	1.1	1.0			
2-d after delivery	39.9	5.1	20.2	2.3	12.5			
2-d after delivery	32.9	4.4	24.6	13.3	1.7			

Abbreviations: CRP, C-reactive protein; IL-8, interleukin-8.

^aDirect effect = the effect of an independent variable on the outcome, controlling for the mediator, reported as estimate (95% confidence interval) and associated *p*-value.

^bIndirect effect = average mediator effect, reported as estimate (95% confidence interval) and associated *p*-value

Supplementary Table S9 Association of prenatal CRP with baseline maternal characteristics and preterm birth after exclusion of patients with second CRP measurement on or after day of delivery

Association by linear regression model	First-trimester log(CRP) n = 523		Third-trimester log(CRP) $n = 523$			
	β (95% CI)	<i>p</i> -Value	β (95% CI)	<i>p</i> -Value		
Maternal age ≥ 35 y	-0.10 (-0.45, 0.25)	0.58	-0.16 (-0.49, 0.16)	0.32		
Maternal education: less than college	0.40 (0.21, 0.60)	$< 0.001^{a}$	0.29 (0.11, 0.47)	$< 0.001^{a}$		
Treatment arm: high-dose prenatal vitamin D (4,400 IU/d)	0.02 (-0.17, 0.21)	0.85	0.03 (-0.14, 0.21)	0.71		
Prepregnancy BMI	0.08 (0.06, 0.09)	$< 0.001^{a}$	0.05 (0.04, 0.07)	$< 0.001^{a}$		
BMI change over pregnancy	$-0.03 \; (-0.06, 0.00)$	0.09	0.01 (-0.02, 0.03)	0.68		
Gravidity (total no.)	0.15 (0.09, 0.21)	$< 0.001^{a}$	0.07 (0.02, 0.13)	0.01 ^a		
Prior premature births (total no.)	0.46 (0.17, 0.76)	$< 0.001^{a}$	0.39 (0.12, 0.66)	0.01^{a}		
Living children (total no.)	0.25 (0.16, 0.34)	$< 0.001^{a}$	0.08 (0.00, 0.17)	0.06		
Birth mode: c-section	0.17 (-0.05, 0.38)	0.13	0.20 (-0.39, 0.00)	0.05		
Perinatal antibiotics	-0.11 (-0.38, 0.08)	0.26	-0.07 (-0.25, 0.11)	0.44		
Unhealthy diet by PCA	0.05 (0.00, 0.11)	0.05^{a}	0.07 (0.02, 0.12)	$< 0.001^{a}$		
Any smoke exposure during pregnancy	-	-	0.18 (-0.05, 0.42)	0.12		
Gestational diabetes	0.43 (0.04, 0.81)	0.03 ^a	-0.05 (-0.41, 0.31)	0.79		
Frequency of uncontrolled asthma in pregnancy	-0.14 (-0.89, 0.61)	0.71	0.53 (-0.17, 1.23)	0.13		
Vitamin D level (first trimester)	-0.02 (-0.03, -0.01) <0.001 ^a		$-0.02 \; (-0.03, -0.01)$	$< 0.001^{a}$		
Vitamin D level (third trimester)			-0.01 (-0.01, 0.00)	0.11		
Association by Kruskal–Wallis H-Test	CRP in mg/L p-Value (median: 25%ile,75%ile)		CRP in mg/L (median: 25%ile,75%ile)	<i>p</i> -Value		
Maternal race/ethnicity						
Black						
Hispanic	17.8 (12.1, 38.1)		17.3 (12.5, 26.5)			
Non-Hispanic	10.0 (3.9, 20.8)		9.5 (4.6, 9.5)			
Other						
Hispanic	10.6 (6.6, 23.3)	$< 0.001^{a}$	7.9 (4.8, 15.1)	$< 0.001^{a}$		
Non-Hispanic	6.9 (3.5, 10.6)		5.6 (2.7, 11.5)			
White						
Hispanic	7.7 (5.2, 16.8)		7.2 (4.0, 12.4)			
Non-Hispanic	6.6 (3.0, 14.9)		6.0 (3.5, 14.5)			
Study site						
Boston	8.8 (4.2, 21.0)	0.27	8.6 (4.4, 17.9)	0.04^{a}		
San Diego	7.8 (3.7, 16.6)		6.6 (3.5, 12.7)			
St. Louis	10.5 (3.6, 19.1)			9.3 (4.3, 17.2)		
Association with preterm birth $(n = 28)$	Adjusted odds ratio (95%	CI)	<i>p</i> -Value			
Log CRP: first trimester	1.05 (0.72, 1.56)		0.79			
Log CRP: third trimester	1.38 (0.91, 2.10)		0.13			
CRP increase	2.91 (1.21, 7.30)		0.02 ^a			

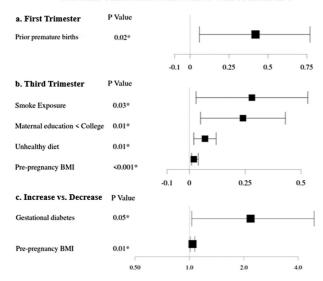
Abbreviations: BMI, body mass index; CI, confidence interval; IU, international units; PCA, principal component analysis (unhealthy diet high in red meat, processed meats, baked goods, and deep-fried foods); SD, standard deviation.

Notes: Missingness: prepregnancy BMI (n = 76), BMI change over pregnancy (n = 97), unhealthy diet and red meat consumption by PCA (n = 1), vitamin D level in third trimester (n = 2), and smoke exposure during pregnancy (n = 6).

Models were adjusted for study site, maternal race/ethnicity, prepregnancy BMI, and any prenatal smoke exposure. Models for biomarker change over pregnancy were additionally adjusted for baseline biomarker value.

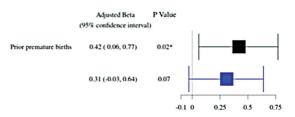
^aDenotes *p*-value less than predefined level of significance, α < 0.05.

Maternal Characteristics Associated with Prenatal IL-8

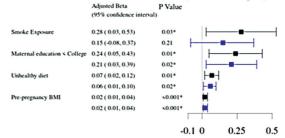


Supplementary Fig. S1 Forest plots depicting the model estimates and 95% confidence intervals of maternal characteristics that were significantly associated with (A) first-trimester log(IL-8) as determined by univariate linear regression (B) third-trimester log(IL-8) as determined by univariate linear regression and c) an increase in IL-8 over pregnancy as determined by logistic regression adjusted for baseline IL-8 level. Maternal characteristics are ordered from highest to lowest β coefficient (A, B) or odds ratio (C). Unhealthy diet was based on principal component analysis of food frequency questionnaire data with higher scores characterized by higher consumption of red or processed meats, baked products, and deep-fried foods. * Denotes p-value less than predefined level of significance, $\alpha < 0.05$

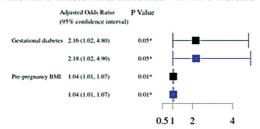
Maternal characteristics associated with log(IL8) at baseline



Maternal characteristics associated with log(IL8) in late pregnancy



Maternal characteristics associated with IL-8 increase



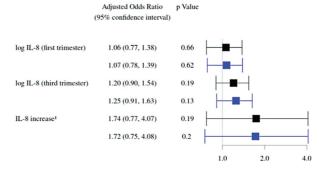
Supplementary Fig. S2 Forest plots depicting the model estimates and 95% confidence intervals with (black) and without (blue) outliers with extreme IL-8 values (>10,000 pg/L) of maternal characteristics and the association with first-trimester log(IL-8) as determined by univariate linear regression (top), third-trimester log(IL-8) as determined by univariate linear regression (middle), and an increase in IL-8 over pregnancy as determined by logistic regression adjusted for baseline IL-8 level (bottom). Maternal characteristics are ordered from highest to lowest β coefficient (top, middle) or odds ratio (bottom). Unhealthy diet was based on principal component analysis of food frequency questionnaire data with higher scores characterized by higher consumption of red or processed meats, baked products, and deep-fried foods. * Denotes p-value less than predefined level of significance, $\alpha < 0.05$.

Association of prenatal IL-8 and all preterm births

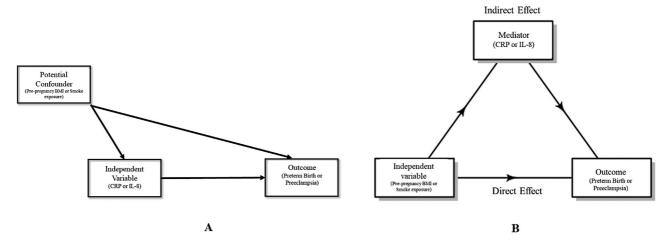
	Crude Odds Ratio (95% confidence interval)	P Value	Adjusted Odds Ratio (95% confidence interval)	P Value			
log IL-8: first trimester	r 1.08 (0.84, 1.32)	0.48	1.06 (0.77, 1.38)	0.66			
log IL-8: third trimeste	er 1.17 (0.89, 1.48)	0.2	1.20 (0.90, 1.54)	0.18	=	-	
IL-8 increase ¹	1.94 (0.94, 4.14)	0.1	1.74 (0.77, 4.07)	0.19		-	
					1.0	2.0	4.0

Supplementary Fig. S3 Forest plots depicting the odds ratio and 95% confidence intervals obtained from logistic regression models of associations between prenatal IL-8 with preterm birth. Five-hundred and twenty-six patients (36 with preterm birth) were included in the crude analysis and 447 patients (31 with preterm birth) were included in the adjusted analysis. Models were adjusted for study site, maternal race/ethnicity, prepregnancy BMI, and any prenatal smoke exposure. ¹ Models for biomarker change over pregnancy were additionally adjusted for baseline biomarker value. * Denotes p-value less than predefined level of significance, α <0.05

Association of prenatal IL-8 and preterm birth with and without extreme outliers



Supplementary Fig. S4 Forest plots depicting the odds ratio and 95% confidence intervals obtained from logistic regression models of the association between prenatal IL-8 in first trimester, third trimester, and increase over pregnancy with outcomes of preterm birth. Results from models including outliers with extreme IL-8 values (>10,000 pg/L) are in black (n=528) and results from models excluding outliers are in blue (n=525). Models were adjusted for study site, maternal race/ethnicity, prepregnancy BMI, and any prenatal smoke exposure. ¹ Models for biomarker change over pregnancy were additionally adjusted for the baseline value.



Supplementary Fig. S5 Directed acyclic graphs (DAG) depicting two different possible relationships between prenatal CRP or IL-8, preterm birth or preeclampsia, and prepregnancy BMI or smoke exposure. The first DAG (A) considers prepregnancy BMI and smoke exposure as potential confounders in the association between CRP or IL-8 and preterm birth or preeclampsia. The second DAG (B) considers prenatal CRP or IL-8 as a mediator in the association between prepregnancy BMI or smoke exposure and preterm birth and preeclampsia. CRP, G-reactive protein; IL, interleukin.