Association of vitamin D intake during pregnancy with small vulnerable newborns: a population-based cohort study

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Supplementary Table 1 Basic characteristics of participants included in the analysis and those excluded[1]

Characteristic	Overall	Included participants	Excluded participants	*P* value
N	3566	2980	586	
Age (years)	29.0 ± 3.6	29.0 ± 3.5	29.2 ± 3.7	0.245
Pre-pregnancy BMI (kg/m^2)	21.1 ± 2.9	21.2 ± 3.0	21.0 ± 2.7	0.113
Gestational weight gain (kg)	15.1 ± 5.3	15.1 ± 5.3	15.2 ± 5.3	0.895
Ethnicity (Han Chinese)	3486 (97.8)	2916 (97.9)	570 (97.3)	0.473
Education levels (years)				0.084
≤ 9	274 (7.7)	215 (7.2)	59 (10.1)	
10–12	531 (14.9)	440 (14.8)	91 (15.5)	
13–15	1113 (31.2)	931 (31.2)	182 (31.1)	
≥ 16	1648 (46.2)	1394 (46.8)	254 (43.3)	
Monthly incomes (CNY)				0.446
≤ 3000	61 (1.7)	53 (1.8)	8 (1.4)	
3000–4999	509 (14.3)	414 (13.9)	95 (16.2)	
5000–9999	1956 (54.9)	1644 (55.2)	312 (53.2)	
≥ 10000	1040 (29.2)	869 (29.2)	171 (29.2)	
Season				<0.001
Winter	998 (28.0)	888 (29.8)	110 (18.8)	
Spring	883 (24.8)	696 (23.4)	187 (31.9)	
Summer	971 (27.2)	800 (26.8)	171 (29.2)	
Fall	714 (20.0)	596 (20.0)	118 (20.1)	
Primiparity (yes)	2721 (76.3)	2292 (76.9)	429 (73.2)	0.061
Smoking (yes)	92 (2.6)	79 (2.7)	13 (2.2)	0.645
Alcohol drinking (yes)	233 (6.5)	183 (6.1)	50 (8.5)	0.040
Regular exercise (yes)	1424 (39.9)	1208 (40.5)	216 (36.9)	0.106
Outdoor activities (yes)	1882 (52.8)	1597 (53.6)	285 (48.6)	0.031
Sun protection (yes)	651 (18.3)	567 (19.0)	84 (14.3)	0.009

[1]Continuous variables were presented as means ± SDs for normally distributed variables and medians (interquartile ranges) for non-normally distributed variables; categorical variables were presented as n (%).

BMI, body mass index; CNY, Chinese Yuan.

Supplementary Table 2 Dietary food and nutrient intake according to the quartiles of total vitamin D intake in the first and second trimesters[1]

	First trimester				Second trimester			
	Overall	Q1	Q4	*P* value	Overall	Q1	Q4	*P* value
N	2049	513	512		1446	362	362	
Foods and total energy intake								
Grains (g/d)	220.00 (172.46, 275.00)	226.57 (177.50, 284.00)	204.30 (165.62, 254.29)	<0.001	271.49 (216.33, 314.24)	279.36 (227.28, 324.64)	260.36 (213.26, 302.14)	0.005
Vegetables (g/d)	268.21 (180.36, 382.14)	275.93 (184.46, 417.86)	254.76 (180.00, 372.36)	0.014	309.83 (227.15, 408.69)	307.57 (230.23, 407.83)	319.02 (222.26, 429.58)	0.589
Fruits (g/d)	396.07 (271.07, 546.25)	382.14 (263.21, 531.61)	390.00 (272.94, 548.04)	0.501	410.20 (290.78, 566.07)	403.30 (279.82, 573.04)	433.40 (307.95, 564.64)	0.443
Meats (g/d)	32.86 (15.00, 56.43)	33.39 (13.57, 54.50)	36.43 (17.14, 60.09)	0.003	51.07 (32.14, 75.00)	47.50 (30.09, 70.98)	53.21 (33.66, 75.67)	0.009
Aquatic products (g/d)	17.86 (7.50, 34.29)	16.04 (6.43, 31.43)	22.05 (10.71, 42.86)	<0.001	27.18 (14.29, 48.57)	22.86 (10.71, 40.00)	33.18 (18.59, 56.07)	<0.001
Eggs (g/d)	28.57 (12.50, 50.00)	25.00 (11.43, 50.00)	40.00 (17.86, 50.00)	<0.001	40.00 (20.00, 50.00)	31.79 (14.29, 50.00)	40.00 (25.00, 50.00)	<0.001
Legumes (g/d)	6.00 (2.57, 11.43)	6.00 (2.29, 12.00)	6.00 (2.57, 10.89)	0.859	6.00 (2.86, 10.71)	6.07 (2.86, 10.96)	6.43 (2.89, 11.30)	0.623
Nuts (g/d)	8.43 (2.68, 16.86)	7.14 (1.79, 15.00)	8.57 (2.86, 18.21)	0.002	11.79 (4.71, 20.71)	10.12 (2.95, 20.22)	12.14 (5.65, 20.86)	0.070
Dairy products (g/d)	132.14 (50.00, 250.00)	107.14 (40.00, 200.00)	225.71 (123.58, 292.86)	<0.001	208.21 (100.00, 285.71)	139.29 (55.53, 250.00)	231.07 (139.46, 321.43)	<0.001
Total energy (kcal/d)	1808.00 (1495.03, 2124.39)	1820.62 (1479.78, 2167.15)	1780.87 (1537.06, 2099.42)	0.054	2134.10 (1847.80, 2449.56)	2121.91 (1821.72, 2399.98)	2122.82 (1857.81, 2417.47)	0.606
Energy-adjusted nutrient intake								
Protein (g/d)	51.23 (46.99, 55.95)	49.72 (45.77, 54.27)	53.97 (50.31, 59.11)	<0.001	60.77 (56.13, 66.59)	58.72 (54.79, 63.34)	63.75 (58.24, 69.46)	<0.001
Fat (g/d)	61.96 (52.63, 71.82)	61.56 (51.39, 70.57)	65.52 (55.61, 75.70)	<0.001	76.01 (65.81, 86.07)	73.25 (62.75, 82.24)	76.92 (67.29, 87.81)	<0.001
Carbohydrates (g/d)	265.23 (242.19, 287.53)	267.43 (246.55, 291.33)	256.41 (229.40, 277.61)	<0.001	299.61 (275.90, 323.58)	308.09 (287.06, 334.71)	294.95 (269.84, 317.19)	<0.001
Cholesterol (mg/d)	270.75 (167.05, 368.44)	250.61 (156.81, 337.54)	338.61 (222.98, 432.17)	<0.001	331.26 (234.71, 422.27)	290.94 (201.92, 384.49)	374.19 (284.94, 445.85)	<0.001
Vitamin A (ug/d)	671.20 (510.08, 872.36)	662.08 (485.07, 845.63)	711.65 (544.81, 902.41)	0.002	806.08 (623.29, 1057.44)	764.01 (603.43, 1002.97)	837.56 (638.11, 1142.67)	0.008
Vitamin C (mg/d)	159.74 (125.70, 202.44)	159.88 (120.02, 200.53)	157.50 (124.82, 194.82)	0.301	170.93 (134.69, 215.75)	166.30 (133.34, 217.94)	178.41 (141.82, 222.78)	0.305

Vitamin E (mg/d)	35.54 (28.65, 43.88)	36.04 (29.49, 44.07)	35.16 (28.11, 42.91)	0.124	40.20 (32.72, 49.47)	40.14 (32.41, 50.00)	40.24 (32.35, 49.66)	0.602
Folic acid (ug/d)	242.41 (201.21, 296.66)	229.06 (190.88, 283.06)	255.97 (210.26, 307.62)	<0.001	277.88 (236.82, 333.33)	270.11 (228.43, 324.46)	287.59 (247.02, 343.19)	0.001
Calcium (mg/d)	479.37 (385.07, 586.66)	455.56 (364.60, 555.07)	549.43 (462.94, 647.11)	<0.001	573.25 (474.01, 692.75)	518.23 (411.96, 629.06)	626.79 (515.62, 742.31)	<0.001
Iron (mg/d)	16.71 (15.52, 18.22)	16.64 (15.44, 18.07)	16.70 (15.50, 18.12)	0.404	19.21 (17.87, 20.71)	19.00 (17.68, 20.46)	19.51 (18.13, 21.01)	0.004
Zinc (mg/d)	8.95 (8.38, 9.60)	8.79 (8.28, 9.36)	9.25 (8.69, 9.92)	<0.001	10.69 (10.07, 11.52)	10.43 (9.95, 11.19)	10.98 (10.28, 11.71)	<0.001
Selenium (ug/d)	31.24 (26.55, 36.58)	30.34 (25.78, 34.91)	34.89 (29.78, 39.58)	<0.001	37.50 (32.27, 44.04)	35.60 (30.85, 41.75)	39.78 (34.92, 47.27)	<0.001
PUFA (g/d)	20.45 (15.24, 26.37)	20.53 (15.02, 26.79)	20.28 (14.92, 26.07)	0.369	24.73 (18.32, 30.76)	24.70 (17.39, 30.31)	24.60 (19.04, 30.34)	0.075

[1]medians (interquartile ranges) were given for non-normally distributed variables and *P* values were from the Kruskal-Wallis rank test. The daily intake of dietary nutrients was adjusted for total energy intake using the nutrient residual method.

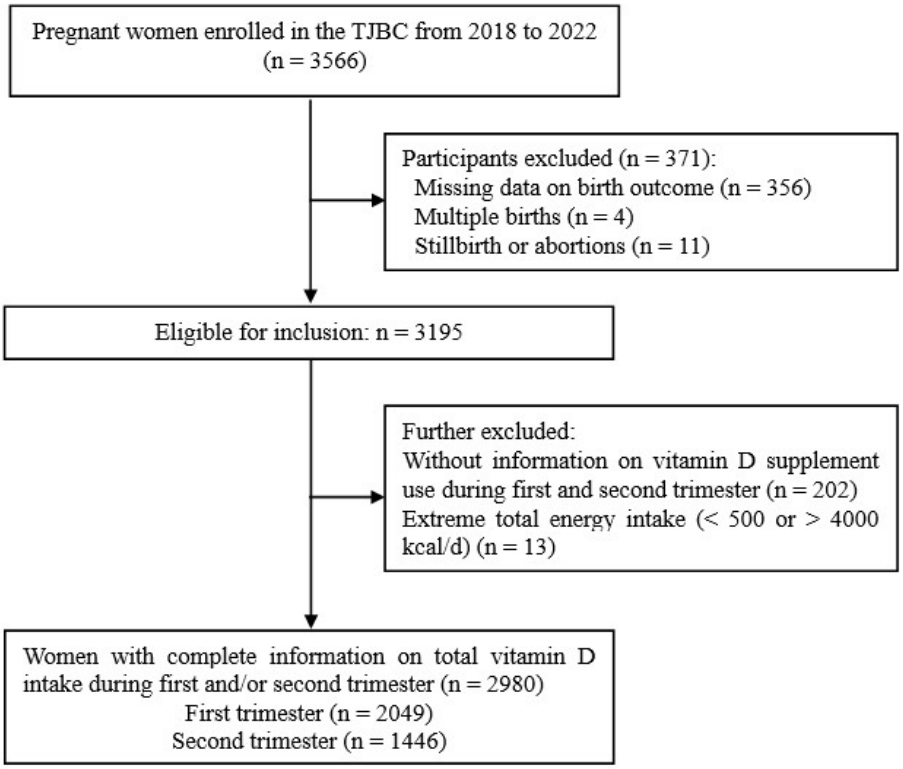
Q, quartile; PUFA, polyunsaturated fatty acids.

Supplementary Table 3 Association between dietary vitamin D intake (per SD increase) from different food sources and risk of small vulnerable newborns in the first and second trimesters[1]

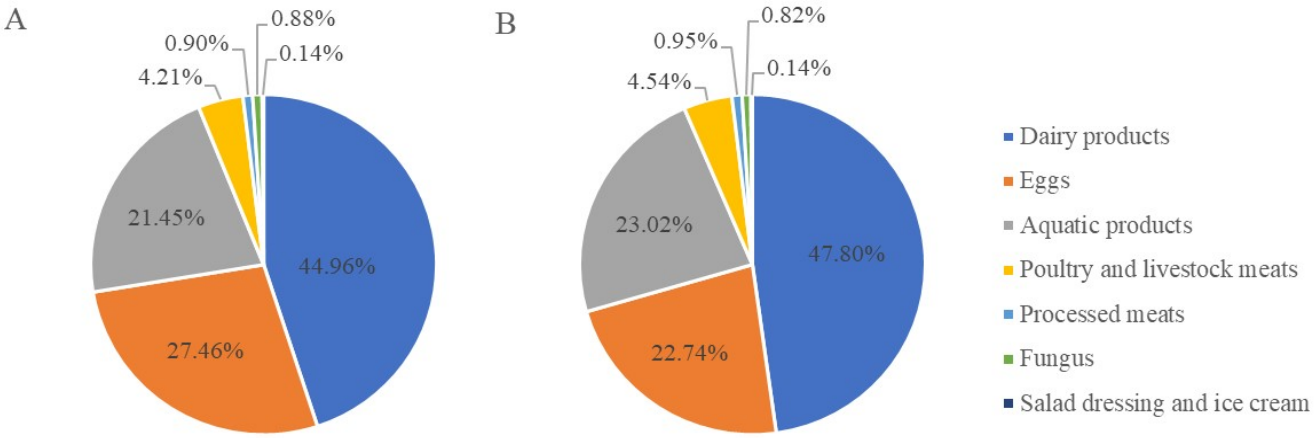
Food groups	LBW	PTB	SGA	SVN
First trimester				
Poultry and livestock meats	1.07 (0.85, 1.35)	0.96 (0.78, 1.18)	0.84 (0.68, 1.03)	0.90 (0.77, 1.05)
Processed meats	1.06 (0.84, 1.34)	1.01 (0.83, 1.23)	0.81 (0.60, 1.08)	0.92 (0.78, 1.09)
Aquatic products	1.06 (0.85, 1.33)	1.05 (0.87, 1.27)	1.09 (0.93, 1.28)	1.07 (0.95, 1.22)
Eggs	0.88 (0.68, 1.14)	0.84 (0.68, 1.04)	1.02 (0.85, 1.22)	0.94 (0.82, 1.09)
Dairy products	1.23 (0.99, 1.53)	1.19 (0.99, 1.43)	0.88 (0.72, 1.08)	1.00 (0.86, 1.15)
Fungus	0.96 (0.71, 1.30)	1.02 (0.84, 1.24)	0.96 (0.79, 1.17)	0.99 (0.86, 1.14)
Salad dressing and ice cream	0.96 (0.75, 1.24)	1.09 (0.94, 1.26)	1.13 (0.99, 1.29)	1.13 (1.02, 1.26)
Second trimester				
Poultry and livestock meats	0.85 (0.57, 1.28)	1.02 (0.75, 1.37)	1.14 (0.91, 1.44)	1.08 (0.89, 1.30)
Processed meats	0.82 (0.41, 1.65)	0.53 (0.23, 1.24)	0.99 (0.78, 1.26)	0.90 (0.69, 1.17)
Aquatic products	1.24 (0.90, 1.70)	1.27 (0.98, 1.63)	0.80 (0.60, 1.06)	0.99 (0.82, 1.20)
Eggs	0.87 (0.59, 1.28)	1.07 (0.80, 1.42)	0.96 (0.76, 1.22)	1.01 (0.84, 1.22)
Dairy products	1.03 (0.79, 1.35)	1.02 (0.86, 1.22)	0.92 (0.60, 1.42)	0.99 (0.84, 1.16)
Fungus	0.64 (0.37, 1.12)	1.17 (0.93, 1.48)	0.89 (0.66, 1.18)	1.03 (0.85, 1.24)
Salad dressing and ice cream	0.82 (0.43, 1.56)	1.14 (0.88, 1.48)	0.82 (0.53, 1.27)	0.99 (0.78, 1.27)

[1]Values were represented as ORs (95% CIs) from logistic regression models and were adjusted for age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, total energy intake, and dietary vitamin D intake from other food groups.

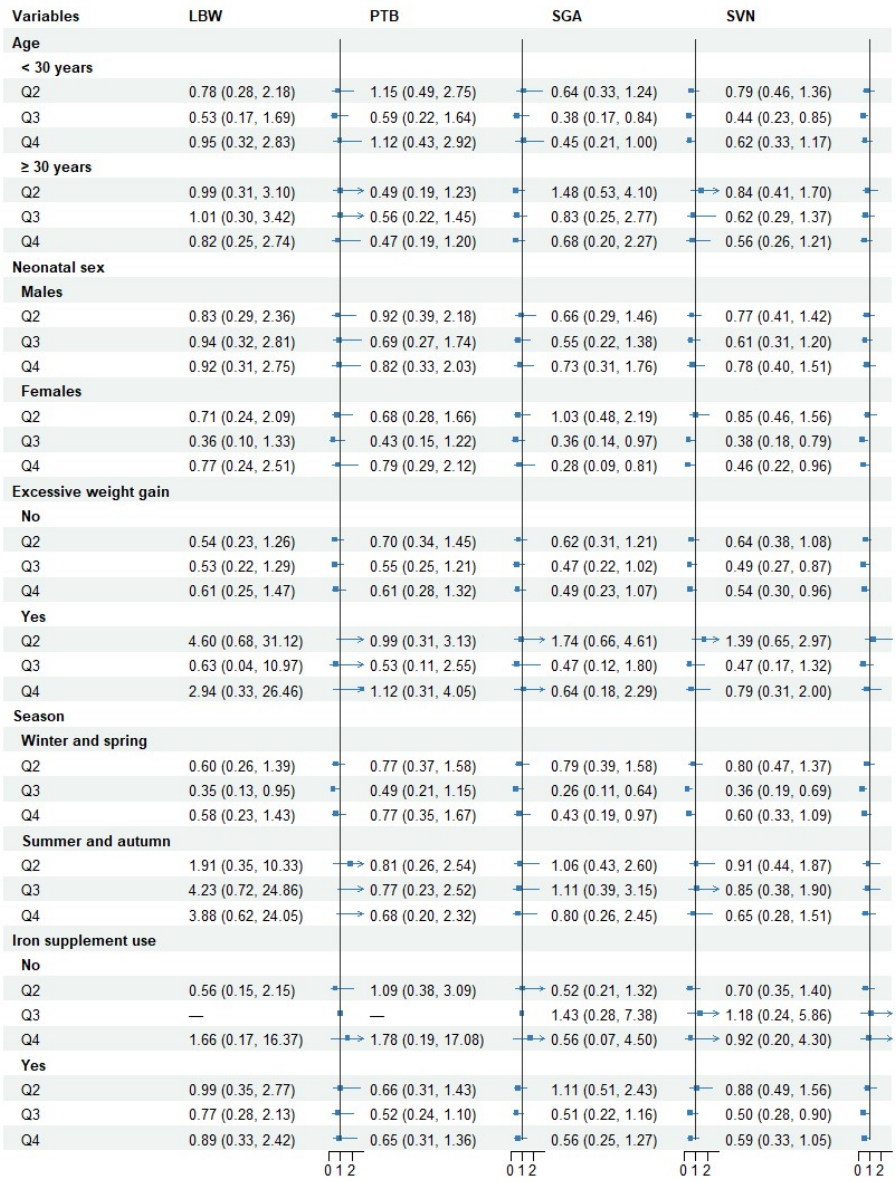
LBW, low birth weight; PTB, preterm birth; SGA, small for gestational age; SVN, small vulnerable newborns.



Supplementary Figure 1 Flow chart for the selection of participants included in the analysis



Supplementary Figure 2 Distribution of dietary vitamin D intake from different food sources in the first (A) and second trimester (B)

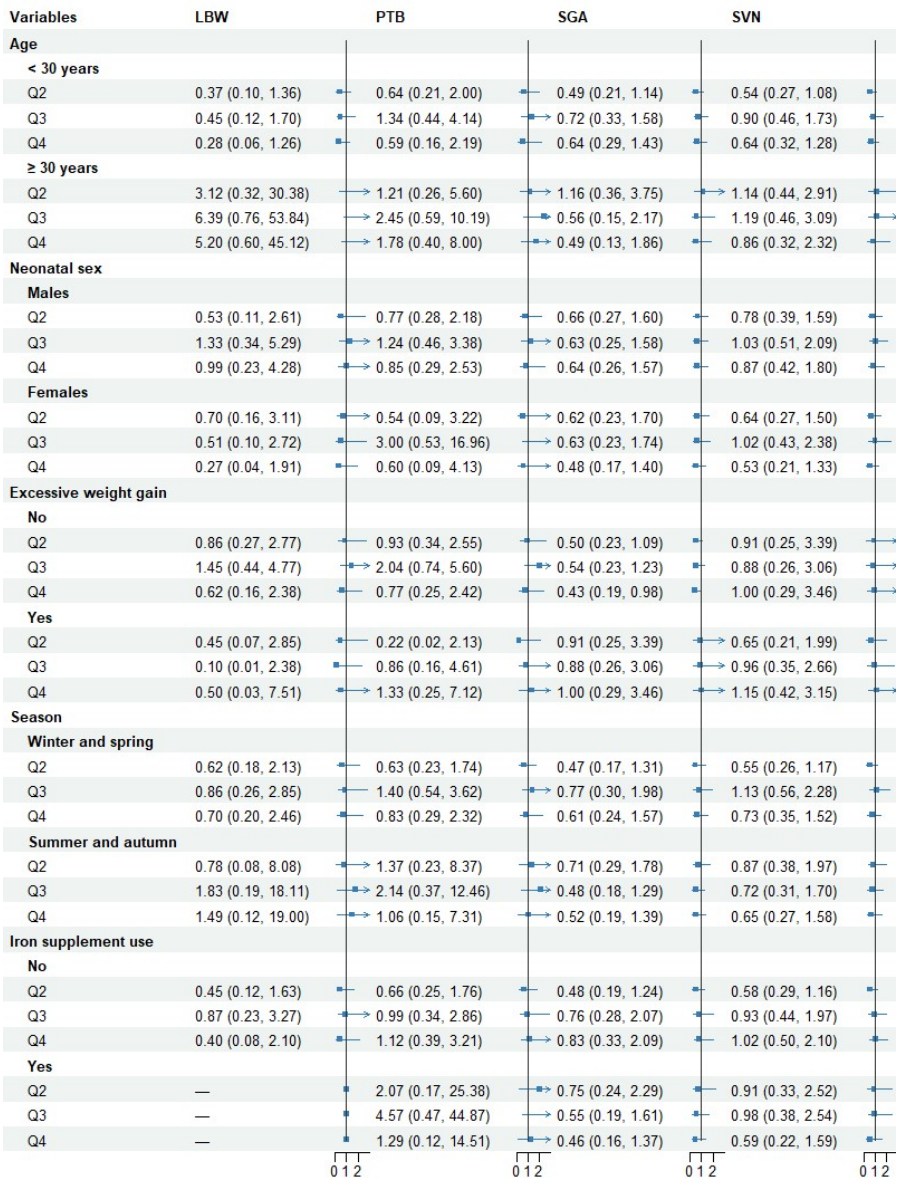


Supplementary Figure 3 Stratified analyses for association of total vitamin D intake in the first trimester with the risk of small vulnerable newborns

Values were represented as ORs (95% CIs) from logistic regression models and were adjusted for age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, and total energy intake. The lowest quartile (Q1) was applied as a reference.

"—" indicates that the sample size of this group is small and the model can not fit effectively.

LBW, low birth weight; PTB, preterm birth; Q, quartile; SGA, small for gestational age; SVN, small vulnerable newborns.

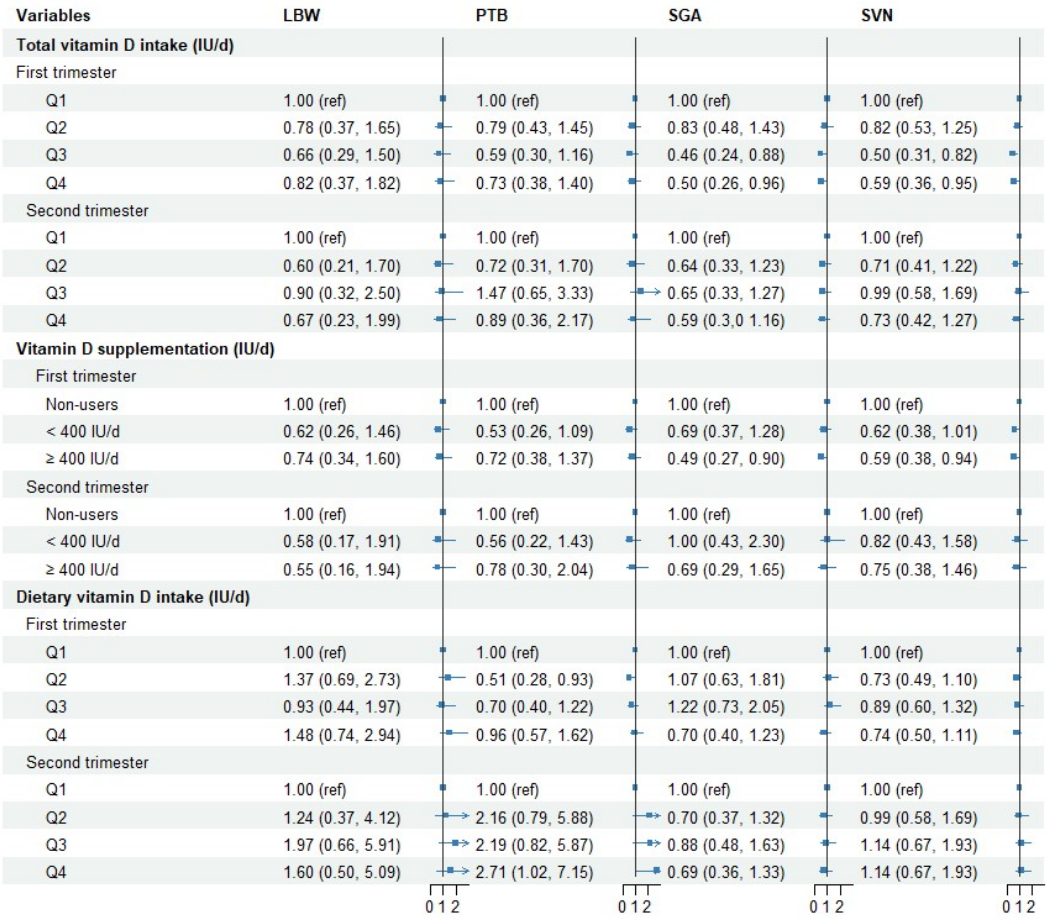


Supplementary Figure 4 Stratified analyses for association of total vitamin D intake in the second trimester with the risk of small vulnerable newborns

Values were represented as ORs (95% CIs) from logistic regression models and were adjusted for age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, and total energy intake. The lowest quartile (Q1) was applied as a reference.

"—" indicates that the sample size of this group is small and the model can not fit effectively.

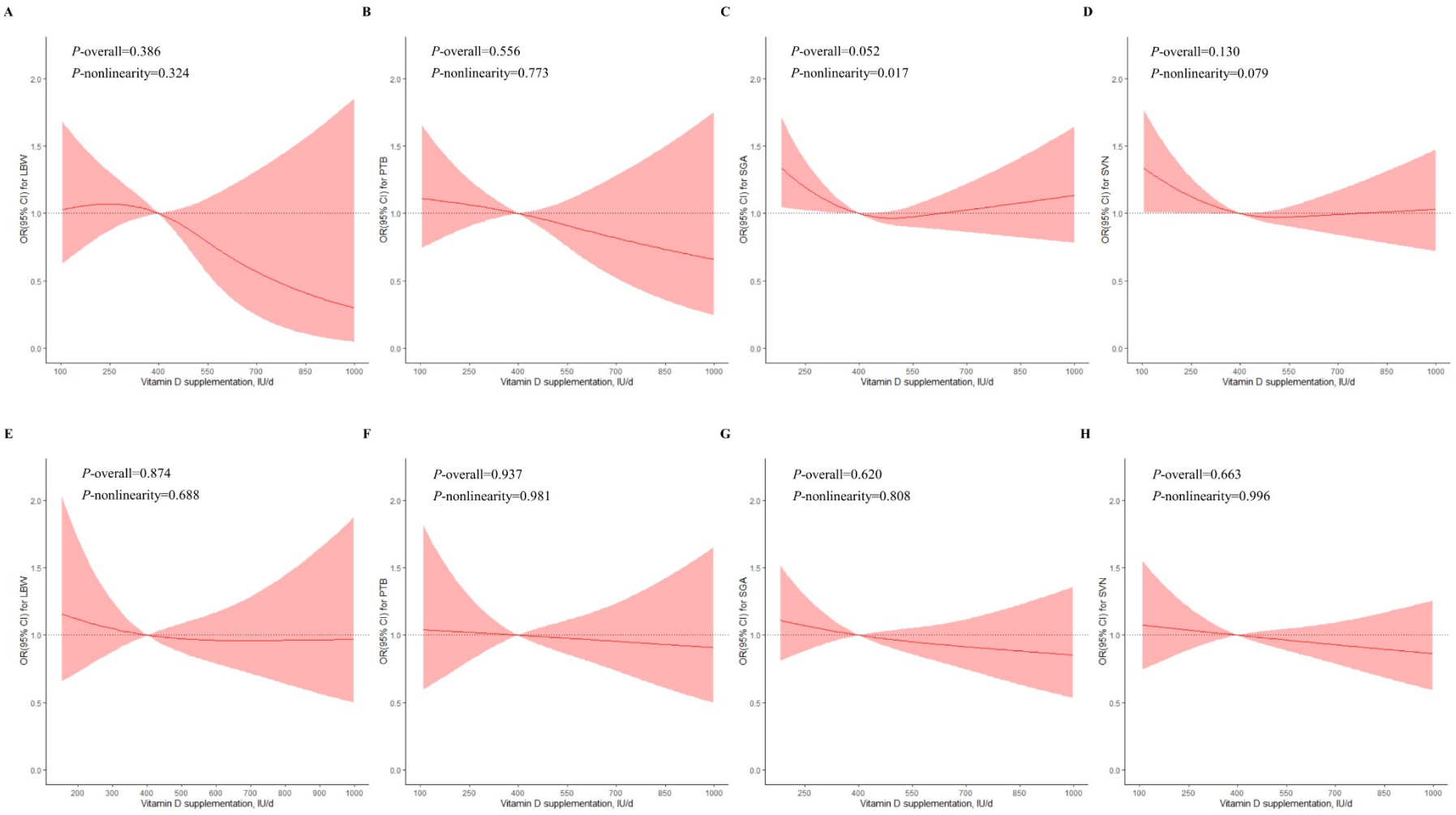
LBW, low birth weight; PTB, preterm birth; Q, quartile; SGA, small for gestational age; SVN, small vulnerable newborns.



Supplementary Figure 5 Association of vitamin D intake in the first and second trimesters with the risk of small vulnerable newborns when additionally adjusted for aMed score

Values were represented as ORs (95% CIs) from logistic regression models and were adjusted for aMed, age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, and total energy intake. The lowest quartile (Q1) was applied as a reference.

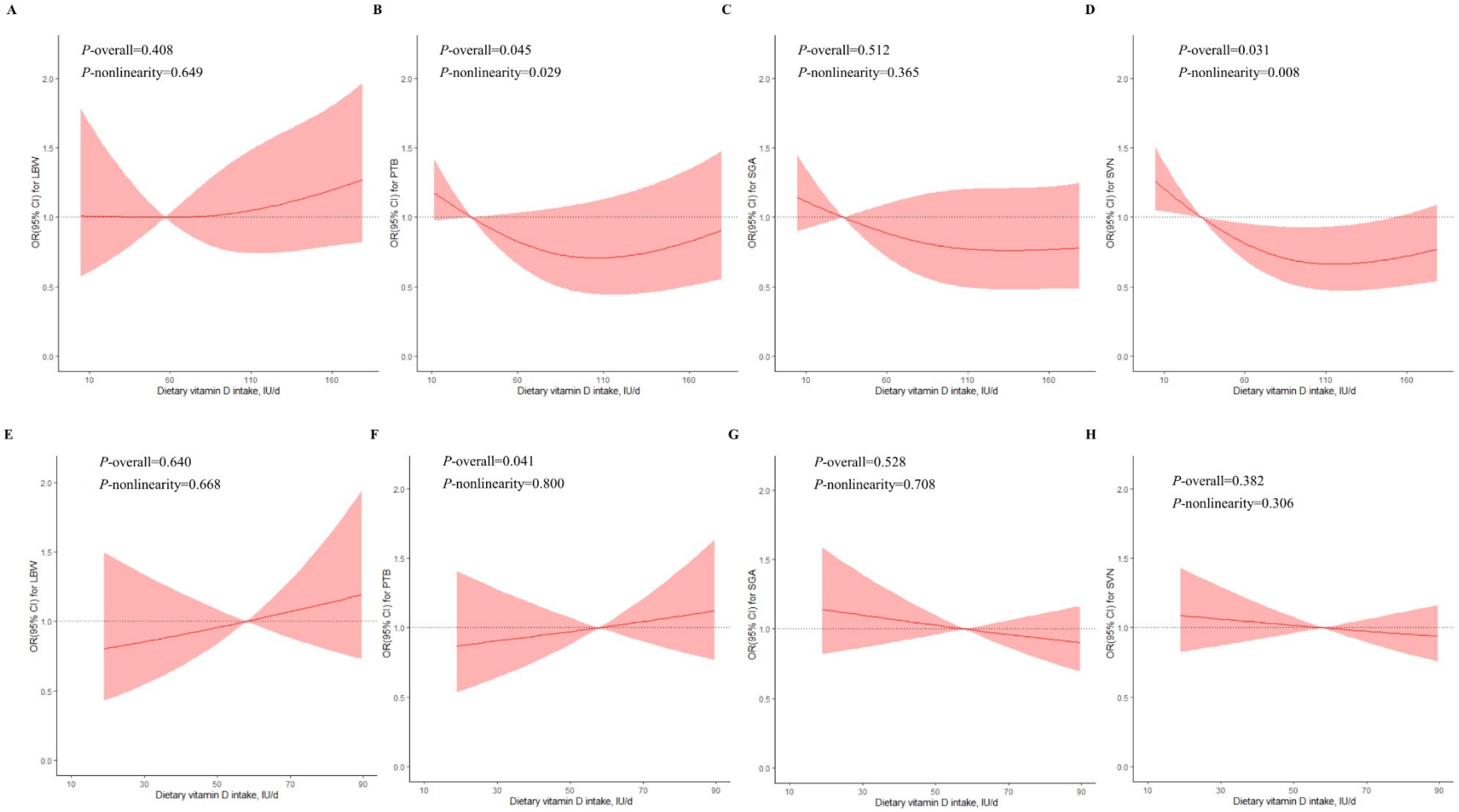
aMed, alternate Mediterranean diet score; LBW, low birth weight; PTB, preterm birth; Q, quartile; SGA, small for gestational age; SVN, small vulnerable newborns.


A
P-overall=0.386
P-nonlinearity=0.324
OR(95% CI) for LBW
B
P-overall=0.556
P-nonlinearity=0.773
OR(95% CI) for PTB
C
P-overall=0.052
P-nonlinearity=0.017
OR(95% CI) for SGA
D
P-overall=0.130
P-nonlinearity=0.079
OR(95% CI) for SVN
E
P-overall=0.874
P-nonlinearity=0.688
OR(95% CI) for LBW
F
P-overall=0.937
P-nonlinearity=0.981
OR(95% CI) for PTB
G
P-overall=0.620
P-nonlinearity=0.808
OR(95% CI) for SGA
H
P-overall=0.663
P-nonlinearity=0.996
OR(95% CI) for SVN
Vitamin D supplementation, IU/d

Supplementary Figure 6 Restricted cubic spline analyses for association of vitamin D supplementation in the first and second trimesters with the risk of small vulnerable newborns

Figures 5A-5D show the correlation between vitamin D supplementation in the first trimester and the risk of LBW, PTB, SGA and SVN, respectively. Figures 5E-5H show the correlation between vitamin D supplementation in the second trimester and the risk of LBW, PTB, SGA and SVN, respectively. In the Odd ratios (solid lines) and 95% CIs (shaded areas) were adjusted for age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, total energy intake, and dietary vitamin D intake. Knots were placed at the 10th, 50th, and 90th percentiles, and the reference value was set at the intake of 400 IU/d.

LBW, low birth weight; PTB, preterm birth; SGA, small for gestational age; SVN, small vulnerable newborns.


A
P-overall=0.408
P-nonlinearity=0.649
OR(95% CI) for LBW
Dietary vitamin D intake, IU/d
B
P-overall=0.045
P-nonlinearity=0.029
OR(95% CI) for PTB
Dietary vitamin D intake, IU/d
C
P-overall=0.512
P-nonlinearity=0.365
OR(95% CI) for SGA
Dietary vitamin D intake, IU/d
D
P-overall=0.031
P-nonlinearity=0.008
OR(95% CI) for SVN
Dietary vitamin D intake, IU/d
E
P-overall=0.640
P-nonlinearity=0.668
OR(95% CI) for LBW
Dietary vitamin D intake, IU/d
F
P-overall=0.041
P-nonlinearity=0.800
OR(95% CI) for PTB
Dietary vitamin D intake, IU/d
G
P-overall=0.528
P-nonlinearity=0.708
OR(95% CI) for SGA
Dietary vitamin D intake, IU/d
H
P-overall=0.382
P-nonlinearity=0.306
OR(95% CI) for SVN
Dietary vitamin D intake, IU/d

Supplementary Figure 7 Restricted cubic spline analyses for association of dietary vitamin D intake in the first and second trimesters with the risk of small vulnerable newborns

Figures 6A-6D show the correlation between dietary vitamin D intake in the first trimester and the risk of LBW, PTB, SGA and SVN, respectively. Figures 6E-6H show the correlation between dietary vitamin D intake in the second trimester and the risk of LBW, PTB, SGA and SVN, respectively. In the Odd ratios (solid lines) and 95% CIs (shaded areas) were adjusted for age, prepregnancy BMI, gestational weight gain, nation, education levels, monthly incomes, primiparity, smoking, drinking, season, regular exercise, outdoor activities, sun protection, iron supplement use, neonatal sex, labor way, total energy intake, and dietary vitamin D intake. Knots were placed at the 10th, 50th, and 90th percentiles, and the reference value was set at the 10th percentiles.

LBW, low birth weight; PTB, preterm birth; SGA, small for gestational age; SVN, small vulnerable newborns.