Supplementary materials for

**Preconception hemoglobin concentration and risk of preterm birth in over 2.7 million Chinese women aged 20-49 years: a population-based cohort study**

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Table S1. Altitude adjustments to measured hemoglobin concentrations and the distribution of participants according to the altitude.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Altitude (m)** | **Measured Hb adjustment (g/L) \*** | **Class I** |  | **Class II** |  | **No. of participants** | **PTB, n (%)** |
| **Anemia** | **normal Hb** | **High Hb** | **severe anemia** | **moderate anemia** | **mild anemia** | **normal Hb** | **mild high Hb** | **moderate high Hb** | **severe high Hb** |
| <1000 | 0 | <110 | 110-149 | ≥150 |  | <70 | 70-99 | 100-109 | 110-149 | 150-159 | 160-160 | ≥160 | 2480775 | 171241 (6.90) |
| 1000-1500 | -2 | <112 | 112-151 | ≥152 |  | <72 | 72-101 | 102-111 | 112-151 | 152-161 | 162-162 | ≥162 | 100448 | 7502 (7.47) |
| 1500-2000 | -5 | <115 | 115-154 | ≥155 |  | <75 | 75-104 | 105-114 | 115-154 | 155-164 | 165-165 | ≥165 | 80867 | 7307 (9.04) |
| 2000-2500 | -8 | <118 | 118-157 | ≥158 |  | <78 | 78-107 | 108-117 | 118-157 | 158-167 | 168-168 | ≥168 | 36663 | 3919 (10.69) |
| 2500-3000 | -13 | <123 | 123-162 | ≥163 |  | <83 | 83-112 | 113-122 | 123-162 | 163-172 | 173-173 | ≥173 | 11985 | 1562 (13.03) |
| 3000-3500 | -19 | <129 | 129-168 | ≥169 |  | <89 | 89-118 | 119-128 | 129-168 | 169-178 | 179-179 | ≥179 | 7657 | 889 (11.61) |
| 3500-4000 | -27 | <137 | 137-176 | ≥177 |  | <97 | 97-126 | 127-136 | 137-176 | 177-186 | 187-187 | ≥187 | 3304 | 333 (10.08) |
| 4000-4500 | -35 | <145 | 145-184 | ≥185 |  | <105 | 105-134 | 135-144 | 145-184 | 185-194 | 195-195 | ≥195 | 342 | 49 (14.33) |
| >=4500 | -45 | <155 | 156-194 | ≥195 | 　 | <115 | 115-144 | 145-154 | 155-194 | 195-204 | 205-205 | ≥205 | 233 | 17 (7.30) |

Hb, hemoglobin. Altitude, meters above the sea level.

\* The measured Hb adjustment values at varying altitudes were developed by the US Centers for Disease Control and Prevention’s (CDC) Pediatric Nutrition Surveillance System using data from a study of children living in mountainous states (17). These adjustment values were also recommended by WHO to define anemia for residents living in elevations above 1000 meters (18). Therefore, Hb concentrations of women who lived in areas with altitude ≥ 1000 meters were adjusted by subtracting the adjustment values from the original Hb concentrations in the current study.

Table S2. Associations between maternal original preconception hemoglobin concentrations and risk of preterm birth.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Hb category** **(g/L)** a | **PTB, n (%)** | **Model I \*** | **Model II #** | **Model III $** |
| **PTB** | **Class I**  |  |  |  |  |
|  | <110 | 17268 (6.75) | 0.95 (0.94-0.97) | 0.96 (0.94-0.98) | 0.96 (0.95-0.98) |
|  | 110-149 | 164720 (7.07) | 1 | 1 | 1 |
|  | ≥150 | 10831 (8.00) | 1.14 (1.12-1.17) | 1.09 (1.06-1.11) | 1.04 (1.02-1.07) |
|  | **Class II**  | 　 |  |  |  |
|  | < 70 | 95 (8.29) | 1.19 (0.96-1.47) | 1.16 (0.93-1.44) | 1.14 (0.92-1.42) |
|  | 70-99 | 5318 (6.93) | 0.98 (0.95-1.01) | 0.98 (0.95-1.01) | 0.98 (0.95-1.01) |
|  | 100-109 | 11855 (6.67) | 0.94 (0.92-0.96) | 0.95 (0.93-0.97) | 0.95 (0.94-0.97) |
|  | 110-149 | 164720 (7.07) | 1 | 1 | 1 |
|  | 150-159 | 7667 (7.75) | 1.10 (1.08-1.13) | 1.06 (1.04-1.09) | 1.03 (1.01-1.05) |
|  | 160-169 | 1981 (8.63) | 1.24 (1.18-1.30) | 1.15 (1.09-1.20) | 1.09 (1.04-1.14) |
|  | ≥ 170 | 1183 (8.70) | 1.25 (1.18-1.33) | 1.16 (1.09-1.24) | 1.10 (1.03-1.17) |
| **MPTB** | **Class I**  |  |  |  |  |
|  | <110 | 14498 (5.73) | 0.94 (0.92-0.96) | 0.94 (0.92-0.96) | 0.95 (0.93-0.96) |
|  | 110-149 | 140211 (6.08) | 1 | 1 | 1 |
|  | ≥150 | 9144 (6.84) | 1.13 (1.11-1.16) | 1.08 (1.06-1.11) | 1.04 (1.02-1.07) |
|  | **Class II**  | 　 |  |  |  |
|  | < 70 | 84 (7.40) | 1.23 (0.99-1.54) | 1.21 (0.96-1.52) | 1.20 (0.95-1.51) |
|  | 70-99 | 4461 (5.88) | 0.96 (0.94-0.99) | 0.96 (0.93-0.99) | 0.96 (0.93-0.99) |
|  | 100-109 | 9953 (5.66) | 0.93 (0.91-0.95) | 0.93 (0.91-0.95) | 0.94 (0.92-0.96) |
|  | 110-149 | 140211 (6.08) | 1 | 1 | 1 |
|  | 150-159 | 6493 (6.64) | 1.10 (1.07-1.13) | 1.06 (1.03-1.09) | 1.03 (0.99-1.05) |
|  | 160-169 | 1663 (7.34) | 1.22 (1.16-1.29) | 1.15 (1.09-1.21) | 1.09 (1.03-1.15) |
|  | ≥ 170 | 988 (7.37) | 1.23 (1.15-1.31) | 1.15 (1.07-1.23) | 1.09 (1.02-1.17) |
| **VPTB** | **Class I**  |  |  |  |  |
|  | <110 | 2770 (1.15) | 1.03 (0.99-1.07) | 1.06 (1.02-1.11) | 1.07 (1.02-1.11) |
|  | 110-149 | 24509 (1.12) | 1 | 1 | 1 |
|  | ≥150 | 1687 (1.34) | 1.19 (1.14-1.25) | 1.09 (1.04-1.15) | 1.05 (0.99-1.11) |
|  | **Class II** | 　 |  |  |  |
|  | < 70 | 11 (1.04) | 0.93 (0.51-1.69) | 0.87 (0.47-1.62) | 0.86 (0.46-1.61) |
|  | 70-99 | 857 (1.19) | 1.06 (0.99-1.13) | 1.08 (1.01-1.17) | 1.09 (1.01-1.17) |
|  | 100-109 | 1902 (1.13) | 1.01 (0.96-1.06) | 1.05 (1.01-1.11) | 1.06 (1.01-1.11) |
|  | 110-149 | 24509 (1.12) | 1 | 1 | 1 |
|  | 150-159 | 1174 (1.27) | 1.14 (1.07-1.20) | 1.06 (1.01-1.13) | 1.03 (0.97-1.10) |
|  | 160-169 | 318 (1.49) | 1.34 (1.19-1.49) | 1.13 (1.01-1.28) | 1.08 (0.96-1.22) |
|  | ≥ 170 | 195 (1.55) | 1.39 (1.20-1.60) | 1.21 (1.04-1.41) | 1.16 (0.99-1.35) |

Hb, hemoglobin; PTB, preterm birth (< 37 weeks of gestation); MPTB, moderate preterm birth (32 to < 37 weeks of gestation); VPTB, very preterm birth (< 32 weeks of gestation).

**a** Class I refers that women were classified into 3 groups (anemia: < 110 g/L; normal Hb level: 110-149 g/L; and high Hb level: ≥ 150 g/L); Class II refers that women were classified into 7 groups (severe anemia: < 70 g/L; moderate anemia: 70-99 g/L; mild anemia: 100-109 g/L; normal Hb level: 110-149 g/L; mild high Hb level: 150-159 g/L; moderate high Hb level: 160-169 g/L; and severe high Hb level: ≥ 170 g/L).

\*Model I: adjust for age; #Model II: adjust for characteristics of women (age, education, ethnic, occupation, region with GDP per capita), smoking, passive smoking and alcohol drinking status at baseline, history of diseases (diabetes, hypertension and thyroid dysfunction), pre-pregnancy body-mass index, parity, history of adverse pregnancy outcomes, and sex of child. $Model III: adjust for variables in model II plus altitude.

Table S3. Subgroup analysis by altitude of the association between maternal original preconception hemoglobin concentrations and PTB risk.

|  |  |  |  |
| --- | --- | --- | --- |
| **Hb category (g/L)** a | **< 1000 meter** |  | **≥ 1000 meter** |
| **PTB, n (%)** | **Multivariable-adjusted OR (95% CI)** **#** | **PTB, n (%)** | **Multivariable-adjusted OR (95% CI) #** |
| **Class I**  |  |  |  |  |  |
| <110 | 16048 (6.59) | **0.96 (0.94-0.98)** |  | 1220 (10.04) | **1.09 (1.02-1.17)** |
| 110-149 | 147365 (6.91) | 1 |  | 17355 (8.81) | 1 |
| ≥150 | 7828 (7.59) | **1.08 (1.05-1.10)** |  | 3003 (9.30) | 0.99 (0.95-1.03) |
| **Class II**  | 　 | 　 |  | 　 | 　 |
| < 70 | 77 (7.80) | 1.11 (0.87-1.42) |  | 18 (11.32) | 1.38 (0.82-2.33) |
| 70-99 | 4909 (6.75) | 0.97 (0.95-1.01) |  | 409 (10.20) | **1.13 (1.01-1.26)** |
| 100-109 | 11062 (6.51) | **0.95 (0.93-0.97)** |  | 793 (9.94) | 1.07 (0.98-1.16) |
| 110-149 | 147365 (6.91) | 1 |  | 17355 (8.81) | 1 |
| 150-159 | 5690 (7.38) | **1.05 (1.02-1.08)** |  | 1977 (9.05) | 0.99 (0.94-1.04) |
| 160-169 | 1316 (8.04) | **1.14 (1.08-1.21)** |  | 665 (10.09) | 1.02 (0.93-1.11) |
| ≥ 170 | 822 (8.44) | **1.21 (1.12-1.30)** |  | 361 (9.35) | 0.94 (0.83-1.06) |

Hb, hemoglobin; PTB, preterm birth; OR, odd ratio.

**a** Class I refers that women were classified into 3 groups (anemia: < 110 g/L; normal Hb level: 110-149 g/L; and high Hb level: ≥ 150 g/L); Class II refers that women were classified into 7 groups (severe anemia: < 70 g/L; moderate anemia: 70-99 g/L; mild anemia: 100-109 g/L; normal Hb level: 110-149 g/L; mild high Hb level: 150-159 g/L; moderate high Hb level: 160-169 g/L; and severe high Hb level: ≥ 170 g/L).

**#** Multivariable-adjusted OR (95% CI) were adjusted for characteristics of women (age, education, ethnic, occupation, region with GDP per capita), smoking, passive smoking and alcohol drinking status at baseline, history of diseases (diabetes, hypertension and thyroid dysfunction), pre-pregnancy body-mass index, parity, history of adverse pregnancy outcomes, and sex of child.