

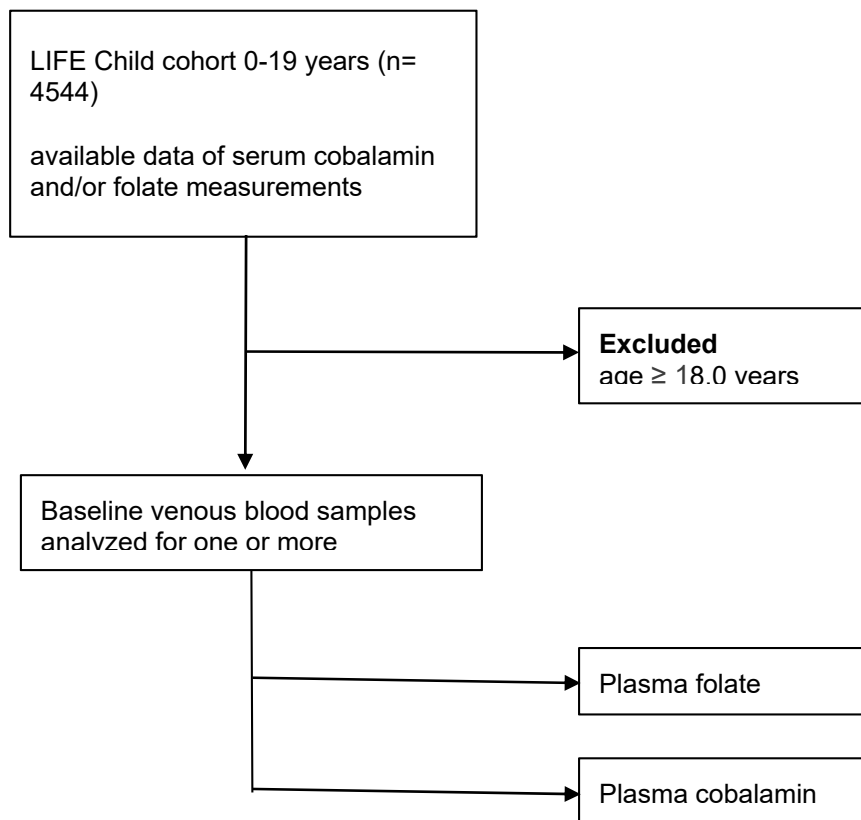
Supplementary Materials

Table S1. A range of the published pediatric reference intervals for serum folate (SF) and cobalamin (B12)

| Study | KiGGS [6] | HELENA [7] | NDNS [8] | Hay et al [9] |
|--------------------------------|---|---|--|--|
| Year | 2009 | 2011 | 2008 | 2008 |
| Country | Germany | 9 European countries | United Kingdom | Norway |
| Population | Population sample | Population sample | Population sample | Children delivered at Aker University Hospital (Oslo, Norway) |
| Age (years) | 3-17.5 | 12.5-17.45 | 4-18 | birth-24 mo |
| Sample size (cases) | B12: 13.050 | 1051 | PF: 840, B12=770 | 1091 |
| Study type, Exclusion criteria | Cross-sectional study, no exclusions | Cross-sectional study, inability to speak language, participation in another trial | Cross-sectional study, no exclusions | Longitudinal study, non-singleton births, gestational period <37w or >43w, birth weight > 2.5th percentile |
| Assay | ECLIA (Elecsys E2010, Roche, Mannheim, Germany) | CLIA (Immulate 2000, DPC Biermann GmbH, Bad Nauheim, Germany) | MEIA (Abbott IMx) | MA (colistin sulfate-resistant strain of <i>Lactobacillus leichmannii</i> (B12) and <i>L. casei</i> (SF)) |
| Method | sex- and age-specific percentiles estimated using an LMS-type method | sex- and age-specific percentiles estimated using an LMS-type method | sex- and age-specific percentiles | Age-specific reference intervals for folate and cobalamin status according to breastfeeding status |
| Results | 3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentile (continuously with age: 3-17.5 y) | 2.4th, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97.5th percentile (continuously with age: 12.5-17.45 y) | 5th, 50th, 90th percentile (4-10y, 11-14y, 15-18 y), stratified by sex for age 15-18 y | 5th, 50th, 95th percentile (birth, 6 mo, 12 mo, 24 mo) |

KiGGS nationwide health survey in children and adolescents carried out by the Robert Koch Institute, Germany; HELENA Healthy Lifestyle in Europe by Nutrition in Adolescence; NDNS National Diet and Nutrition Survey (NDNS); w = weeks; mo = month; y = years; ECLIA = electrochemiluminescence immunoassay; CLIA = chemiluminescent competitive immunoassay; MEIA = microparticle enzyme immunoassay; MA = microbiological assays; LMS = L skewness, M median, S coefficient of variation.

Figure S1. Composition of the generally healthy pediatric reference population from the LIFE Child cohort



The flowchart indicates the inclusion and exclusion criteria for the study cohort. n = number of cases.

Table S2. Percentile distribution of plasma folate (nmol/l) as a function of age (0-18 years) derived from censored data based on the LIFE Child cohort of generally healthy children and adolescents (n=4171)

| Sex | Age | P 2.5 | P 10 | P 50 | P90 | P 97.5 | Mu | Sigma | Nu |
|------|-----|-------|-------|-------|-------|--------|-------|-------|------|
| Male | 0.5 | 21.64 | 27.09 | 40.48 | 59.87 | 73.91 | 40.48 | 0.30 | 0.06 |
| | 1.0 | 20.12 | 25.21 | 37.70 | 55.82 | 68.95 | 37.70 | 0.31 | 0.06 |
| | 1.5 | 18.76 | 23.52 | 35.22 | 52.20 | 64.51 | 35.22 | 0.31 | 0.06 |
| | 2.0 | 17.60 | 22.07 | 33.09 | 49.09 | 60.70 | 33.09 | 0.31 | 0.06 |
| | 2.5 | 16.63 | 20.88 | 31.32 | 46.52 | 57.55 | 31.32 | 0.31 | 0.06 |
| | 3.0 | 15.86 | 19.92 | 29.92 | 44.48 | 55.06 | 29.92 | 0.31 | 0.06 |
| | 3.5 | 15.26 | 19.18 | 28.84 | 42.92 | 53.15 | 28.84 | 0.31 | 0.06 |
| | 4.0 | 14.80 | 18.61 | 28.02 | 41.73 | 51.72 | 28.02 | 0.31 | 0.06 |
| | 4.5 | 14.44 | 18.18 | 27.39 | 40.85 | 50.65 | 27.39 | 0.31 | 0.06 |
| | 5.0 | 14.17 | 17.84 | 26.91 | 40.17 | 49.84 | 26.91 | 0.31 | 0.06 |

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|------|-------|-------|-------|-------|-------|-------|------|------|
| 5.5 | 13.94 | 17.56 | 26.53 | 39.64 | 49.20 | 26.53 | 0.31 | 0.06 |
| 6.0 | 13.74 | 17.33 | 26.20 | 39.19 | 48.68 | 26.20 | 0.31 | 0.06 |
| 7.0 | 13.39 | 16.91 | 25.62 | 38.40 | 47.75 | 25.62 | 0.32 | 0.06 |
| 8.0 | 13.02 | 16.46 | 25.00 | 37.56 | 46.75 | 25.00 | 0.32 | 0.06 |
| 9.0 | 12.61 | 15.96 | 24.29 | 36.56 | 45.56 | 24.29 | 0.32 | 0.06 |
| 10.0 | 12.16 | 15.40 | 23.50 | 35.45 | 44.23 | 23.50 | 0.32 | 0.06 |
| 11.0 | 11.65 | 14.78 | 22.60 | 34.16 | 42.67 | 22.60 | 0.32 | 0.06 |
| 12.0 | 11.03 | 14.02 | 21.49 | 32.55 | 40.70 | 21.49 | 0.32 | 0.06 |
| 13.0 | 10.33 | 13.14 | 20.19 | 30.65 | 38.37 | 20.19 | 0.33 | 0.06 |
| 14.0 | 9.62 | 12.26 | 18.87 | 28.71 | 35.99 | 18.87 | 0.33 | 0.06 |
| 15.0 | 8.99 | 11.47 | 17.70 | 26.99 | 33.86 | 17.70 | 0.33 | 0.06 |
| 16.0 | 8.45 | 10.79 | 16.70 | 25.52 | 32.05 | 16.70 | 0.33 | 0.06 |
| 17.0 | 7.97 | 10.19 | 15.80 | 24.21 | 30.44 | 15.80 | 0.33 | 0.06 |
| 18.0 | 7.54 | 9.66 | 15.01 | 23.04 | 29.01 | 15.01 | 0.33 | 0.06 |

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|--------|------|-------|-------|-------|-------|-------|-------|------|------|
| Female | 0.5 | 24.07 | 29.27 | 41.62 | 59.20 | 71.98 | 41.62 | 0.27 | 0.00 |
| | 1.0 | 22.43 | 27.31 | 38.91 | 55.44 | 67.49 | 38.91 | 0.27 | 0.00 |
| | 1.5 | 20.95 | 25.53 | 36.45 | 52.04 | 63.42 | 36.45 | 0.27 | 0.00 |
| | 2.0 | 19.66 | 23.98 | 34.30 | 49.07 | 59.86 | 34.30 | 0.27 | 0.00 |
| | 2.5 | 18.56 | 22.66 | 32.48 | 46.55 | 56.85 | 32.48 | 0.28 | 0.00 |
| | 3.0 | 17.65 | 21.58 | 30.99 | 44.51 | 54.41 | 30.99 | 0.28 | 0.00 |
| | 3.5 | 16.93 | 20.72 | 29.81 | 42.89 | 52.50 | 29.81 | 0.28 | 0.00 |
| | 4.0 | 16.36 | 20.05 | 28.90 | 41.67 | 51.05 | 28.90 | 0.28 | 0.00 |
| | 4.5 | 15.92 | 19.53 | 28.21 | 40.75 | 49.98 | 28.21 | 0.28 | 0.00 |
| | 5.0 | 15.57 | 19.12 | 27.68 | 40.06 | 49.19 | 27.68 | 0.28 | 0.00 |
| | 5.5 | 15.28 | 18.79 | 27.25 | 39.52 | 48.59 | 27.25 | 0.28 | 0.00 |
| | 6.0 | 15.03 | 18.50 | 26.89 | 39.07 | 48.09 | 26.89 | 0.29 | 0.00 |
| | 7.0 | 14.56 | 17.96 | 26.21 | 38.25 | 47.19 | 26.21 | 0.29 | 0.00 |
| | 8.0 | 14.07 | 17.40 | 25.50 | 37.36 | 46.19 | 25.50 | 0.29 | 0.00 |
| | 9.0 | 13.52 | 16.76 | 24.66 | 36.28 | 44.96 | 24.66 | 0.30 | 0.00 |
| | 10.0 | 12.90 | 16.03 | 23.69 | 35.01 | 43.48 | 23.69 | 0.30 | 0.00 |
| | 11.0 | 12.24 | 15.24 | 22.62 | 33.57 | 41.80 | 22.62 | 0.30 | 0.00 |
| | 12.0 | 11.58 | 14.45 | 21.54 | 32.10 | 40.06 | 21.54 | 0.31 | 0.00 |

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|------|-------|-------|-------|-------|-------|-------|------|------|
| 13.0 | 10.95 | 13.70 | 20.52 | 30.71 | 38.42 | 20.52 | 0.31 | 0.00 |
| 14.0 | 10.40 | 13.04 | 19.61 | 29.49 | 36.98 | 19.61 | 0.31 | 0.00 |
| 15.0 | 9.91 | 12.46 | 18.82 | 28.42 | 35.74 | 18.82 | 0.32 | 0.00 |
| 16.0 | 9.46 | 11.92 | 18.09 | 27.44 | 34.59 | 18.09 | 0.32 | 0.00 |
| 17.0 | 9.02 | 11.40 | 17.37 | 26.47 | 33.45 | 17.37 | 0.32 | 0.00 |
| 18.0 | 8.61 | 10.91 | 16.70 | 25.57 | 32.38 | 16.70 | 0.33 | 0.00 |

n = number of measurements; P = percentile; Mu = location parameter; Sigma = spread parameter; Nu = skewness parameter

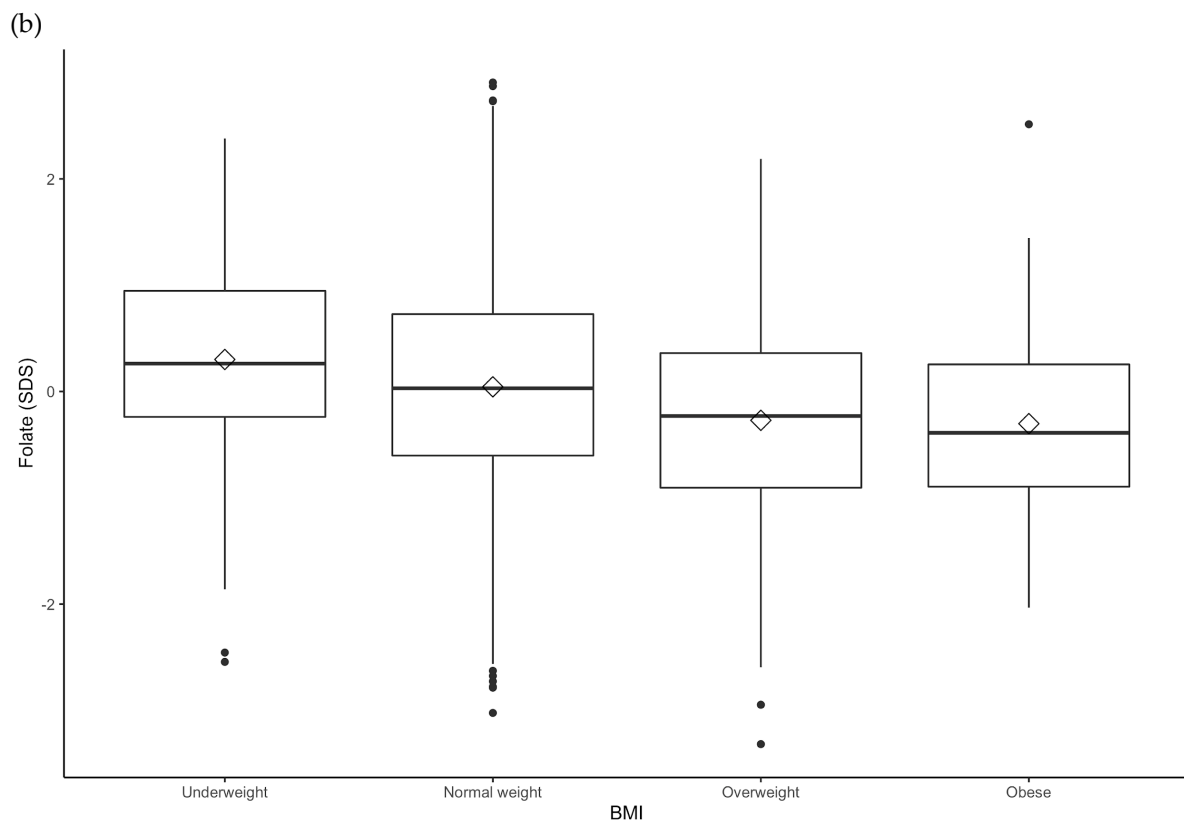
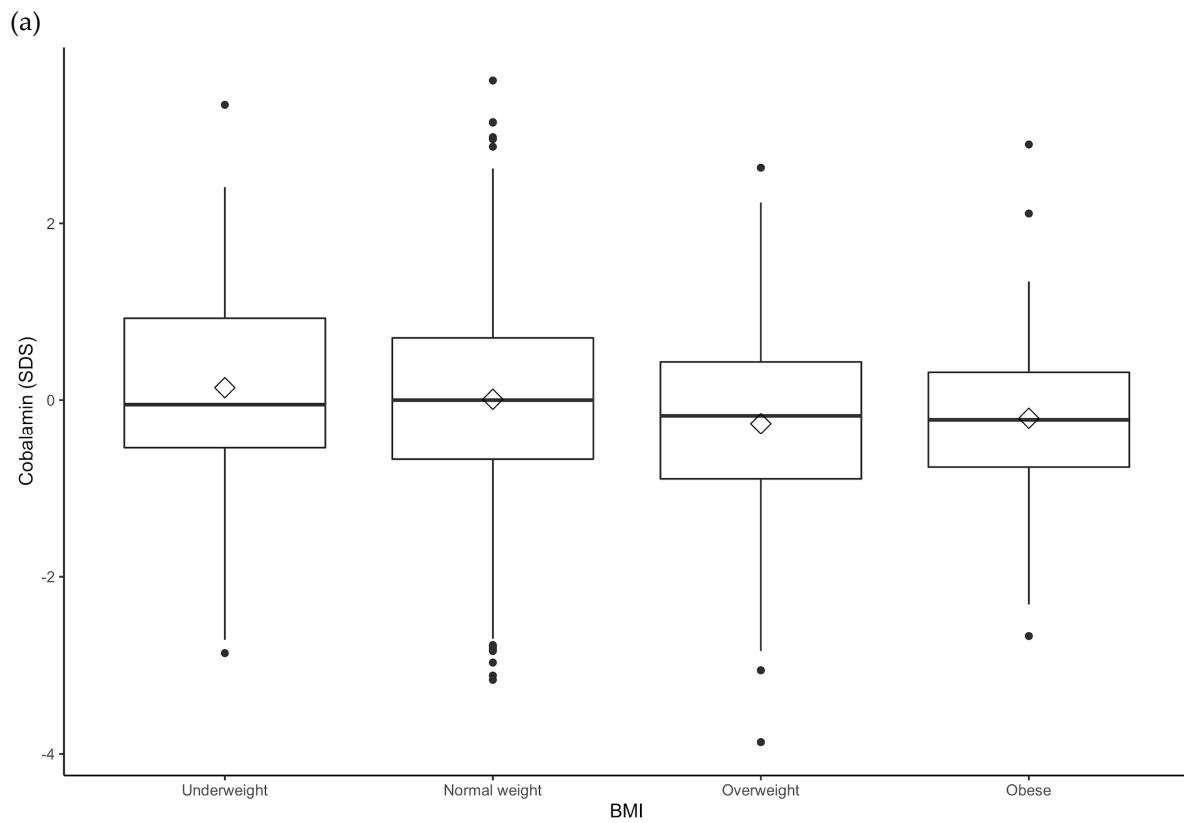
Table S3. Percentile distribution of plasma cobalamin (pmol/l) as a function of age (0-18 years) based on the LIFE Child cohort of generally healthy children and adolescents (n=4229)

| Sex | Age | P 2.5 | P 10 | P 50 | P90 | P 97.5 | Mu | Sigma | Nu |
|------|--------|--------|--------|--------|--------|--------|--------|-------|-------|
| Male | 0.5 | 132.98 | 174.47 | 297.50 | 522.44 | 713.15 | 297.50 | 0.43 | -0.10 |
| | 1 | 147.53 | 192.52 | 322.95 | 552.76 | 741.09 | 322.95 | 0.41 | -0.07 |
| | 1.5 | 163.02 | 211.59 | 349.47 | 584.39 | 771.22 | 349.47 | 0.40 | -0.05 |
| | 2 | 178.89 | 230.99 | 376.11 | 616.16 | 802.19 | 376.11 | 0.38 | -0.03 |
| | 2.5 | 194.43 | 249.88 | 401.74 | 646.59 | 832.20 | 401.74 | 0.37 | 0.00 |
| | 3 | 208.97 | 267.43 | 425.20 | 674.03 | 859.17 | 425.20 | 0.36 | 0.01 |
| | 3.5 | 221.85 | 282.85 | 445.37 | 696.94 | 881.21 | 445.37 | 0.35 | 0.03 |
| | 4 | 232.50 | 295.41 | 461.26 | 714.01 | 896.79 | 461.26 | 0.34 | 0.04 |
| | 4.5 | 240.43 | 304.55 | 472.14 | 724.48 | 905.16 | 472.14 | 0.34 | 0.05 |
| | 5 | 245.32 | 309.91 | 477.67 | 728.09 | 906.18 | 477.67 | 0.33 | 0.06 |
| | 5.5 | 247.31 | 311.67 | 478.14 | 725.33 | 900.43 | 478.14 | 0.33 | 0.06 |
| | 6 | 246.90 | 310.43 | 474.41 | 717.38 | 889.29 | 474.41 | 0.33 | 0.06 |
| | 7 | 242.40 | 303.27 | 460.48 | 694.27 | 860.43 | 460.48 | 0.32 | 0.04 |
| | 8 | 236.39 | 294.20 | 444.02 | 668.71 | 829.87 | 444.02 | 0.32 | 0.01 |
| | 9 | 229.71 | 284.39 | 426.42 | 640.87 | 795.88 | 426.42 | 0.32 | -0.01 |
| | 10 | 221.09 | 272.58 | 406.36 | 608.91 | 755.88 | 406.36 | 0.31 | -0.03 |
| | 11 | 208.38 | 256.91 | 383.17 | 574.76 | 714.05 | 383.17 | 0.31 | -0.04 |
| 12 | 191.93 | 237.73 | 357.20 | 538.84 | 670.94 | 357.20 | 0.32 | -0.02 | |
| 13 | 175.56 | 218.88 | 332.06 | 503.82 | 628.27 | 332.06 | 0.33 | 0.00 | |
| 14 | 163.64 | 205.01 | 312.74 | 475.00 | 591.60 | 312.74 | 0.33 | 0.02 | |
| 15 | 157.15 | 197.07 | 300.22 | 453.52 | 562.34 | 300.22 | 0.33 | 0.05 | |
| 16 | 154.78 | 193.75 | 293.43 | 439.32 | 541.55 | 293.43 | 0.32 | 0.07 | |
| 17 | 155.17 | 193.61 | 290.84 | 430.94 | 527.89 | 290.84 | 0.31 | 0.09 | |

| | | | | | | | | | |
|--------|--------|--------|--------|--------|--------|--------|--------|-------|-------|
| | 18 | 156.76 | 194.78 | 289.84 | 424.66 | 516.77 | 289.84 | 0.30 | 0.10 |
| Female | 0.5 | 129.08 | 174.53 | 310.81 | 558.85 | 765.44 | 310.81 | 0.45 | -0.03 |
| | 1 | 146.71 | 194.85 | 334.90 | 579.86 | 777.80 | 334.90 | 0.43 | -0.02 |
| | 1.5 | 165.53 | 216.26 | 359.81 | 601.94 | 792.22 | 359.81 | 0.40 | -0.02 |
| | 2 | 184.97 | 238.10 | 384.74 | 624.09 | 807.52 | 384.74 | 0.38 | -0.02 |
| | 2.5 | 204.27 | 259.51 | 408.64 | 645.09 | 822.29 | 408.64 | 0.36 | -0.01 |
| | 3 | 222.46 | 279.43 | 430.32 | 663.55 | 834.97 | 430.32 | 0.34 | -0.01 |
| | 3.5 | 238.60 | 296.88 | 448.71 | 678.38 | 844.39 | 448.71 | 0.32 | 0.00 |
| | 4 | 251.90 | 311.03 | 463.03 | 688.88 | 849.89 | 463.03 | 0.31 | 0.00 |
| | 4.5 | 261.84 | 321.41 | 472.91 | 694.87 | 851.39 | 472.91 | 0.30 | 0.01 |
| | 5 | 268.22 | 327.86 | 478.34 | 696.52 | 849.16 | 478.34 | 0.29 | 0.01 |
| | 5.5 | 271.21 | 330.56 | 479.57 | 694.16 | 843.51 | 479.57 | 0.29 | 0.02 |
| | 6 | 271.20 | 329.97 | 477.12 | 688.34 | 834.97 | 477.12 | 0.29 | 0.02 |
| | 7 | 264.67 | 321.65 | 464.45 | 669.87 | 812.81 | 464.45 | 0.29 | 0.01 |
| | 8 | 252.37 | 307.02 | 445.05 | 645.97 | 787.21 | 445.05 | 0.29 | -0.01 |
| | 9 | 237.32 | 289.46 | 422.74 | 620.32 | 761.43 | 422.74 | 0.30 | -0.03 |
| | 10 | 222.85 | 272.88 | 402.53 | 598.73 | 741.36 | 402.53 | 0.31 | -0.05 |
| | 11 | 209.83 | 258.41 | 386.05 | 583.10 | 728.74 | 386.05 | 0.32 | -0.07 |
| | 12 | 197.94 | 245.63 | 372.69 | 572.62 | 722.64 | 372.69 | 0.33 | -0.07 |
| 13 | 186.10 | 232.84 | 359.01 | 561.01 | 714.63 | 359.01 | 0.34 | -0.07 | |
| 14 | 173.57 | 218.45 | 340.83 | 539.46 | 692.11 | 340.83 | 0.35 | -0.07 | |
| 15 | 161.40 | 203.50 | 319.10 | 508.78 | 655.99 | 319.10 | 0.36 | -0.08 | |
| 16 | 151.24 | 190.38 | 298.56 | 478.32 | 619.64 | 298.56 | 0.36 | -0.10 | |
| 17 | 143.39 | 179.97 | 281.94 | 454.51 | 592.82 | 281.94 | 0.36 | -0.13 | |
| 18 | 136.87 | 171.27 | 268.23 | 436.10 | 573.97 | 268.23 | 0.36 | -0.17 | |

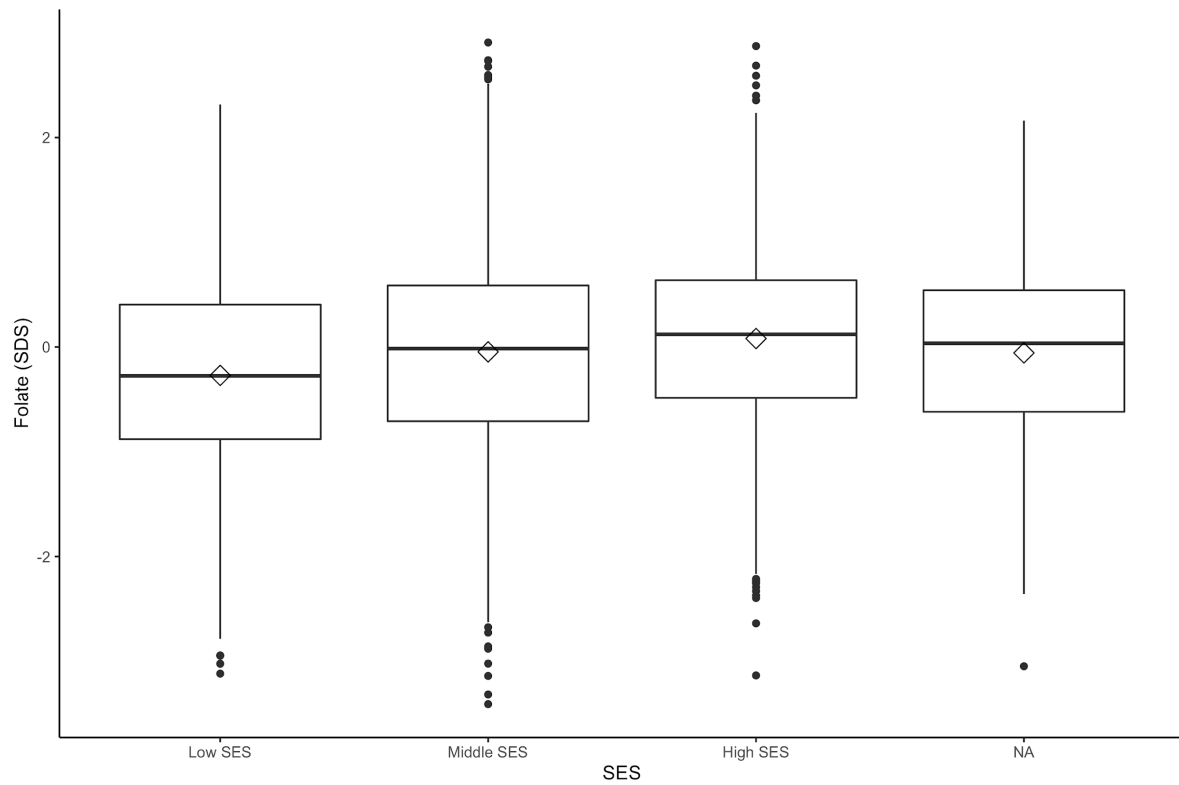
n = number of measurements; P = percentile; Mu = location parameter; Sigma = spread parameter; Nu = skewness parameter

Figure S2. (a) Cobalamin, (b) folate according to BMI



Higher BMI was significantly associated with lower serum vitamin concentrations ($p < 0.001$). Mean (square shape); 25th, 50th, 75th percentile are depicted. BMI-SDS groups: underweight: BMI-SDS < -1.28 ; normal weight: BMI-SDS -1.28 to < 1.28 ; overweight: BMI-SDS > 1.28 to 1.88 ; obese: BMI-SDS > 1.88 . SDS = standard deviation score; BMI = body mass index.

Figure S3. Folate according to SES



Higher SES was significantly associated with higher serum folate concentrations. SES groups: low: WI 3-8.4; middle: WI 8.5-15; high: 15.5-21. SES = socioeconomic status; WI = Winkler Index; SDS = standard deviation score.