

**Table S1.** List of folate terms

| <b>Term</b>                            | <b>Definition</b>   |
|--|---|
| <b>Naturally Occurring Food Folate</b> | Polyglutamate folate form found naturally in foods and not added through fortification                                  |
| <b>Folic Acid from Fortified Foods</b> | Synthetic folic acid added to certain foods through a process known as fortification                                    |
| <b>Food Folate</b>                     | Total folate derived from food, reflecting both folic acid from fortified foods and naturally occurring food folate     |
| <b>Supplemental Folic Acid</b>         | Synthetic folic acid intake from vitamins   |
| <b>Folate from All Sources</b>         | Total folate derived from naturally occurring food folate, folic acid from fortified foods, and supplemental folic acid |
| <b>Total Synthetic Folic Acid</b>      | Total synthetic acid from supplements (supplemental folic acid) and folic acid from fortified foods                     |

Folate terms used to describe different sources of folate with brief definitions.

**Table S2.** Demographics of participants by recruitment source

|   | <b>Facebook<br/>(n=33)</b> | <b>Craigslist<br/>(n=159)</b> | <b>Hospital<br/>(n=73)</b> |
|---|----------------------------|-------------------------------|----------------------------|
| <b>Age (years) ± SD</b>                           | 18.5 ± 0.6                 | 24.0 ± 4.4                    | 24.9 ± 3.7                 |
| <b>Self-reported Race<br/>(White / non-White)</b> | 18 / 15                    | 106 / 53                      | 52 / 21                    |
| <b>Education (years) ± SD</b>                     | 12.2 ± 1.3                 | 15.4 ± 2.4                    | 16.5 ± 2.0                 |
| <b>Sex (Male / Female)</b>                        | 11 / 22                    | 81 / 78                       | 26 / 47                    |

Demographic information reported for participants recruited from Facebook, Craigslist, and from Hospital-wide electronic recruitment resources.

**Table S3.** Demographic differences of participants included and excluded in the regression

|   | <b>Included<br/>(n = 180)</b> | <b>Excluded<br/>(n = 85)</b> | <b>Statistics</b> | <b>p-value</b> |
|---|-------------------------------|------------------------------|-------------------|----------------|
| <b>Age (years) ± SD</b>                           | 23.9 ± 4.5                    | 22.8 ± 4.0                   | $t = 1.97$        | 0.06           |
| <b>Self-reported Race<br/>(White / non-White)</b> | 123 / 57                      | 53 / 32                      | $\chi^2 = .68$    | 0.41           |
| <b>Education (years) ± SD</b>                     | 15.4 ± 2.5                    | 15.1 ± 2.5                   | $t = 1.06$        | 0.29           |
| <b>FOLH1 genotype<br/>(TT / C-carrier)</b>        | 94 / 86                       | 37 / 29                      | $\chi^2 = 0.15$   | 0.70           |
| <b>Sex (Male / Female)</b>                        | 85 / 95                       | 52 / 33                      | $\chi^2 = 1.33$   | 0.25           |

Demographic characteristics reported for participants included in and excluded from the regression analysis. Chi-square and independent samples *t*-tests were used to test the significance of differences between groups.

**Table S4.** Synthetic folic acid predictors of RBC folate status

| Variables                                     | Beta | <i>p</i> -value | Adjusted R <sup>2</sup> | Significance of R <sup>2</sup> Change |
|---|------|-----------------|-------------------------|---------------------------------------|
| <b>Log of supplemental folic acid</b>         | 0.20 | 0.006           | 0.059                   | 0.002                                 |
| <b>Log of folic acid from fortified foods</b> | 0.17 | 0.02            |                         |                                       |

Regression of log-transformed synthetic folic acid intake (from supplements and from fortified foods) on RBC folate level.

### ***MTHFR* Supplemental Analysis**

Prior research suggests different variants of the common *MTHFR* C677T polymorphism are associated with an altered distribution of folate forms in red blood cells [44], which could in turn influence RBC folate measurements [45,46]. Therefore, we conducted a one-way ANOVA to determine whether RBC folate levels differed amongst the three *MTHFR* genotypes. Additionally we then used chi-square tests to determine whether the frequency of *MTHFR* genotypes differed between the two *FOLH1* groups (T/T and C-carrier) for all subjects with valid genotype, nutrition, and RBC folate data.

For all Caucasian subjects with valid genotype and RBC folate measurements included in the later regression analysis (n = 123) there were no significant differences in RBC folate level across each of the three *MTHFR* genotypes (CC, 36.6%; CT, 49.6%; and TT, 13.8%),  $F(2,120) = 1.62$ ,  $p = 0.20$ . As previous research suggests *MTHFR* effects on RBC folate may be primarily driven by the T allele [53], we conducted a chi-square test to see if the distribution of *MTHFR* genotypes differed between *FOLH1* 484 T-allele homozygotes and C-allele carriers. There was no significant difference in the frequency of *MTHFR* genotypes between the *FOLH1* T-allele homozygotes (CC, 40.7%; CT, 44.4%; TT, 14.8%) and C-allele carriers (CC, 33.3%; CT, 53.6%; TT, 13.0%),  $\chi^2 = 1.04$ ,  $p = 0.60$ . Consequently, *MTHFR* genotype was not accounted for in regression modeling.