PYRIDOXAL 5’-PHOSPHATE (PLP), the principal active coenzyme form of vitamin B₆, is involved in almost 100 enzymatic reactions.¹ One function of vitamin B₆ is its role in the 1-carbon metabolic pathway, which involves the transfer of 1-carbon groups for DNA synthesis and DNA methylation. Deficiency of vitamin B₆ has been associated with considerably impaired 1-carbon metabolism in animals.² Hence, low vitamin B₆ levels may increase colorectal cancer risk through aberrations in DNA synthesis, repair, and methylation.³ Vitamin B₆ may also suppress colorectal carcinogenesis by reducing cell proliferation, angiogenesis, oxidative stress, inflammation, and nitric oxide synthesis.⁴⁻⁶ Major food sources of vitamin B₆ include fortified cereals, meat, fish, poultry, starchy vegetables, and some fruits (eg, bananas and avocado).¹

Findings from prospective studies that have examined the association between vitamin B₆ intake or PLP levels in the blood and the risk of colorectal cancer have been inconsistent. The aim of this review was to evaluate the evidence from prospective studies on vitamin B₆ intake or blood levels of PLP and the risk of colorectal cancer by summarizing it quantitatively with a meta-analytic approach.

Context Mounting evidence indicates that vitamin B₆, a coenzyme involved in nearly 100 enzymatic reactions, may reduce the risk of colorectal cancer.

Objective To conduct a systematic review with meta-analysis of prospective studies assessing the association of vitamin B₆ intake or blood levels of pyridoxal 5’-phosphate (PLP, the active form of vitamin B₆) with risk of colorectal cancer.

Data Sources Relevant studies were identified by a search of MEDLINE and EMBASE databases to February 2010, with no restrictions. We also reviewed reference lists from retrieved articles.

Study Selection We included prospective studies that reported relative risk (RR) estimates with 95% confidence intervals (CIs) for the association between vitamin B₆ intake or blood PLP levels and the risk of colorectal, colon, or rectal cancer.

Data Extraction Two authors independently extracted data and assessed study quality. Study-specific RRs were pooled using a random-effects model.

Data Synthesis Nine studies on vitamin B₆ intake and 4 studies on blood PLP levels were included in the meta-analysis. The pooled RRs of colorectal cancer for the highest vs lowest category of vitamin B₆ intake and blood PLP levels were 0.90 (95% CI, 0.75-1.07) and 0.52 (95% CI, 0.38-0.71), respectively. There was heterogeneity among studies of vitamin B₆ intake (P=.01) but not among studies of blood PLP levels (P=.95). Omitting 1 study that contributed substantially to the heterogeneity among studies of vitamin B₆ intake yielded a pooled RR of 0.80 (95% CI, 0.69-0.92). The risk of colorectal cancer decreased by 49% for every 100-pmol/mL increase (approximately 2 SDs) in blood PLP levels (RR, 0.51; 95% CI, 0.38-0.69).

Conclusion Vitamin B₆ intake and blood PLP levels were inversely associated with the risk of colorectal cancer in this meta-analysis.

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Eligibility Criteria
Studies were included in the meta-analysis if they met the following criteria: (1) prospective design; (2) the exposure of interest was intake of vitamin B₆ or blood (plasma or serum) levels of PLP; (3) the outcome of interest was colorectal, colon, or rectal cancer; and (4) relative risk (RR) estimates with 95% confidence intervals (CIs) (or data to calculate these) were reported. If data were duplicated in more than 1 study, we included the study with the largest number of cases.

Data Extraction
The following data were extracted from each study: the first author's last name, publication year, country where the study was performed, study period, participant sex and age, sample size (cases and controls or cohort size), measure and range of exposure, variables adjusted for in the analysis, and RR estimates with corresponding 95% CIs (or data to calculate these) were reported. If data were duplicated in more than 1 study, we included the study with the largest number of cases.

Statistical Analysis
Study-specific RR estimates were combined using a random-effects model, which considers both within-study and between-study variation. For 1 study that reported results for colon and rectal cancer separately, we combined the 2 RR estimates and then included the pooled RR estimate in the meta-analysis. If results were reported for both dietary and total vitamin B₆ intake, we used the results for total vitamin B₆ in the main analysis. In the dose-response meta-analysis of blood PLP levels, we used the method proposed by Greenland and Longnecker and Orsini et al to compute the trend from the correlated log RR estimates across categories of PLP levels. For each study, the median level of PLP for each category was assigned to each corresponding RR estimate. We examined a potential nonlinear dose-response relationship between PLP levels and colorectal cancer by modeling PLP levels using restricted cubic splines with 3 knots at percentiles 25%, 50%, and 75% of the distribution. A P value for nonlinearity was calculated by testing the null hypothesis that the coefficient of the second spline is equal to 0.

Statistical heterogeneity among studies was evaluated by using the Q and I² statistics. We performed a sensitivity analysis in which one study at a time was removed and the rest analyzed to evaluate whether the results could have been affected markedly by a single study. We also conducted analyses stratified by geographic area, study quality, range of exposure, and source of vitamin B₆ intake (foods only or foods and supplements combined). Publication bias was evaluated with the use of the Egger regression asymmetry test. All statistical analyses were performed with Stata software, version 10 (Stata Corp, College Station, Texas). P < .05 was considered statistically significant.

RESULTS

Literature Search
The detailed steps of our literature search are shown in Figure 1. Briefly, we identified 11 potentially relevant articles concerning vitamin B₆ intake and 4 articles on blood PLP levels in relation to risk of colorectal, colon, or rectal cancer. Three articles on vitamin B₆ intake were excluded because of duplicate reports from the same study population. The remaining articles, including 8 on vitamin B₆ intake (including 9 studies because 1 article reported results from 2 independent cohorts) and 4 on blood PLP levels, were included in the meta-analysis.

Study Characteristics
The 9 studies on vitamin B₆ intake (8 cohort studies and 1 nested case-control study) were published between 2002 and 2009 (Table 1) and...
Table 1. Characteristics of Prospective Studies on Vitamin B₆ Intake and Colorectal Cancer

<table>
<thead>
<tr>
<th>Source</th>
<th>Location/Period</th>
<th>Sex</th>
<th>Age, y</th>
<th>No. of Cases (Cancer Type)</th>
<th>No. of Participants</th>
<th>Measure/Range of Exposure, mg/d(^a)</th>
<th>Study Quality(^b)</th>
<th>Adjustment for Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harnack et al,(^{11}) 2002</td>
<td>United States, 1986-1998</td>
<td>F</td>
<td>55-69</td>
<td>598 (CC) 123 (RC)</td>
<td>41 836</td>
<td>Dietary vitamin B₆; &lt;1.59 (Q1), ≥4.36 (Q5)</td>
<td>6</td>
<td>Age, BMI, smoking pack-years, estrogen use, intakes of energy, calcium, and vitamin E</td>
</tr>
<tr>
<td>Larsson et al,(^{18}) 2005</td>
<td>Sweden, 1997-2004</td>
<td>F</td>
<td>40-76</td>
<td>805 (CRC) 547 (CC) 252 (RC)</td>
<td>61 433</td>
<td>Dietary vitamin B₆; &lt;1.53 (Q1), ≥2.05 (Q5)</td>
<td>6</td>
<td>Age, education, BMI, intakes of red meat, saturated fat, calcium, folate, beta-carotene, and cereal fiber</td>
</tr>
<tr>
<td>Le Marchand et al,(^{8}) 2005(^c)</td>
<td>United States, 1993-2000</td>
<td>F/M</td>
<td>45-75</td>
<td>383 (CRC)</td>
<td>971</td>
<td>Dietary vitamin B₆; &lt;1.63 (T1), ≥2.46 (T3)</td>
<td>6</td>
<td>Age, sex, and race/ethnicity</td>
</tr>
<tr>
<td>Zhang et al,(^{12}) 2006</td>
<td>United States, 1992-2004</td>
<td>F/M</td>
<td>≥45</td>
<td>220 (CRC) 171 (CC) 44 (RC)</td>
<td>37 916</td>
<td>Dietary vitamin B₆; &lt;1.69 (Q1), ≥2.40 (Q5) Total vitamin B₆; &lt;1.78 (Q1), ≥4.00 (Q5)</td>
<td>6</td>
<td>Age, randomized treatment assignment, BMI, physical activity, smoking status, family history of colorectal cancer, history of colon polyps, aspirin use, menopausal status, postmenopausal hormone use, multivitamin use, intakes of alcohol, energy, and red meat</td>
</tr>
<tr>
<td>Ishihara et al,(^{19}) 2007</td>
<td>Japan, 1995-2002</td>
<td>F/M</td>
<td>45-74</td>
<td>191 (CRC) 335 (CRC) (M)</td>
<td>43 077 (F) 38 107 (M)</td>
<td>Dietary vitamin B₆ (F); 1.02 (Q1), 1.80 (Q4) Dietary vitamin B₆ (M); 1.09 (Q1), 1.91 (Q4)</td>
<td>7</td>
<td>Age, study area (public health centers), BMI, physical activity, smoking, supplement use, intakes of alcohol, calcium, vitamin D, and meat</td>
</tr>
<tr>
<td>de Vogel et al,(^{20}) 2008</td>
<td>Netherlands, 1986-1999</td>
<td>F/M</td>
<td>55-69</td>
<td>960 (CRC) (F) 682 (CC) (F) 254 (RC) (F) 1389 (CRC) (M) 849 (CC) (M) 501 (RC) (M)</td>
<td>Subcohort: 2078 (F) 2000 (M)</td>
<td>Dietary vitamin B₆ (F); 1.05 (Q1), 1.63 (Q5) Dietary vitamin B₆ (M); 1.22 (Q1), 1.88 (Q5)</td>
<td>6</td>
<td>Age, BMI, smoking status, family history of colorectal cancer, intakes of alcohol, energy, meat, fat, fiber, calcium, iron, folate, methionine, and riboflavin</td>
</tr>
<tr>
<td>Schernhammer et al,(^{21}) 2008</td>
<td>United States, 1980-2002</td>
<td>F</td>
<td>34-59</td>
<td>389 (CC)</td>
<td>88 691</td>
<td>Total vitamin B₆; &lt;1.30 (Q1), ≥3.51 (Q5)</td>
<td>7</td>
<td>Age, BMI, physical activity, smoking, screenign sigmoidoscopy, family history of colorectal cancer, colon polyps, aspirin use, multivitamin use, intakes of alcohol, beef, calcium, folate, vitamin B₁₂, and methionine</td>
</tr>
<tr>
<td>Schernhammer et al,(^{21}) 2008</td>
<td>United States, 1986-2002</td>
<td>M</td>
<td>40-75</td>
<td>277 (CC)</td>
<td>47 371</td>
<td>Total vitamin B₆; &lt;1.90 (Q1), ≥5.81 (Q5)</td>
<td>7</td>
<td>Age, BMI, physical activity, smoking, screenign sigmoidoscopy, family history of colorectal cancer, colon polyps, aspirin use, multivitamin use, intakes of alcohol, beef, calcium, folate, vitamin B₁₂, and methionine</td>
</tr>
<tr>
<td>Shrubsole et al,(^{22}) 2009</td>
<td>China, 1996-2006</td>
<td>F</td>
<td>40-70</td>
<td>394 (CRC)</td>
<td>72 861</td>
<td>Dietary vitamin B₆; 1.36 (Q1), 2.33 (Q5)</td>
<td>7</td>
<td>Age, education, income, BMI, physical activity, smoking status, drinking status, diabetes, menopausal status, postmenopausal hormone use, family history of colorectal cancer, colorectal polyps, NSAID use, vitamin B₁₂ supplementation use, intakes of energy, fruits, vegetables, red meat, and calcium</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CC, colon cancer; CRC, colorectal cancer; NSAID, nonsteroidal anti-inflammatory drug; PC, rectal cancer; T, tertile; Q, quartile/percentile. Dietary vitamin B₆ includes vitamin B₆ from foods only and total vitamin B₆ includes vitamin B₆ from foods and supplements. Range of exposure indicates the cut points for the highest and lowest categories of daily vitamin B₆ intake. Study quality was judged based on the Newcastle-Ottawa Scale (range, 1-9 stars). Nested case-control study; the number of cases and controls in the group with the CC genotype (wild-type) of 5,10-methylenetetrahydrofolate reductase.
involved a total of 6064 cases. Five studies were conducted in the United States, 2 in Europe, and 2 in Asia. In the 3 studies that reported baseline characteristics of the study population by vitamin B₆ intake, high vitamin B₆ intake tended to be associated with older age, more physical activity, less smoking, lower alcohol consumption, and higher folate and red meat intakes. Only 2 reports provided results for total vitamin B₆ intake from foods and supplements combined, and none reported results for vitamin B₆ supplement use alone. The 4 nested case-control studies on blood PLP levels (comprising a total of 883 cases and 1424 controls) were published between 2005 and 2009; 3 were conducted in the United States and measured plasma PLP levels and 1 was conducted in Finland and measured serum PLP levels (Table 2). The studies on blood PLP levels met more quality criteria (8-9 stars) than the studies on vitamin B₆ intake (6-7 stars). Studies with a lower quality score generally did not adjust for physical activity. Most studies provided risk estimates that were adjusted for age (all 13 studies), body mass index (12 studies), smoking (10 studies), physical activity (9 studies), alcohol consumption (9 studies), and red meat (10 studies); fewer were adjusted for folate (7 studies) and calcium (7 studies).

### High vs Low Vitamin B₆ or PLP Levels
The multivariable-adjusted RRs for each study and all studies combined for the highest vs lowest categories of vitamin B₆ intake or blood PLP level are shown in Figure 2. Results from studies on vitamin B₆ intake in relation to colorectal cancer risk were inconsistent, with both inverse and positive associations reported. All studies on the association of blood PLP levels with colorectal cancer risk showed an inverse association, which was statistically significant in 3 studies. The pooled RRs of colorectal cancer for the highest vs lowest categories of vitamin B₆ intake and blood PLP level were, respectively, 0.90 (95% CI, 0.75-1.07) and 0.52 (95% CI, 0.38-0.71). There was statistically significant heterogeneity among studies of vitamin B₆ intake (P=.01; F=56%; 95% CI, 0%-76%) but not among studies of blood PLP levels (P=.95; F=0%; 95% CI, 0%-68%). The Egger test showed no evidence of publication bias for vitamin B₆ intake (P=.10) or blood PLP levels (P=.94).

### Sensitivity Analyses
To explore the heterogeneity among studies of vitamin B₆ intake and colorectal cancer, we performed sensitivity and stratified analyses. A sensitivity analysis omitting 1 study at a time and calculating the pooled RRs for the remainder of the studies showed that the study by de Vogel et al substantially influenced the pooled RR. After excluding this single study, there was no study heterogeneity (P=.23; F=24%; 95% CI, 0%-64%), and the RR for the highest vs lowest category of vitamin B₆ intake was 0.80 (95% CI, 0.69-0.92). Stronger associations between vitamin B₆ intake and colorectal cancer were found in studies that met more

### Table 2. Characteristics of Prospective Studies on Blood PLP Levels and Colorectal Cancer

<table>
<thead>
<tr>
<th>Source</th>
<th>Location/Period</th>
<th>Sex</th>
<th>Age, y</th>
<th>No. of Cases/Controls</th>
<th>Measure/Range of Exposure, pmol/mL</th>
<th>Study Quality</th>
<th>Adjustment for Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wei et al, 2005</td>
<td>United States, 1989-2000</td>
<td>F</td>
<td>43-69</td>
<td>188/371</td>
<td>Plasma PLP: 23.9 (Q1), 131.2 (Q4)</td>
<td>8</td>
<td>Age, date of blood collection, fasting status, BMI, physical activity, smoking, menopausal status, postmenopausal hormone use, aspirin use, family history of colorectal cancer, history of endoscopy, plasma vitamin D, use of vitamin B supplements and multivitamins, intakes of alcohol, red meat, folate, and methionine</td>
</tr>
<tr>
<td>Weinstein et al, 2008</td>
<td>Finland, 1985-2002</td>
<td>M</td>
<td>50-69</td>
<td>275/275</td>
<td>Serum PLP: 12.7 (Q1), 77.7 (Q5)</td>
<td>8</td>
<td>Age at randomization, date of blood collection, BMI, physical activity, intakes of vitamin D and iron</td>
</tr>
<tr>
<td>Lee et al, 2009</td>
<td>United States, 1982-2000</td>
<td>M</td>
<td>40-84</td>
<td>197/371</td>
<td>Plasma PLP: 43 (Q1), 144 (Q4)</td>
<td>8</td>
<td>Age, smoking status, fasting status, BMI, exercise, multivitamin use, aspirin assignment, intakes of alcohol, red meat, and cold cereals, plasma levels of folate, vitamin B₁₂, homocysteine, tumor necrosis factor receptor 2, C-reactive protein, and interleukin 6</td>
</tr>
<tr>
<td>La Marchand et al, 2009</td>
<td>United States, 2001-2006</td>
<td>F/M</td>
<td>53-83</td>
<td>223/407</td>
<td>Plasma PLP: ≤26.6 (Q1), &gt;101 (Q4)</td>
<td>9</td>
<td>Age, sex, ethnicity, date of blood collection, fasting duration, BMI, physical activity, pack-years of smoking, family history of colorectal cancer, colorectal cancer screening, plasma folate levels, intakes of processed meat and alcohol</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; PLP, pyridoxal 5'-phosphate; Q, quartile/quintile.  
*Median blood PLP levels in the lowest and highest categories or the cut points for the highest and lowest categories.*  
*Study quality was judged based on the Newcastle-Ottawa Scale (range, 1-9 stars).*
quality criteria (7 stars; RR, 0.80; 95% CI, 0.67-0.96) than in studies that met fewer quality criteria (6 stars; RR, 0.99; 95% CI, 0.74-1.34).

Stratifying by geographic region, the RRs were 0.86 (95% CI, 0.70-1.06) for studies conducted in the United States, 1.04 (95% CI, 0.63-1.73) for studies in Europe, and 0.79 (95% CI, 0.59-1.05) for studies in Asia. Among 6 studies that provided results for colon cancer, the RR was 0.97 (95% CI, 0.81-1.17). We could not conduct analyses stratified by colon subsites because only 2 studies reported results for proximal and distal colon sites.12,20 The risk estimates for rectal cancer (4 studies) were too heterogeneous to pool (P < .001; I² = 82%; 95% CI, 49%-91%). When we stratified the analysis by source of vitamin B₆ intake, the RRs were 0.89 (95% CI, 0.72-1.10) for dietary vitamin B₆ and 0.90 (95% CI, 0.73-1.11) for total vitamin B₆. Associations between vitamin B₆ intake and colorectal cancer were stronger in studies with a wider range of exposure (>1.5-mg difference in median intake comparing extreme categories; RR, 0.79; 95% CI, 0.75-1.07) compared with studies with a more narrow range of exposure (≤1.5-mg difference; RR, 0.95; 95% CI, 0.73-1.23).

Only 4 reports (5 studies) provided both age-adjusted and multivariable RRs for the association between vitamin B₆ intake and colorectal cancer risk.11,12,18,21 For these studies, the age-adjusted and multivariable RRs for the highest vs lowest categories of vitamin B₆ intake were, respectively, 0.79 (95% CI, 0.70-0.90) and 0.85 (95% CI, 0.68-1.07).

**Dose-Response Meta-analysis**

We next assessed the dose-response relationship between blood PLP levels and colorectal cancer risk. We found no evidence of statistically significant departure from linearity (P = .44). A 100-pmol/mL increment (about 2 SDs) in blood PLP level conferred an RR of 0.51 (95% CI, 0.38-0.69) (FIGURE 3). Excluding the study conducted in Finland that measured serum PLP levels did not change the results appreciably (RR, 0.52; 95% CI, 0.37-0.71).

**COMMENT**

The findings from this meta-analysis of prospective studies indicate that increased blood PLP levels are associated with a reduced risk of colorectal cancer. Overall, the risk of colorectal cancer decreased by 49% for every 100-pmol/mL increase in blood PLP level, corresponding to approximately 2 SDs in the majority of the studied population. The observed heterogeneity among studies of vitamin B₆ intake and colorectal cancer risk seemed to be explained by 1 large cohort study in the Netherlands.20 After exclusion of this single study, there was a statistically significant inverse association between vitamin B₆ intake and risk of colorectal cancer (20% decreased risk when comparing high vs low intake) without evidence of study heterogeneity. The disparate results for the Netherlands cohort may be due to the very narrow

![Figure 2. Adjusted Relative Risks of Colorectal Cancer for the Highest vs Lowest Categories of Vitamin B₆ Intake or Blood PLP Level](image)

![Figure 3. Dose-Response Relationship Between Blood PLP Level and Relative Risk of Colorectal Cancer](image)
range of exposure in that study (0.6- to 0.7-mg difference in median vitamin B6 intake between the highest and lowest quintiles) compared with the other studies (Figure 2). In fact, a statistically significant 21% reduction in colorectal cancer risk comparing high vs low vitamin B6 intake was observed among studies with a wider range of exposure (>1.3-mg difference).

Although vitamin B6 is found in a wide variety of foods, many older people do not obtain an adequate intake of this nutrient. In the United States, the prevalence of inadequate vitamin B6 intake for adults older than 50 years is about 20% for men and 40% for women.30

A strength of this study is that our quantitative assessment was based on prospective studies. This minimizes the possibility that our results were due to recall or selection bias, which could be of concern in retrospective case-control studies. Our study also has several limitations. First, a meta-analysis is not able to solve problems with confounding factors that could be inherent in the included studies. Inadequate control for confounders may bias the results in either direction, toward exaggeration or underestimation of risk estimates. Although most studies adjusted for other known risk factors for colorectal cancer, residual or unknown confounders cannot be excluded as a potential explanation for the observed findings. Vitamin B6 intake tends to be associated with healthy behaviors that may be protective against colorectal cancer, such as higher physical activity, less smoking, lower alcohol consumption, and higher folate intake.12,18,19 However, all but 1 of the studies on blood PLP levels adjusted for major potential confounders, including physical activity, smoking, and intakes of alcohol and folate. A second limitation is that our results are likely to be affected by some degree of misclassification of exposure. Only 2 reports on vitamin B6 intake updated the information about diet during follow-up.18,21 Misclassification of vitamin B6 intake may have been present in the 6 studies that assessed diet at baseline only,8,11,12,19,20,22 which could lead to an underestimation of the RR estimates. The associations between blood PLP level and colorectal cancer were stronger than those between vitamin B6 intake and colorectal cancer. This may be because of measurement error in the assessment of vitamin B6 intake, leading to an attenuation of the observed association between vitamin B6 intake and colorectal cancer risk. Dietary and total vitamin B6 intake has been shown to be reasonably strongly correlated with serum (r = 0.46)27 and plasma (r = 0.42)28 PLP levels, respectively. Third, heterogeneity may be introduced because of methodological differences among studies, including different ranges of exposure. In addition, some studies measured vitamin B6 intake from diet only, whereas other studies combined dietary and supplemental vitamin B6 intake. Nevertheless, results were similar for dietary and total vitamin B6 intake. Finally, in a meta-analysis of published studies, publication bias could be of concern because small studies with null results tend not to be published. In this meta-analysis, we found no evidence of publication bias.

The association between vitamin B6 intake and risk of colorectal cancer has been assessed in several case-control studies, with most studies showing a statistically significant inverse association.31 In a meta-analysis of 6 case-control studies, the odds ratio of colorectal cancer for the highest vs lowest categories of vitamin B6 intake was 0.67 (95% CI, 0.60-0.75), with borderline evidence of heterogeneity among studies (P = .09).31

Recent results from a randomized clinical trial of B vitamin supplementation (folic acid and vitamins B6 and B12) showed no association between very high doses of vitamin B6 supplementation (40 mg/d) and colorectal cancer during a median 39 months of intake or exposure and an additional 38 months of posttrial observational follow-up.32 However, the number of colorectal cancer cases was limited. For colorectal cancer incidence, 26 cases were diagnosed in the vitamin B6 group and 22 cases in the placebo group. The corresponding number of deaths due to colorectal cancer was 5 in the vitamin B6 group and 7 in the placebo group.

Studies on plasma PLP levels in relation to risk of colorectal adenomas have observed an inverse association.26,31 In the Aspirin/Folate Polyp Prevention Study, a randomized trial of folic acid supplementation and incidence of new colorectal adenomas in individuals with a history of adenomas, those in the highest quartile of baseline plasma PLP level had a 22% lower risk of new adenoma compared with those in the lowest quartile (RR, 0.78; 95% CI, 0.61-1.00).33 Likewise, in the Nurses’ Health Study, women in the highest quartile of plasma PLP level had a non–statistically significant lower risk of distal colorectal adenoma than did women in the lowest quartile after adjustment for potential confounders (RR, 0.69; 95% CI, 0.41-1.15).26

In summary, findings from this meta-analysis of prospective studies indicate that blood PLP levels are inversely associated with risk of colorectal cancer. There was no significant association between vitamin B6 intake and colorectal cancer risk. The findings from these observational studies need to be confirmed in large randomized clinical trials of vitamin B6 supplementation.

Author Contributions: Dr Larsson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Larsson, Orsini, Wolk. Acquisition of data: Larsson, Orsini. Analysis and interpretation of data: Larsson, Orsini, Wolk. Drafting of the manuscript: Larsson, Orsini. Critical revision of the manuscript for important intellectual content: Larsson, Orsini, Wolk. Statistical analysis: Larsson, Orsini. Obtained funding: Wolk. Administrative, technical, or material support: Wolk. Study supervision: Wolk.

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