high-impact journals that do not publish details on the “Role of the Funding Source/Sponsor,” which was needed to assess trial collaboration. Our results suggest that, in addition to disclosure of industry funding source, greater transparency of industry funders’ role in trial design, analysis, and reporting might be valuable for assessing potential bias in trial findings.

Nitin Roper, MD
Nasen Zhang, MD
Deborah Korenstein, MD

Author Affiliations: Weill Cornell Medical College, New York, New York (Roper); Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York (Zhang); American College of Physicians, Philadelphia, Pennsylvania (Korenstein).

Corresponding Author: Nitin Roper, MD, Weill Cornell Medical College, 535 East 70th St, Sixth Floor, New York, NY 10021 (nitinroper@gmail.com).


Author Contributions: Dr Roper 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: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Roper.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Roper.

Administrative, technical, or material support: Roper, Zhang.

Study supervision: Korenstein.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We acknowledge Jatin Roper, MD, for helpful editing of the manuscript. No financial compensation was provided for the contribution.


Editor’s Note

It’s Not Just About the Money, Money, Money...

Global funding for biomedical research now approaches $270 billion per year, nearly two-thirds of which comes from industry, including pharmaceutical, biotechnology, and medical device companies. While industry’s investment in research has spawned breakthroughs and innovations, these investments have also fueled concerns that industry-funded clinical trials are more likely to have proindustry conclusions, potentially distorting the evidence base to favor more expensive, brand name products on which manufacturers continue to spend research dollars.

Having examined a year’s worth of clinical trials published in high-impact biomedical journals, the findings of Roper et al suggest that the problem may go beyond funding and instead be a consequence of collaboration. When compared with trials not funded by industry, trials funded by industry were no different with respect to key design features suggestive of methodological rigor or likelihood of reporting proindustry conclusions. However, trials funded by industry that also involved collaboration in its design, analysis, or reporting used less rigorous methods and were more likely to report proindustry conclusions.

Appropriate research collaborations focused on patient benefits should be fostered, taking advantage of the skills and knowledge of those in industry and academia (and government). However, perhaps collaboration breeds sufficient familiarity and generosity that decisions are affected, even if only subtly, in a way that diminishes the rigor and robustness of the research. Ensuring that these collaborations are made fully transparent, including the process of study design and decisions relevant to study conduct and statistical analysis, may help, as might independent oversight or advisory committees. By human nature, I suspect we are all inclined to make small concessions to those with whom we work, regardless of whether they are employed by a pharmaceutical company funding our research or work at the front desk of our clinics. So we must be mindful and remember, it’s not just about the money.

Joseph S. Ross, MD, MHS


Low Yield of Outpatient Serum Folate Testing: Eleven Years of Experience

Since the United States began folate acid fortification in 1998, the prevalence of folate deficiency in the general population has decreased. Despite this, folate testing continues to be recommended for the evaluation of macrocytic anemia and is commonly performed to evaluate macrocytosis without anemia, normocytic anemia, dementia, delirium, and peripheral neuropathy. We aimed to determine the utility of serum folate testing in an outpatient population.

Methods | We conducted a retrospective review of all outpatient serum folate tests performed at a large academic medical center in Boston, Massachusetts, from January 1, 2003, through December 31, 2013. The study was reviewed by the Beth Israel Deaconess Medical Center Institutional Review Board and was determined to be exempt. No informed consent was required because this study was retrospective and observational (and thus did not affect patient care in any way). Serum folate values were determined using a chemiluminescent competitive binding protein assay on an Elecsys analyzer as prescribed by the manufacturer (Roche Diagnostics Corporation). Serum folate levels were defined as deficient (<3.0 ng/mL; to convert to nanomoles per liter, multiply by 2.266), low-normal (3.0-3.9 ng/mL), normal (4.0-19.9 ng/mL), or high (>19.9 ng/mL). To determine whether changes in the number of serum folate tests ordered were specific to
folate or were reflective of a general trend in overall ordering of laboratory tests, we compared the number of serum folate tests performed with the number of serum creatinine tests performed as a function of time. In addition, we performed cost, reimbursement, and charge analyses of serum folate testing based on 2014 institutional cost and charge figures (<$2.00 per test and $128.00 per test, respectively) and the 2014 Massachusetts Medicare fee schedule figure ($20.02 per test). Descriptive statistics were used to analyze the data.

Results | From January 1, 2003, through December 31, 2013, a total of 84,187 serum folate levels were measured in 77,627 individuals. There were 47 deficient (0.056%), 166 low-normal (0.197%), 57,411 normal (68.20%), and 26,563 high (31.55%) levels (Table 1). The mean (SE) slope of folate to creatinine by year was −0.000474 (0.000305), with $t_9 = −1.554$ and $P = .15$, which indicates that year does not have a significant effect on the ratio of serum folate to serum creatinine levels performed. Cost, charge, and reimbursement analyses are given in Table 2.

Discussion | In this retrospective review, we determined the rate of serum folate deficiency to be exceedingly low in the outpatient population because only 0.056% of serum folate levels measured were in the deficient range. This finding likely represents the significant reduction in folate deficiency since folic acid fortification began in 1998, in addition to an extreme overuse of serum folate testing. Despive the low rate of serum folate deficiency, there has been no change in ordering habits relative to routinely ordered tests, such as creatinine. We also performed cost, charge, and reimbursement analyses. From January 1, 2003, through December 31, 2013, the overall costs, charges, and reimbursements were $168,374, $10,775,936, and $1,685,423.74, respectively. This amount represents a net surplus of $1,577,050 ($137,913 per year) for the medical center.

The low rate of deficiency, high rate of overuse, and favorable payment status of serum folate testing present an interesting financial dilemma to the medical center. Every physician and medical center should aim to provide high-value care. In the case of serum folate, this would mean a significant reduction, or perhaps elimination, of testing, which in fee-for-service payment models would result in a significant loss in revenue to the medical center. The weakness of this report is that it is a retrospective study from a single institution. The results may not be generalizable to other institutions or populations.

In summary, serum folate testing is overused and deficiency is rare in the outpatient setting. Although this test generates revenue for medical centers, the goal of providing high-value patient care suggests that serum folate testing should be significantly reduced or even eliminated in the outpatient setting.

Jesse Theisen-Toupal, MD
Gary Horowitz, MD
Anthony Breu, MD

Table 1. Serum Folate Level Results

<table>
<thead>
<tr>
<th>Level</th>
<th>No. (%) of Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficient (&lt;3 ng/mL)</td>
<td>47 (0.06)</td>
</tr>
<tr>
<td>Low-normal (3.0-3.9 ng/mL)</td>
<td>166 (0.20)</td>
</tr>
<tr>
<td>Normal (4.0-19.9 ng/mL)</td>
<td>57,411 (68.20)</td>
</tr>
<tr>
<td>High (&gt;19.9 ng/mL)</td>
<td>26,563 (31.55)</td>
</tr>
</tbody>
</table>

Table 2. Cost, Reimbursement, and Charge Analyses*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total, $</th>
<th>Per Deficient Result, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>168,374.00</td>
<td>3582.43</td>
</tr>
<tr>
<td>Charge</td>
<td>10,775,936.00</td>
<td>229,275.23</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>1,685,423.74</td>
<td>35,860.08</td>
</tr>
</tbody>
</table>

* Cost per test was $2.00. Charge per test was $128.00. Reimbursement based on Medicare fee schedule per test was $20.02.

In summary, serum folate testing is overused and deficiency is rare in the outpatient setting. Although this test generates revenue for medical centers, the goal of providing high-value patient care suggests that serum folate testing should be significantly reduced or even eliminated in the outpatient setting.

Jesse Theisen-Toupal, MD
Gary Horowitz, MD
Anthony Breu, MD

Author Affiliations: Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Theisen-Toupal); Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Horowitz); Medical Service, VA Boston Healthcare System, West Roxbury, Massachusetts (Breu).

Accepted for Publication: June 4, 2014.

Corresponding Author: Jesse Theisen-Toupal, MD, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Span 2, Boston, MA 02215 (jttoupal@bidmc.harvard.edu).


Author Contributions: Drs Theisen-Toupal and Horowitz had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Theisen-Toupal, Breu.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Theisen-Toupal, Breu.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Theisen-Toupal, Horowitz.

Study supervision: Breu.

Conflict of Interest Disclosures: None reported.


Invited Commentary | HEALTH CARE REFORM

Folate Testing: Time to Retire Your VCR

I was coming home from a long work week at the hospital and thought of stopping by the video store to rent a copy of the latest Hollywood blockbuster video. I called my wife from my office telephone to tell her I’d be late. I wasn’t sure where the store was, but I had a map in my car and found directions. The store was in a strip mall. In the parking lot, there was a drive-through film developing store that advertised return of prints in less than 1 hour. Great! I’d drop off my film, go to the video store, and, if I had some ex-