In Reply: The overall objective of our study was to examine whether a lifelong lowering of HDL cholesterol levels, without corresponding higher levels of plasma triglycerides or atherogenic remnant lipoproteins, was associated with increased risk of IHD. To test this hypothesis, we used heterozygotes for mutations in ABCA1 associated with low cellular cholesterol efflux, as well as with substantial, lifelong lowering of HDL levels, and showed no increase in risk. These results question the hypothesis of reverse cholesterol transport, an active research field. We agree with Dr Brunham and colleagues that genetic variants in ABCA1 may have effects on atherosclerosis independent of effects on HDL levels. However, there are some inaccuracies in their letter.

First, it is correct that the unadjusted reduction in HDL levels in ABCA1 heterozygotes compared with noncarriers was 28% (Table 2); however, the age- and sex-adjusted mean percentile for HDL levels in heterozygotes in the CCHS was at the 16th percentile compared with noncarriers (Figures 2 and 3). The 17-mg/dL lower HDL levels observed in ABCA1 heterozygotes were associated with an estimated hazard ratio for IHD of 1.70 (95% confidence interval [CI], 1.57-1.85) in the CCHS, similar to other studies and consistent with an inverse relationship between HDL level and risk. However, the adjusted odds ratio for heterozygotes vs noncarriers and IHD was 0.93 (95% CI, 0.53-1.62), suggesting no increase in risk of IHD.

Second, we agree that cholesterol efflux studies are generally of questionable significance given the relatively large variability of this assay. However, in our study, the lower in vitro cholesterol efflux, which in vivo mainly reflects liver efflux, is indeed reflected in the lower plasma HDL level. The important point is that cholesterol efflux due to this effect on HDL level has been used as a surrogate marker for atherosclerosis. In humans it has been assumed but never shown that a low cholesterol efflux causes atherosclerosis. Third, our findings are consistent with our previous reports on the same cohort showing that polymorphisms and mutations in ABCA1 may or may not affect HDL levels, but that risk of IHD is independent of these HDL effects. Fourth, it is not correct that to state that heterozygosity for the 3 rare mutations in the CCHS (P106S, G1216V, or R214H; n=6) was associated with a 25% reduction in LDL cholesterol levels compared with noncarriers because this was not statistically significant. Furthermore, in the Copenhagen General Population Study, median LDL levels in heterozygotes (n=6) and noncarriers of these rare mutations were 124 mg/dL (interquartile range, 112-139 mg/dL) and 124 mg/dL (interquartile range, 100-151 mg/dL), respectively (P>.99). Therefore, it is unlikely that LDL levels in rare heterozygotes could explain the lower-than-expected risk.

Our conclusion remains that a lifelong reduction in HDL levels due to mutations in ABCA1 is not associated with an increased risk of IHD.

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Updated Estimates of Pharmaceutical Company Payments to Physicians in Vermont

To the Editor: We previously examined the experiences of Vermont and Minnesota with state laws requiring that pharmaceutical companies disclose payments to health care professionals. However, in Vermont, companies were
permitted to designate payments as trade secrets, preventing their inclusion in our study. Public Citizen subsequently obtained disclosed trade-secret-designated payments through litigation against the companies. We present updated findings and comparison of trade-secret- and non-trade-secret-designated payments.

Methods. Our methods have been described previously. Vermont law requires disclosure of payments of $25 or more. We categorized each payment by recipient and purpose; recipient names were typically not disclosed as part of the settlement. We conducted a descriptive analysis, summarizing all payments over the study period stratified by whether or not they were initially designated trade secret. We focused on payments of $100 or more because these exceed guidelines by the American Medical Association and Pharmaceutical Research and Manufacturers of America for gifts to physicians. We used χ² and Brown-Mood 1-way analyses of variance with medians to compare trade-secret- and non-trade-secret-designated payments. Analyses were performed using SAS 9.1 (SAS Institute Inc, Cary, North Carolina). All statistical tests were 2-tailed, using a type I error rate of .002 to account for multiple comparisons.

Results. From July 1, 2002, to June 30, 2004, there were 21,409 payments of any value to all health care professionals and organizations, totaling $4.90 million (median, $52; range, $0.22-$63,458). This sum is $0.69 million less than the $5.59 million calculated by the Vermont attorney general, $0.22-$63 458). This sum is $0.69 million less than the $5.59 million calculated by the Vermont attorney general, a discrepancy accounted for by our exclusion of dis

Table. Disclosed Payments of $100 or More From Pharmaceutical Companies in Vermont, July 2002 Through June 2004

<table>
<thead>
<tr>
<th>Payment Recipient</th>
<th>Physicians</th>
<th>Nonphysicians</th>
<th>Organizations</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTSD</td>
<td>TSD</td>
<td>NTSD</td>
<td>TSD</td>
<td>NTSD</td>
</tr>
<tr>
<td>Amount Paid, $ (%)</td>
<td>2146 (85.5)</td>
<td>2327 (85.8)</td>
<td>273 (9.7)</td>
<td>298 (11.0)</td>
</tr>
<tr>
<td>Payment Purpose</td>
<td>Consulting</td>
<td>84 (3.5)</td>
<td>184 (7.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Detailing</td>
<td>616 (25.5)</td>
<td>132 (5.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Education</td>
<td>688 (28.4)</td>
<td>1004 (43.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Marketing</td>
<td>218 (9.0)</td>
<td>98 (4.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Speaker</td>
<td>341 (14.1)</td>
<td>749 (32.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>76 (3.2)</td>
<td>27 (1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Unspecified</td>
<td>395 (16.4)</td>
<td>133 (5.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall</td>
<td>2416 (51.0)</td>
<td>2327 (49.0)</td>
<td>&lt;.001</td>
<td>1,012,492 (31.7)</td>
</tr>
</tbody>
</table>

Abbreviations: NTSD, non-trade-secret-designated; TSD, trade-secret-designated.

P value for comparison of non-trade-secret- and trade-secret-designated payments.

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tiff, not the general public. Trade-secret-designated payments were of greater value and many were for food. Currently proposed federal legislation (S.2029 and HR.5605) does not permit trade-secret designation of payments. However, proposed state bills, such as in Washington, do include trade-secret provisions, which prevent disclosure of substantial numbers of payments. Variation in designation among companies and among payment purposes raises concerns about the appropriateness of trade-secret designation and its practical usage.

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Study concept and design: Ross, Lurie, Lackner, Krumholz.
Acquisition of data: Ross, Nazem, Lurie.
Analysis and interpretation of data: Ross, Lurie, Krumholz.
Drafting of the manuscript: Ross.
Critical revision of the manuscript for important intellectual content: Ross, Nazem, Lurie, Lackner, Krumholz.
Statistical analysis: Ross.
Administrative, technical, or material support: Lurie, Krumholz.
Study supervision: Lurie, Krumholz.

Financial Disclosures: Drs Ross and Krumholz reported having served as consultants at the request of plaintiffs for recent suits against Merck and Co Inc related to Vioxx. Dr Krumholz reported having research contracts with the American College of Cardiology and the Colorado Foundation for Medical Care; being on an advisory board for UnitedHealthcare; serving as a subject matter expert for VHA Inc; and being editor-in-chief of Circulation: Cardiovascular Quality and Outcomes and Journal Watch Cardiology of the Massachusetts Medical Society. Dr Krumholz reported that in the past 5 years he has received a research grant from Boehringer-Ingelheim; served as a consultant to Centegen; and served as an advisory board member for Alera, CV Therapeutics, and Amgen. No other disclosures were reported.

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