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 to state that heterozygosity for the 3 rare mutations in the CCHS (P1065S, G1216V, or R2144X; 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). (To convert to mmol/L, multiply by 0.0259.) 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.

Anne Tybjærg-Hansen, MD, DMSc
Department of Clinical Biochemistry
Rigshospitalet
Børge G. Nordestgaard, MD, DMSc
Department of Clinical Biochemistry
Herlev Hospital
Ruth Frikke-Schmidt MD, PhD
Department of Clinical Biochemistry
Rigshospitalet
University of Copenhagen
Copenhagen, Denmark

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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 required to report payments to all physicians; in Minnesota, payments to facilities were not included. In the states with the law, companies reported payments to physicians, and in the absence of a disclosure law, companies did not report payments.
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, a discrepancy accounted for by our exclusion of discount and rebate payments (not required to be disclosed by law) reported by a single company. Of these 21,409 payments, 9,182 (42.9%) totaling $2.72 million (55.5%) were designated trade secret. There was a nonsignificant difference between the median trade-secret- and non-trade-secret-designated payments ($53 vs $51; P=.06), although a greater proportion of trade-secret-designated payments were for $100 or more (29.6% vs 25.0%; P<.001).

There were 5,539 payments that exceeded $100, totaling $4.20 million (median, $250; range, $100-$63,458) (Table). Of these, 2,713 (49.0%) totaling $2.44 million (58.1%) were designated trade secret; the median trade-secret-designated payment was significantly greater than the median non-trade-secret-designated payment ($500 vs $184; P<.001).

Approximately 86% of trade-secret and non-trade-secret-designated payments exceeding $100 were to physicians, comprising 4,743 payments totaling $3.20 million (median, $250; range, $100-$20,000). Among these, the median trade-secret-designated payment was significantly greater than the median non-trade-secret-designated payment ($500 vs $177; P<.001) (Table). Trade-secret-designated payments to physicians were more likely to be for education or speakers, and less likely to be for detailing or unspecified purposes, when compared with non-trade-secret-designated payments (P values <.001) (Table), and were less likely to be in the form of food (25.3% vs 67.5%; P<.001).

Among all payments of any value, 30 companies did not designate any trade secrets, 7 designated all trade secrets, and 14 designated some but not all trade secrets. Among payments to physicians that exceeded $100, 46 companies provided 4,743, totaling $3.20 million (median number per company, 21; range, 1-973; median total amount, $13,549; range, $116,594-$567).

Comment. Data about nearly half of payments exceeding $100 to physicians from pharmaceutical companies in Vermont, accounting for two-thirds the total value, were obtained through litigation; they were available only to the plain-

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><strong>Payments, No. (%)</strong></td>
<td>NTSD</td>
<td>TSD</td>
<td>NTSD</td>
<td>TSD</td>
</tr>
<tr>
<td>Physicians</td>
<td>2146 (85.5)</td>
<td>2327 (85.0)</td>
<td>.77</td>
<td>1,012,492 (57.6)</td>
</tr>
<tr>
<td>Nonphysicians</td>
<td>273 (9.7)</td>
<td>298 (11.0)</td>
<td>.1</td>
<td>115,314 (6.6)</td>
</tr>
<tr>
<td>Organizations</td>
<td>134 (4.8)</td>
<td>88 (3.2)</td>
<td>.003</td>
<td>628,967 (35.8)</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>2826 (51.0) b</td>
<td>2713 (49.0) b</td>
<td>.1</td>
<td>1,756,773 (41.9) b</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Payment Purpose</strong></th>
<th>NTSD</th>
<th>TSD</th>
<th>NTSD</th>
<th>TSD</th>
<th>NTSD</th>
<th>TSD</th>
<th>NTSD</th>
<th>TSD</th>
<th>NTSD</th>
<th>TSD</th>
<th>P Value a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consulting</td>
<td>84 (3.5)</td>
<td>184 (7.9)</td>
<td>&lt;.001</td>
<td>52,013 (5.1)</td>
<td>179,265 (8.2)</td>
<td>&lt;.001</td>
<td>250 (100–5000)</td>
<td>300 (100–8000)</td>
<td>.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detailing</td>
<td>616 (25.5)</td>
<td>132 (5.7)</td>
<td>&lt;.001</td>
<td>137,694 (13.6)</td>
<td>22,020 (1.0)</td>
<td>&lt;.001</td>
<td>158 (100–2703)</td>
<td>149 (100–338)</td>
<td>.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>686 (28.4)</td>
<td>1004 (43.2)</td>
<td>&lt;.001</td>
<td>170,389 (16.8)</td>
<td>916,165 (41.7)</td>
<td>&lt;.001</td>
<td>132 (100–20,000)</td>
<td>340 (100–9044)</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marketing</td>
<td>218 (9.0)</td>
<td>96 (4.2)</td>
<td>&lt;.001</td>
<td>51,070 (5.0)</td>
<td>21,584 (1.0)</td>
<td>&lt;.001</td>
<td>135 (100–7230)</td>
<td>147 (100–1100)</td>
<td>.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker</td>
<td>341 (14.1)</td>
<td>749 (32.2)</td>
<td>&lt;.001</td>
<td>351,659 (34.7)</td>
<td>946,476 (43.2)</td>
<td>&lt;.001</td>
<td>1000 (100–7607)</td>
<td>1000 (100–7607)</td>
<td>.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>76 (3.2)</td>
<td>27 (1.2)</td>
<td>&lt;.001</td>
<td>46,282 (4.6)</td>
<td>5668 (0.3)</td>
<td>&lt;.001</td>
<td>153 (100–3477)</td>
<td>100 (100–2000)</td>
<td>.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td>395 (16.4)</td>
<td>133 (5.7)</td>
<td>&lt;.001</td>
<td>203,385 (20.1)</td>
<td>103,391 (4.7)</td>
<td>&lt;.001</td>
<td>368 (100–5000)</td>
<td>483 (113–5000)</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>2416 (51.0) b</td>
<td>2327 (49.0) b</td>
<td>.77</td>
<td>1,012,492 (31.7) b</td>
<td>2,191,018 (68.3) b</td>
<td>&lt;.001</td>
<td>177 (100–20,000)</td>
<td>500 (100–9044)</td>
<td>&lt;.001</td>
<td></td>
<td></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. Represents row percentage: proportion of total number of payments or amount paid. For payments of $100 or more from pharmaceutical companies to physicians only.

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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.

Joseph S. Ross, MD, MHS
joseph.ross@mssm.edu
Department of Geriatrics and Adult Development
Mount Sinai School of Medicine
New York, New York

Alexander G. Nazem, BS
Yale University School of Medicine
New Haven, Connecticut

Peter Lurie, MD, MPH
Health Research Group
Public Citizen
Washington, DC

Josh E. Lackner, BS
University of Minnesota School of Medicine
Minneapolis

Harlan M. Krumholz, MD, SM
Department of Medicine
Yale University School of Medicine

Author Contributions: Dr Ross had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis. 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.

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