domized, controlled investigations with a sufficient number of patients are needed. However, the general public and the medical community should be reassured by our study that the severity of the problem is probably much less than initially thought.

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REFERENCES


REPLY

We appreciate Dr. Dieter’s interest in our article and the opportunity to respond to his letter. Patients in CAPRIE were intensively monitored for neutropenia, and severe neutropenia (<450 per microliter) was observed in six patients, four of whom were receiving clopidogrel (three women, one man, all of whom were Caucasian). Although these patients did develop neutropenia while receiving clopidogrel, we disagree with Dr. Dieter’s conclusion that clopidogrel “caused” the neutropenia in these patients. One patient was receiving chemotherapy for a malignancy when the neutropenia occurred. Two patients developed only transient neutropenia, which did not resume after clopidogrel was reinitiated, and they continued to receive clopidogrel for the duration of the study. We should mention that a fifth clopidogrel patient was described in the CAPRIE manuscript as having developed neutropenia but was found to have aplastic anemia and was, therefore, not considered by the Food and Drug Administration to have developed “neutropenia.” This fifth clopidogrel patient does not appear in the labeling for clopidogrel. (Similarly, two additional aspirin patients were described in the CAPRIE manuscript as having developed neutropenia; one had actually developed acute myelogenous leukemia, and one was found to have been neutropenic at study entry.)

Despite the “association” between clopidogrel and neutropenia in these four patients, we are no more convinced that clopidogrel caused their neutropenia than we are convinced that aspirin caused the neutropenia in the two patients in the aspirin group. It is important to distinguish between the frequency of "background"

Table 1.

<table>
<thead>
<tr>
<th>Age</th>
<th>Mitral Regurgitation</th>
<th>Aortic Regurgitation</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>26–39</td>
<td>0.186</td>
<td>0.142</td>
</tr>
<tr>
<td>40–49</td>
<td>0.302</td>
<td>0.361</td>
</tr>
<tr>
<td>50–59</td>
<td>0.442</td>
<td>0.383</td>
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<tr>
<td>60–69</td>
<td>0.07</td>
<td>0.115</td>
</tr>
<tr>
<td>70–83</td>
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<td>0</td>
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<td>&gt;83</td>
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<tr>
<td>Expected prevalence</td>
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<td>Total expected prevalence</td>
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<td>0.021</td>
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<tr>
<td>Observed prevalence</td>
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<td>0.066</td>
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<td>Prevalence ratio</td>
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<td>3.13</td>
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<tr>
<td>95% confidence limits</td>
<td>0.41–4.35</td>
<td>0.99–9.85</td>
</tr>
</tbody>
</table>

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REFERENCES
