Cigarette smoking is associated with an increased risk of developing type 2 diabetes, results of a meta-analysis suggest. Active smokers had an increased risk of developing type 2 diabetes, compared with nonsmokers, with a pooled relative risk of 1.44,“ study investigators reported. The researchers conducted a meta-analysis of all 25 prospective cohort studies of the issue in the United States, Europe, Japan, and Israel that were published between 1992 and 2006. All of the studies examined a possible link between smoking and irregularities of glucose metabolism, and all but one found a positive association, Dr. Carol Willi of the University of Lausanne (Switzerland) and her associates wrote.

The number of study subjects ranged from 630 people to more than 700,000 people, for a total of 1.2 million subjects and 45,844 cases of incident diabetes in the meta-analysis. Overall, 35% of the people were current smokers. Follow-up ranged from 5 to 30 years.

The association between smoking and diabetes remained robust through numerous statistical analyses that explored study factors as well as clinical variables. The findings also suggested a dose-response relationship, because the association with diabetes was stronger among heavy smokers than among light smokers, and was stronger in active smokers than in former smokers.

Given this consistency, they conclude that the relevant question is no longer whether this association exists, but rather whether this established association is causal," Dr. Willi and her associates said (JAMA 2008;299:2654-2664).

“There is theoretical biological plausibility for causality in that smoking may lead to insulin resistance or inadequate

### Table 1: Treatment-emergent adverse reactions in controlled trials in Neuropathic Pain Associated with Diabetic Peripheral Neuropathy

<table>
<thead>
<tr>
<th>Body System</th>
<th>LYRICA (N=77)</th>
<th>LYRICA (N=212)</th>
<th>LYRICA (N=321)</th>
<th>LYRICA (N=369)</th>
<th>LYRICA (N=979)</th>
<th>LYRICA (N=459)</th>
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<tbody>
<tr>
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<td></td>
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<tr>
<td>Dizziness</td>
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<td>9</td>
<td>23</td>
<td>29</td>
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<td>5</td>
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<tr>
<td>Abnormal thinking</td>
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<td>Somnolence</td>
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<td>7</td>
<td>10</td>
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<td>1</td>
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</table>
compensatory insulin secretion responses according to several but not all studies," they wrote.

They noted that "Smoking also has a clinical significant effect on both oral and intravenous glucose tolerance tests that could influence diabetes detection."

The adverse effect of smoking on diabetes risk "has been generally underrecognized," Dr. Eric L. Ding and Dr. Frank B. Hu of the Harvard School of Public Health, Boston, said in an editorial accompanying the report. Dr. Ding and Dr. Hu estimated that 12% of all type 2 diabetes in the United States may be attributable to smoking, based on this study's estimates, statistics on smoking prevalence, and an accepted population-attributable risk formula (JAMA 2007;298:2675-6).

In addition, "an estimated 2.3 million cases of diabetes in the United States and a corresponding $14.9 billion of the annual U.S. $132 billion diabetes cost burden may be attributable to smoking," they said.

Although the exact mechanism by which smoking may contribute to the development of diabetes has not been identified, smoking is known to be related to central adiposity, to increase inflammation and oxidative stress, to directly damage beta cell function, to impair endothelial function, and to impair insulin sensitivity and glucose tolerance, Dr. Ding and Dr. Hu said.

Given the findings of Dr. Willi and her associates, it is "important and prudent for clinicians to screen for and carefully monitor glucose levels among current and former smokers," they added.

Active smokers had a pooled relative risk of 1.44 for developing type 2 diabetes compared with nonsmokers.