**INVESTIGATING Cumulative Marijuana Use and Risk of Cardiovascular Disease in Middle Age With Longitudinal Data**

Never before have so many people expressed such strong interest in knowing the impact of marijuana legalization on human behavior and health.\(^1,2\)

There is a global trend toward legalizing marijuana. According to the National Organization for the Reform of Marijuana Laws, 29 US states permit marijuana use (http://norml.org/laws). However, research from diverse sources has produced mixed findings regarding the impact of marijuana laws.\(^3,4\)

A recent *AJPH* article by Reis et al. addressed cumulative marijuana exposures and cardiovascular disease (CVD).\(^5\) In this timely research, the authors used data from a long-established project (the Coronary Artery Risk Development in Young Adults [CARDIA] study), funded by the National Institutes of Health, in which cardiovascular events were determined via standard diagnostic procedures. Reis et al. used a Cox proportional hazards model and a trend test to assess the impact of marijuana exposures. However, we believe that their evidence is inadequate to conclude, as they did from their findings, that “[n]either cumulative lifetime nor recent use of marijuana is associated with the incidence of CVD in middle age.”\(^5(p601)\)

As an example, lifetime marijuana use is not a good measure for this purpose given that it is a compound indicator encompassing (1) those who use marijuana continuously after initiation, (2) those who quit after initiation, and (3) those who initiated use recently.\(^6\) To illustrate this point, Table 1 summarizes results from the Reis et al. study. CARDIA’s 26.9 years of follow-up with 5113 participants showed that 4286 were lifetime users, 827 had never used marijuana, and 960 were current users. These data indicate that 3326 of the 4286 (4286 \(−\) 960) lifetime users, or 77.6%, were ex-users. In other words, 77.6% of the Reis et al. figure on lifetime exposure is a reflection of the effect of quitting rather than using marijuana.

Reis et al. noted that self-reported marijuana exposure is subject to error. However, they derived a dosage measure by multiplying reported use in a given month by years of follow-up, amplifying the error. This may explain the inconsistent dose–response relationships reported. We conducted a quick analysis with a dichotomized measure of current marijuana use, and the results showed a cumulative relative risk for current marijuana exposure of 1.63 (95% confidence interval = 1.22, 2.19; \(P<.01\)).

On the basis of our observations, we recommend a reinvestigation of the same study hypotheses with alternative approaches, such as adding a group of former marijuana users to allow an exploration of the effects of quitting, using binary measures of marijuana exposure before searching for dose–response relationships, and implementing new methods of assessing long-term exposures (e.g., developmental trajectory analyses).\(^7\)

**ABOUT THE AUTHORS**

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**CONTRIBUTORS**

X. Chen drafted and revised the letter, D.-G. Chen conducted the data analysis and interpreted the results, and B. Yu contributed to the first draft of the letter and revised the final version.

**REFERENCES**


**TABLE 1—Summary of Reis et al. Study Results**

<table>
<thead>
<tr>
<th>Type of Marijuana Use</th>
<th>Lifetime Users, No. (%)</th>
<th>Never Users, No. (%)</th>
<th>Total, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime</td>
<td>4286 (83.8)</td>
<td>827 (16.2)</td>
<td>5113</td>
</tr>
<tr>
<td>Current</td>
<td>960 (18.8)</td>
<td>4153 (81.2)</td>
<td>5113</td>
</tr>
<tr>
<td>Difference</td>
<td>3326 (77.6(^a))</td>
<td>3326 (402.2(^b))</td>
<td>0</td>
</tr>
</tbody>
</table>

Note. Current use indicates use prior to the diagnosis of a cardiovascular event or death. Source. Data are from the study by Reis et al.\(^5\)

\(^a\)Quitters.

\(^b\)Initiators.

