**RESEARCH**

**Title: Explaining Differences in Cardiovascular Disease Occurrence for Cigarette Users**

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**Background** Smoking has been associated with negative cardiovascular outcomes. The Population Assessment of Tobacco and Health (PATH) Study collects data from a sample of both tobacco users and nonusers in the United States about their general health and relationship with tobacco. This data includes levels for several biomarkers that have evidence of association with tobacco use.

**Objectives** PATH Study data was analyzed to see if there was any evidence that certain biomarkers collected were related to cardiovascular disease occurrence through cigarette and e-cigarette use and could be used as a signal for cardiovascular health risk.

**Methods** 1,436 participants who did not develop a cardiovascular condition during the PATH Study Waves 1 through 5 and 140 participants who did were used for the analysis. Participants were either cigarette users, e-cigarette users, or nonusers. Mediation analysis was conducted to understand both the association between a given biomarker and cardiovascular disease occurrence and the association between that biomarker and smoking status.

**Results** There was evidence thatthe biomarkers soluble intercellular adhesion molecule-1 (sICAM-1) and high-sensitivity C-reactive protein (hsCRP) partially explained the effect of cigarette use on the occurrence of cardiovascular disease. The relative indirect effects for sICAM-1 and hsCRP were 73.3% (95% CI: 41.6% - 100.0%) and 28.3% (95% CI: 9.8% - 59.9%), respectively. Unlike cigarette use, e-cigarette use was not associated with cardiovascular disease occurrence.

**Conclusions** Biomarkers sICAM-1 and hsCRP collected from the PATH Study Wave 1 participants show evidence of influencing the effect that smoking cigarettes has on cardiovascular disease occurrence.

**Recommendations** This research provides support for the idea of using biomarkers to measure cigarette use and disease risk and their relationship with one another.

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