

# e-Cigarette Use and Subsequent Tobacco Use by Adolescents New Evidence About a Potential Risk of e-Cigarettes

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**Few topics in public health** and medicine are as contentious as electronic cigarettes (e-cigarettes), novel handheld battery-operated nicotine-delivery devices that resemble



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conventional tobacco cigarettes and simulate the experience of smoking a cigarette.<sup>1-3</sup> Unlike cigarettes that burn tobacco to generate smoke, e-cigarettes heat a liquid consisting of nicotine, propylene glycol or glycerin, flavorings, and other chemicals to create a vapor that is inhaled. Both conventional cigarettes and e-cigarettes deliver nicotine, the addictive agent in tobacco, but e-cigarettes do not expose the user to the many other tobacco smoke constituents responsible for causing tobacco-related diseases. e-Cigarettes therefore offer the tantalizing prospect that they could reduce the harms of conventional tobacco use, the leading cause of preventable death and disability in the United States and worldwide.<sup>4</sup>

e-Cigarettes have substantial consumer appeal, generating an estimated \$2.2 billion in revenue in the United States in 2014.<sup>5</sup> Their use by adults and adolescents in the United States has increased substantially.<sup>6,7</sup> Their novel design and consumer appeal make e-cigarettes a “disruptive technology,”<sup>3</sup> and their potential benefits and harms are substantial and hotly debated.<sup>1,2</sup> Meanwhile, the characteristics of these products are evolving; newer generations deliver more nicotine and resemble cigarettes less.<sup>8</sup> Thus, e-cigarettes raise many questions for which there are few answers. The evidence base is limited because e-cigarettes entered the marketplace without being regulated as either drugs or devices.

The primary potential benefit of e-cigarettes is to reduce the prevalence of tobacco use by helping current smokers to quit or to switch completely and permanently from combustible tobacco to e-cigarette use. Dual use involving substituting some conventional cigarettes with e-cigarettes would provide far less benefit. However, any benefit of e-cigarettes would be offset to the extent that these products are harmful.

The 3 principal public health concerns about e-cigarettes are their potential to renormalize cigarette use if they are permitted in venues where cigarettes are banned; their potential appeal to nonsmokers, especially to children and adolescents; and their possible health risks as a result of users' exposure to e-cigarette constituents, such as flavorings or propylene glycol, or to e-cigarette contaminants.<sup>9</sup>

e-Cigarettes could increase tobacco use initiation rates if youths who would not have otherwise tried conventional ciga-

rettes try e-cigarettes, become addicted to nicotine, and transition to using combustible tobacco products. Adolescents may be especially susceptible to develop nicotine addiction after e-cigarette exposure because their brains are still developing and are particularly sensitive to nicotine.<sup>4</sup> There is universal agreement that this is not a good outcome, and there is concern that it could occur because e-cigarettes are marketed in ways that appeal to youth.<sup>8</sup>

Whether adolescents' use of e-cigarettes predisposes them to initiate conventional tobacco use is a critical question for assessing the net public health effect of e-cigarettes. The existing evidence derives from cross-sectional studies. In a nationally representative sample of US middle and high school students from 2011-2013, ever use of e-cigarettes was associated with conventional tobacco product use and with a measure of susceptibility to start smoking in the future,<sup>10</sup> consistent with an earlier analysis.<sup>11</sup> In a national survey of US young adults from 2012-2013, ever use of e-cigarettes was associated with an openness to smoke conventional cigarettes.<sup>12</sup> The associations observed in these studies persisted after statistical adjustment for potential confounders, but cross-sectional study designs cannot establish causality or the temporal direction of observed relationships.<sup>13</sup>

A longitudinal study can help untangle the temporality of these relationships. In this issue of *JAMA*, Leventhal and colleagues<sup>14</sup> report findings from such a study. The authors used a repeated-measures prospective observational study design to assess combustible tobacco and e-cigarette use among a diverse cohort of 2530 ninth graders attending 10 public high schools in Los Angeles, California, from 2013-2014.<sup>14</sup> At baseline, all students were nonsmokers (defined as never having used a combustible tobacco product, including cigarettes, cigars, blunts, and hookah); 222 (8.8%) of them had ever used an e-cigarette. Nonsmokers with previous exposure to e-cigarettes at initial interview compared with those without exposure to e-cigarettes were more likely to report use of a combustible tobacco product during the next 6 months (30.7% vs 8.1%, respectively) and 12 months (25.2% vs 9.3%, respectively). Significant associations also were found for each individual tobacco product, including cigarettes, cigars, and hookah. The investigators carefully adjusted the analysis for many known sociodemographic, family, environmental, and intrapersonal factors associated with e-cigarette and combustible tobacco use. This adjustment substantially lowered the magnitude of the association between e-cigarettes and subsequent tobacco use (odds ratio [OR] declined from 4.27 [95% CI, 3.19-5.71] to 2.73 [95% CI, 2.00-3.73]), suggesting that these fac-

tors were important confounders, but the ORs remained statistically significant. However, the relationship between e-cigarette and combustible tobacco product use was bidirectional; a history of tobacco smoking at baseline was associated with initiation of e-cigarette use during follow-up.

The measures of exposure (e-cigarette use) and outcome (combustible tobacco product use) had limited detail. Because the only outcome measure was any use of a tobacco product during the past 6 months, the analysis could not distinguish students who had just tried a few cigarettes from those who progressed to regular smoking during follow-up. The latter is the greater concern, and the current study cannot determine whether e-cigarette exposure was associated with that outcome. Similarly, the single exposure measure, lifetime e-cigarette use, did not permit the authors to look for a dose-response relationship between the degree of prior e-cigarette use and subsequent smoking, which could have strengthened a causal inference.

This study is the first prospective report associating adolescents' use of e-cigarettes with subsequent uptake of combustible tobacco products. The authors are appropriately cautious in interpreting their findings, acknowledging the limitations of observational studies for inferring causation, and calling for additional prospective studies to confirm their findings. At least 1 large nationally representative US study, the Population Assessment of Tobacco and Health, is already under way.<sup>15</sup> Nevertheless, the report by Leventhal and colleagues<sup>14</sup> is the strongest evidence to date that e-cigarettes might pose a health hazard by encouraging adolescents to start smoking conventional tobacco products.

Regardless of whether e-cigarettes are a gateway to tobacco product initiation, there is no reason for adolescents to

use a product for which the hypothesized public health benefit is harm reduction for adult smokers. However, there is ample evidence that e-cigarettes are marketed in ways that appeal to children and adolescents.<sup>8</sup> Prompt, effective action is needed to protect youth and reduce the demand for e-cigarettes by nonsmokers of all ages. A rational approach is to extend to e-cigarettes the same sales, marketing, and use restrictions that apply to combustible cigarettes.

Actions have already begun. In April 2014, the US Food and Drug Administration (FDA), which has the authority to regulate the manufacture, marketing, and distribution of conventional cigarettes, proposed to extend its jurisdiction to e-cigarettes.<sup>16</sup> The proposed regulations set the age of 18 years as the minimum age of sale, require health warnings on e-cigarettes, and open the door for future product standards. The FDA should move swiftly to finalize this rule, which to date has not been issued and is overdue. The agency also should prioritize future regulatory actions such as banning product flavorings and restricting advertising on television and in youth-targeted publications and media. Additional actions to discourage youth uptake of e-cigarettes are beyond the FDA's authority. One example is to apply restrictions on cigarette smoking in public places and workplaces to e-cigarettes to avoid renormalizing cigarettes. States and communities have already started to take these actions.<sup>17</sup>

In the meantime, to support future actions, researchers must seek to understand how to balance the benefits and risks of e-cigarettes and thereby to maximize public health and reduce the enormous toll of tobacco-related disease. The study by Leventhal and colleagues<sup>14</sup> represents an important new contribution to the much-needed evidence base.

#### ARTICLE INFORMATION

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