Institute of Mental Health, Doris Duke Charitable Foundation, Genentech, and California Health Care Foundation and personal fees from Uncommon Bold outside the submitted work. She is a founding member of TIME’S UP Healthcare but receives no financial compensation from that organization. Dr Roubinov reported grants from the National Institute of Mental Health and Canadian Institute for Advanced Research outside of the submitted work. Dr Jaggi reported grants from the National Cancer Institute/National Institutes of Health, Doris Duke Charitable Foundation, Komen Foundation, Blue Cross Blue Shield of Michigan, and Genentech, grants and personal fees from Greenwall Foundation, personal fees from Amgen, Vizient, Sheridan & Hasso, and Dressman Benziger, Lavelle outside the submitted work, serving as an advisory board member from Equity Quotient, and is an uncompensated founding member of TIME’S UP Healthcare. No other disclosures were reported.


Trends in e-Cigarette Use in Adults in the United States, 2016-2018

e-Cigarettes are generally perceived to be less harmful than traditional cigarettes. A considerable public health challenge is their use among young adults who have never smoked and among vulnerable subgroups, including individuals with mental health conditions and pregnant women. The rapidly evolving e-cigarette market, outdated tobacco laws and regulations, and the recent outbreak of e-cigarette or vaping product use–associated lung injuries highlight the need for up-to-date data on e-cigarette use.

Methods | We analyzed 1156411 participants from the nationally representative Behavioral Risk Factor Surveillance System 2016-2018 with information on e-cigarette use, which was categorized as never, former, or current (daily/occasional) use. We defined sole e-cigarette users as those who never use combustible cigarettes but who currently use e-cigarettes. Participants self-reported demographic information, cigarette smoking status, chronic health conditions, and health-risk behaviors (other tobacco use, heavy alcohol use, marijuana use, and binge drinking, defined elsewhere). Data were analyzed in October 2019. Sampling weights and methodology are described elsewhere.

Current e-cigarette use prevalence was analyzed by year, and absolute differences in percentage prevalence were calculated. Trends across the years were tested using logistic regression with survey year as a continuous variable. In 2018, only 33 states had e-cigarette use documented; we therefore conducted subanalysis of trends in only these states. The data used were publicly available and deidentified; thus, this study was exempt from was institutional review board review based on the Federal Policy for the Protection of Human Subjects Revised Common Rule. The statistical software used was Stata version 15.1 (StataCorp).

Results | The weighted overall current e-cigarette use prevalence was 4.5% (95% CI, 4.4%-4.6%) in 2016, remained stable at 4.4% (95% CI, 4.3%-4.5%) in 2017, then increased to 5.4% (95% CI, 5.2%-5.6%) in 2018. This translates to approximately 11 200 000 adults using e-cigarettes in the US in 2016, 11 000 000 in 2017, and 13 700 000 in 2018. These trends were similar across sociodemographic subgroups. The youngest age group (18-24 years) had the largest increase in prevalence, from 9.2% in 2016 to 15% in 2018, as did students, whose use increased from 6.3% in 2016 to 12% in 2018 (Figure, A). Among those who never smoked, there was a significant increase in prevalence of e-cigarette use from 1.4% in 2016 to 2.3% in 2018. Participants who participated in health-risk behaviors, including marijuana use, had higher increases in e-cigarette use prevalence compared with those who did not (Table).

Daily and occasional use prevalence increased from 2016 to 2018, with the largest change observed among 18- to 24-year-olds. Among those who never smoked, e-cigarette use prevalence increased from 1.4% in 2016 to 2.3% in 2018, translating to approximately 3 500 000 adults in 2016 and 5 800 000 adults in 2018. The group of 18- to 24-year-olds had the highest prevalence of sole use each year (Figure, C). Trends in e-cigarette use in the 50 states and 3 territories included in the Behavioral Risk Factor Surveillance System were heterogeneous but showed generally similar trends; trend analysis in the 33 states with complete data were consistent with the overall findings of this study.

Discussion | Findings from this nationally representative sample of US adults, including state-level analysis, show stable e-cigarette use prevalence between 2016 and 2017, followed by a marked increase from 2017 to 2018. We observed a shift toward daily use and sole e-cigarette use, and a significant increase in use among younger adults, especially students.

While our study is the largest analysis to date that assesses the trends in current e-cigarette and sole e-cigarette use in U.S. adults, it has a few limitations. All data were also self-reported, so we cannot exclude some misclassification and information bias. Additionally, social desirability and recall bias may have led to underreporting of e-cigarette use and cigarette smoking status.

Previous studies report a strong association between exposure to e-cigarette marketing and its subsequent use. We speculate that increased e-cigarette advertisement expenditure over the years and increased social media presence correlates with increased e-cigarette use, especially in the youngest age group. The significant increase in daily e-cigarette use suggests that more users are becoming dependent on e-
Table. Characteristics and Trends of e-Cigarette Use Prevalence Among Adults in the US, 2016-2018

<table>
<thead>
<tr>
<th>Variable</th>
<th>2016 Weighted % (95% CI)</th>
<th>2017 Weighted % (95% CI)</th>
<th>2018 Weighted % (95% CI)</th>
<th>2016 vs 2017 (95% CI)</th>
<th>2017 vs 2018 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall current e-cigarette use</td>
<td>4.5 (4.4 to 4.6)</td>
<td>4.4 (4.3 to 4.5)</td>
<td>5.4 (5.2 to 5.6)</td>
<td>−0.1 (−0.3 to 0.1)</td>
<td>1.0 (0.8 to 1.3)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.6 (5.3 to 5.8)</td>
<td>5.4 (5.2 to 5.7)</td>
<td>6.9 (6.5 to 7.2)</td>
<td>−0.1 (−0.4 to 0.2)</td>
<td>1.4 (1.0 to 1.9)</td>
</tr>
<tr>
<td>Female</td>
<td>3.5 (3.4 to 3.7)</td>
<td>3.4 (3.2 to 3.6)</td>
<td>4.1 (3.9 to 4.4)</td>
<td>−0.1 (−0.3 to 0.1)</td>
<td>0.7 (0.4 to 1.0)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>9.2 (8.7 to 9.8)</td>
<td>10.0 (9.4 to 10.7)</td>
<td>15.0 (14.0 to 16.1)</td>
<td>0.8 (−0.1 to 1.7)</td>
<td>5.0 (3.8 to 6.2)</td>
</tr>
<tr>
<td>25-29</td>
<td>7.5 (6.9 to 8.1)</td>
<td>7.2 (6.7 to 7.9)</td>
<td>9.7 (8.8 to 10.7)</td>
<td>−0.2 (−1.0 to 0.6)</td>
<td>2.5 (1.3 to 3.6)</td>
</tr>
<tr>
<td>30-34</td>
<td>5.7 (5.3 to 6.2)</td>
<td>5.9 (5.4 to 6.4)</td>
<td>8.1 (7.2 to 9.1)</td>
<td>0.2 (−0.5 to 0.9)</td>
<td>2.2 (1.1 to 3.3)</td>
</tr>
<tr>
<td>35-39</td>
<td>5.2 (4.8 to 5.7)</td>
<td>5.1 (4.7 to 5.6)</td>
<td>7.4 (6.6 to 8.4)</td>
<td>−0.1 (−0.8 to 0.6)</td>
<td>2.3 (1.3 to 3.4)</td>
</tr>
<tr>
<td>40-44</td>
<td>4.6 (4.1 to 5.2)</td>
<td>4.4 (3.9 to 5.0)</td>
<td>4.5 (4.0 to 5.1)</td>
<td>−0.2 (−1.0 to 0.6)</td>
<td>0.1 (−0.7 to 0.9)</td>
</tr>
<tr>
<td>45-49</td>
<td>4.4 (3.9 to 5.0)</td>
<td>3.5 (3.1 to 3.9)</td>
<td>4.6 (3.9 to 5.3)</td>
<td>−0.9 (−1.6 to −0.3)</td>
<td>1.1 (0.3 to 1.9)</td>
</tr>
<tr>
<td>50-54</td>
<td>3.9 (3.5 to 4.3)</td>
<td>3.6 (3.2 to 3.9)</td>
<td>3.7 (3.2 to 4.3)</td>
<td>−0.3 (−0.9 to 0.3)</td>
<td>0.1 (−0.5 to 0.8)</td>
</tr>
<tr>
<td>55-59</td>
<td>3.5 (3.2 to 3.9)</td>
<td>3.0 (2.7 to 3.4)</td>
<td>3.0 (2.7 to 3.3)</td>
<td>−0.5 (−1.0 to 0.03)</td>
<td>−0.1 (−0.5 to 0.4)</td>
</tr>
<tr>
<td>≥60</td>
<td>1.5 (1.4 to 1.6)</td>
<td>1.4 (1.3 to 1.5)</td>
<td>1.4 (1.3 to 1.6)</td>
<td>−0.1 (−0.4 to 0.3)</td>
<td>−0.2 (−0.7 to 0.3)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>5.1 (4.9 to 5.2)</td>
<td>5.0 (4.8 to 5.2)</td>
<td>5.8 (5.6 to 6.1)</td>
<td>−0.1 (−0.3 to 0.1)</td>
<td>0.9 (0.6 to 1.1)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>3.4 (3.1 to 3.8)</td>
<td>3.2 (2.8 to 3.6)</td>
<td>3.7 (3.2 to 4.2)</td>
<td>−0.2 (−0.8 to 0.3)</td>
<td>0.5 (−0.2 to 1.1)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.9 (2.6 to 3.3)</td>
<td>2.9 (2.6 to 3.3)</td>
<td>4.9 (4.2 to 5.7)</td>
<td>0.0 (−0.4 to 0.5)</td>
<td>1.9 (1.1 to 2.7)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>4.8 (4.4 to 5.3)</td>
<td>4.6 (4.2 to 5.0)</td>
<td>5.4 (4.8 to 6.1)</td>
<td>−0.2 (−0.8 to 0.4)</td>
<td>0.8 (0.1 to 1.6)</td>
</tr>
<tr>
<td>High school and some college</td>
<td>5.5 (5.3 to 5.7)</td>
<td>5.5 (5.3 to 5.7)</td>
<td>6.6 (6.3 to 6.9)</td>
<td>−0.03 (−0.3 to 0.3)</td>
<td>1.1 (0.8 to 1.5)</td>
</tr>
<tr>
<td>College graduate</td>
<td>2.2 (2.1 to 2.3)</td>
<td>2.0 (1.9 to 2.1)</td>
<td>2.8 (2.6 to 3.0)</td>
<td>−0.2 (−0.3 to 0.0)</td>
<td>0.8 (0.6 to 1.1)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>4.9 (4.8 to 5.1)</td>
<td>4.7 (4.6 to 4.9)</td>
<td>6.1 (5.8 to 6.4)</td>
<td>−0.3 (−0.5 to 0.1)</td>
<td>1.4 (1.0 to 1.7)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>5.6 (5.3 to 6.0)</td>
<td>5.5 (5.2 to 5.9)</td>
<td>5.9 (5.4 to 6.4)</td>
<td>−0.1 (−0.5 to 0.3)</td>
<td>0.4 (−0.2 to 1.0)</td>
</tr>
<tr>
<td>Student</td>
<td>6.3 (5.6 to 7.0)</td>
<td>7.2 (6.4 to 8.0)</td>
<td>12.0 (10.6 to 13.6)</td>
<td>0.9 (−0.2 to 1.9)</td>
<td>4.8 (3.1 to 6.5)</td>
</tr>
<tr>
<td>Retired</td>
<td>1.4 (1.3 to 1.5)</td>
<td>1.3 (1.2 to 1.4)</td>
<td>1.4 (1.2 to 1.7)</td>
<td>−0.1 (−0.3 to 0.0)</td>
<td>0.1 (−0.1 to 0.4)</td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below poverty line</td>
<td>5.4 (5.0 to 5.8)</td>
<td>5.3 (4.9 to 5.8)</td>
<td>6.9 (6.3 to 7.5)</td>
<td>−0.1 (−0.7 to 0.5)</td>
<td>1.5 (0.8 to 2.3)</td>
</tr>
<tr>
<td>Within 100%-200% above poverty line</td>
<td>5.2 (5.0 to 5.5)</td>
<td>4.6 (4.3 to 4.9)</td>
<td>6.1 (5.6 to 6.6)</td>
<td>−0.7 (−1.1 to −0.2)</td>
<td>1.5 (0.9 to 2.1)</td>
</tr>
<tr>
<td>&gt;200% above poverty line</td>
<td>4.0 (3.8 to 4.2)</td>
<td>3.8 (3.6 to 4.0)</td>
<td>5.0 (4.7 to 5.2)</td>
<td>−0.2 (0.4 to 0.0)</td>
<td>1.2 (0.9 to 1.5)</td>
</tr>
<tr>
<td>Metropolitan area</td>
<td>2.8 (2.6 to 3.1)</td>
<td>2.4 (2.1 to 2.7)</td>
<td>2.4 (2.0 to 2.8)</td>
<td>−0.4 (−0.8 to −0.1)</td>
<td>0.0 (−0.4 to 0.5)</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Weighted % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016</td>
</tr>
<tr>
<td>Same county as center city</td>
<td>2.7 (2.4 to 3.0)</td>
</tr>
<tr>
<td>Suburban county</td>
<td>3.0 (2.6 to 3.3)</td>
</tr>
<tr>
<td>Outside metropolitan area</td>
<td>3.5 (3.1 to 4.0)</td>
</tr>
<tr>
<td>Combustible cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.4 (1.3 to 1.5)</td>
</tr>
<tr>
<td>Former</td>
<td>5.3 (5.0 to 5.6)</td>
</tr>
<tr>
<td>Current</td>
<td>14.7 (14.1 to 15.2)</td>
</tr>
<tr>
<td>Use of other tobacco products&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.3 (4.2 to 4.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>9.4 (8.5 to 10.4)</td>
</tr>
<tr>
<td>Heavy alcohol use</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.2 (4.1 to 4.3)</td>
</tr>
<tr>
<td>Yes</td>
<td>8.6 (7.9 to 9.3)</td>
</tr>
<tr>
<td>Marijuana use</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.9 (3.7 to 4.2)</td>
</tr>
<tr>
<td>Yes</td>
<td>16.2 (14.4 to 18.2)</td>
</tr>
<tr>
<td>Binge drinking</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.7 (3.5 to 3.8)</td>
</tr>
<tr>
<td>Yes</td>
<td>8.6 (8.2 to 9.1)</td>
</tr>
<tr>
<td>Cardiovascular disease&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.7 (4.6 to 4.8)</td>
</tr>
<tr>
<td>Yes</td>
<td>7.1 (6.0 to 8.3)</td>
</tr>
<tr>
<td>Cancer&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.8 (4.6 to 4.9)</td>
</tr>
<tr>
<td>Yes</td>
<td>6.5 (5.6 to 7.5)</td>
</tr>
<tr>
<td>Asthma&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.5 (4.4 to 4.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>6.7 (6.2 to 7.2)</td>
</tr>
<tr>
<td>COPD&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.5 (4.4 to 4.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>10.2 (9.2 to 11.2)</td>
</tr>
<tr>
<td>Diabetes&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.8 (4.7 to 5.0)</td>
</tr>
<tr>
<td>Prediabetes</td>
<td>5.0 (3.8 to 6.4)</td>
</tr>
<tr>
<td>Yes</td>
<td>5.0 (4.4 to 5.7)</td>
</tr>
<tr>
<td>Chronic kidney disease&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4.8 (4.6 to 4.9)</td>
</tr>
<tr>
<td>Yes</td>
<td>6.5 (5.3 to 8.0)</td>
</tr>
<tr>
<td>Depression&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.9 (3.8 to 4.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>9.1 (8.7 to 9.5)</td>
</tr>
</tbody>
</table>

Abbreviation: COPD, chronic obstructive pulmonary disease.

<sup>a</sup> Defined as current use of chewing tobacco, snuff, or snus every day or some days.

<sup>b</sup> Defined as history of myocardial infarction, stroke, angina, or coronary heart disease.

<sup>c</sup> Age standardized estimates are shown.
cigarettes rather than merely experimenting with them. This is concerning among younger adults because early use of e-cigarettes has been associated with subsequent cigarette smoking, as well as drug and alcohol use. The increase in e-cigarette use among individuals exhibiting other health-risk behaviors, particularly marijuana use, is concerning especially in light of the outbreak of e-cigarette, or vaping, product use–associated lung injuries that has been linked to the vaping of tetrahydrocannabinoids.

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Author Contributions: Dr Obisesan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Figure. e-Cigarette Use Among Adults in the Behavioral Risk Factor Surveillance System, 2016 to 2018

A Current use
B Daily use
C Current e-cigarette use prevalence among never smokers

Concept and design: Obisesan, Osei, Uddin, Dzaye, Mirbolouk, Blaha. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Obisesan, Osei, Uddin, Dzaye, Mirbolouk. Critical revision of the manuscript for important intellectual content: Obisesan, Osei, Uddin, Dzaye, Stokes, Blaha. Statistical analysis: All authors. Obtained funding: Dzaye, Blaha. Administrative, technical, or material support: Osei, Blaha. Supervision: Uddin, Dzaye, Mirbolouk, Blaha.

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Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the US Food and Drug Administration, or the American Heart Association.

Characteristics and Strength of Evidence of COVID-19 Studies Registered on ClinicalTrials.gov

The coronavirus disease 2019 (COVID-19) pandemic has led to a massive activation of clinical research. The methodological strength of these studies is not well characterized but has implications for the quality of evidence produced. We evaluated the characteristics and expected strength of evidence of COVID-19 studies registered on ClinicalTrials.gov.

Methods | For this cross-sectional analysis, we searched ClinicalTrials.gov on May 19, 2020, using the terms COVID-19, SARS-CoV-2, 2019-nCov, 2019 novel coronavirus, and severe acute respiratory syndrome coronavirus 2 and extracted all structured data fields.1 We excluded withdrawn, suspended, terminated, or expanded-access studies. We categorized reported outcomes and graded studies using the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) level of evidence framework.2 A single reviewer (K.P.) verified studies for inclusion and removed duplicates, and 2 reviewers (A.C.P. and M.P.T.) audited results. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Results | We identified 1551 studies registered from March 1, 2011, to May 19, 2020, meeting inclusion criteria: 911 (58.7%) interventional (including 664 randomized clinical trials [RCTs]) and 640 (41.3%) observational studies (Table); 1180 (76.1%) were single center. Frequently reported primary and secondary outcomes include mortality (526 [33.9%]), ventilation requirement (413 [26.6%]), and treatment complications (359 [23.1%]). Of the 1551 studies, 451 (29.1%) could potentially yield OCEBM level 2 evidence, or the highest level of individual study evidence.2

Across 664 RCTs, the primary outcome most frequently pertained to clinical course (323 [48.6%]); 51 (7.7%) had a primary outcome of mortality, and 42 (6.3%) had a composite end point including mortality (Figure). Blinding (required for OCEBM level 2 evidence) was reported for 364 RCTs, of which 195 (29.3%) were placebo-controlled, 238 (35.8%) planned enrollment of more than 100 participants, and 113 (17.0%) reported at least 2 study centers or sites. Only 75 RCTs (11.3%) were placebo-controlled and blinded with at least 2 study centers (60 with enrollment >100 participants; 24 with >500 participants). Most RCTs evaluated drugs and biologic compounds (486 [73.2%]); 155 (23.3%), hydroxychloroquine or chloroquine; 7 (1.1%), remdesivir; 48 (7.2%), other antivirals; 21 (3.2%), tocilizumab; and 20 (3.0%), corticosteroids.

Of the 640 observational studies, 517 (80.8%) were single center and 123 (19.2%) were multicenter, 36 of which had 10 or more centers. Eighty-seven studies (13.6%) were prospective cohort studies that could yield level 2 evidence.

Discussion | Although a few large multicenter trials may generate high-quality evidence, the large proportion of studies with an expected low level of evidence is concerning. Rapid dissemination of studies with low-quality evidence studies can influence public opinion, government actions, and clinical practice in potentially harmful ways,3 especially with a rising tide of COVID-19 study dissemination via preprint or other strategies ahead of peer review.

A number of measures can mitigate these issues. Preprint results could be accompanied by transparent data sharing.