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## State-Level Temporal Trends in Smokeless Tobacco and Cigarette Use Among U.S. Adults



Smokeless tobacco (SLT) is a term used to describe noncombustible forms

of tobacco products, and includes loose leaf, plug, twist, snus, or snuff. SLT use has been linked with an increased risk for cancers and cardiovascular and cerebrovascular diseases. Recent estimates have shown that SLT use has been on the rise. Data from the Centre for Disease Control has shown that between 2000 and 2015, the consumption of combustible forms of tobacco decreased by 38.7%, whereas that of SLT increased by 23.1% in the United States.<sup>1</sup> However, the regional variations in the use of cigarettes and SLT, which may be affected by state-specific policies as well as regional differences in perceptions of these products is not well studied. We therefore evaluated the state-level temporal trends from 2016 to 2018 in the prevalence of SLT and cigarette use using data from the nationally administered and self-reported Behavioral Risk Factor Surveillance System survey. SLT use was defined as use of chewing tobacco, snus, or snuff every day or on some days. Current cigarette use was defined as use on some days or every day. We first ascertained current cigarette use and current SLT use for respondents from each US state in 2016 and in 2018. Relative change in SLT or cigarette use was then calculated as: (prevalence in 2018 - prevalence in 2016)/prevalence in 2016, and plotted using heat maps. We also classified states based on SLT use as low prevalence (below median prevalence in 2016) and high prevalence (above median prevalence in 2016) and reported their relative change in 2018.

There were 909,754 survey respondents in total. The overall prevalence of current SLT use was 3.62% in 2016 and 3.58% in 2018 whereas that of current cigarette use was 16.33% in 2016 and 15.53% in 2018. Overall, a relative decrease was observed for cigarette use, median (interquartile range) -4.5% (-9.1%, -0.7%), and SLT, -1.5% (-9.6%, 14.7%) between 2016 and 2018. Twenty-five states (47.2%) reported concomitant decrease in SLT and cigarette use, whereas, 19 states (35.8%) showed a relative increase in SLT use despite a decrease in cigarette

use. Five states (9.4%) reported a concomitant increase in SLT and cigarette use while 4 states (7.5%) demonstrated a relative increase in cigarette use despite a decrease in SLT use (Figure 1).

Further, 52% (14/27) states with low prevalence of SLT use in 2016 (i.e., below median prevalence of 4.0%) showed a relative increase in SLT use in 2018, whereas 38% (10/26) states with high prevalence of SLT use in 2016 showed a relative increase in SLT use in 2018.

There has been a steady decline in the overall prevalence of cigarette smoking in the United States in the last two decades, mostly owing to the widespread implementation of public health campaigns and legal measures.<sup>1</sup> At the same time, the use of SLT has shown a heterogeneous trend, with an increase in use in certain demographics and a decrease in others, with limited data available for recent years. Our study highlights that while the trends for SLT use may not be too impressive when viewed on a national level, there exists significant geographical variation in terms of its public health burden. The prevalence and increase of SLT use, while seemingly small actually translates to millions of U.S. adults who use SLT. The aggressive marketing of SLT products as a safer alternative and as a means to quit smoking, its affordability, ease of use of SLT in smoke-free zones, and rising cigarette bans are other avenues that are often stressed upon by SLT advertisements, and that has driven a number of seasoned smokers to switch to SLT or in some cases become dual users.

These trends provide actionable information to public health professionals in these states and pave the way for federal and the state-level policy making to regulate the marketing and the use of SLT.

## Disclosures

The authors have no conflicts of interest to declare.

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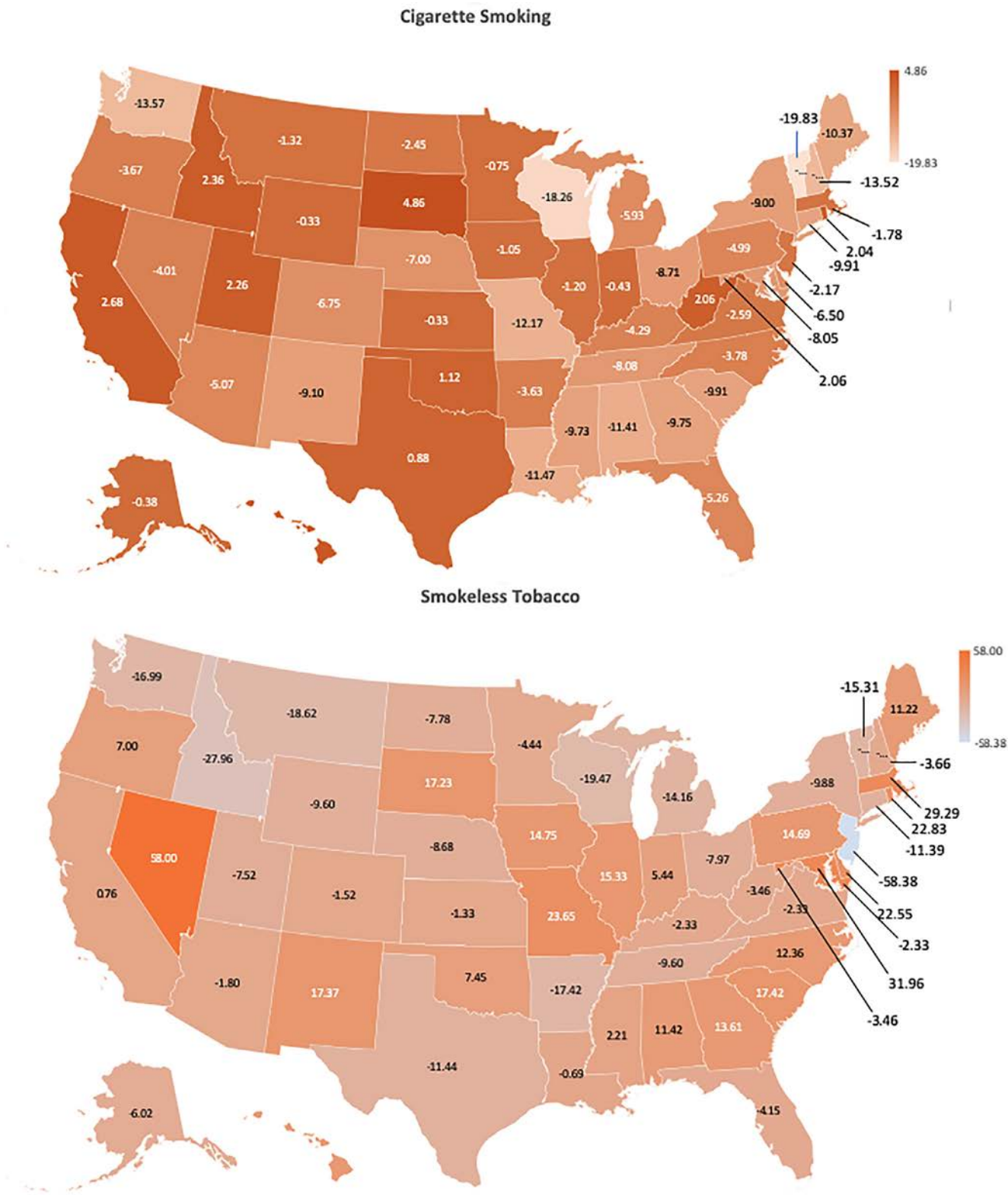


Figure 1. Heat maps demonstrate the relative change in the prevalence of cigarette smoking (above) and smokeless tobacco use (below) across the United States between 2016 and 2018.

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However, due to the lack of prospective randomized data, the choice and duration of OAC remain unclear.

We performed a systematic search of online databases PubMed, Embase, Cochrane Central Register of Controlled Trials and Scopus until 31 August 2020 for studies comparing non-vitamin K OAC (NOAC) to vitamin K antagonists (VKA) for the treatment of patients with LVT. We used an advanced search strategy utilizing the terms ([VKA] OR [Warfarin]) AND ([direct OAC] OR [novel OAC] OR [non-VKA OAC]) AND ([LVT] OR [left ventricular thrombi]). Two reviewers (YG and NS) independently performed the search and literature screen, with disputes resolved by consensus following discussion with a third author (MF). We included studies that met all of the following inclusion criteria: (1) all studies comparing NOAC to VKA in patients with LVT, and (2) reporting clinical outcomes that included embolic events, and if available, bleeding events and/or documented LVT resolution. We excluded individual case reports or series or studies not reporting on the clinical outcomes of interest.

The study primary outcome was the occurrence of embolic events. Secondary outcomes were the occurrence of LVT resolution and bleeding events, including major and minor bleeding.

Pooled odds ratios (OR) with 95% confidence interval (CI) were estimated for binary variables using a random-effects model by the method of DerSimonian and Laird. Heterogeneity between individual studies was explored by  $X^2$  statistic and characterized with  $I^2$  statistic. Meta-regression analysis was performed to examine the log transformed OR of embolic events or LVT resolution on OAC and the study reported percentage of ischemic cardiomyopathy. All analyses were performed using RevMan Version 5.4.0 software and Stata version 15.1.

Our initial search yielded a total of 277 potential studies, of which 15 studies were retrieved and screened for eligibility (Figure 1). Of these, 3 studies were excluded as only single-arm studies,<sup>3–5</sup> 1 study did not distinguish between the type of OAC used<sup>6</sup> and the last study only reported echocardiographic findings.<sup>7</sup> The remaining 10 studies were included and they

adopted the retrospective observational design.<sup>8–17</sup> Table 1 shows the breakdown of reported baseline characteristics of each study. A total of 2,103 patients were included in the analysis with 524 on NOAC and 1,579 patients on VKA, namely warfarin. All 10 studies reported the primary outcome of the occurrence of embolic events.

There was no significant difference in the occurrence of embolic events between patients taking NOAC and warfarin (9.7% vs 11.2%, OR 0.9; 95% CI 0.58 to 1.4,  $p = 0.65$ ) (Figure 2). Eight studies reported the incidence of LVT resolution and bleeding. There was no significant difference in the occurrence of LVT resolution between NOAC and warfarin treated patients (69.6% vs 74.4%, OR 1.02; 95% CI 0.56 to 1.86,  $p = 0.96$ ) (Figure 3). Similarly, there was no significant difference in all bleeding events between patients taking NOAC and those taking warfarin (9.3% vs 8.9% OR 0.93; 95% CI 0.55 to 1.56,  $p = 0.77$ ) (Figure 4A). Furthermore, there was no significant difference in major bleeding (4.4% vs 6.2%, OR 0.86; 95% CI 0.22 to 3.4,  $p = 0.83$ ) (Figure 4B) or minor bleeding events (1.5% vs 2.2%, OR 0.62; 95% CI 0.25 to 1.51,  $p = 0.29$ ) between the 2 groups (Figure 4C). Regression analyses showed no relationship between the etiology of LVT and either the occurrence of embolic events ( $p = 0.13$ ) or LVT resolution with OAC ( $p = 0.23$ ).

This systematic review and meta-analysis of 10 observational studies demonstrates no significant difference between patients treated with NOAC or warfarin for LVT with respect to the occurrence of embolic events over a median follow up of 12 months. Moreover, there was no difference in rate of LVT resolution or bleeding complications between patients treated with NOAC or warfarin (Figure 5). Furthermore, there was no difference between patients with ischemic and nonischemic etiology of LVT in terms of the efficacy or safety between the 2 OAC approaches. In the absence of randomized studies, our meta-analysis therefore lends support to the use of NOAC in the treatment of LVT.

In the current meta-analysis, an embolic rate of 10.8% was documented with OAC, whereas historical papers from the 1990s report embolic event rates of around 11% in

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## Non-Vitamin K Antagonist Oral Anticoagulants Versus Warfarin for Patients With Left Ventricular Thrombus: A Systematic Review and Meta-Analysis



Left ventricular thrombus (LVT) formation is a recognized complication in patients with left ventricular dysfunction, especially following acute myocardial infarction, but may also occur in patients with nonischemic cardiomyopathy.

The importance of LVT is that it is frequently associated with systemic embolism, which can be life-threatening. A meta-analysis of observational studies demonstrated that patients with mural thrombus exhibit an increased risk of embolic events when compared to patients without (11% vs 2%).<sup>1</sup> Treatment with systemic anticoagulation reduces embolic event rates by 33% compared to untreated patients.<sup>1</sup> This has led to the international recommendations for the treatment of LVT with oral anticoagulation (OAC).<sup>2</sup>

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