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Modeling the Effects of E-Cigarettes on Smoking Behavior: Implications for Future Adult Smoking Prevalence

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Abstract

Background—Electronic cigarette (e-cigarette) use has increased rapidly in recent years. Given the unknown effects of e-cigarette use on cigarette smoking behaviors, e-cigarette regulation has become the subject of considerable controversy. In the absence of longitudinal data documenting the long-term effects of e-cigarette use on smoking behavior and population smoking outcomes, computational models can guide future empirical research and provide insights into the possible effects of e-cigarette use on smoking prevalence over time.

Methods—Agent-based model examining hypothetical scenarios of e-cigarette use by smoking status and e-cigarette effects on smoking initiation and smoking cessation.

Results—If e-cigarettes increase individual-level smoking cessation probabilities by 20%, the model estimates a 6% reduction in smoking prevalence by 2060 compared to baseline model (no effects) outcomes. In contrast, e-cigarette use prevalence among never smokers would have to rise dramatically from current estimates, with e-cigarettes increasing smoking initiation by more than 200% relative to baseline model estimates in order to achieve a corresponding 6% increase in smoking prevalence by 2060.

Conclusions—Based on current knowledge of the patterns of e-cigarette use by smoking status and the heavy concentration of e-cigarette use among current smokers, the simulated effects of e-cigarettes on smoking cessation generate substantially larger changes to smoking prevalence relative to their effects on smoking initiation.

INTRODUCTION

Electronic cigarette (e-cigarette) use has increased substantially in recent years, from 1.0% of U.S. adults reporting ever using e-cigarettes in 2009 to 13% in 2013.^{1,2} The prevalence of current e-cigarette use among U.S. adults has also grown from 0.3% in 2010 to 6.8% in 2013.¹ To date, almost all research examining e-cigarette use by smoking status has shown that current smokers are more likely to currently use, initiate use of, and experiment with e-

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cigarettes.²⁻⁶ While the majority of current e-cigarette users are also current cigarette smokers, nearly a third are former or never smokers.^{1,7} The rapid increase in e-cigarette use is of growing concern to public health authorities as e-cigarettes are being marketed as smoking cessation aids and safe alternatives to traditional cigarettes⁸, without consistent scientific evidence supporting these claims. Some experts believe that e-cigarettes have the potential to reduce the toll of cigarette smoking on population health,⁹ while others are concerned that e-cigarettes may weaken tobacco control efforts by renormalizing smoking behavior and serving as a gateway for cigarette smoking initiation among young adults.¹⁰

While public health surveillance efforts continue to monitor rates of e-cigarette trial and experimentation, particularly among youth¹¹, longitudinal data evaluating the long-term effects of continued or current e-cigarette use on traditional cigarette smoking cessation or initiation in youth and adult populations are not yet available. Two small randomized controlled studies, both lasting less than two years, suggest that e-cigarette use among cigarette smokers increases smoking cessation relative to placebo e-cigarettes, with efficacy comparable to other cessation aids.^{12,13} Conversely, one recent longitudinal study found an association between ever use of e-cigarettes and initiation of cigarette smoking among high school students in Los Angeles, suggesting that gateway effects may indeed exist.¹⁴ However, most evidence of e-cigarette initiation and cessation relies on self-reported smoking behaviors and convenience samples with known limitations.^{2,15}

In the absence of robust, longitudinal empirical data, computational models can support decision-making by investigating a range of possible outcomes under different scenarios.¹⁶ Agent-based models (ABMs) have the unique benefit of generating population-level outcomes from aggregated individual-level behaviors. These models have been used to explore complex social dynamics and health behaviors where feedbacks between individuals (e.g., in cessation and initiation behaviors of traditional tobacco and alternative products) generate complex interactive landscapes that affect relevant health outcomes.¹⁷⁻²⁰ A recent Institute of Medicine (IOM) report highlighted the value of simulation models when there is need for regulatory policy on public health issues for which existing empirical data are insufficient.²¹ An ABM approach is particularly amenable to questions of smoking and e-cigarette use given the potential for behavioral feedback dynamics to occur as individuals experiment with new products. In particular, the likelihood of e-cigarette initiation differs by individual characteristics such as smoking status and propensity to try e-cigarettes as they become more popular, which can drive changes to e-cigarette use prevalence and incidence at the population level. Positive feedback mechanisms over time and trait heterogeneity are difficult to capture using traditional statistical methods and population-level compartmental models, which are subject to exponentially increasing programming complexity problems as more individual-level traits are included.^{21,22}

In this study, we develop a computational model of traditional cigarette smoking (smoking) and e-cigarette use to examine how different levels of e-cigarette effects on adult smoking behaviors (i.e., smoking initiation and cessation) generates changes to population-level smoking patterns under a range of hypothetical scenarios. In particular, we simulate the potential population-level outcomes generated from individual-level e-cigarette use under the following scenarios: 1) e-cigarettes inhibit smoking cessation; 2) e-cigarettes support

smoking cessation; 3) e-cigarettes encourage smoking initiation; and 4) e-cigarettes discourage smoking initiation. We do not simulate the health risks of e-cigarette use independent of their effects on cigarette smoking, though some early studies have characterized such potential risks.^{23,24} The objective of this study is to identify a range of relative changes to population-level smoking prevalence generated by varying e-cigarette effects on smoking behavior.

METHODS

Model Overview

We developed an agent-based model (ABM) that simulates cigarette smoking as well as e-cigarette use. ABMs provide flexibility and modularity for model development, enabling us to apply a range of magnitudes and directions of e-cigarette effects on smoking behavior according to smoking status at the individual level. Additionally, the modularity of this approach can be readily extended to include other alternative tobacco products (e.g., chewing tobacco and snuff), an eventual future research objective. We used data from the National Health Interview (NHIS)²⁵, the U.S. Census²⁶, the CDC^{11,27}, the Cancer Intervention and Surveillance Modeling Network (CISNET)^{28,29}, in addition to epidemiological, clinical, and modeling studies.^{1,2,7,30–32} This model simulates a population of U.S. adults, aged 18 to 85, and their smoking and e-cigarette use status starting in the year 1997 and ending in 2070. The model has four binary (yes/no) nicotine-use states: 1) exclusive e-cigarette user (e-cigarette user), 2) exclusive cigarette smoker (smoker), 3) dual user of both e-cigarettes and cigarettes (dual user), and 4) never user of either product (never user). A model diagram illustrating all possible nicotine use states and transitions is available as supplementary material (eFigure 1). Individuals' smoking status affects their transitions between nicotine-use states and their probability of death each year. Reflecting our input data sources, we define current e-cigarette use in this model as any individual using e-cigarettes every day or some days. We define current smoking as having smoked at least 100 cigarettes in one's lifetime and currently smoking every day or some days.

Model Assumptions

Our model assumes that e-cigarette use status emulates smoking status, with transitions from never user to current user, to former user. Age-specific smoking cessation rates in our model are based on CISNET estimates, which assume that individuals have quit for at least two years with no relapse. We assume no relapse back to e-cigarette use once an individual quits e-cigarette use. Individuals in our model do not initiate smoking after age 30, consistent with evidence showing almost no smoking initiation beyond that age.³³ We also assume no e-cigarette initiation beyond age 30, given dramatically higher rates of e-cigarette initiation and current use among young adults (age < 25) compared to older adults.^{1,2,34} This assumption places a conservative bound on the magnitude of decline to population-level smoking prevalence due to positive e-cigarette effects on smoking cessation. The annual probability of quitting e-cigarettes is set to 0.026, reflecting annual population smoking cessation rate estimates in 2009.³⁵ Consistent with observed patterns of e-cigarette use, never and former smokers in this model are 15 and 6 times less likely than current smokers, respectively, to initiate e-cigarette use, which closely approximates data on reported e-

cigarette prevalence.^{1,7} Finally, this study focuses on the impact of e-cigarettes on estimated adult smoking prevalence, so we assume no further negative health effects due to e-cigarette use independent of their effects on cigarette smoking behavior.

Model Description

At each time step, every simulated person ages by one year and either stays in the current nicotine-use state, moves to a different state (e.g., a never smoker starting to smoke), or dies. Movement between nicotine-use states are probabilistic and determined by a combination of: individual age, empirical data on the risk of transition from one state to another (e.g., the annual probability that a 22 year-old non-smoker, current e-cigarette user, initiates smoking), and model parameters representing e-cigarette effects. Every year, new 18 year-olds enter the population through a “birth rate” that reflects the 1997 birth rate as reported by the CDC.²⁷ In order to account for early youth initiation of e-cigarettes,^{1,11} approximately 14% of 18 year-olds enter the population as current e-cigarette users, regardless of smoking status, beginning in 2009. Table 1 presents a subset of model parameter descriptions used in this article. In this model, the scenario that generates the lowest smoking prevalence would simulate a 200% increase in smoking cessation rates with a 100% decrease to smoking initiation due to e-cigarettes (i.e., 3 times greater cessation and no smoking initiation). In contrast, the scenario that would generate the highest smoking prevalence would simulate a 100% decrease in smoking cessation rates with a 200% increase in smoking initiation (i.e., no smoking cessation and 3 times greater smoking initiation). Please refer to the supplementary material of this manuscript for a complete model description (eSection 3.1–3.4), pseudo-code (eSection 5.2), as well as a list of all model parameters, equations, and citations for the assumptions and rules governing the model (eTable 1 and eTable 2).

Model Calibration

To achieve baseline estimates of future smoking prevalence, we calibrated a “smoking only model” to historical and projected smoking estimates in the U.S. using data from NHIS and CISNET.^{28,29} For the years 1997–2013, smoking prevalence estimates from this model were within the 95% confidence intervals for smoking prevalence as reported by NHIS for all years except in 2002 (eTable 3). Next, in order to calibrate e-cigarette use prevalence by smoking status to the current literature, we incorporated e-cigarettes in a “baseline” model. The baseline model simulates e-cigarette initiation and cessation using a time-based sigmoidal function representing the rapid uptake of e-cigarettes in the population and eventual plateau due to saturation, analogous to the diffusion of innovations theory often used in systems science research.³⁶ Using this sigmoid function, the e-cigarette initiation rate among current smokers is low in 2009, two years after the first introduction of e-cigarettes into the U.S. market, and when empirical research of e-cigarette use first begins to emerge.³⁷ This initiation rate then grows exponentially until 2016, when the initiation rate plateaus to a maximum level that is then held constant until the end of our simulations in 2070 (the timing and level of the plateau are tunable model parameters). The baseline model assumes no e-cigarette effects on smoking behavior to serve as a platform for experiments examining the independent e-cigarette effects on smoking prevalence. Please refer to the supplementary material for full calibration outcomes (eTable 3), discussion of these outcomes (eSection 4.1), detailed parameter descriptions and values (eTable 2 and eTable 1),

and additional information about the sigmoidal function referenced in this section (eFigure 3 and eSection 3.1).

E-cigarette Effects on Smoking Initiation and Cessation

After establishing the baseline model, we performed experiments allowing e-cigarette use to alter the rate of smoking initiation, smoking cessation, or both in order to assess the outcomes of the potential harm-inducing and harm-reducing effects of e-cigarettes. While holding the parameters that determine e-cigarette use prevalence by smoking status constant, we modify e-cigarette effects on smoking initiation and cessation with increases of 0% to 200%, or decreases of 0% to 100%, relative to baseline (i.e., no effect) rates. E-cigarette use effects below 100% result in decreases to annual baseline estimates of smoking initiation and cessation, while e-cigarette effects above 100% result in increases to annual baseline estimates of smoking initiation and cessation. For example, with an e-cigarette cessation effect of 200%, a 30-year-old smoker would increase their annual probability of quitting traditional cigarettes from a baseline of 0.026²⁸ to 0.078. Table 1 shows parameter descriptions and a range of values that this model explored.

Sensitivity Analyses

To assess the robustness of our results and to examine unexpected changes to the model resulting from the interaction of parameters, we performed sensitivity analyses parameters governing the operationalization of our model assumptions. Sensitivity analyses were conducted on the following parameters in scenarios with and without e-cigarettes to identify any potential interaction abnormalities: 1) maximum age at e-cigarette initiation, 2) rate which e-cigarette initiation rates increase over time, 3) maximum probability of e-cigarette initiation, 4) amount of time from e-cigarette introduction to maximum e-cigarette initiation, and 5) smoking cessation rates by birth cohort.

RESULTS

E-Cigarette Prevalence by Smoking Status Projections at Baseline

Figure 1 shows projected population e-cigarette prevalence by smoking status from 2010 to 2070 using the baseline smoking model (i.e., e-cigarettes have no effect on smoking initiation or cessation), which is fit to match past and present data, projected into the future.^{25,30} E-cigarette use outcomes from 2010–2014 are fit to existing e-cigarette use literature by smoking status,^{1,7} whereas future projections of e-cigarette use are based on the e-cigarette initiation and cessation parameters generated from the process of model fitting and the assumptions described previously. For all groups, e-cigarette prevalence increases steadily over time except among current smokers whose e-cigarette use prevalence plateaus. Rising population e-cigarette prevalence in the baseline model is primarily driven by current smokers in earlier years and then by former and never smokers in later years. While the majority of e-cigarette users remain former and current smokers, the baseline model also projects a continued rise in e-cigarette use prevalence among never smokers.

Exploring E-Cigarette Effects

Figure 2 shows smoking prevalence outcomes resulting from seven hypothetical scenarios of e-cigarette effects on smoking behavior, assuming e-cigarette use patterns described in Figure 1. This includes the baseline scenario that assumes no e-cigarette effects on smoking behavior and hypothetical scenarios of e-cigarette effects to the baseline scenario. A 20% decrease in smoking cessation due to the introduction of e-cigarette use (i.e., addiction-sustaining effects), increases smoking prevalence in 2060 by approximately 7.5% compared to baseline smoking prevalence estimates, bringing smoking prevalence from an initial baseline projection of 13.4% to 14.4%. In the case that e-cigarettes increase smoking initiation by 20% (i.e., addiction inducing “gateway” effects), smoking prevalence would increase by 0.8% in 2060 compared to baseline (13.4% to 13.5%). Under the assumption that e-cigarettes aid smoking cessation, a 20% increase in smoking cessation due to e-cigarettes generates a 6% reduction in smoking prevalence compared to the baseline scenario (13.4% to 12.6%). In contrast, e-cigarettes would have to increase smoking initiation by over 200% in the absence of any effect on smoking cessation in order to generate a 6% increase to baseline smoking prevalence. Overall, we observe that e-cigarette effects on smoking cessation, by either increasing or decreasing cessation, generate substantially larger changes to population-level smoking prevalence by 2070 than e-cigarette effects on smoking initiation in this model.

Figure 3 shows smoking prevalence projections in 2030 and 2060 relative to baseline model outcomes under varying e-cigarette effects on smoking cessation (horizontal dimension) and smoking initiation (vertical dimension). Values above 1.0 (i.e., 100%) are increases to smoking prevalence relative to the baseline scenario, and values below 1.0 are reductions to smoking prevalence relative to baseline. The baseline scenario estimates 14.3% and 13.4% smoking prevalence for the years 2030 and 2060, respectively. There is an absence of major variation according to e-cigarette effects on smoking initiation (along the vertical axis), suggesting that population smoking prevalence is driven primarily by e-cigarette effects on smoking cessation. For instance, if e-cigarettes increase both smoking initiation and cessation by 50%, we estimate smoking prevalence to be approximately 90% of baseline estimates in 2060. That is, despite equal effects on smoking initiation and cessation, e-cigarettes would generate lower smoking prevalence in 2060. If e-cigarettes increase smoking cessation by 100% (i.e. double the likelihood of cessation), assuming baseline smoking initiation values, the smoking prevalence would reduce by 23% relative to baseline. A similar change in e-cigarettes effects on smoking initiation (i.e. they increase smoking initiation by 100%) increases baseline smoking prevalence by 1.03 times, or 3%, when assuming baseline cessation values. The figure also shows greater variation in smoking prevalence in 2060 than in 2030. These patterns emerge because e-cigarette prevalence among never smokers, current smokers, and former smokers changes over time, resulting in changes to the size of exposure groups (i.e., those who are e-cigarette users). Additionally, projected smoking prevalence declines from 2030 to 2060, thus modifying the relative share of the population that are eligible to quit smoking (smokers) and start smoking (never smokers).

Figure 4 shows smoking prevalence in 2060 relative to baseline scenario by prevalence of e-cigarette use among never smokers (y-axis) and e-cigarette cessation effects (x-axis). The panels assume 10%, 50%, 100%, and 200% increases to individual smoking initiation rates due to e-cigarette use (i.e. addiction inducing “gateway” effects). Assuming e-cigarette exposure increases the likelihood of smoking initiation, the changing color gradient in the vertical dimension for Figures 4A–4D shows that projected smoking prevalence is higher relative to baseline with increasing e-cigarette use among never smokers. The panels illustrate that unless e-cigarettes increase smoking initiation by more than 100% (i.e., 2 times baseline smoking initiation), they have almost no noticeable effect on smoking prevalence, even if e-cigarettes prevalence reaches 60% in never smokers. In the case that e-cigarettes increase initiation rates by 200% (Figure 4D), approximately 50% of never-smokers would need to use e-cigarettes in order to increase smoking prevalence by 15% compared to baseline. In this same scenario, if e-cigarette use prevalence is less than 20% among never smokers, smoking prevalence increases by approximately 4%–6% relative to baseline regardless of the smoking cessation effects of e-cigarettes. E-cigarette effects on smoking cessation (horizontal gradient) become more noticeable in this extreme scenario at higher levels of e-cigarette use prevalence in never smokers, suggesting a feedback between smoking initiation and smoking cessation effects of e-cigarettes, where e-cigarettes can lead to smoking initiation first, and then also to higher rates of smoking cessation.

Sensitivity Analyses

Results from sensitivity analyses across a range of parameters and parameter values suggest that our model assumptions do not substantially change our main results. The largest variation in smoking prevalence outcomes due to e-cigarettes occur when using birth cohorts earlier than the one used in the baseline model (1970). These cohorts were observed to have much lower rates of smoking cessation²⁹, and thus generated smoking prevalence trends much higher than current and future predictions.^{30,33,38} The sensitivity analyses performed generate similar (relative) results to those presented above when exploring a range of values for parameters governing the maximum age at e-cigarette initiation, rates of adoption of e-cigarettes, the period over which e-cigarette adoption occurs, and the amount of time from e-cigarette introduction to maximum e-cigarette initiation. Additional discussion of these analyses and their results are available in the supplementary material (eFigures 4–10).

DISCUSSION

Under a variety of hypothetical scenarios of the possible effects of e-cigarettes on smoking behavior, our model shows that smoking prevalence is far more sensitive to e-cigarette effects on smoking cessation than on smoking initiation. Additionally, given current values of population smoking initiation and cessation and the relative prevalence of e-cigarette use between never, current and former smokers, if e-cigarettes induce smoking in never smokers, even small increases in smoking cessation due to e-cigarettes would counteract the potential negative impact on overall population smoking prevalence. Finally, if e-cigarettes decrease smoking cessation by allowing current smokers to continue smoking, population smoking prevalence could increase considerably.

The results from our model are largely due to three main factors: First, we assumed relatively high rates of e-cigarette initiation among current smokers compared to never smokers in light of current evidence from the literature.^{1,7} Accordingly, there are more smokers than never smokers using e-cigarettes in the simulated population, which means that there are more smokers susceptible to benefit from potential smoking cessation effects of e-cigarettes compared to the number of never smokers that could be affected by their potential effects on smoking initiation. Second, declining smoking initiation rates in the baseline scenario^{3,21,28} generate small effect outcomes of e-cigarettes on smoking initiation rates among never smokers. That is, we multiply e-cigarette effects in the model by the underlying smoking initiation and cessation rates (e.g. 1.5 times initiation rate). Given declining smoking initiation rates, even a 200% increase in smoking initiation results in relatively small absolute changes to annual age-specific smoking initiation probabilities. Third, smoking prevalence is more sensitive in the short-term to changing smoking cessation rates because there are greater time delays between an increase in smoking initiation rates and their eventual impact on the number of smokers in the population. Thus, our analyses suggest that e-cigarettes would have to act as an extremely effective gateway to cigarette smoking in order to increase smoking prevalence substantially, and never smokers would have to use e-cigarettes much more than the current evidence suggests.

Results from our model reveal complex feedbacks that occur when investigating e-cigarette effects on smoking behavior. If e-cigarettes undermine smoking cessation efforts, our results suggest that we may experience a substantial increase in smoking prevalence as more never smokers use e-cigarettes, regardless of e-cigarette effects on smoking initiation. That is, if these never smokers eventually become smokers, they would be less likely to quit smoking due to their e-cigarette use, thus raising population smoking prevalence. However, in the event that e-cigarettes both increase smoking initiation and smoking cessation, the effects on smoking initiation would have to be extremely large (i.e., increase over 200%) in order to offset even small cessation effects on smoking (Figures 4A–4D).

The conclusions of this study should be considered with several limitations in mind. First, our results and interpretation emphasize the general patterns produced by the model, and not the actual values, due to the challenges of quantifying e-cigarette effects, and uncertainty surrounding the sparse longitudinal data that currently exist. In particular, values presented in this paper are outcomes relative to our baseline model and represent model- and parameter-specific relative estimates. Therefore, these results serve only as an educated guess of the potential impact of e-cigarettes on future adult smoking prevalence. Second, our model used a variety of data sources that provide estimates of e-cigarette initiation and cessation values that can range widely across various reports and are challenging to measure accurately. Third, our model does not explore any potential direct and independent health effects of e-cigarette use. Fourth, our results are largely dependent on the low and decreasing smoking initiation rate in the U.S. Our outcomes are not applicable to countries or settings with relatively high, stable, or increasing smoking prevalence. Finally, we made simplifying assumptions about e-cigarette use behavior and smoking behavior in order to account for high variability in the e-cigarette data, and improve interpretability of our model and its outcomes. While these assumptions do not meaningfully change our primary conclusions, as

demonstrated in our sensitivity analyses, future work should continue to explore and refine these assumptions as further data become available.

Our study contributes to a growing literature that examines systems-level feedbacks and interactions relevant to smoking behavior that could not otherwise be explored using conventional statistical modeling research methods.^{25,28–30} In light of the recent IOM report specifically emphasizing the utility of ABMs for decision-making related to tobacco policies,²¹ this model may be of interest to those considering how simultaneous e-cigarettes and alternative tobacco product effects for individuals might translate into broader changes to population cigarette smoking patterns. These study results can also provide useful insights given the uncertain regulatory environment surrounding e-cigarettes. The U.S. Food and Drug Administration (FDA) previously proposed a rule extending its regulatory authority over additional tobacco products including e-cigarettes.³⁹ The agency applies the “Public Health Standard” in developing regulations for new products like e-cigarettes, which considers a product’s risks and benefits to the population as a whole, in addition to the individual user.⁴⁰ In exploring the possible net effects of e-cigarettes on the population by simulating such risks and benefits with respect to smoking status, this model can provide useful information for future tobacco regulation. However in order to precisely determine the eventual net impact of e-cigarettes on smoking prevalence, researchers must continue to empirically evaluate the effects of e-cigarettes on smoking initiation and cessation. Robust longitudinal¹⁴ studies that assess the consequences of e-cigarette use for smoking behaviors remain paramount. As these data become available, modeling can serve as a framework to assess the potential impact of e-cigarettes under varying scenarios of use prevalence and their effects on smoking patterns. Given the potential for e-cigarettes to sustain addiction by promoting dual use with cigarettes, the continued pattern of high e-cigarette use among current smokers remains a major public health concern. In this particular instance, we find that under current patterns of e-cigarette use by smoking status and a range of hypothesized e-cigarette effects on smoking behavior, it is unlikely that the potential “gateway” effects of e-cigarettes will substantially increase smoking prevalence, unless they also reduce smoking cessation rates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Mcmillen RC, Gottlieb MA, Shaefer RM, Winickoff JP, Klein JD. Trends in Electronic Cigarette Use Among U.S. Adults : Use is Increasing in Both Smokers and Nonsmokers. 2015; 17(10):1195–1202.
2. Pepper JK, Brewer NT. Electronic nicotine delivery system (electronic cigarette) awareness, use, reactions and beliefs: a systematic review. *Tob Control*. 2013; 23(5):375–384. [PubMed: 24259045]
3. Hughes K, Bellis MA, Hardcastle KA, et al. Associations between e-cigarette access and smoking and drinking behaviours in teenagers. *BMC Public Health*. 2015; 15:244. [PubMed: 25886064]
4. Grana R, Benowitz N, Glantz SA. E-cigarettes: A scientific review. *Circulation*. 2014; 129(19):1972–1986. [PubMed: 24821826]
5. Delnevo CD, Giovenco DP, Steinberg MB, et al. Patterns of Electronic Cigarette Use Among Adults in the United States. *Nicotine Tob Res*. 2015 [E-pub ahead of publication].
6. Brose LS, Hitchman SC, Brown J, West R, McNeill A. Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up. *Addiction*. 2015; 110(7):1160–1168. [PubMed: 25900312]
7. Zhu SH, Gamst A, Lee M, et al. The Use and Perception of Electronic Cigarettes and Snus among the U.S. Population. *PLoS One*. 2013; 8(10):e79332. [PubMed: 24250756]
8. Cobb NK, Brookover J, Cobb CO. Forensic analysis of online marketing for electronic nicotine delivery systems. *Tob Control*. 2015; 24(2)
9. Abrams D. Promise and Peril of E-Cigarettes: Can Disruptive Technology Make Cigarettes Obsolete? *JAMA*. 2014; 311(2):135–136. [PubMed: 24399548]
10. Dutra LM, Glantz SA. Electronic Cigarettes and Conventional Cigarette Use Among US Adolescents: A Cross-Sectional Study. *JAMA Pediatr*. 2014; 168(7):610–617. [PubMed: 24604023]
11. Centers for Disease Control and Prevention. Tobacco Use Among Middle and High School Students -- United States 2013. *Morb Mortal Wkly Rep*. 2014; 63(45):1021–1026.
12. Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. *Lancet*. 2013; 382(9905):1629–1637. [PubMed: 24029165]
13. Caponnetto P, Campagna D, Cibella F, et al. Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as Tobacco Cigarettes Substitute: A Prospective 12-Month Randomized Control Design Study. *PLoS One*. 2014; 9(1):e66317.
14. Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence. *JAMA*. 2015; 314(7):700–707. [PubMed: 26284721]
15. McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P. Electronic cigarettes for smoking cessation and reduction. *Cochrane Database Syst Rev*. 2014; 12
16. Cerdá M, Tracy M, Ahern J, Galea S. Addressing population health and health inequalities: The role of fundamental causes. *Am J Public Health*. 2014; 104(S4):S609–S619. [PubMed: 25100428]
17. Chao D, Hashimoto H, Kondo N. Dynamic impact of social stratification and social influence on smoking prevalence by gender: An agent-based model. *Soc Sci Med*. 2015; 147:280–287. [PubMed: 26610078]
18. Resnicow K, Page SE. Embracing chaos and complexity: A quantum change for public health. *Am J Public Health*. 2008; 98(8):1382–1389. [PubMed: 18556599]
19. Auchincloss AH, Riolo RL, Brown DG, Diez Roux A. An Agent-Based Model of Income Inequalities in Diet in the Context of Residential Segregation. *Am J Prev Med*. 2013; 40(3):303–311. [PubMed: 21335261]
20. Diez Roux A. Complex systems thinking and current impasses in health disparities research. *Am J Public Health*. 2011; 101(9):1627–1634. [PubMed: 21778505]
21. IOM (Institute of Medicine). *Assessing the Use of Agent-Based Models for Tobacco Regulation*. Washington, DC: The National Academies Press; 2015.

22. Siebert U, Alagoz O, Bayoumi AM, Jahn B. State-Transition Modeling : A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3. *Value Health*. 2012; 15(6):812–820. [PubMed: 22999130]
23. Kim JW, Baum CR. Liquid Nicotine Toxicity. *Pediatr Emer Care*. 2015; 31(7):517–521.
24. Lerner CA, Sundar IK, Yao H, et al. Vapors Produced by Electronic Cigarettes and E-Juices with Flavorings Induce Toxicity, Oxidative Stress, and Inflammatory Response in Lung Epithelial Cells and in Mouse Lung. *PLoS One*. 2015; 10(2):e0116732. [PubMed: 25658421]
25. National Center for Health Statistics. National Health Interview Survey 1997–2013. 1997. <http://www.cdc.gov/nchs/nhis.htm>
26. U.S. Census Bureau. Profiles of General Demographic Characteristics (1997–2010). 2010. <http://www.census.gov/data.html>
27. Centers for Disease Control and Prevention. Table 1-1, “Live Births, Birth-Rates, and Fertility Rates, by Race: United States, 1909–2000”. 2005. <http://www.cdc.gov/nchs/data/statab/t001x01.pdf>
28. Holford TR, Meza R, Warner KE, et al. Tobacco control and the reduction in smoking-related premature deaths in the United States, 1964–2012. *JAMA*. 2014; 311(2):164–171. [PubMed: 24399555]
29. Holford TR, Levy DT, McKay LA, et al. Patterns of birth cohort-specific smoking histories, 1965–2009. *Am J Prev Med*. 2014; 46(2):e31–e37. [PubMed: 24439359]
30. Vugrin ED, Rostron BL, Verzi SJ, et al. Modeling the Potential Effects of New Tobacco Products and Policies: A Dynamic Population Model for Multiple Product Use and Harm. *PLoS One*. 2015; 10(3):e0121008. [PubMed: 25815840]
31. Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet*. 2013; 382(9905):1629–1637. [PubMed: 24029165]
32. Sanders-Jackson AN, Tan AS, Bigman CA, Henriksen L. Knowledge About E-Cigarette Constituents and Regulation: Results From a National Survey of U.S. Young Adults. *Nicotine Tob Res*. 2014; 17(10):1247–1254. [PubMed: 25542915]
33. United States Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress A Report of the Surgeon General. 2014
34. Durta L, Glantz S. Electronic Cigarettes and Conventional Cigarette use Among US Adolescents. *JAMA Pediatr*. 2014; 168(7)
35. Pizacani BA, Maher JE, Rohde K, Drach L, Stark MJ. Implementation of a smoke-free policy in subsidized multiunit housing: Effects on smoking cessation and secondhand smoke exposure. *Nicotine Tob Res*. 2012; 14(9):1027–1034. [PubMed: 22318686]
36. Sterman, JD. S-Shaped Growth: Epidemics, Innovation Diffusion, and the Growth of New Products. In: Sterman, JD., editor. *Business Dynamics: Systems Thinking and Modeling for a Complex World*. Boston, MA: Irwin McGraw-Hill; 2000. p. 294-349.
37. Noel JK, Rees VW, Connolly GN. Electronic cigarettes: a new “tobacco” industry? *Tob Control*. 2011; 20(1):81. [PubMed: 20930060]
38. Mendez D, Warner KE, Courant PN. Has smoking cessation ceased? Expected trends in the prevalence of smoking in the United States. *Am J Epidemiol*. 1998; 148(3):249–258. [PubMed: 9690361]
39. U.S. Department of Health and Human Services. Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products. Food and Drug Administration. 2014
40. P.L. 111-31. Family Smoking Prevention and Tobacco Control Act. 2009 Section 906(d).

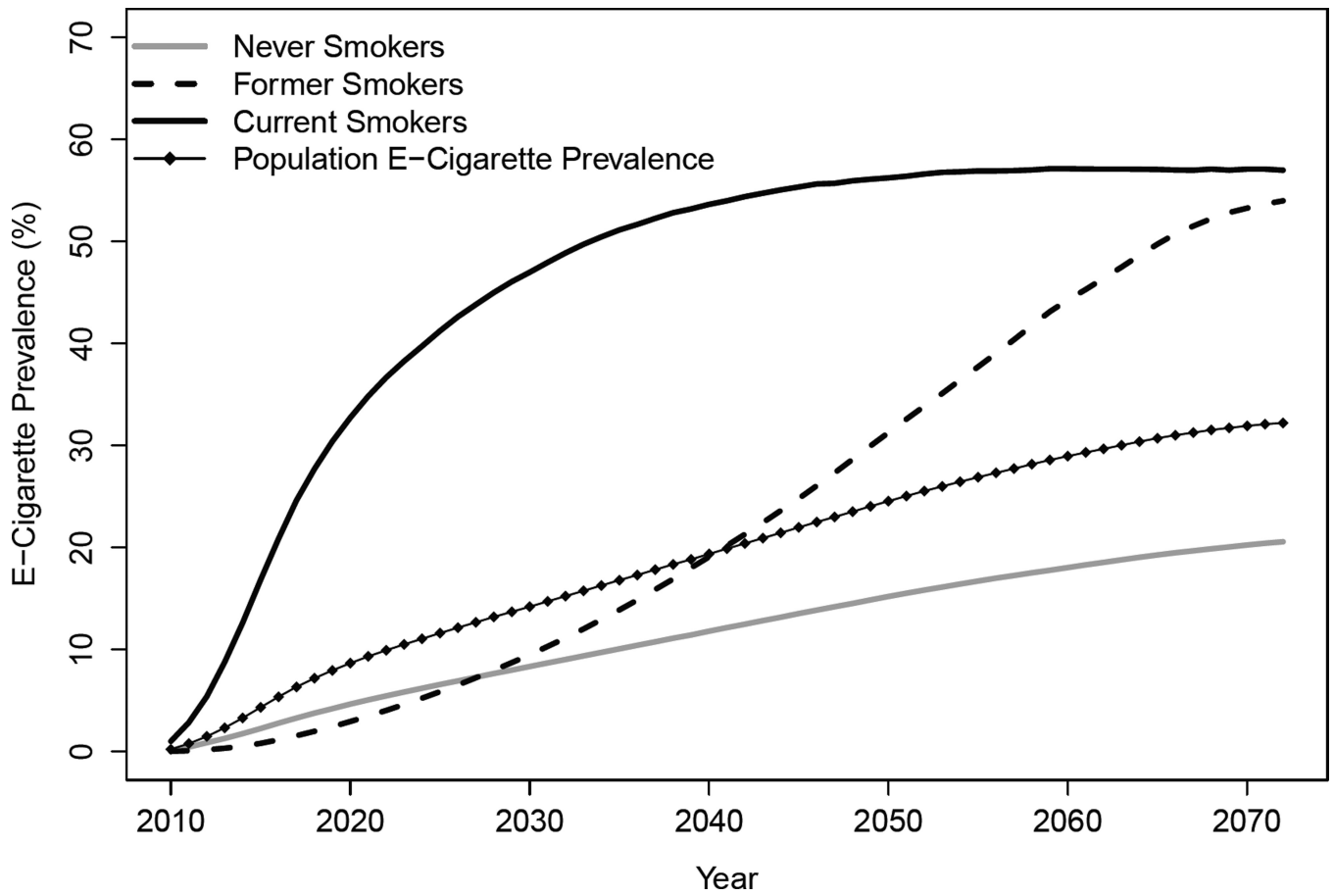


Figure 2. E-cigarette use prevalence by smoking status (extended baseline model). Includes e-cigarette initiation and cessation, with no e-cigarette effects on smoking.

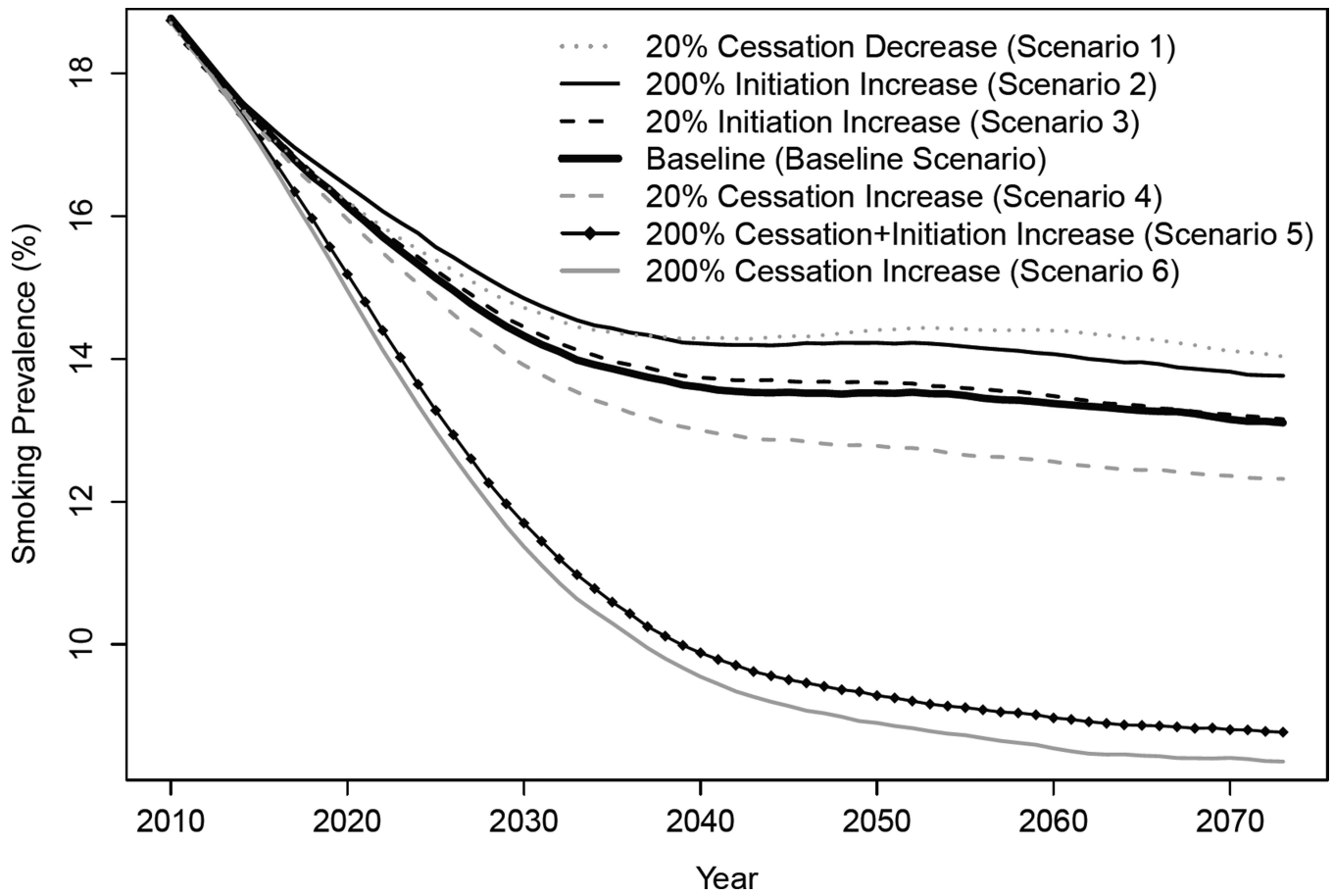


Figure 3. Baseline smoking projections and select model scenarios of e-cigarette effects on smoking, 2010 to 2070.

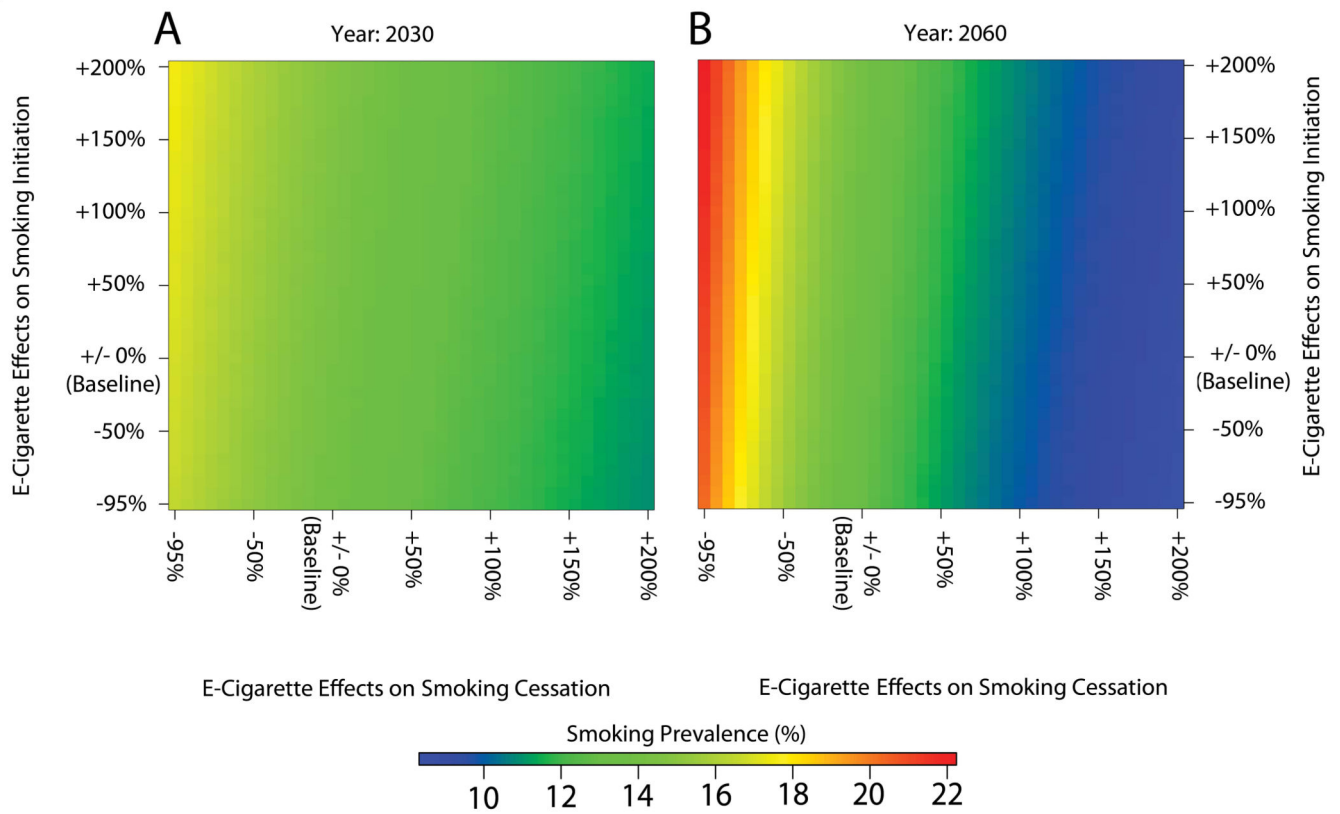


Figure 3. Smoking prevalence projections relative to baseline prevalence by e-cigarette effects on smoking initiation and cessation, 2030 and 2060.

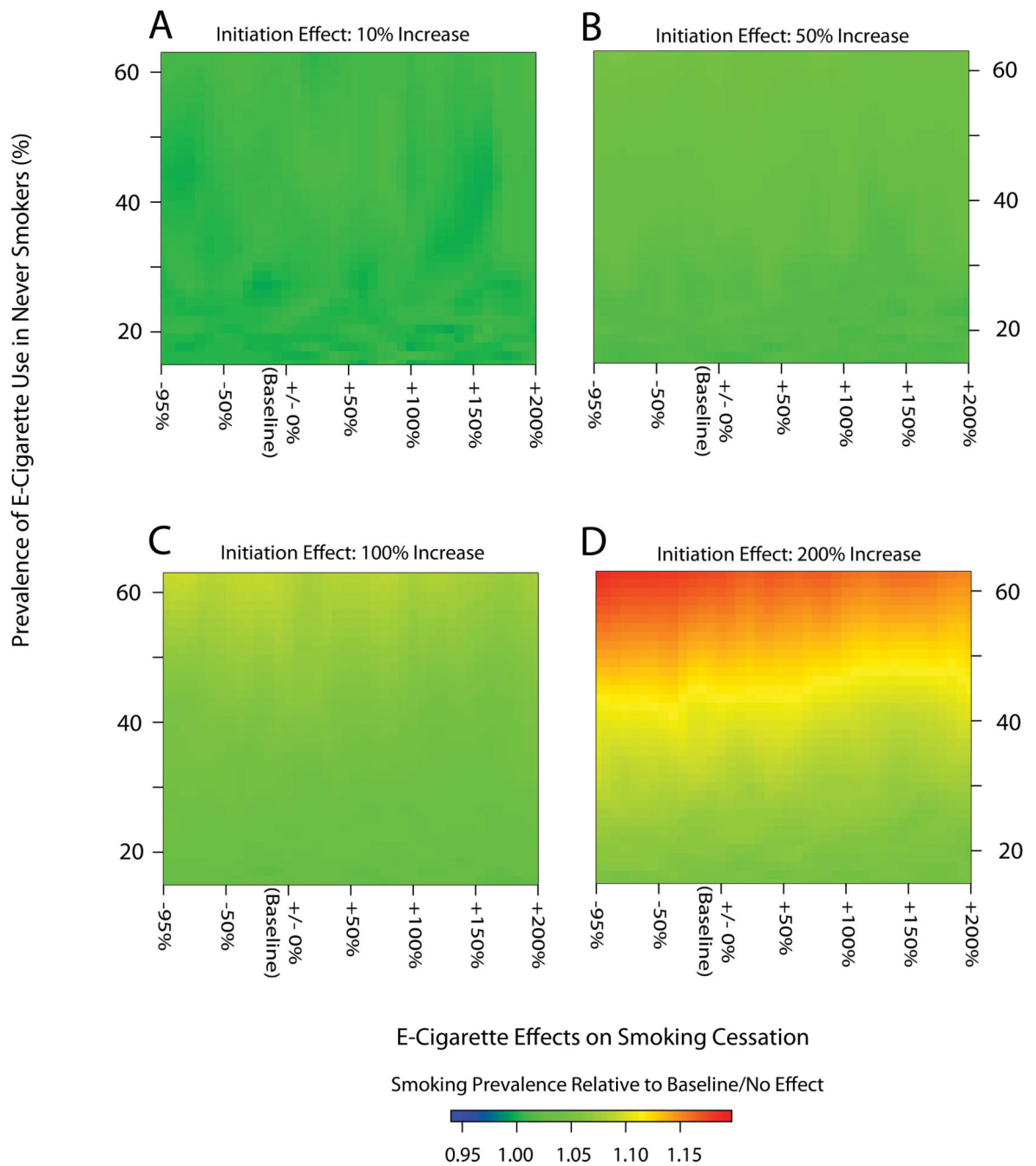


Figure 4. Smoking prevalence projections relative to baseline prevalence by e-cigarette prevalence among never smokers and effects on smoking cessation, 2060. Panels A–D show relative changes to smoking prevalence assuming e-cigarettes increase smoking initiation rates by 10%, 50%, 100%, and 200%.

Table 1

Subset of primary model parameters and descriptions.

Parameters [†]	Description
Smoking Cessation Rate	Yearly age-specific smoking cessation rates [1997–2070] ²⁸
Smoking Initiation Rate	Yearly age-specific smoking initiation rates [1997–2070]
E-Cigarette Smoking Cessation Effect [*]	E-cigarette effect on smoking cessation [–100% to 200%]. Effects represent the percentage change relative to baseline, where values less than 0 are decreases in smoking cessation rates (e.g. –50% effect is equal to a reduction of the baseline smoking cessation rate by half); values greater than 0 are increases in smoking cessation rates (e.g. 200% effect is equivalent to 3× the baseline cessation rate)
E-Cigarette Smoking Initiation Effect [*]	E-cigarette effect on smoking initiation [–100% to 200%]. Effects represent the percentage change relative to baseline, where values less than 0 are decreases in smoking initiation rates (e.g., –50% effect is equal to a reduction of the baseline smoking initiation rate by half); values greater than 0 are increases in smoking initiation rates (e.g., 200% effect is equivalent to 3× the baseline initiation rate)
E-Cigarette Initiation Sigmoid Function	E-cigarette initiation rate is derived from a time-based sigmoidal function to mimic the rapid uptake of e-cigarettes with growing use (theory of innovations)
E-cigarette Quit Rate	Rate at which e-cigarette users quit using e-cigarettes
Maximum Age of E-Cigarette Initiation	Maximum age that an individual can initiate e-cigarette use
Maximum Age of Cigarette Initiation	Maximum age that an individual can initiate traditional smoking behavior ³³
Death Rate	Death rates based on smoking status (i.e., relative risk of mortality among former smokers, never smokers, and current smokers)

[†]All parameter descriptions, citations, and parameter values can be found in the supplementary material

^{*}Experimental parameters

Evidence and assumptions derived from a combination of recent peer-reviewed studies