SUPPLEMENTARY MATERIAL

eSection 1. Summary of the Supplementary Material

1.1 Content Overview

This supplementary material is divided into five sections: 1) Summary of the supplementary material; 2) Modeling methodology; 3) Model parameterization; 4) Model Outcomes; and 5) Programming. Section 1 describes the purpose of the supplementary material and provides an overview of its content. Section 2 discusses the use of agent-based modeling (ABM) in our study and how the potential effects of e-cigarettes on smoking behavior present a research problem amenable to an ABM approach. Section 3 details the parameters used to operationalize mortality, smoking initiation, smoking cessation, e-cigarette initiation, e-cigarette cessation, and other processes in the model. Section 4 describes model outcomes, specifically as they relate to validating model output against empirical data, and discusses the results of our sensitivity analyses. Section 5 presents model pseudo code, and additional notes about programming the model. This supplementary content is referenced in the main text of the manuscript with the appropriate numbered header for each subsection.

1.2 Purpose

The content provided in this supplementary material was written with three main goals in mind: 1) To provide additional information regarding both the modeling methodology and the validation of the model presented in the main manuscript: "Modeling the Effects of E-Cigarettes on Smoking Behavior: Implications for Future Adult Smoking Prevalence"; 2) To further justify the modeling approach, and detail the specifics of model validation not presented in the main text of the manuscript; and 3) To provide technical programming guidance and model process equations so that readers are able to reproduce the model and its outcomes as they were presented in the manuscript.

eSection 2. Modeling Methodology

2.1 Agent-Based Modeling Approach

Agent-based models (ABMs) have been used across a wide variety of disciplines to understand how macro-level phenomena can be driven by micro-level interactions between individuals and their environment. They are especially well suited for modeling individual-to-individual or individual-to-environment feedback mechanisms and adaptation. Many have emphasized the utility of ABMs in the practice of epidemiology and public health when examining causal inference.[1–4] A recent Institute of Medicine (IOM) report highlighting the value of ABMs in tobacco research concluded that the use of ABMs has not been fully explored in the tobacco regulatory space,[5] despite their more common application in other public health areas (e.g., obesity[6–8] and infectious disease[9]). ABMs differ philosophically and programmatically from traditional compartmental models often used in epidemiological research. Philosophically speaking, ABMs seek to explain outcomes from an individual-level and generative perspective (e.g., feedbacks, adaptations, evolution), while compartmental models explain outcomes from an aggregate (i.e., group) perspective. This leads to differences in computational modeling methods. While ABMs are more amenable to an object-oriented programming approach, where individuals are considered unique objects, compartmental models typically take the form of structured programming approaches (e.g., matrices and arrays).

We chose to use an ABM approach for three reasons:

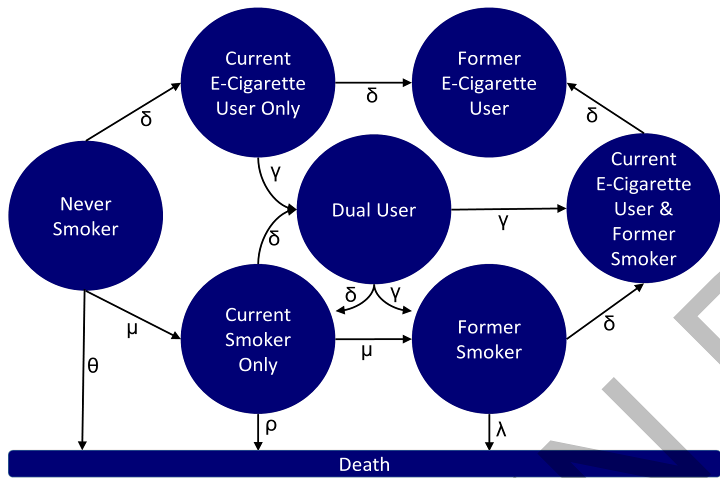
1) The generative and modular nature of this ABM leaves room for further model development examining dynamics at the individual level as more data about e-cigarettes become available. The purpose of this initial model was to demonstrate the variety of possible outcomes dependent upon the effects that e-cigarettes may have on smoking. This model can be extended to incorporate other tobacco products, like smokeless tobacco, in particular snuff and snus, and social network and environmental effects on e-cigarette use;

2) The simplicity of a bottom-up approach from an object-oriented perspective provides greater model clarity and modularity. While a traditional compartmental model would have generated similar results, the structural approach typically used in dynamical systems models would involve programming the set of individual-traits and their various levels of heterogeneity, leading to state explosion.[10] Furthermore, from a practical standpoint, ABMs are an aggregate of N compartmental models operating in parallel, where N represents the number of individuals. Specifically, our agent-specific traits, unique to every individual in our model includes: a) smoking status (former, never, current) b) e-cigarette status (former, never, current), c) dual user (former, current), d) never user of e-cigarettes and cigarettes, e) age (18-85), f) probability of smoking initiation, and g) probability of e-cigarette initiation. The object-oriented programming approach in the backend of the ABM method allows us to store these traits and trait histories to follow an individual's experience trajectory; and

3) Our goal was to explore how individual-level e-cigarette use changes population-level smoking prevalence. Smoking status, probability of smoking initiation, and probability of e-cigarette initiation are either dynamic and/or heterogeneous outcomes/states

across the individuals in our model, a problem well-suited for ABMs. eFigure 1 presents a model overview of all possible nicotine use states in our model, excluding age.

eFigure 1. Model diagram illustrating all possible nicotine use states (i.e., excludes age), transition pathways, and descriptive transition rates between states. Our model assumes that death rates change only by smoking behavior, and not by e-cigarette use (see model assumptions subsection in the methods section of the main text).



μ No E-cigarette effects (rates from data)
γ E-Cigarette use effects (experiments)
δ Model generated rates (validated to data)
θ Never smoker death rate (rates from data)
λ Current smoker death rate (rates from data)
ρ Former smoker death rate (rates from data)

eSection 3. Model Parameterization

Please refer to eTable 1 for detailed parameter explanations.

3.1 E-Cigarette Initiation and Cessation Rate

We assume that the probability of e-cigarette initiation among never, former, and current smokers follows a diffusion of innovations sigmoid function[11] (eFigure 3). This function is additionally described in detail in eTable 1 (i.e., under ecigInitSmoker) and also more broadly in the main paper. Parameters for the slope of the curve (ecigNetSlope), the maximum probability of initiation among smokers (eCigProbMax), years until maximum e-cigarette initiation probability is reached (timeToMaxECigInit), and years until e-cigarettes are introduced in the model (modelBurnIn), are used in by the sigmoid function to generate e-cigarette incidence by smoking status (i.e., never, current, and former smoker). This is done in order to approximate current e-cigarette use by smoking status as reported in recent literature.[12–14]

eFigure 3 shows the e-cigarette initiation sigmoid curve for former, never, and current smoker initiation rates by year using baseline parameter values. After the year 2016, the probability of e-cigarette initiation by smoking status remains constant through the end of the model in 2070. Current smokers have the highest probability of e-cigarette initiation and serve as the reference group for e-cigarette initiation among former smokers and never smokers. For each time point on the sigmoid curve, if an individual is a never smoker, the probability of initiating e-cigarette use for that individual is the e-cigarette initiation rate on the curve divided by the parameter divECigNeverSmoker (equal to 15 in our baseline model). This divisor may be an overestimate given recent data showing never smokers are approximately 30 times less likely to use e-cigarettes than current smokers.[13] Nonetheless, in the context of our results, this assumption is conservative (i.e., allows for larger negative effects of e-cigarettes on smoking initiation relative to baseline). Results from additional sensitivity analyses conducted on these parameters are available upon request. Similarly, current e-cigarette prevalence among former smokers was reported as 6 times less than that of current smokers – if an individual is a former smoker, the probability of initiating e-cigarette use is the e-cigarette initiation rate for smokers, divided by the parameter: divECigFormerSmoker. For simplicity and because of scarce data on e-cigarette cessation patterns, we assumed e-cigarette cessation rates to be similar to traditional smoking cessation rates (e.g., 0.026 at baseline, see eTable1).

3.2 Smoking Cessation and Initiation Rates

We calibrated the model using smoking cessation data from the 1970 birth cohort, the most recent cohort with all of the data available through the Cancer Intervention and Surveillance Modeling Network (CISNET) website.[15] Though we relied on 1970 birth cohort quit rates for the main analysis, we also assess CISNET estimates of age-specific (ages 18-85) smoking cessation rates for those born in the years 1940, 1950, 1960, and 1970, corresponding to the parameter smokeQuitCohort. In particular, 1940 corresponds with smokeQuitCohort = 1, 1950 with smokeQuitCohort = 2, etc. Earlier birth cohorts generally have lower smoking cessation rates, so we performed additional simulations to examine smoking prevalence outcomes resulting from these lower smoking cessation rates as part of our sensitivity analyses. We found that the 1970 cohort had cessation rates that generated smoking prevalence levels for 2013-2070 that most closely resembled available projected adult smoking prevalence data.[16–18] Using cessation rates from birth cohorts earlier than 1970 combined with recent smoking initiation estimates generated higher than expected smoking prevalence values than those reported by NHIS[19] and other studies[16–18]. The lower panels in eFigures 4 – 9 present sensitivity analyses of birth cohort effects on smoking prevalence (i.e., the parameter "smokeQuitCohort").

We used survival analysis (i.e., the cumulative hazard function) to calculate smoking initiation rates based on reported NHIS smoking prevalence among 18-24 year olds from 1997 to 2013. Our calculation assumes that the smoking initiation rate for those ages 0-12 years old is zero. This is consistent with research indicating that smoking uptake can occur as early as age 12, with most initiation occurring by age 18.[20–22] The survival and hazard equations are as follows:

$$S(t) = e^{-H(t)}, \text{ where } H(t) = \int_0^t \lambda(u)du, \text{ and } t \text{ denotes age}$$

$$h(t) = -\frac{S'(t)}{S(t)}$$

We assume a smoking initiation of 0 from age 0 to 12, and a constant rate from that age forward (λ) until age 30, when smoking initiation is disallowed, such that:

$$H(t) = \lambda(t-12)$$

$$S(t) = e^{-\lambda(t-12)}$$

Therefore:

$$\lambda = \frac{-\log\big(S(t)\big)}{t-12}$$

We then performed simple linear regression on these values to project smoking initiation rates into the year 2027 (30 years after model initialization), after which initiation rates remain constant through 2070. These decisions were made to best approximate historical estimates and future projections[15,17,23] of smoking prevalence in the US. eFigure 2 presents the regression line, along with the corresponding slope and intercept values used to project future smoking initiation rates.

3.3 Death and "Birth" Rates

Mortality rates for smokers and former smokers are determined by using reported values of relative risk of death among current (smokerDeathRiskRelative) and former smokers (formerSmokerDeathRiskRelative) compared to never smokers. We used data from the US Census, the Human Mortality Database, and the Lee-Carter method to calculate age- and year- specific death rates among never smokers[24–27]. In order to achieve population equilibrium and to approximate observed prevalence for current and former smoking, we used an annual birth rate of 14.2 per 1,000 persons[28] (i.e., replacement of 18 year olds in the model) and examined a range of values for relative risks of all-cause mortality for current and former smokers. We determined the relative risk for all-cause mortality to be 2.9 for current smokers and 1.5 for former smokers. For example, in our model, a 19 year never smoker in 1998 has a 0.000895 probability of death. For a 19 year old never smoker, this probability of death is 0.0025955.[24] These values are within 95% confidence bounds of all-cause mortality for smokers and former smokers reported by Freedman et al.[29], and Lynch et. al.[30],respectively.

3.4 E-Cigarette Effects

The magnitude of the effect of e-cigarettes on smoking cessation and smoking initiation are driven by parameter values dualUseQuitMultiplier and ecigSmokeInitInc which range from 0.0 to 3.0. These values are multipliers applied to baseline annual probabilities of smoking cessation or initiation. Values above 1 increase smoking initiation or smoking cessation probabilities relative to baseline values. Likewise, values below 1 decrease smoking initiation or smoking cessation probabilities relative to baseline. Baseline probabilities were taken directly from CISNET data by cohort.[31] These values are presented as percentages in the main paper for simplicity (i.e. 100% decrease in value to 200% increase in value). For example, a value of 1 is equivalent no decrease or increase to smoking initiation or cessation, a value of 1.5 is equivalent to a 50% increase to smoking initiation or cessation, and a value of 0.85 is a 15% decrease to smoking initiation or cessation.

eSection 4. Model Outcomes

4.1 Model Validation

Our study objective was to estimate the effects of e-cigarettes on smoking prevalence relative to baseline projections of smoking prevalence in the absence of e-cigarettes. All aspects of this model are approximations of potential effects given the current state of knowledge on smoking and e-cigarette use. We reviewed a range of studies on patterns of e-cigarette use and validated model outcomes against e-cigarette prevalence estimates between 2010 and 2014 (see eTable 3). A large proportion of our estimates fell within 95% confidence intervals reported in one or more studies.[12,13,32,33] eTable 3 provides model generated outcomes compared to data sources available at the time of model creation. The majority of our baseline smoking estimates are within the 95% confidence intervals for NHIS reported smoking prevalence from 1997 to 2013, with the exception of 2002. Our model prevalence estimates for 2002 were slightly lower than that reported by NHIS. We speculate that this lower estimate is primarily due to increases in tobacco product marketing occurring between 2001 and 2002 that this model does not account for. However, our smoking prevalence estimates return to the NHIS 95% confidence interval bounds after 2002. We projected a smoking prevalence of 12.8% by 2070—consistent with an upper level projection of a recent IOM report on raising the minimum age of cigarette smoking[26], and comparable to projected smoking prevalence by 2050 as estimated by Vugrin et. al.[17]

To illustrate the extreme worst- and best-case scenarios of e-cigarette use effects on smoking prevalence, we projected estimates of e-cigarette use prevalence such that baseline estimates of e-cigarette effects (harm-reducing or harm-inducing) are likely overestimates (See Figure 1 in main paper). Pending additional observational data, e-cigarette use may increase beyond the scenario extremes examined in our study, though they may also fall short of our e-cigarette prevalence estimates. Given the possible overestimation of e-cigarette prevalence, we explored how e-cigarette use prevalence could ultimately affect our outcomes (See Figure 4 in the main paper). In addition, we mapped initiation effects of e-cigarettes on smoking behavior against the prevalence of e-cigarette use among never smokers, as presented in the Results section of our main paper.

4.2 Sensitivity Analyses

In eFigures 4 – 9, we show sensitivity analyses for different e-cigarette initiation and cessation effect levels varying the following parameters: maximum age of e-cigarette initiation (ageStopECigInit), years until maximum e-cigarette initiation is reached (timeToMaxECigInit), annual probability of e-cigarette cessation (eCigProbMax), the slope of the sigmoid function for e-cigarette initiation (ecigNetSlope), e-cigarette initiation rate divisor for never smokers relative to current smokers (divECigNeverSmoker), and smoking cessation rates across different birth cohorts (smokeQuitCohort). The colored bar legend represents smoking prevalence, and axes are labeled according to the parameters used within the model (See eTable 1). The largest differences in smoking prevalence are generated by experiments examining age- and year- specific smoking cessation probabilities by birth cohort. This property is discussed further in the main paper. The remaining differences in smoking prevalence generated from the entire set of sensitivity analyses range from a 0.01 to 0.6 absolute difference in smoking prevalence. Due to the comparative nature of the model (i.e., e-cigarette effects on smoking behavior compared to the baseline model), the differences in absolute smoking prevalence from these sensitivity analyses are negligible in the context of our study, and do not affect our conclusions. In short, we are more concerned with the directionality and magnitude of the relative outcomes, and not the absolute differences of these outcomes. In eFigure 10, to better understand the range of outcomes that our model generates resulting from our assumptions, we explore the sensitivity of smoking prevalence in our model at the extreme values of all combinations of the following model parameters (as performed in eFigures 4 – 9): ecigNetSlope, timeToMaxECigInit, eCigProbMax, and their interaction with the maximum age of e-cigarette initiation allowed in the model on the horizontal axis (ageStopECigInit). From this analysis, we find that extreme variations and combinations of our parameters do not change the smoking prevalence values substantially by ageStopECigInit at baseline or when e-cigarettes only increase smoking initiation rates. However, we observe a slight downward trend in smoking prevalence by ageStopECigInit, and greater minimum and maximum smoking prevalence differences when e-cigarettes result in greater smoking cessation rates. The results of this analysis suggest that our baseline model outcomes and results are conservative estimates of the relative advantage of e-cigarette cessation effects over e-cigarette initiation effects. In other words, the downward trend by ageStopECigInit indicates that we would observe even lower smoking prevalence (even at the extreme values of other parameters) than we report in our results when allowing individuals over the age of 30 to initiate e-cigarettes. Although we believe it is likely that older adults over the age of 30 could use e-cigarettes as a smoking cessation aid, the results from this sensitivity analysis indicate that allowing individuals in our model to initiate e-cigarettes after the age of 30 would reinforce our findings of the relative strength of e-cigarette cessation effects compared to e-cigarette initiation effects on smoking behavior.

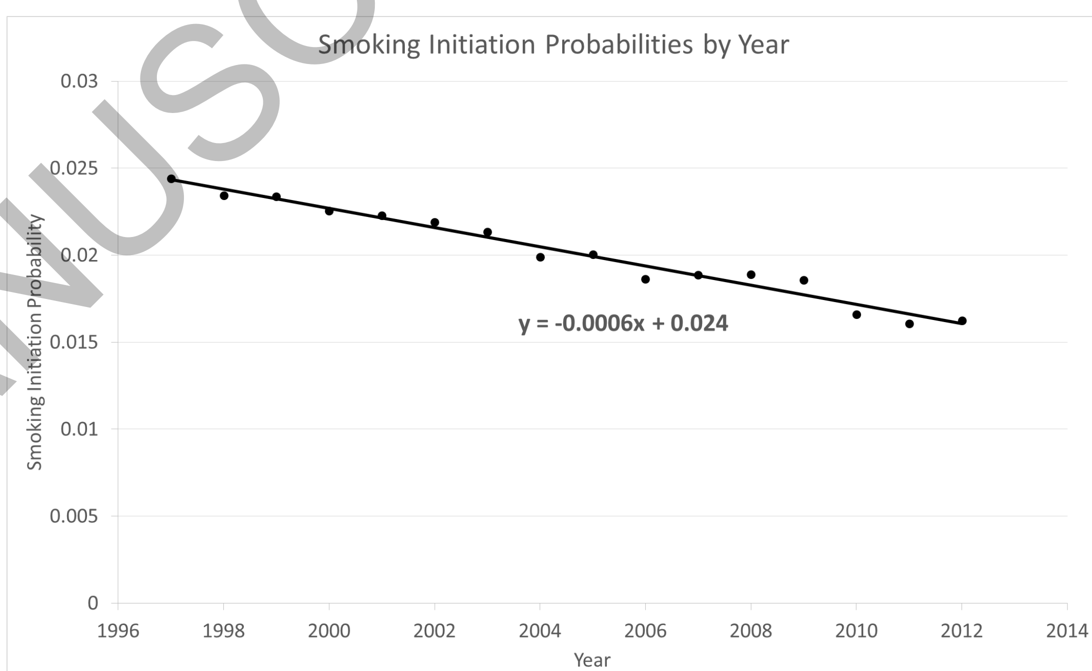
eTable 1 Baseline Model Parameters*

Parameters	Values	Description
ecigNetSlope	0.20	Slope of sigmoid function governing e-cigarette initiation
dualUseQuitMultiplier	1.0	Multiplier applied to baseline smoking quit rates for dual users. While this is set to 1.0 (i.e., no effect) in the baseline model, this is an experimental parameter that takes a range of values. Figure 3, Figure 4, and eSection 4.2 of this supplement provide results for these experiments.
smokerDeathRiskRelative	2.9	Relative risk of mortality for smokers compared to never smokers
formerSmokerDeathRiskRelative	1.5	Relative risk of mortality for former smokers compared to never smokers
eCigProbMax	0.23	Maximum probability of e-cigarette initiation of current smokers
modelBurnIn	12.0	Number of years until e-cigarettes are introduced (1997-2009)
ecigQuitProb	0.026	Annual probability of e-cigarette cessation
ecigSmokeInitInc	1.0	Multiplier on baseline smoking initiation rates among e-cigarette users. While this is set to 1.0 (i.e., no effect) in the baseline model, this is an experimental parameter that takes a range of values. Figure 3, Figure 4, and eSection 4.2 of this supplement provide results for these experiments.
smokeQuitCohort	4.0	CISNET smoking cessation rates based on cohort.† Here, cohort 4.0 is equivalent to the 1970 birth cohort
divECigNeverSmoker	15.0	E-cigarette initiation rate divisor for never smokers
divECigFormerSmoker	6.0	E-cigarette initiation rate divisor for former smokers
timeToMaxECigInit	7.0	Time (in years) to maximum e-cigarette initiation rate after their introduction
ageStopECigInit	30.0	Maximum age of e-cigarette initiation

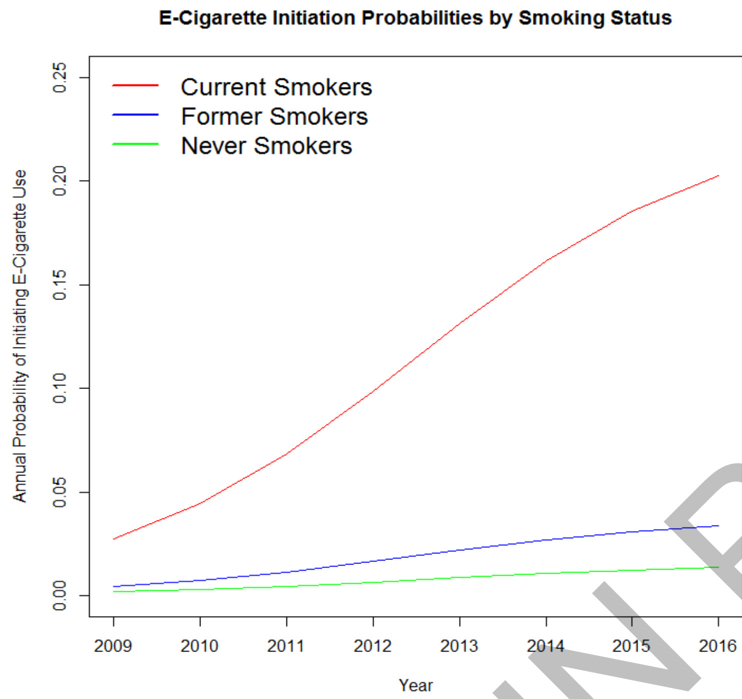
*Parameter values are those used in the baseline model calibrated to e-cigarette use prevalence among never, former, and current smokers in 2010 and 2013, and adult smoking prevalence from 1997 to 2013. Note: We use parameter variable names in the model pseudo code.

†See eSection 3.2 Smoking Cessation and Initiation Rates for additional information.

eFigure 2. Smoking initiation probabilities generated by the cumulative hazard function, using linear regression to project initiation rates by year.



eFigure 3. Sigmoid functions determining the probability of e-cigarette initiation by smoking status.



eTable 2. Model equations and parameters

Variable and Calculation Method	Function	Description
smokingInit	-0.0006*MIN(time,25) + 0.024	The probability of becoming a smoker dependent on the model time step (year)
Survival rates by prevalence (calculated from historical prevalence and then fitted to linear function)		
smokingCess	Table	The probability of quitting dependent on the model time step (year)
CISNET annual smoking cessation probabilities from the 1970 male and female cohort (averaged)[15,23]		
deathRate	Table	The probability of death dependent on the model time step (year)
US death rates table (past, present, and future projections) using Census data[25], the Human Mortality Database[24], and the Lee-Carter method[26,27]		
birthrate	14.2 per 1000 persons	Stable birth rate in the model
Reported by the CDC in 1997[28]		
smokingPrevAtInit	Table	Age-specific population level smoking prevalence in 1997 -- Model individuals are initialized at these age-specific levels
NHIS smoking prevalence values by age groups 18-24, 25-44, 45-64, and 65+ [19]		
ecigInitSmoker	$\frac{\text{eCigProbMax}}{1+e^{(-\text{timeVal}*\text{ecigNetSlope})}}$ where: $\text{timeVal} = (\text{time-modelBurnIn})*\left(\frac{20}{\text{timeToMaxECigInit}}\right)\text{-10}$	The probability of a current smoker becoming an e-cigarette user dependent on the model time step (year)
Sigmoidal function from the theory of innovations, based in time[11]		

Model parameters are used within equations that govern transition probabilities between nicotine use states and life-cycle states (i.e., age, alive/dead). Note: These equation variable names are also used in the pseudo code; some equation variables are generated from parameter values.

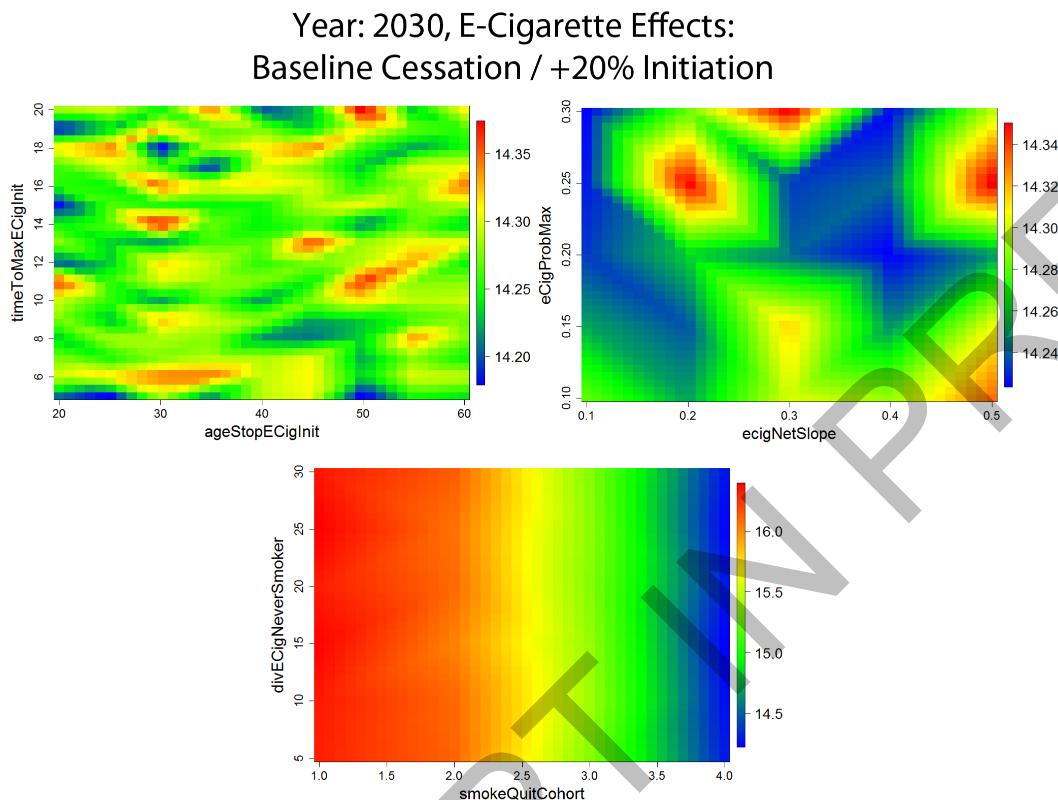
eTable 3. Model generated outcomes compared to data sources

Current E-Cigarette Use Prevalence by Smoking Status (%)				
Year	2010	2011	2012	2013
Model Population Prevalence	0.8	1.5	2.4	3.4
McMillen et al. Population Prevalence[13]	0.3	0.8	2.6	6.8
Schmidt et al. Population Prevalence[12]	NA	NA	NA	1.3
Zhu et al. Population Prevalence[32]	NA	NA	1.4	NA
Model Current Smokers	0.1	0.1	8.7	12.6
McMillen et al. Current Smokers	1.4	5.0	10.8	30.3
Zhu et al. Current Smokers	NA	NA	6.3	NA
Model Former Smokers	0.1	0.2	0.3	1.0
McMillen et al. Former Smokers	0.3	0.1	1.1	5.4
Zhu et al. Long Term Former Smokers	NA	NA	0.2	NA
Zhu et al. Recent Former Smokers	NA	NA	6.1	NA
Model Never Smokers	0.5	1.0	1.5	2.0
McMillen et al. Never Smokers	0.1	0.1	0.1	1.4
Zhu et al. Never Smokers	NA	NA	0.04	NA
Adult Smoking Prevalence (%)				
Year	1997	2002	2007	2012
Model Smoking Prevalence	24.2	21.1	19.1	17.6
NHIS Smoking Prevalence	24.7	22.5	19.7	18.1
NHIS (95% CI)	(24.1,25.3)	(21.9, 23.1)	(19.0, 20.6)	(17.5, 18.7)

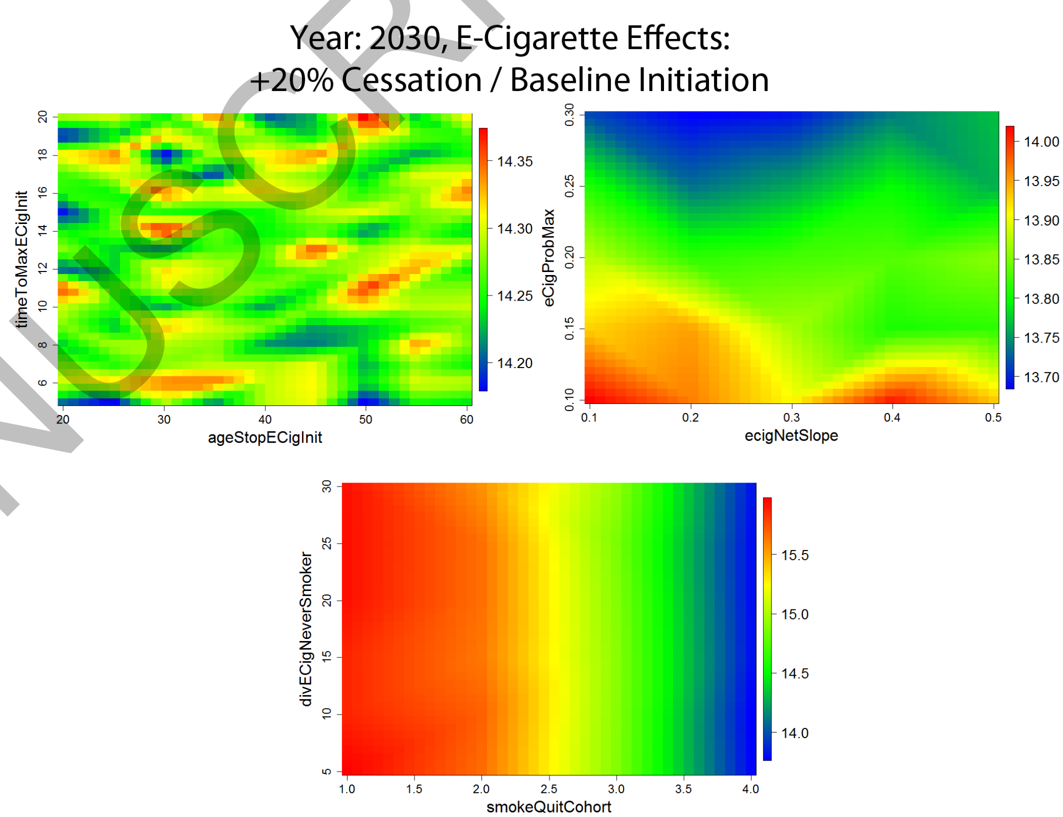
Note: McMillen et al. and Schmidt et al. define current use as “everyday” or “someday” use of e-cigarettes. Zhu et al. define current use as “use of e-cigarettes in the past 30 days.”

*Color axes in subsequent heatmap figures (eFigures 4 – 9) represent smoking prevalence (%) outcomes.

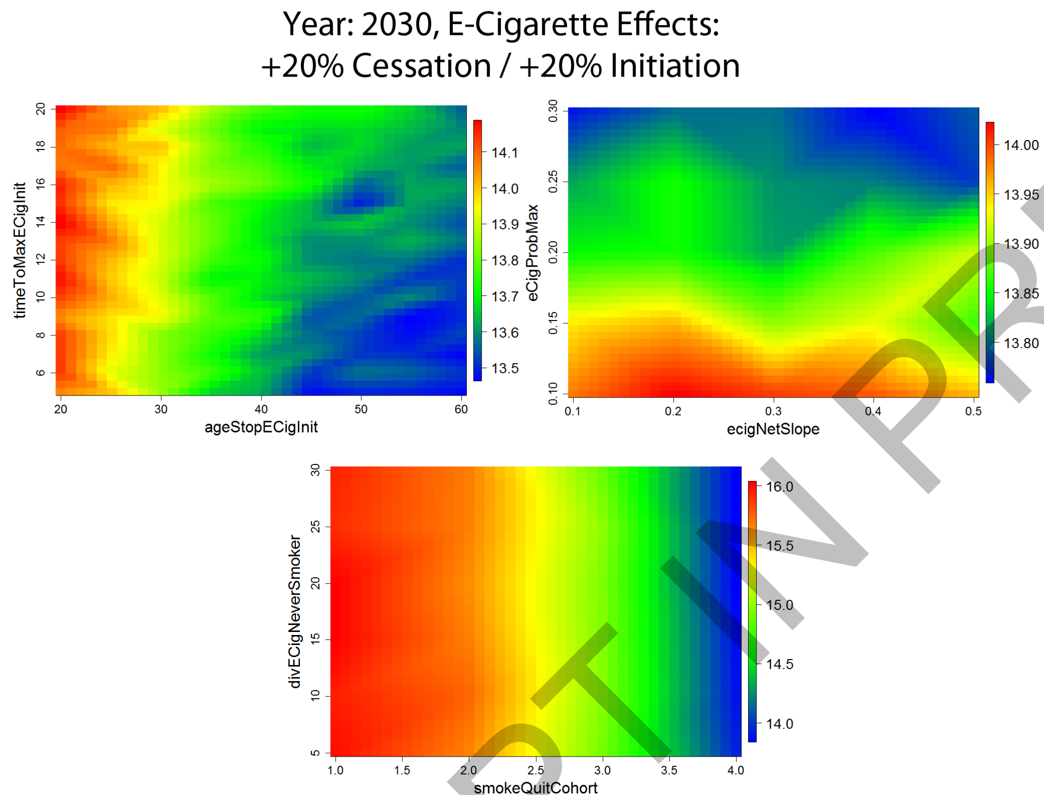
eFigure 4. Smoking prevalence outcomes in 2030: e-cigarette use results in a 20% increase to individual-level smoking initiation probability and does not affect smoking cessation, relative to baseline.*



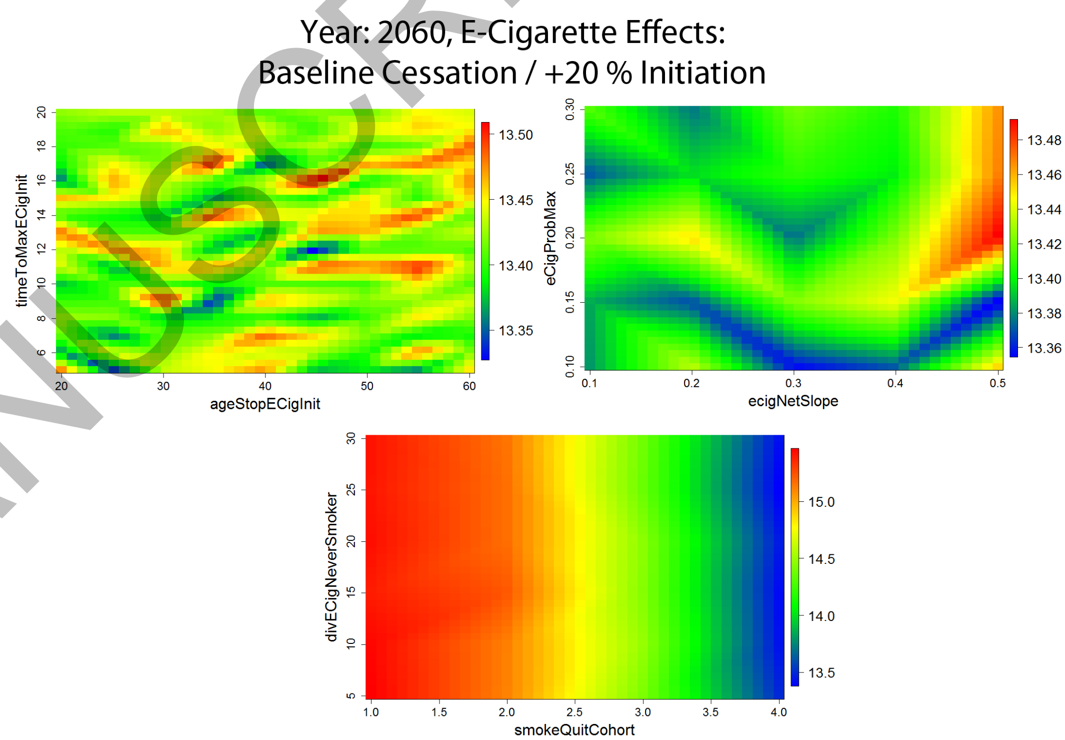
eFigure 5. Smoking prevalence outcomes in 2030: e-cigarette use results in a 20% increase to individual-level smoking cessation probability and does not affect smoking initiation, relative to baseline.*



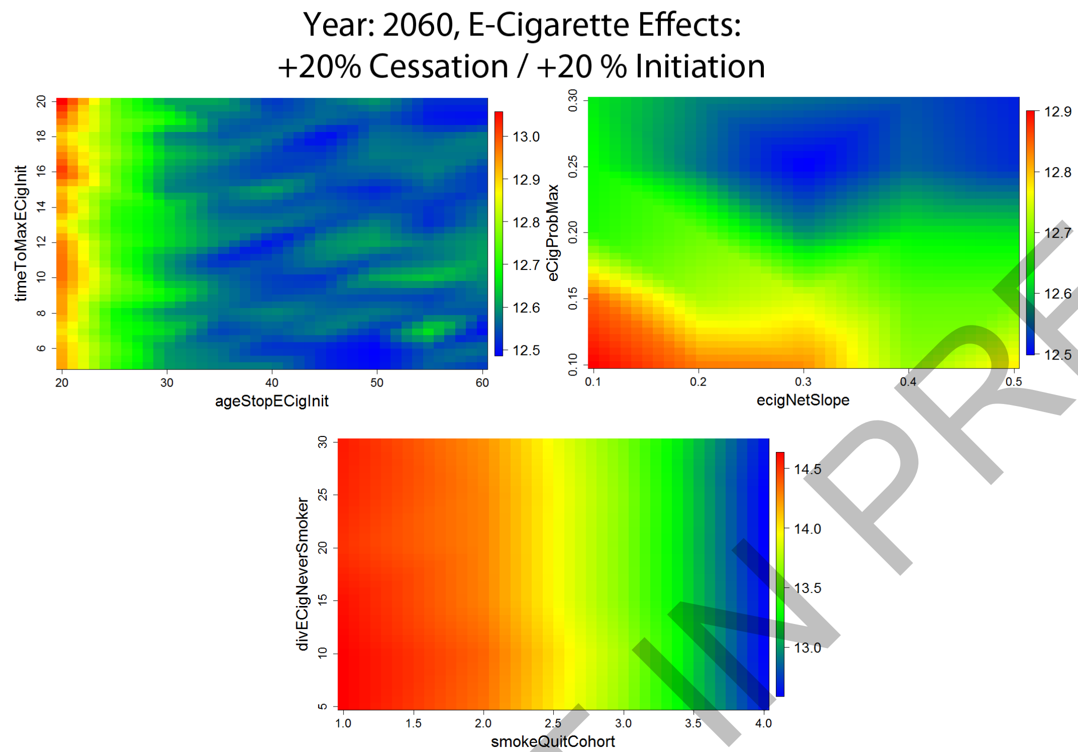
eFigure 6. Smoking prevalence outcomes in 2030: e-cigarette use results in a 20% increase to both individual-level smoking cessation probability and individual-level smoking initiation probability, relative to baseline*



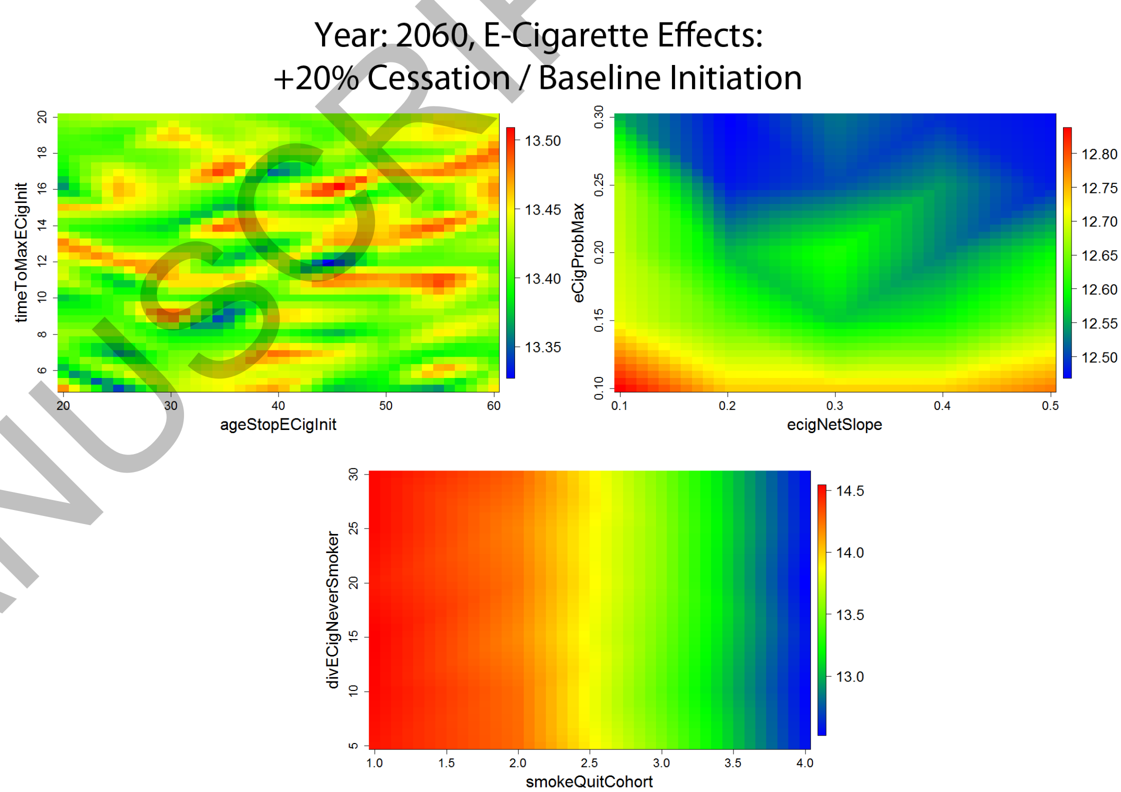
eFigure 7. Smoking prevalence outcomes in 2060: e-cigarette use results in a 20% increase to individual-level smoking initiation probability, and does not affect smoking cessation, relative to baseline.*



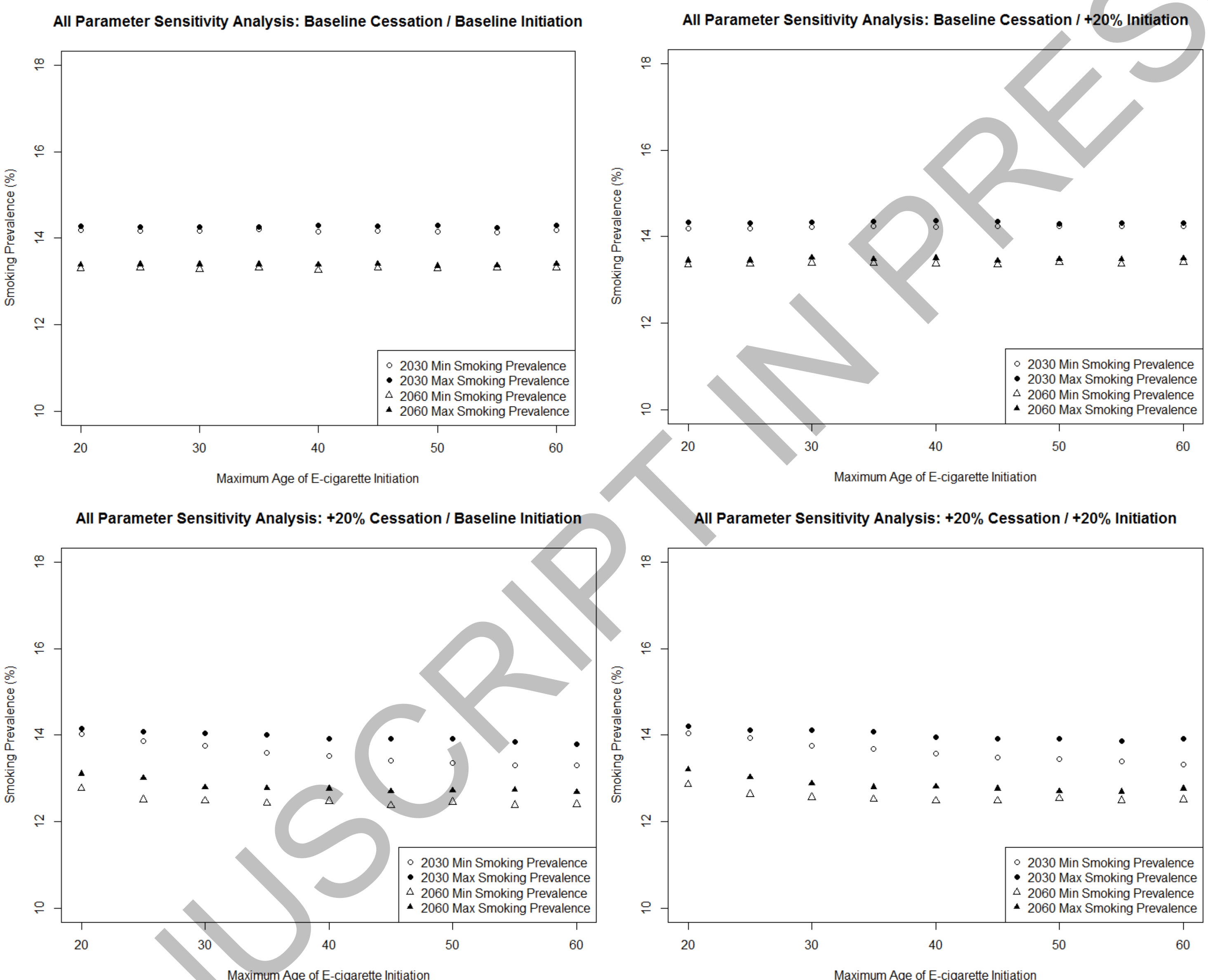
eFigure 8. Smoking prevalence outcomes in 2060: e-cigarette use results in a 20% increase to both individual-level smoking cessation probability and smoking initiation probability, relative to baseline.*



eFigure 9. Smoking prevalence outcomes in 2060: e-cigarette use results in a 20% increase to individual-level smoking cessation probability and does not affect smoking initiation, relative to baseline.*



eFigure 10. Smoking prevalence outcomes in 2030 and 2060 using extreme ranges of all parameters by a range of maximum age at e-cigarette initiation values (x-axes). Upper Left: Baseline Model. Upper Right: e-cigarette use results in a 20% increase to individual-level smoking initiation probability and does not affect smoking cessation. Bottom Left: e-cigarette use results in a 20% increase to individual-level smoking cessation probability and does not affect smoking initiation. Bottom Right: e-cigarette use results in a 20% increase to both individual-level smoking cessation and individual-level smoking initiation probabilities.



eSection 5. Programming

5.1 Programming Notes

- Model was programmed using Python
- Model output was analyzed using Python-Pandas and R
- Primary assumptions: No relapse of smoking or e-cigarette use after quitting
- No smoking initiation after age 30
- No e-cigarette initiation after age 30
- Variable names used here are described in the eTable 1 and eTable 2

5.2 Model Pseudo Code

```
OBJECT agent;
    age;
    current_smoking_status;
    smoking_history;
    current_electronic_cigarette_status;
    electronic_cigarette_history;
    alive_or_dead;

PROGRAM smoking_model;
   initialize agents to 1997 US population age and smoking status demographics;
   for every year from 1997 to 2075:
      repeat for all agents in the model:
            if  (age >= 85) or probability of death by age, smoking status, history:
               die;
            if smoker:
               if not e-cigarette user:
                  start e-cigarettes at P(ecigInitSmoker);
                  quit smoking at P(smokingCess);
                if e-cigarette user:
                    quit smoking at P(smokingCess) * dualUseQuitMultiplier;
                    quit e-cigarettes at P(ecigQuitProb);
            if former smoker:
                if e-cigarette user:
                    quit e-cigarettes at P(ecigQuitProb);
                if not e-cigarette user:
                   start e-cigarettes at P(ecigInitSmoker)/divECigFormerSmoker;
            if never smoker:
                if e-cigarette user:
                   start smoking at P(somkingInit)*ecigSmokeInitInc;
                   quit e-cigarettes at P(ecigQuitProb);
                if not e-cigarette user:
                   start e-cigarettes at P(ecigInitSmoker)/divECigNeverSmoker;
         increment age;
      birth new 18 year olds at set birth rate to maintain stable population counts;
      calculate model and agent statistics;
      write model and agent statistics to outputs;
      clear model and agent statistics for this step;
```

REFERENCES

1. Resnicow K, Page SE. Embracing chaos and complexity: A quantum change for public health. *Am J Public Health*. 2008;98(8):1382-1389. doi:10.2105/AJPH.2007.129460.

2. Auchincloss AH, Diez Roux A. A new tool for epidemiology: The usefulness of dynamic-agent models in understanding place effects on health. *Am J Epidemiol*. 2008;168(1):1-8. doi:10.1093/aje/kwn118.

3. Diez Roux A. Complex systems thinking and current impasses in health disparities research. *Am J Public Health*. 2011;101(9):1627-1634. doi:10.2105/AJPH.2011.300149.

4. Marshall BL, Galea S. Formalizing the Role of Agent-Based Modeling in Causal Inference and Epidemiology. *Am J Epidemiol*. 2015;181(2):92-99. doi:10.1093/aje/kwu274.

5. IOM (Institute of Medicine). *Assessing the Use of Agent-Based Models for Tobacco Regulation*. Washington, DC: The National Academies Press. 2015.

6. Zhang D, Giabbanelli PJ, Arah OA, Zimmerman FJ. Impact of Different Policies on Unhealthy Dietary Behaviors in an Urban Adult Population: An Agent-Based Simulation Model. *Am J Public Health*. 2014;104(7):1217-1222. doi:10.2105/AJPH.2014.301934.

7. Orr MG, Galea S, Riddle M, Kaplan GA. Reducing racial disparities in obesity: Simulating the effects of improved education and social network influence on diet behavior. *Ann Epidemiol*. 2014;24(8):563-569. doi:10.1016/j.annepidem.2014.05.012.

8. 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. doi:10.1016/j.amepre.2010.10.033.

9. Epstein JM, Goedecke DM, Yu F, Morris RJ, Wagener DK, Bobashev G V. Controlling Pandemic Flu: The Value of International Air Travel Restrictions. *PLoS One*. 2007;2(5):e401. doi:10.1371/journal.pone.0000401.

10. 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. doi:10.1016/j.jval.2012.06.014.

11. Sterman JD. S-Shaped Growth: Epidemics, Innovation Diffusion, and the Growth of New Products. In: Sterman, JD. *Business Dynamics: Systems Thinking and Modeling for a Complex World*. Boston, MA: Irwin McGraw-Hill. 2000:294-349

12. Schmidt L, Reidmohr A, Harwell TS, Helgerson SD. Prevalence and Reasons for Initiating Use of Electronic Cigarettes Among Adults in Montana, 2013. *Prev Chronic Dis.* 2014;11:140283. doi:10.5888/pcd11.140283.

13. 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. doi:10.1093/ntr/ntu213.

14. 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. doi:10.1136/tobaccocontrol-2013-051122.

15. 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. doi:10.1001/jama.2013.285112.

16. 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.

17. 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. doi:10.1371/journal.pone.0121008.

18. Jeon J, Meza R, Krapcho M, Clarke L, Bryne J, Levy DT. Actual and Counterfactual Smoking Prevalence Rates in the US population via Micro-simulation. *Risk Anal.* 2012;32(s1). doi: 10.1111/j.1539-6924.2011.01775.x.

19. National Center for Health Statistics. *National Health Interview Survey 1997-2013*. 1997. http://www.cdc.gov/nchs/nhis.htm.

20. Anderson C, Burns D. Patterns of adolescent smoking initiation rates by ethnicity and sex. *Tob Control*. 2000;9(SUPPL2):ii4-ii8. doi:10.1136/tc.9.suppl_2.ii4.

21. Pierce JP, White VM, Emery SL. What public health strategies are needed to reduce smoking initiation? *Tob Control*. 2012;21(2):258-264. doi:10.1136/tobaccocontrol-2011-050359.

22. Huxley RR, Yatsuya H, Lutsey PL, et. al. Impact of age at smoking initiation, dosage, and time since quitting on cardiovascular disease in African Americans and whites: The Atherosclerosis Risk in Communities Study. *Am J Epidemiol*. 2012;175(8):816-826. doi:10.1093/aje/kwr391.

23. Cancer Intervention and Surveillance Modeling Network. *Publication support and modeling resources*. 2014. https://resources.cisnet.cancer.gov/projects/#shg/tce/summary.

24. University of California Berkeley (USA), Max Planck Institute for Demographic Research (Germany). *The Human Mortality Database*. www.mortality.org or www.humanmortality.de.

25. U.S. Census Bureau. *Profiles of General Demographic Characteristics (1997-2010)*; 2010. http://www.census.gov/data.html.

26. IOM (Institute of Medicine). *Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products*. 2015. Washington, DC: The National Academies Press.

27. Janssen F, van Wissen LJG, Kunst AE. Including the Smoking Epidemic in Internationally Coherent Mortality Projections. *Demography*. 2013;50(4):1341-1362. doi:10.1007/s13524-012-0185-x.

28. 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.

29. Carter BD, Abnet CC, Feskanich D, et al. Smoking and Mortality — Beyond Established Causes. *N Engl J Med.* 2015;372(7):631-640. doi:10.1056/NEJMsa1407211.

30. Lynch JW, Kaplan GA, Cohen RD, Tuomilehto J, Salonen JT. Do cardiovascular risk factors explain the relation between socioeconomic status, risk of all-cause mortality, cardiovascular mortality, and acute myocardial infarction? *Am J Epidemiol*. 1996;144(10):934-942. doi:10.1093/oxfordjournals.aje.a008863.

31. 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. doi:10.1016/j.amepre.2013.10.022.

32. Zhu SH, Gamst A, Lee M, Cummins S, Yin L, Zoref L. The Use and Perception of Electronic Cigarettes and Snus among the U.S. Population. *PLoS One*. 2013;8(10):e79332. doi:10.1371/journal.pone.0079332.

33. Dutra LM, Glantz SA. Electronic Cigarettes and Conventional Cigarette Use Among US Adolescents: A Cross-sectional Study. *JAMA Pediatr*. 2014;168(7):610-617. doi:10.1001/jamapediatrics.2013.5488.