Reducing the Smoking-Related Health Burden in the US through Diversion to Electronic Cigarettes: A System Dynamics Simulation Study

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Abstract

Background: Electronic cigarettes ("e-cigarettes") have altered tobacco use trends, and their impacts are controversial. Given their lower risk relative to conventional cigarettes, e-cigarettes have potential for harm reduction. This study presents a simulation-based analysis of an e-cigarette harm reduction policy set in the US.

Methods: A system dynamics simulation model was constructed, with separate aging chains representing different stages of use for both cigarette smokers and e-cigarette users. These structures interact with a policy module to close the gap between actual (simulated) and goal numbers of cigarette smokers, chosen to reduce the tobacco-attributable death rate to that due to all accidents in the general population. The policy is two-fold, removing existing flavor bans and providing an informational campaign promoting e-cigarettes as a lower-risk alternative. Realistic practical implementation challenges are modeled in the policy sector, including time delays, political resistance, and budgetary limitations. Effects of e-cigarettes on conventional smoking occurs through three mechanisms: 1) diversion from ever initiating conventional smoking; 2) reducing progression to established smoking; and 3) increasing smoking cessation. An important unintended effect was included, which increases the tobacco-related mortality accordingly with an increase in nicotine users due to e-cigarettes.

Results: The base-case model replicated the historical exponential decline in smoking and the exponential increase in e-cigarette use since 2010. The ideal-case policy was able to reduce conventional smoking to the goal level approximately 40 years after implementation. Implementation obstacles (time delays, political resistance, and budgetary constraints) delayed and weakened the effect of the policy by up to 95% in the worst case, relative to the ideal-case scenario; however, these discrepancies substantially decreased over time in dampened oscillations as negative feedback loops stabilize the system after the one-time "shock" introduced by policy changes.

Conclusions: Current findings demonstrate that the promotion of e-cigarettes as a harm-reduction policy is a viable strategy, given current knowledge of e-cigarettes' effects on conventional smoking. Given the strong effects of implementation challenges on policy effectiveness in the short term, accurately modeling such obstacles is essential in policy design. Ongoing research is needed with forthcoming data on e-cigarette use prevalence and possible effects on cigarette smoking.

Introduction

Cigarette smoking is a causal factor in a wide range of adverse health effects including cancers virtually anywhere in the body, cardiovascular disease, diabetes, macular degeneration, birth defects, rheumatoid arthritis, inflammation, and impaired immune function (1). Through a combination of public policy (e.g. cigarette taxes, age restrictions on purchasing, and bans on advertising to youth) and increased public awareness of the health dangers of smoking, the US has had success in drastically reducing the smoking prevalence over the past several decades, from 42% in 1965 to about 16% currently (1); however, recent

years show this reduction hitting a plateau (2), possibly due to "hardening" of remaining smokers as detailed below. As a result, reductions in smoking-related morbidity and mortality have stagnated, and cigarette smoking remains the primary cause of preventable death and disease in the US (1).

Adverse health outcomes attributable to smoking are primarily tied to combustible elements of conventional cigarettes (3, 4) as well as tars and arsenic (5). For example, lung cancer is perhaps the most well-known health risk of cigarette smoking, and approximately 90% of cases are attributable to smoking (1). Despite reductions in smoking prevalence, the incidence of lung cancer has remained high (incidence rates of 100 per 100,000 in 1980, with only a slight reduction to 70 cases per 100,000 in 2010) (1). Even more concerningly, cigarettes seem to be becoming deadlier over time: despite the declines in smoking prevalence, lung cancer incidence as well as mortality has increased, particularly adenocarcinoma. The increased cancer burden is thought to be due to changes in the composition and processing of cigarettes (1). Additionally, cigarettes cause a wide range of other health effects beyond lung cancer, including other cancers, respiratory diseases, cardiovascular diseases, diabetes, and immune disorders (1).

Although nicotine is the major, but not only addictive component in cigarettes (6), nicotine itself is not much more harmful than caffeine (5) as evidenced by low risk profiles of nicotine replacement therapy (NRT) products such as nicotine patches and gum (5). Given the vastly different risk profile of nicotine alone vs. other components in cigarettes, a great deal of harm reduction can be achieved by encouraging smokers to transition away from conventional cigarettes to other nicotine products (5). Though some tobacco control advocates including the US Surgeon General argue for heavily regulating all nicotine products (7), studies supporting the "hardening hypothesis" (2, 8, 9) raise doubts that nicotine use can be eliminated entirely. That is, the population of smokers today have higher levels of nicotine dependence (2, 8) and higher rates of mental health comorbidities (9), relative to in the past, suggesting that today's smokers are the remaining "hardened" group who face greater difficulties in smoking. For example, over 60% of individuals suffering from schizophrenia smoke, which maybe be due to self-medication of their symptoms with nicotine (10). Taken together, diverting users to other sources of nicotine is a valid and likely effective harm reduction strategy.

Electronic cigarettes (e-cigarettes) are an alternate tobacco product that electronically heats nicotine liquid into vapor, and thus lacks the harmful combustible elements of conventional cigarettes (11). E-cigarettes first appeared on the market around 2010, and have continually increased in popularity since then, resulting in more of today's youth using e-cigarettes than conventional cigarettes. Though long-term health data on e-cigarettes will not be available for some time, they are estimated to be only 5% as harmful as conventional cigarettes (11) and thus represent an important and appealing harm reduction alternative (5). Many established smokers use e-cigarettes to offset or quit conventional smoking (12-15), and despite not being approved for this purpose by the Federal Drug Administration (FDA) in the US, e-cigarettes may be more effective than NRT for cessation (16).

A special consideration in smoking harm reduction is adolescents who are nicotine-naïve. Though recent research supports e-cigarette use as a harm reduction method among established, nicotine-dependent smokers who have difficulty quitting (17), much literature has encouraged restricting youth access to and interest in e-cigarettes, for example via flavor bans (18, 19). The motivation for restricting adolescent e-cigarette use stems from fears of e-cigarettes acting as a "gateway" to tobacco use, including conventional cigarettes (20, 21). Evidence for the gateway mechanism includes e-cigarette users being at much higher risk for subsequent conventional smoking relative to nonusers (21, 22); however, these adolescents have pre-existing risk factors that predisposed them to smoking, suggesting they would have gone on to use conventional cigarettes anyway (23, 24). Population trend modeling studies have also raised doubts about a gateway effect, as declines in conventional smoking among youth have accelerated after the appearance of e-cigarettes (25, 26). This suggests a possible "primary prevention" effect of e-cigarettes, which has been understudied (27) but is supported by recent studies showing that e-cigarettes may be diverting adolescents from ever using conventional cigarettes (28, 29).

The current study tests a harm reduction policy of promoting e-cigarette use in order to divert current or would-be smokers away from conventional cigarettes, using system dynamics simulation modeling. The model developed here is set in the US, though it can easily be adapted to other settings by re-calibrating relevant parameters. System dynamics modeling is used to first replicate historical trends in youth use of cigarette and e-cigarette use, and then to project trends into the future under a base-case scenario and a policy scenario. The policy acts through two mechanisms: removing existing flavor bans on e-cigarettes (as one method of increasing access to e-cigarettes), and a public health marketing campaign promoting e-cigarettes as a lower-risk alternative to cigarettes. Effects of this policy on the model are threefold: 1) diverting nicotine-naïve adolescents from ever using conventional cigarettes; 2) reducing conventional smoking behavior among existing smokers; and 3) increasing the cessation rate of conventional cigarettes. The model was calibrated using data from the US National Youth Tobacco Survey (NYTS) (30, 31). Long-term outcomes of cigarette smoking prevalence are examined as a function of different policy variants.

Methods

Causal Loop Diagram

A causal loop diagram showing the minimal essential set of relationships describing cigarette use, e-cigarette use, their hypothesized relationship between them, and the policy under examination is shown in Figure 1. This conceptual diagram guides the development of the subsequent simulation model (see below). The causal loop diagram shows primarily feedback loops, either positive/reinforcing (whereby a change in one variable accelerates its own future change through the chain of causal relationships) or negative/balancing (whereby a change in one variable limits its own future change).

Loop B1 and B2 describe the central dynamic in this model: that established cigarette use leads to an unacceptable number of preventable deaths (relative to some goal). The term "tobacco-related deaths" is

an umbrella term meant to include deaths from both cigarettes and e-cigarettes; though e-cigarettes are not derived from tobacco, this terminology reflects the FDA's designation of e-cigarettes as a tobacco product. The unacceptably high number of tobacco-related deaths motivates a harm reduction policy, which in this case is twofold: 1) implementing an informational campaign which promotes e-cigarettes as a less risky alternative to cigarettes (B1); and 2) removing existing flavor bans (which are in effect in many places) (B2). This in turn increases e-cigarette initiation. Increasing e-cigarette initiation has 3 intended effects: 1) decreasing the cigarette progression rate by offsetting of cigarettes with e-cigarettes (B1), 2) reducing the cigarette initiation rate by diversion away from conventional cigarettes (B3), and increasing the smoking cessation rate (B4). An important unintended consequence is also included: progression to established e-cigarette use will increase the preventable deaths (though not as much as conventional cigarettes), which can counteract the policy to some degree (R1).

Stock-and-Flow Diagram

Based on the CLD above, a stock-and-flow diagram (Figure 2) was constructed in Stella Architect, version 1.9.5 (32), which consists of "aging chains" for both cigarette and e-cigarette use (a structure consisting of stocks in series, here representing different stages of use, with appropriate inflows and outflows, representing transition rates). Each aging chain has an initial inflow dependent on the rate of individuals maturing into adolescence (i.e. turning 12 years old), which occurs continuously throughout the length of the simulation. The cigarette aging chain has three stocks: experimenters, established users, and former users; while the e-cigarette aging chain only has the first two. Ex-e-cigarette users were intentionally excluded from the model because there is lack of available data on this group to calibrate parameters. Instead, a simplifying assumption was made (e.g. due to the hardening hypothesis) that once a person becomes an established e-cigarette user, they remain there for life. This is a conservative assumption (see Limitations). The flows from one stock to another are assumed to encompass two mechanisms: 1) a "social-recruitment" mechanism, in which the new initiation rate is positively affected by the proportion of established users; and 2) a "self-recruitment" mechanism in which there is a stable base of nicotine users regardless of usage in the population, consistent with the hardening hypothesis (2). The social recruitment mechanism parameter was set to 2, meaning that each user influences 2 other users per year (see Calibration Testing below).

The two aging chains feed into the Goal-Gap of Tobacco-Related Mortality Module, which calculates the discrepancy between the actual tobacco-related deaths (from both cigarettes and e-cigarettes, based on the respective stocks of established users, as this is the relevant measure from a health perspective (33)) and a goal value. Since it is unrealistic to entirely eliminate tobacco-related deaths, a goal value approximating the death rate from accidents of any type in the general population was chosen (1%/year), below the death rate due to poor diet/physical inactivity and alcohol consumption (34). The discrepancy in the actual vs. desired deaths in turn affects the policy implementation, as a much higher-than-desired tobacco-related death rate motivates regulatory policy.

The policy itself, captured in the Policy Implementation Module, consists of removing existing flavor bans (as one type of policy which increases access to e-cigarettes) as well as an educational campaign promoting e-cigarettes as a less harmful alternative. The effect of the policy is to increase the e-cigarette initiation rate, which has a 3-pronged effect on the cigarette aging chain: increasing diversion away from conventional cigarette initiation, reducing smoking and thus progression rates to established use, and increasing smoking cessation. E-cigarette initiation rate can be increased beyond that of cigarette initiation, indicating that the model allows for never-smokers to initiate e-cigarettes; the e-cigarette and cigarette initiation rates are both capped at the maximum of individuals becoming adolescents each year (maturation rate into adolescence). The Policy Implementation Module includes pragmatic considerations, such as political resistance to overturning a flavor ban, and resources for implementing an informational campaign (both budgetary and workforce-related). The structure of this model allows for ideal, best-case scenarios (no resistance and sufficient resources) as well as more realistic, limited scenarios through changing corresponding parameters (i.e. the likelihood of removing a flavor ban; the proportion of required funding that is approved, and time delays). The overall initiation of the policy is linked to a binary "switch" that can be turned on or off. It is important to note that, while the decision to initiate the policy is a binary variable, the policy itself once switched "on" can still cover a range of specific implementations, including uncertainty of further approval in the case of flavor bans.

The model was run over the period 2000-2100, with e-cigarettes first appearing around 2010, and the policy also being implemented in 2010. The detailed model structure and equations, including the modules, can be downloaded for free (35); the model can be opened and run using the free software isee Player (36).

Model Calibration

The model was calibrated to match the "behavior modes" (i.e. the fundamental shape of the trend, such as exponential growth or exponential decline) observed in youth cigarette and e-cigarette use in the US over the period 2000-2019 (most recently available data), based approximately on the National Youth Tobacco Survey (NYTS) (30, 31) for dynamics relevant to youth (i.e. initiation and progression to established use) and the National Health Interview Survey (NHIS) (37) for dynamics relevant to adults (i.e. smoking-related fractional death rates). Since this model is not intended to finely replicate historical behavior or provide precise future projections, calibration to a broad behavior mode was sufficient. Some parameters were selected based on external data (lifetime probability of quitting cigarettes, self-recruitment effect; experimenting and cessation rates; tobacco-related *raw* death rates and life expectancies; cessation rates; diversion, smoking reduction, and cessation effects, times to established use; and all population numbers), while others (social contagion effects; tobacco-related *fractional* death rates) were calibrated by running "live" simulations over a range of parameters to determine the optimal value with respect to stocks of established users (cigarettes and e-cigarettes), as these are the stocks relevant for public health. Stocks of established cigarette and e-cigarette users according to NYTS (30, 31) and the NHIS (37) show approximately goal-seeking behavior towards a plateau (based on the proportion who are self-recruiters), and exponential growth for established e-cigarette use. Remaining

parameters of flows (i.e. social contagion effect) were calibrated to achieve a reasonable match between simulated and historical data, based on the observed behavior mode and approximate magnitude (e.g. estimates of 46.5 million smokers in the US in 2000 (38). Specifically, the social contagion parameter was tuned over a wide range of plausible range values (0, meaning no social influence, to 10, meaning that each user influences 10 other users), and the value that produces an initial decline followed by a plateau through the end of the time horizon (i.e. year 2100) was selected, consistent with the hardening hypothesis. Values higher than 2 (the final parameter value) produce a continuous decline, while values higher than 2 produce an *increase* in smoking prevalence, both of which are unrealistic.

Parameters for the three-fold effects of e-cigarette use on cigarette smoking (diversion, smoking reduction, and cessation) were quantified as follows. With no existing empirical estimates for a diversion effect, this was quantified based on a separate study (28, under review) as 37.8% of e-cigarette users per year being diverted from initiating cigarettes. No empirical estimates exist for a smoking reduction effect either, and this was quantified using the rationale that, among adolescent tobacco users, about 30% preferentially use e-cigarettes historically (1, 5); therefore, e-cigarettes may offset 30% of ever-smokers who progress to established smoking. The cessation effect was quantified based e-cigarettes having an approximately 20% success rate for smoking cessation in a randomized trial (39).

Model Validation

A range of validation tests were performed on the model, which identified errors that were corrected in the final model. Boundary conditions were examined conceptually to determine which variables and causal relationships were included in the model. Parameter assessment was based on external data sources and calibration to observed data. Extreme conditions testing was conducted by setting inflows and initial values of stocks to 0 and very high values, and ensuring the model behaved reasonably (e.g. stocks do not fall negative).

Model Analysis

A base-case model was constructed to replicate approximate trends in cigarette and e-cigarette use among US adolescents and adults across 2000-2019 (26, 36, 37, 40) and projected into the future (year 2100). Several policy scenarios were run, including an ideal-world, best-case scenario (no practical obstacles to implementation), and scenarios where policy implementation is delayed, faces resistance (i.e. low likelihood of removing flavor bans, due to controversy), and faces limited funding for an informational campaign. Specifically, time delays for the best-case scenario were set to 0.1 years (for time to approve both policies, time to approve funding, and time to hire and train workforce) and 10 years (for workforce turnover rate); and in the time-delayed model, were set to larger values (time to approve removal of flavor bans = 2 years, time to approve informational campaign = 1 year, time to adjust workforce = 1 year, time to train workforce = 0.25 years, and time to approve funding = 1 year). With respect to uncertainty in approving the removal of flavor bans, probability of approval was set to 1 and 0.5 for the ideal-case and uncertain-approval scenarios, respectively. With respect to budgetary constraints, the fraction of required budget that is approved is set to 1 (full budget) and 0.7 in the ideal-

case and budget-restricted scenarios, respectively. Additionally, the model is publicly available and can be run through a web interface, allowing users to vary policy implementation parameters and other assumptions of the model (e.g. the strength of diversion, smoking reduction, and cessation effects).

Results

The base model was able to successfully replicate the approximate behavior modes (Figure 3) observed in historical data (15, 19) and NHIS (37), namely the slow, approximately exponential decline in established cigarette use over 2000-2019 (40) and NHIS (37), and approximately exponential increase in established e-cigarette use from 2010-2019 (40).

Figure 4 shows the base-case simulation run through the year 2100, under the scenario of the status quo (no policy) and the ideal-case policy scenario relative to the goal number of established cigarette smokers (which increases over time with population growth). Under the status quo, the (simulated) number of established cigarette users declines, continuing the preexisting trend of exponential decline from 2000-2019; however, it remains higher than the target number. This persistent discrepancy leads to an unacceptably high number of preventable tobacco-related deaths throughout this time horizon. The ideal-policy scenario shows the policy (implemented in 2010) accomplishing its goal shortly after 2050, and subsequently showing some minor oscillations around that goal. These oscillations are caused by delays in the implementation (e.g. workforce adjustment for the informational campaign); delays within negative feedback loops are well-understood in system dynamics to produce oscillations, as by the time decisions are fully implemented (e.g. hiring and training of staff), the adjustment needed to meet the goal has already changed due to pre-existing dynamics (41).

Figure 5 shows the e-cigarette initiation rates, since this is the flow being regulated by the policy. The desired initiation rate (i.e. the e-cigarette initiation rate required to achieve the policy goal) is shown against what is achievable within the practical constraints of the policy (e.g. time needed for potential e-cigarette users to adjust their expectations) even if the policy were implemented with minimal delay, no political resistance, and full budgetary resources. The desired initiation rate is zero before 2010, as the policy is not yet implemented before then. The initial spike in desired e-cigarette initiation is due to the larger discrepancy between actual and desired cigarette users in 2010, and the sudden enactment of the policy. This then closes as the actual cigarette users approaches its goal. However, the achievable e-cigarette initiation rate is slower and lacks the initial overshoot, as it takes time for potential users to adjust their expectations about e-cigarettes and convert to use. Around 2060, the desired e-cigarette initiation rate suddenly drops to 0 because the stock of cigarette users crosses below the goal (see Figure 4); desired e-cigarette initiation rate drops to 0 shortly after (with a lag due to the delays in the implementation module). In other words, the harm reduction policy is no longer needed, as the goal cigarette users has been met and surpassed; once this change is "registered" in policy, the desired e-cigarette initiation rate is 0, as further offsetting of conventional cigarette use is unnecessary..

Figure 6 shows the ideal-case e-cigarette initiation rate (i.e. the achievable rate shown in Figure 5) against more realistic scenarios that include time delays to policy implementation and/or uncertainty in removing flavor bans and reduced budgetary resources for an informational campaign. Compared to the ideal-case scenario, time delays in policy implementation produce a lagged response in e-cigarette initiation rates accomplished by the policy, which is most severe at first, due to delay in policy approval. E-cigarette initiation rates then overshoots the ideal-case scenario while maintaining a discrepancy with the ideal-case scenario, due to continuing delays in workforce adjustment related to the informational campaign. That is, due to the delays in hiring and training workforce, current workforce lags desired workforce; and when desired workforce decreases, the actual workforce remains higher than necessary until the system adjusts again, temporarily resulting in higher-than-needed e-cigarette initiation rates. This lagged response of actual workforce behind desired workforce persists as long as the system is in disequlibrium (41). A scenario with time delays in addition to uncertain approval of removing flavor bans shows similar behavior, with less overshoot in e-cigarette initiation rates relative to the ideal case during the first peak (through about 2055). In the subsequent undershoot, this scenario similarly shows a dampened and delayed response compared to the ideal-case scenario, though this time in the opposite direction. A scenario with time delays in addition to budgetary constraints shows a delay and consistent undershoot in e-cigarette initiation rates relative to the ideal-case scenario during the first peak, followed by similarly dampened and delayed responses during the subsequent undershoot. Finally, a scenario with all constraints (time delays, uncertain approval, and budgetary constraints) shows a delayed and consistently undershooting e-cigarette initiation rate relative to the ideal case during the first peak, and a similar overshot and delay during the subsequent undershoot.

In order to quantify these differences between the ideal-case and scenarios that include realistic practical limitations, values from 2012 are examined (2 years after policy implementation, and the year of approximately greatest spread in e-cigarette initiation rates across scenarios). In the ideal case, 2.22 million people/year initiate e-cigarette use; versus approximately 171,000 in both the time-delayed and time-delayed with reduced budget scenarios (a 92% difference relative to the ideal-case scenario at the same time point); 108,000 in the time-delayed plus uncertain approval scenario (a 95% difference); and 107,000 in the scenario with all three types of limitation (a 95% difference). This discrepancy closes as time passes: all policies start to converge in 2050. However, oscillations persist into the future whenever the effective policy status changes (i.e. when established cigarette users oscillates past the goal value, and the need to actively encourage e-cigarette initiation is present or absent). These oscillations are dampened: for example, in the second phase of the first oscillation (approximately 2060), the ideal-case scenario shows approximately 613,000 people/year initiating e-cigarettes, versus 943,000 in the time-delayed scenario (a 54% difference relative to the ideal-case scenario at the same time point), 960,000 in the time-delayed plus uncertain approval scenario (a 57% difference), 949,000 in the time-delayed plus reduced budget scenario (a 55% difference), and 964,000 in the scenario with all three types of limitations (a 57% difference). Thus, the more time passes, the closer all scenarios become to each other, indicating that the system has recovered from the initial implementation obstacles.

Finally, since the time delay required for legislative approval is uncertain, several simulations were run (Figure 7) using the default delays (2 years for each policy, which proceed in parallel: this includes 2 years to approve overturning existing flavor bans; and 1 year to approve the informational campaign followed by another year to approve the budget) as well as delays which take half as long (1 year) or twice as long (4 years). As the approval delays get longer, the time for e-cigarette initiation to increase is correspondingly delayed, and the increase has a steeper curve. This is due to the fact that more potential e-cigarette initiators are present by the time the policy takes effect.

With respect to the distal goal of reducing tobacco-attributed preventable deaths to the rate of accidental deaths in the general population, this policy achieves its goal around 2039 (29 years after policy implementation) (data available on downloadable model (35)), and subsequently the preventable deaths remains far below the goal (3.28 million simulated deaths/year vs. a goal of 6.9 million deaths/year in 2021). Notably, this figure includes the potential unintended consequence of preventable deaths attributable to e-cigarettes.

A user-friendly and interactive interface is publicly available on the web (42). This interface version allows the user to modify the above parameters related to implementation obstacles along their full possible ranges, as well as other parameters (namely, the hypothesized strength of the diversion, smoking reduction, and smoking cessation effects of e-cigarettes, across the possible range of each effect, i.e. 0 to 100% effect on the corresponding rate). In addition, the full model is also available for download (35), and can be viewed and run using the free software isee Player (36). This can allow continued utility of this model as forthcoming data provide more precise estimates of relevant parameter values in the model.

Discussion

This study presents a novel system dynamics model examining the promotion of e-cigarettes as a harm reduction policy towards the goal of reducing tobacco-related death and disease, which is primarily due to conventional cigarettes. This simulated policy, which acts through removing existing flavor bans and implementing an informational campaign promoting e-cigarettes as a less harmful alternative, has a 3-pronged effect: 1) diverting adolescents from ever using conventional cigarettes; 2) reducing smoking among recent initiators, thereby lowering the progression rate to established cigarette use; and 3) increasing smoking cessation. Policy simulations show that promoting e-cigarettes can achieve a successful reduction of cigarette smokers to the goal number, given the assumptions in this model. Achieving this goal would move tobacco use from its current place as the leading behavioral cause of death, to below that attributable to poor diet/physical inactivity and alcohol consumption (34). Realistic obstacles to policy implementation such as delays in decision-making, uncertain approval, and budgetary limitations have the effect of delaying and weakening the policy's effects (by up to 95% in the first years after policy implementation, though these effects diminish over time). This system dynamics model is publicly available both as a full model (35) and useable via a user-friendly web format (42), allowing

decision makers to test out the effects of different parameters and assumptions within a simulation setting.

E-cigarette policy remains a controversial topic. Some argue for strict regulation comparable to that of conventional cigarettes, based on health concerns and the addictive potential of nicotine, particularly on young and/or novice users (7). Due to the more favorable risk profile of e-cigarettes (11), many agree that highly addicted, established smokers who have difficulty quitting are better off switching to e-cigarettes (5). On the other hand, e-cigarette use among adolescents and/or novice users remains controversial, due to fears of a "gateway" effect whereby e-cigarettes cause youth to become nicotine-dependent and increase their risk of later conventional cigarette smoking (21). However, given recent research supporting a common-liability hypothesis which postulates that the apparent relationship between e-cigarette use and smoking is attributable to a pre-existing liability for nicotine use (23, 24), the question of primary prevention becomes relevant (27). That is, for youth who have a propensity to use a tobacco product, it is important to direct them to a less harmful product. Furthermore, tightening restrictions on e-cigarettes too strictly may have the unintended consequence of directing would-be nicotine users back to conventional cigarettes (43-45), which are more harmful due to the nature of combustible smoking (3, 5).

Through simulation modeling, the current study shows that a harm reduction policy promoting e-cigarettes could successfully reduce conventional smoking prevalence through a combination of diversion, smoking reduction, and cessation. In turn, the preventable, tobacco-attributed deaths eventually (after dampened oscillations) approach goal value (i.e. the rate of accidental deaths in the general population). This reduction in tobacco-attributable deaths remains substantial even after accounting for the important unintended consequence of deaths from e-cigarettes: this model allows for e-cigarettes to increase the population of users of any tobacco product (cigarettes or e-cigarettes) and consequently the total deaths from e-cigarettes. This is consistent with previous research on the trade-off between the prevalence of use and the risk profile of a product: that is, a greater number of users are allowable from a public health perspective when using a less-risky product (46).

These results should be continually reconsidered with relevant external events and policies that impact the system. For example, the US recently increased the legal age to purchase cigarettes from age 18 to 21, and this is not reflected in the current model. If the increase in purchasing age has its intended effect, the smoking prevalence will decrease beyond what is accounted for in the current model. Future improvements to the model can take into account such external changes, especially if forthcoming literature is able to quantify the effects on smoking initiation and other variables in the system.

Limitations

This study should be interpreted in the context of important limitations. The central limitation of system dynamics modeling is that the results may not reflect what occurs in reality; however, the series of validation tests performed increase confidence that this model captures the relevant causal relationships in the real-world system. Though additional elements can be added to the model, parsimony is desirable once the minimally essential features have been captured. A specific simplifying assumption was

excluding ex-e-cigarette users from the model. Since the stocks relevant to tobacco-related death and disease are established users, excluding a stock for ex-users has the effect of assuming established users remain at the same risk for life. Thus, this is a conservative assumption that likely overestimates the mortality from established e-cigarette use.

Other model assumptions are based on imperfect data, and impact the magnitude and trends of e-cigarette initiation rates and stocks of established cigarette and e-cigarette users. In particular, the strength of the diversion, smoking reduction, and cessation effects are based on estimates from current literature, which may be limited. The diversion effect is particularly controversial, as much existing literature has argued for a gateway effect of e-cigarettes, which is an opposing effect. However, recent studies show that population-level trends are inconsistent with a gateway account, as the cigarette smoking prevalence continues to decline and may even have accelerated after the introduction of e-cigarettes (25, 26). This suggests a net diversion effect (29), the magnitude of which is estimated based on the diversion effect necessary to account for the accelerating decline in conventional smoking after e-cigarettes appeared (28). The current system dynamics model will be updated as new data emerge. Additionally, these assumptions and their implications on simulation results can be further tested using the publicly available web interface for this model.

Additional limitations of the model include the focus on only two tobacco products (cigarettes and e-cigarettes). Other products may alter the dynamics presented here, especially with cigar use surpassing cigarette use among youth (47). Similarly, the current policy was limited to overturning existing flavor bans and delivering an informational campaign; however, additional policies could alter the findings, such as altering existing age restrictions on purchasing e-cigarettes, which is a different method of restricting access to e-cigarettes. Additional implementation challenges that were not included in the model may also be relevant, and would have the effect of delaying and weakening the policy effects. Future research is necessary to explore other policies and implementation challenges in more detail, as the goal of the current study was to show general feasibility of a harm reduction policy promoting e-cigarettes, rather than to compare and contrast specific policies for doing so.

Strengths

The current study is novel in its examination of a harm reduction policy promoting e-cigarettes, particularly with respect to 3 possible mechanisms by which e-cigarette use can decrease the conventional cigarette smoking prevalence. The question of diversion, or primary prevention of cigarette use, is particularly novel, as this is a difficult effect to estimate empirically and has thus been understudied to date (27). Additionally, the use of system dynamics modeling allows for a systematic examination of different scenarios, ranging from the status quo (no policy) to an ideal-world policy, as well as a range of realistic scenarios in between that present obstacles and delays to policy implementation. The current model has its focus on practical considerations with respect to policy implementation, ranging from time delays to political resistance to budgetary limitations. Finally, the

model is publicly available via a user-friendly web interface (42) as well as a downloadable full model (35), allowing further testing of policy scenarios and assumptions of the model.

Conclusions

The system dynamics simulation model presented here demonstrates that promoting e-cigarettes as a less harmful alternative can be a successful harm-reduction policy for reducing the conventional smoking prevalence and consequently the tobacco-attributable deaths in the population. Practical challenges such as delays and limited resources can substantially weaken and delay the effect of the policy, at least initially; therefore, it is important to account for such obstacles when designing policy and projecting its effects. Ongoing evaluation of these findings is warranted with forthcoming data on the likely effects of e-cigarettes on conventional smoking, particularly with respect to a diversion effect.

Abbreviations

CLD: Causal loop diagram

FDA: Food and Drug Administration

NRT: Nicotine replacement therapy

NYTS: National Youth Tobacco Survey

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The full simulation model is downloadable from: https://exchange.iseesystems.com/models/player/arielle-selya/e-cigarette-harm-reduction-policy. This simulation model can be viewed (including model structure, equations, and documentation) and run using the free software isee player (36). A user-friendly, interactive web interface is available at: https://exchange.iseesystems.com/public/arielle-selya/e-cigarette-harm-reduction-policy-interface-tool

Competing interests

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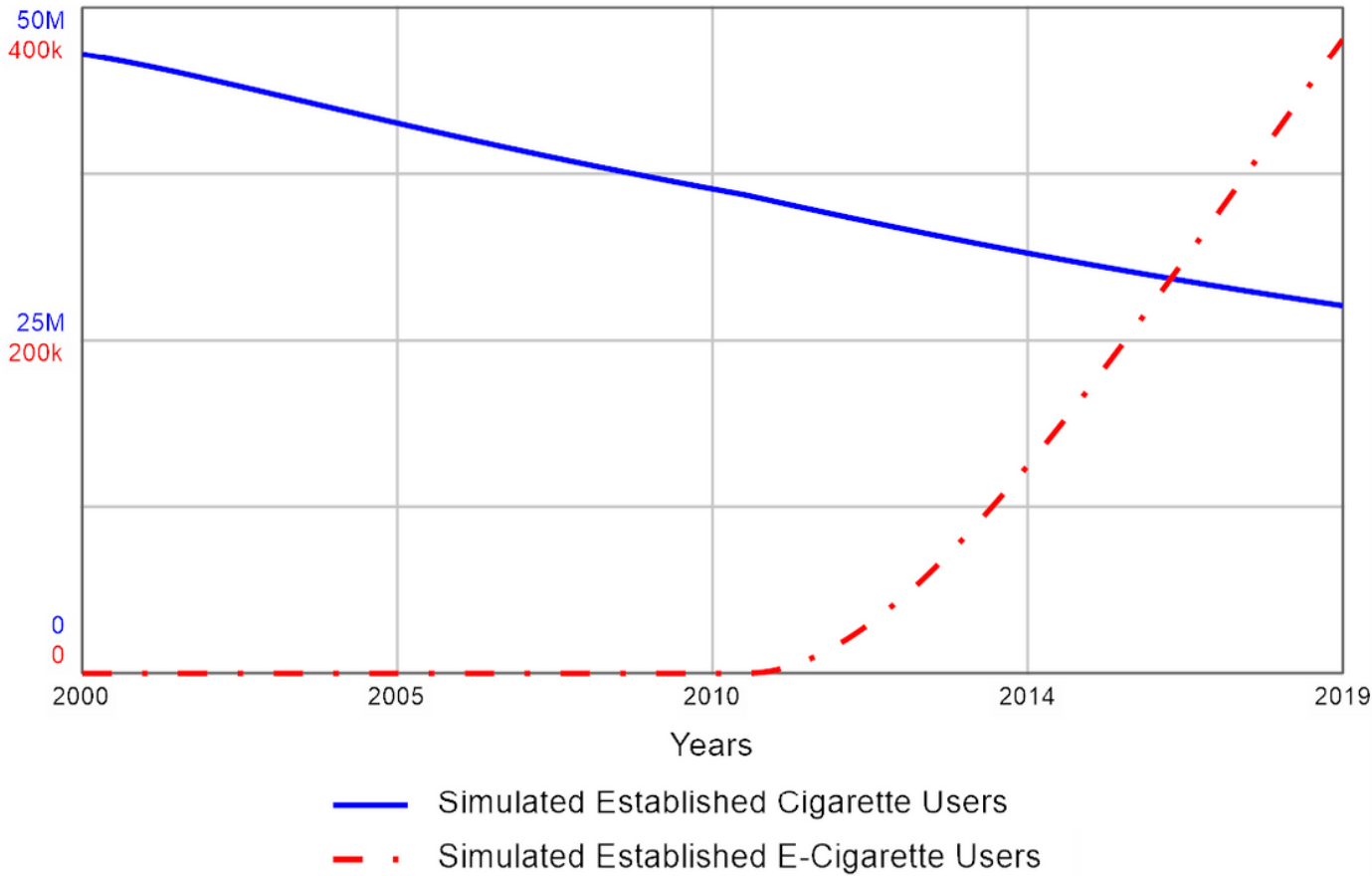
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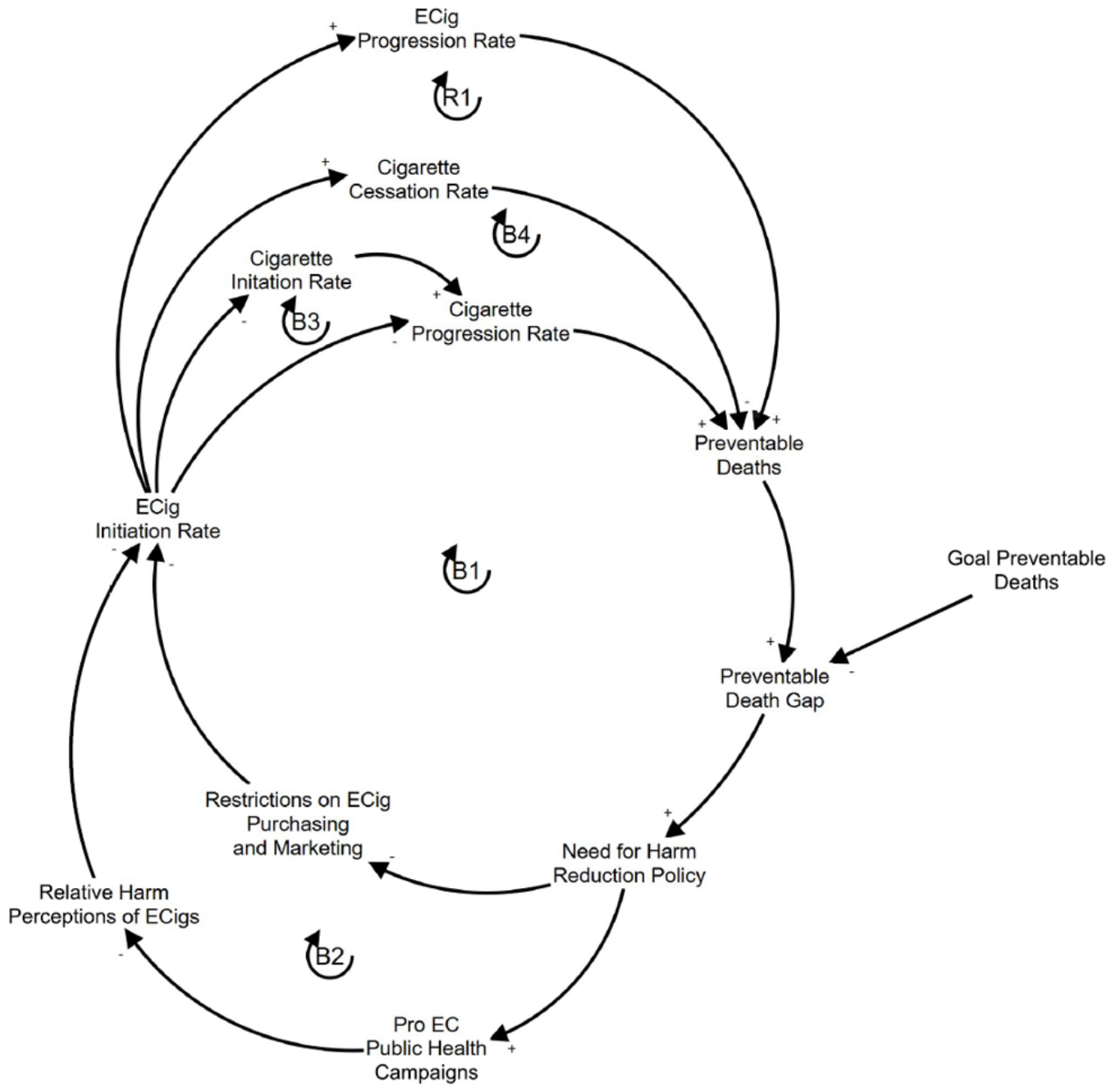
Figure 1

Causal loop diagram of the major feedback loops in cigarette smoking, e-cigarette use, and the current policy. Arrows denote causal links, and the polarity (+/-) at the arrow head denotes a positive relationship and an inverse relationship, respectively. Loops are denoted with an R (reinforcing/positive reinforcing loop) or B (balancing/negative reinforcing loop) and are numbered accordingly. The policy is twofold (public health campaigns that promote e-cigarettes as a less harmful alternative to cigarettes; removing restrictions on e-cigarette purchasing (here, removing flavor bans)). E-cigarettes have 3 possible intended effects on cigarette smoking (diversion from initiation, offsetting consumption, and increasing cessation) and one possible unintended effect (deaths from e-cigarette use, since they are not completely safe).
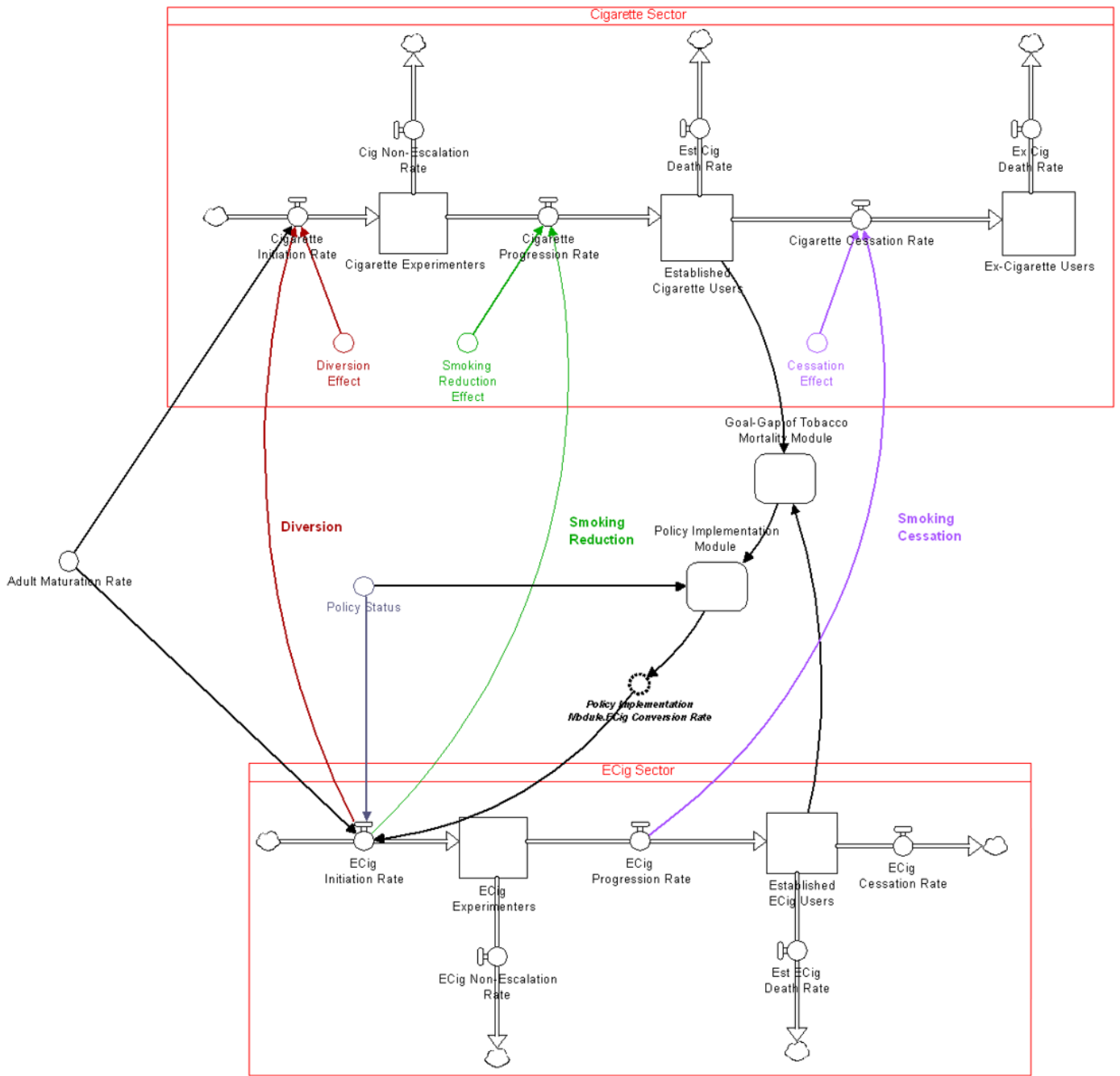
Figure 2

Simplified structure of the stock-and-flow model. Separate aging chains represent cigarette use (top sector) and e-cigarette use (bottom sector) with stocks (represented as squares) for different stages of use, and corresponding flows (represented as valves). The stock of established cigarette and e-cigarette users drives mortality, and this motivates policy implementation which targets e-cigarette initiation rate. This policy acts in 3 ways: diversion from cigarette initiation, reduction of the smoking progression rate, and increasing the cigarette cessation rate.

Simulated Behavior Modes

Figure 3

Simulated Behavior Modes for Exclusive Cigarette and E-Cigarette Use, 2000-2019. After model calibration, simulations show approximately exponential decline in established cigarette use (solid blue line), and exponential increase in established e-cigarette use (dot-dashed red line), between 2000-2019 (40). No policy is implemented in this simulation. Note the different y-axis scales for each line.
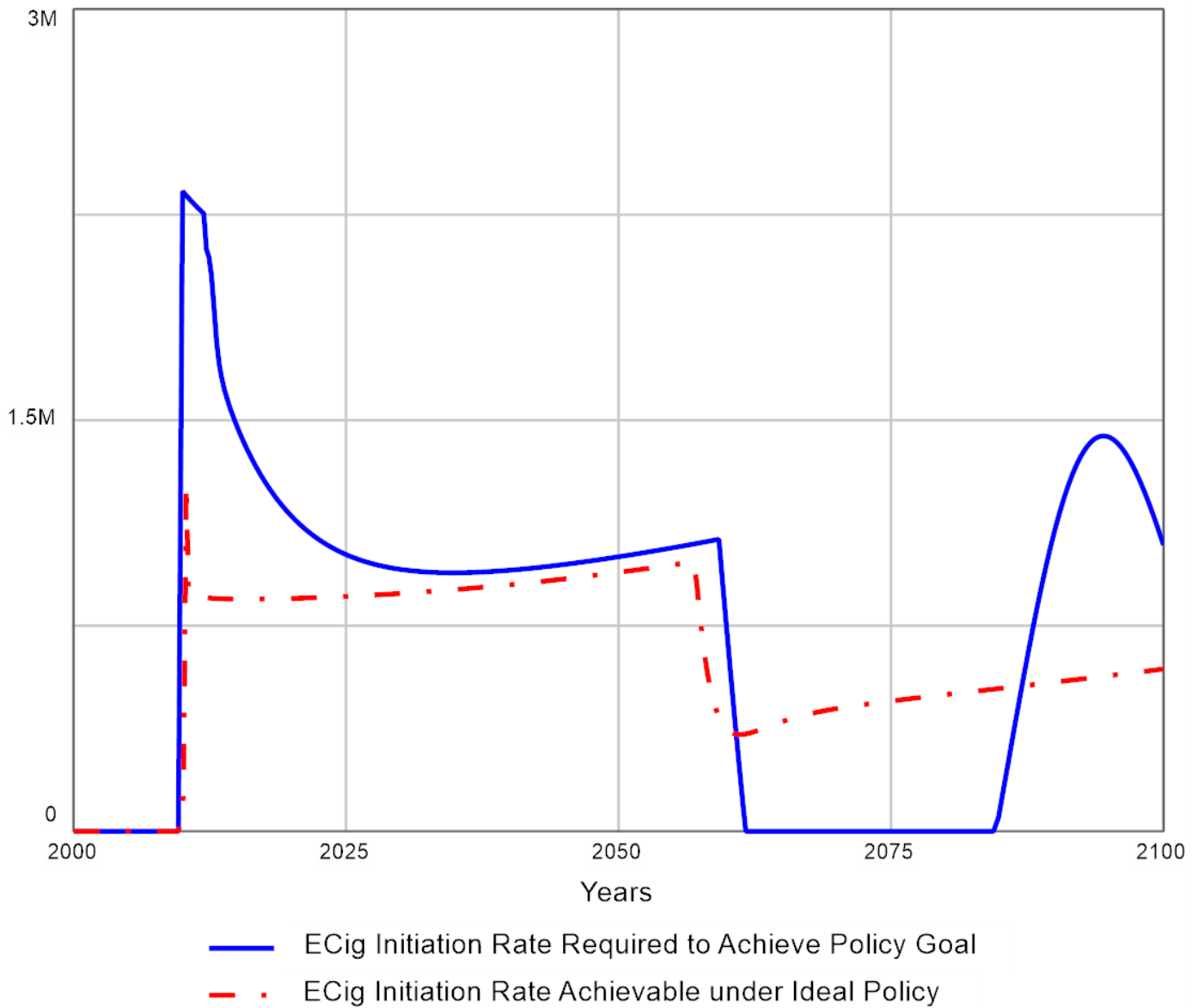
Base Case Simulation
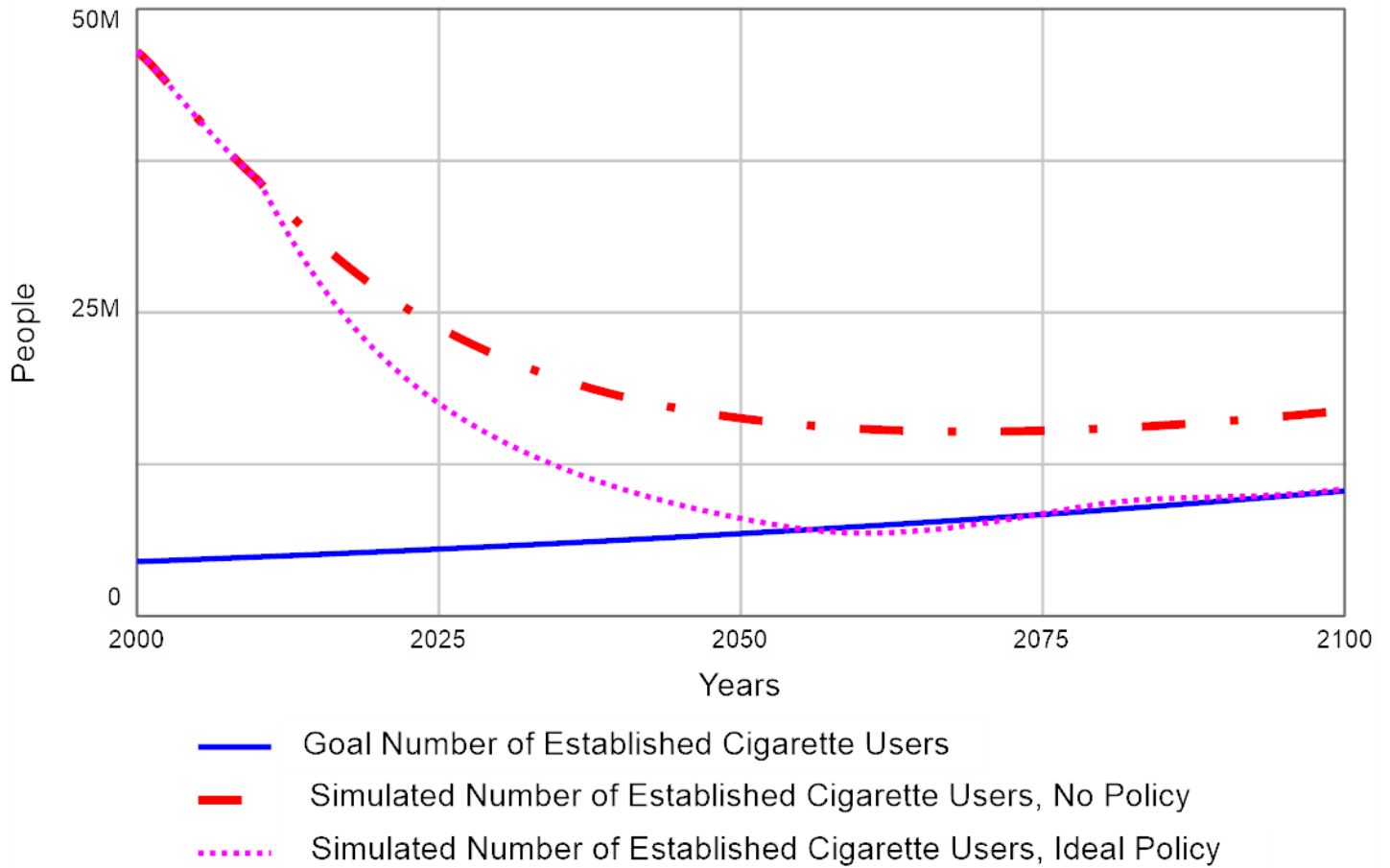
Figure 4

Simulated vs. Goal Established Cigarette Users. The goal number of established cigarette users (solid blue line) is based on the rate of accidental death in the general population, and increases over time with population growth. The simulated number of established cigarette users are shown in the status quo scenario (no policy; dot-dashed red line) and the ideal-policy scenario (starting in 2010; dotted pink line) throughout the time horizon under examination (through 2100).
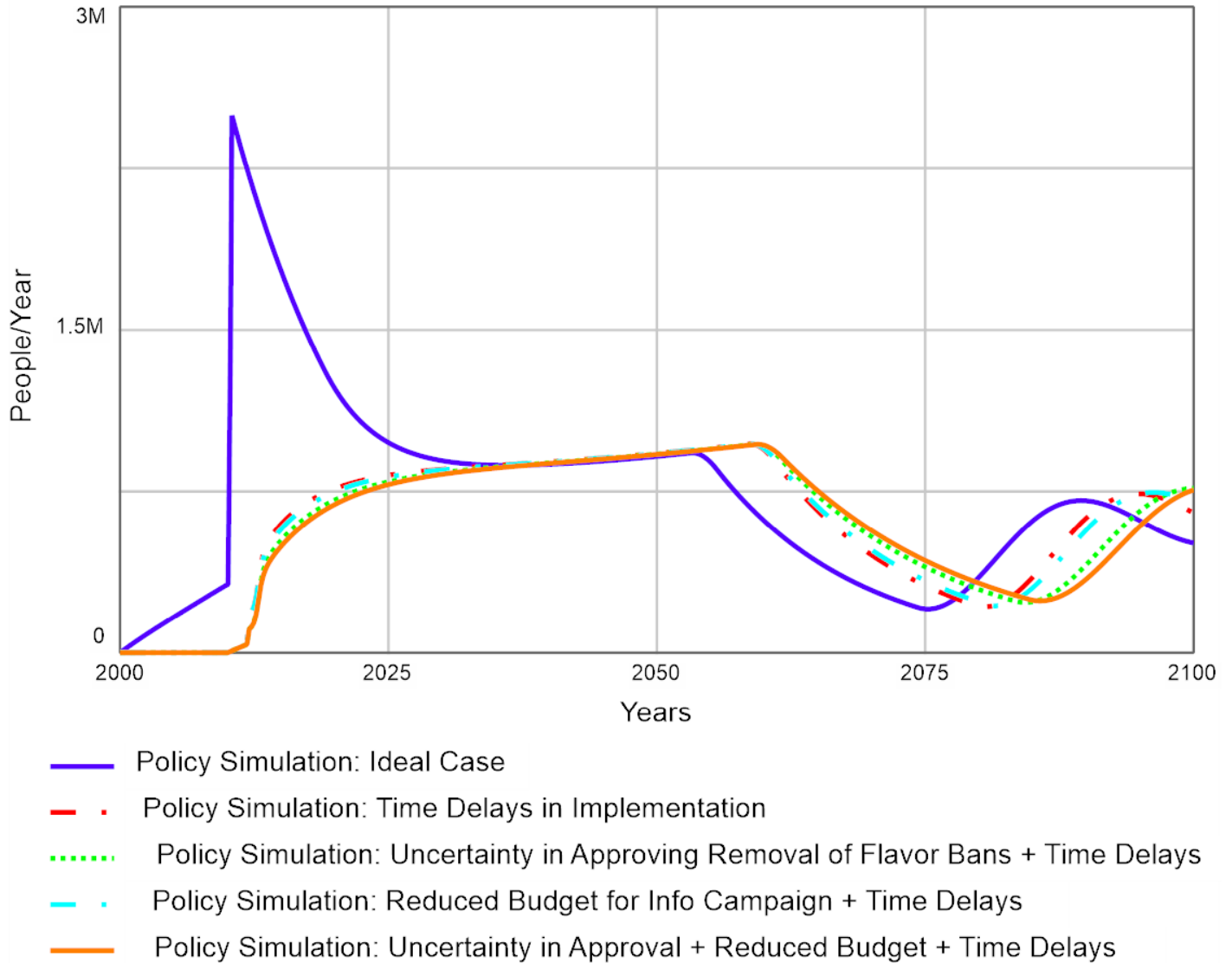
Goal vs. Actual E-Cigarette Initiation Rate

Legend:
— ECig Initiation Rate Required to Achieve Policy Goal
– · – ECig Initiation Rate Achievable under Ideal Policy

Figure 5

Optimal vs. Achievable E-Cigarette Initiation Rates. The flow of e-cigarette initiation rates is the direct target of the policy. The e-cigarette initiation rate required to achieve the goal instantly (solid blue line) is shown against the e-cigarette initiation rate achievable within the limitations of the system (dot-dashed red line).
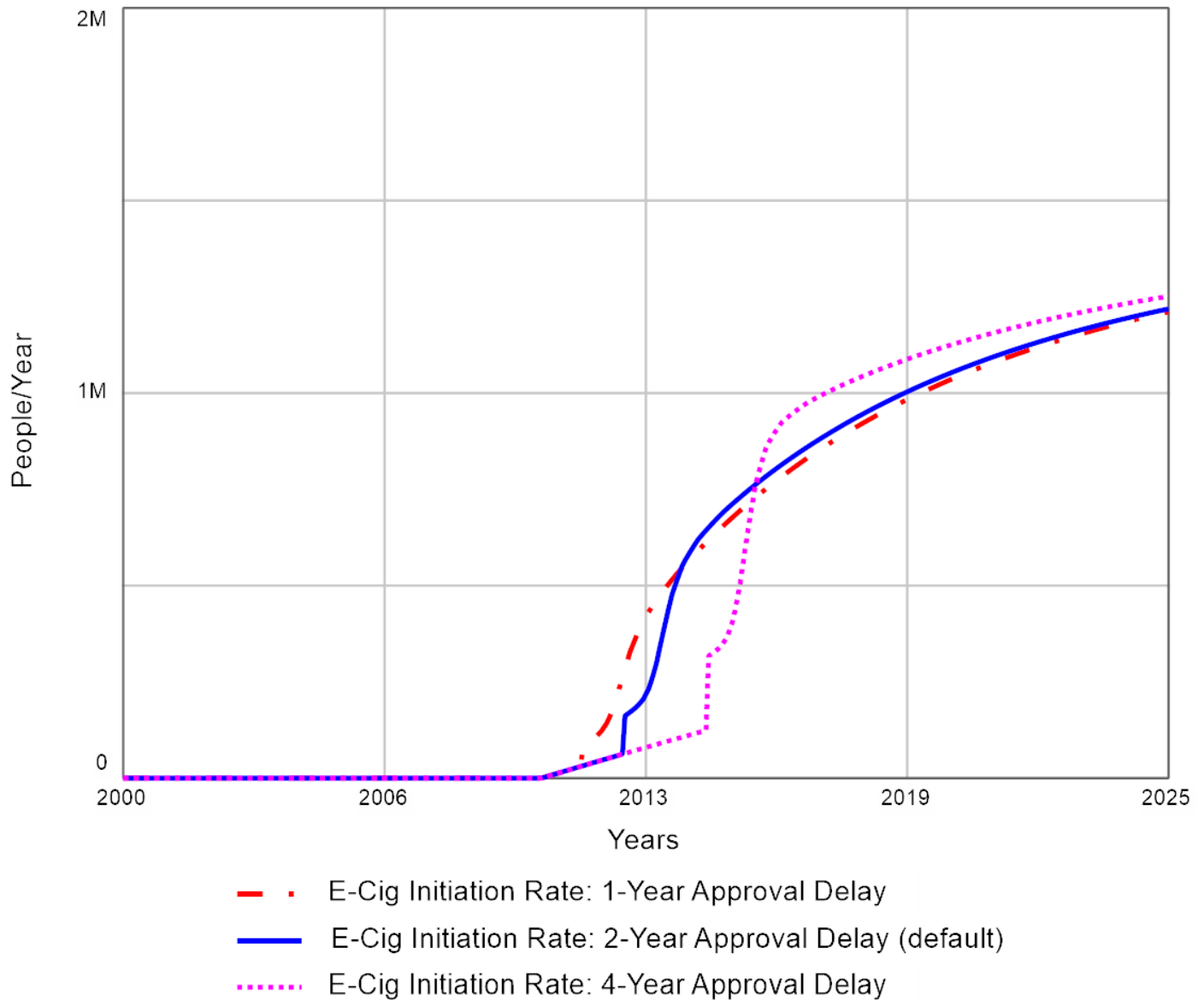
E-Cigarette Initiation Rate

Legend:
- Policy Simulation: Ideal Case
- Policy Simulation: Time Delays in Implementation
- Policy Simulation: Uncertainty in Approving Removal of Flavor Bans + Time Delays
- Policy Simulation: Reduced Budget for Info Campaign + Time Delays
- Policy Simulation: Uncertainty in Approval + Reduced Budget + Time Delays

Figure 6

Policy Simulations showing E-Cigarette Initiation Rates under Ideal Case vs. Practical Limitations. The ideal case (solid blue line) is contrasted with policies with time delays in implementation, alone (dot-dashed red line), with uncertain approval for removing flavor bans (dotted green line), with reduced budget for informational campaigns promoting e-cigarettes as a less harmful alternative (dot-dashed cyan line), and with both uncertain approval and reduced budget (solid orange line).

Figure 7

E-Cigarette Initiation Rates under Different Lengths of Approval Delay. The default delay in the model is 2 years for each policy (referring to a 2-year delay in revoking existing flavor bans; and a 1-year delay in approving an informational campaign followed by a 1-year delay in approving the budget for the campaign), which proceed in parallel. The default 2-year delay (solid blue line) is shown in comparison to scenarios in which each of these delays are halved (dashed red line) or doubled (dotted pink line).