Methodological Approach to Modeling the Potential Impact of a Nicotine Product Standard on Tobacco Use, Morbidity, and Mortality in the U.S.

Center for Tobacco Products
Food and Drug Administration
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1 Background

Nicotine is the primary addictive constituent in tobacco and the "fundamental reason that individuals persist in using tobacco products" (U.S. Department of Health and Human Services, 2010). While nicotine itself is not the direct cause of smoking-related diseases, addiction to the nicotine in tobacco products is the proximate driver of these diseases because it sustains tobacco use (Benowitz, 2010; Henningfield et al., 1998). The addiction caused by the nicotine in tobacco smoke is critical in the transition of smokers from experimentation to sustained smoking and in the maintenance of smoking (U.S. Department of Health and Human Services, 2010; U.S. Department of Health and Human Services, 2014). Combusted tobacco products, including cigarettes, are responsible for the overwhelming burden of disease and death from tobacco product use (U.S. Department of Health and Human Services, 2010; U.S. Department of Health and Human Services, 2014). Moreover, other combusted products, such as little cigars and cigarillos, can share many of the same product characteristics as cigarettes and often function as substitutes for them (Delnevo, 2006). These combusted products also produce many of the same toxic constituents in their smoke as cigarettes, and users receive similar toxicant exposure as cigarette smokers (Pickworth et al., 2017; Pickworth et al., 2018). Noncombusted products such as e-cigarettes and smokeless tobacco have harmful health effects, but they may be less harmful than cigarettes (Levy et al., 2004; National Academies of Sciences, Engineering, and Medicine, 2018).

The Food and Drug Administration (FDA) is considering a tobacco product standard to limit the level of nicotine in cigarettes and certain other combusted tobacco products so that they are minimally addictive or nonaddictive. Such a product standard would be based on FDA's authority to establish a tobacco product standard under section 907 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 387g) as amended by the Family Smoking Prevention and Tobacco Control Act (2009) and would be promulgated through notice-and-comment rulemaking.

This document provides detailed information on the methodology of an analysis to quantify the potential public health impact of a nicotine product standard for cigarettes and certain other combusted tobacco products in the United States (U.S.). It is assumed for the purposes of this analysis that the nicotine product standard would apply to cigarettes (which FDA has previously interpreted to include kreteks and bidis), cigarette tobacco, roll-your-own (RYO) tobacco, cigars other than so-called "premium" cigars (Food and Drug Administration), and pipe tobacco. The standard would not apply to "premium" cigars, waterpipe/hookah tobacco, smokeless tobacco (including chewing tobacco, snuff, and snus), electronic cigarettes (e-cigarettes) and other electronic nicotine delivery systems (ENDS), heated tobacco products, and oral nicotine products such as pouches and lozenges. These exclusions are consistent with instructions given to experts in elicitation processes designed to provide informed estimates for tobacco use transition parameters in the event of a nicotine product standard.

Details of this modeling approach have been previously published in two peer-reviewed publications. Vugrin et al. (2015) provides detail on the model construction, whereas Apelberg et al. (2018) estimates the potential public health impact of a proposed nicotine product standard, utilizing model inputs and assumptions from a 2015 expert elicitation. In line with the previous modeling, we utilize a population projection model using inputs derived from available empirical evidence and expert opinion to estimate the impact of a range of behavioral responses to a potential nicotine product standard on four main outcomes: (1) prevalence of cigarette smoking and noncombusted tobacco use; (2) tobacco-attributable mortality; (3) life years lost due to tobacco use; and (4) quality-adjusted life years (QALYs) lost due to cigarette smoking-attributable morbidity in the U.S. population over time.

The main purpose of this document is to update the models presented in Vugrin et al. (2015) and Apelberg et al. (2018). We document the framework and methodology of the computational model and describe the source of the data inputs that informed creation of an updated baseline for the population health model, including:

1. Updates to input model parameters, assuming 2021 as baseline year, accounting for recent changes in population distribution, mortality, and tobacco product use prevalence;
2. Updates to smoking initiation and cessation rates based on smoking histories from the 1965-2018 National Health Interview Survey (NHIS) data;
3. Updates to assumptions in regard to noncombusted tobacco product (smokeless tobacco, e-cigarette, heated tobacco product, and oral nicotine product) use initiation;
4. Updates to assumptions in regard to switching from cigarettes to noncombusted tobacco products, and from dual use to exclusive cigarette use or noncombusted tobacco product use, using the Population Assessment of Tobacco and Health (PATH) Study data;
5. Updates to smoking-attributable mortality risk estimates considering the 2019 NHIS Linked Mortality Files data, which considers NHIS participants from 1997 through 2018 followed for mortality through the end of 2019; and
6. Utilization of inputs and assumptions from a 2018 expert elicitation, which was repeated considering the 2015 methodology and expert input (seven of the original panel members agreed to participate), but accounting for recent changes in the U.S. tobacco product marketplace and recent scientific results on clinical trials using cigarettes with reduced nicotine content.

In addition, we use the outputs from this updated modeling to analyze the mortality impact of reduced secondhand smoke exposure, smoking-related perinatal conditions, smoking-related fires, and use of non-premium cigars and pipe tobacco based on the ratios of observed deaths from these causes to deaths from cigarette smoking in the U.S. We also conduct a series of sensitivity analyses to examine the impact of key modeling assumptions on the main outcome metrics of interest and the impact of a range of estimates with respect to potential illicit trade.

In 2022, FDA issued proposed product standards to prohibit menthol as a characterizing flavor in cigarettes (87 FR 26454, May 4, 2022) and to prohibit all characterizing flavors (other than tobacco) in cigars (87 FR 26396, May 4, 2002). If finalized, these rules will reduce overall youth initiation and increase cessation among individuals who smoke cigarettes and cigars. In Section 6 of this document, we also describe how we adjust the model by utilizing estimates of the likely population health impact of these rules, quantified in peer-reviewed publications, and discussed in the rules, to adjust the baseline inputs for initiation of combusted and noncombusted products, as well as cessation of combusted products and likelihood of switching to incorporate the impact of the rules in the proposed nicotine product standard.

2 Methodology

FDA has developed a population health model that projects the impact of changes in tobacco product initiation, cessation, switching, and dual use on tobacco use prevalence, morbidity, and mortality in the U.S., considering two types of tobacco products. The model presented here is useful in estimating potential impacts of the nicotine product standard from changes in tobacco use behavior. A

detailed description of the overall model in terms of the inputs, transition behaviors, and outputs that it contains has previously been reported, along with results from a simulation involving use of cigarettes and a hypothetical new product in the U.S. population over time (Vugrin et al., 2015). In the analysis presented in this document, we update the model presented in Apelberg et al. (2018), which describes the impact of a potential product standard that limits the level of nicotine in cigarettes, cigarette tobacco, RYO tobacco, non-premium cigars, and pipe tobacco so that they are minimally addictive or nonaddictive. We estimate the potential impacts of a nicotine product standard by modeling a baseline scenario that specifically incorporates use of two tobacco product classes – 1) cigarettes and 2) noncombusted tobacco products, a class that includes smokeless tobacco, e-cigarettes and other ENDS, heated tobacco products, and oral nicotine products. These product classes were selected because of the magnitude of population health effects from cigarette smoking and the likelihood of product switching to noncombusted products, especially e-cigarettes.

We then compare the baseline scenario to a product standard scenario characterized by the introduction of a potential nicotine product standard that would apply to cigarettes, RYO tobacco, non-premium cigars, and pipe tobacco. Estimates of changes in mortality from other exposures including non-premium cigar and pipe tobacco use are not produced directly by the model but are derived from model outputs instead. The model presented here uses updated inputs derived from empirical evidence and expert opinion to estimate the effect of a potential nicotine product standard on the prevalence of tobacco use, tobacco-related mortality and life years gained. The implementation of a nicotine product standard is expected to increase the likelihood of cigarette smoking cessation and reduce the likelihood of initiation of regular use by reducing the level of nicotine, the major driver of the maintenance of tobacco dependence and use, to minimally addictive or nonaddictive levels. A nicotine product standard may also result, however, in current smokers switching to other tobacco products or becoming dual users, and non-users who have been dissuaded from smoking taking up the use of another tobacco product instead. In the sections below, we summarize the methodology used to project impacts to the population as a whole, and describe the data inputs, data sources, and assumptions used to derive estimates of the potential impact of a nicotine product standard on population health. assumptions used to derive estimates of the potential impact of a nicotine product standard on population health.

2.1 Modeling Approach

2.1.1 Conceptual Framework

The analysis begins with an initial population, divided into subgroups defined by age, sex, and tobacco product use status, accounting for all combinations of current, former, and never use for cigarettes and noncombusted tobacco products, that is representative of the U.S. population in a particular year. The analysis then projects the population changes for subsequent years in one-year time increments, while accounting for births, net migration, and deaths. The full set of product use states and transitions for a two-product model formulation are represented in Figure 1. The number of members of a population subgroup who change tobacco use states is calculated as a function of sex, age, and tobacco product use history. The number of members of a subgroup who survive or die is also a function of sex, age, and tobacco product use status, including time since cessation for former users.

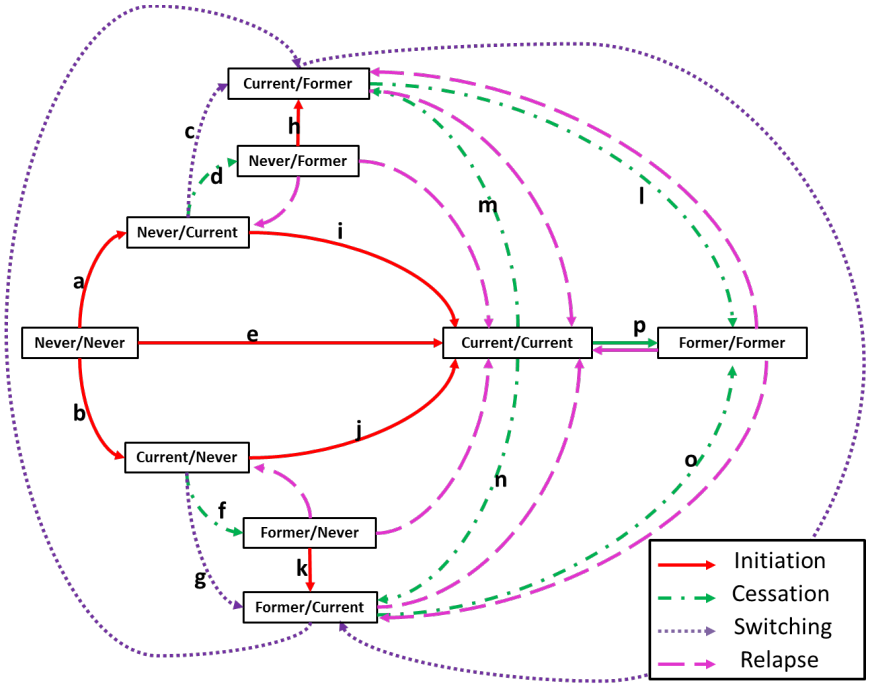


Figure 1. Tobacco Use Status Transitions for a Two-Product Model Formulation. Transition behaviors (illustrated by directed edges) are categorized into four groups: initiation, cessation, switching, and relapse based on the current, former, or never use of the two product classes. Nine possible use states are represented as boxes in which the first and second terms correspond to use of cigarettes and noncombusted tobacco products, respectively.

2.1.2 Implementation

The model is implemented as a discrete dynamical systems model that tracks the number of persons in the population and its constituent subpopulations over time, also referred to as a compartmental model (Tolles et al., 2020).[1] Each subpopulation is defined by a unique combination of sex, age, and tobacco product use. In all the simulations presented in this document, age and time are characterized by single year. The members of each subpopulation have a specified probability of dying and set of probabilities for transitioning from one tobacco use state to another. At each discrete time step in a simulation, the model updates the number of members of each subpopulation by calculating the number of individuals that transition to the subpopulation and remain alive during the time step. The sizes of the subpopulations are also updated by births and net international migration. Details regarding baseline data inputs and sources used in all the simulations are presented in Appendix A of this document. Details on the mathematical implementation and model validation are presented in Appendices B and C, respectively, and in Vugrin et al. (2015). The model is implemented in MATLAB version 9.13.0 (R2022b) (2022).

[1] As Tolles & Luong (2020) explain in their *Journal of the American Medical Association Guide to Statistics and Methods* paper, "In compartmental models, individuals within a closed population are separated into mutually exclusive groups, or compartments, based on their disease status. Each individual is considered to be in 1 compartment at a given time, but can move from one compartment to another based on the parameters of the model."

2.1.3 Scope of the Analysis

The analysis presented in this document estimates the potential public health impact of a tobacco product standard that limits the level of nicotine in cigarettes, cigarette tobacco, RYO tobacco, non-premium cigars and pipe tobacco so that they are minimally addictive or nonaddictive; these products were included in the deliberations of the panel of experts participating in the 2015 and 2018 elicitation process. RYO tobacco, non-premium cigars, and pipe tobacco were included because they are the combusted products that people who smoke cigarettes would be most likely to use as substitutes in order to sustain addiction (Apelberg et al., 2018). Premium cigars and waterpipe/hookah tobacco are assumed to not be covered by a potential product standard because their use patterns make them less likely to serve as substitutes for cigarettes and therefore be used to maintain nicotine addiction (National Academies of Sciences, 2022; Robinson et al., 2017). The population model used in this analysis incorporates transitions and projections related to two types of tobacco products from the year 2021, using a projection period from 2022 through 2100, and assuming implementation of a potential nicotine product standard in 2027. In this analysis, the model tracks use and harm from the following two types of tobacco products: (1) cigarettes, and (2) noncombusted tobacco products (i.e., smokeless tobacco, e-cigarettes, heated tobacco products, and oral nicotine products). While the document describes the impact of a potential nicotine product standard that would include cigarettes and certain other combusted products (i.e., RYO tobacco, non-premium cigars, and pipe tobacco), the main product standard scenario presents the impact of a potential nicotine product standard on cigarette smoking and related morbidity and mortality. We first estimate the impact of a potential nicotine standard on cigarettes because the data are most robust, cigarettes are the most widely used combusted tobacco product, and consequently, the cause of most morbidity and mortality from combusted tobacco product use.

We assess the impact of a potential nicotine product standard on four main outcomes: (1) prevalence of cigarette smoking and noncombusted tobacco use, (2) tobacco-attributable mortality, (3) life years lost due to tobacco use, and (4) QALYs lost due to cigarette smoking-attributable morbidity in the U.S. population over time. We scale the projected changes in avoided tobacco-attributable deaths under the main product standard scenario to estimate the mortality impact of the potential nicotine product standard on other combusted products, including non-premium cigars and pipe tobacco. We use the model outputs to separately estimate the mortality impacts of reduced secondhand smoke, fires caused by smoking, and perinatal conditions. We also examine the potential impact of cigarette smokers switching completely to noncombusted tobacco products (specifically, smokeless tobacco, e-cigarettes, heated tobacco products, and oral nicotine products) rather than quitting tobacco use entirely, as well as the potential for continuing smokers to become dual users of cigarettes and noncombusted tobacco products. In addition, we estimate the impact of dissuaded smoking initiates, i.e., non-users who have been dissuaded from smoking, who instead initiate use of a noncombusted tobacco product.

The values and ranges for the behavioral impact of a potential nicotine product standard for tobacco users and non-users were derived from a formal expert elicitation process conducted in 2018 by Industrial Economics, Incorporated (IEc) through a contract with the FDA (see Section 2.3). Given the inherent uncertainty associated with estimating behavioral responses to a future policy action that has never been implemented, we examine the impact of uncertainty regarding behavioral responses to a nicotine product standard and underlying data inputs and assumptions on model projections and

results. In the subsequent sections, we describe the model inputs and data sources used to quantify the potential population health impact of a nicotine product standard.

2.2 Baseline Scenario Data Inputs and Assumptions

A detailed description of the sources of data used for baseline demographic inputs, cigarette and noncombusted tobacco use transitions, tobacco-related mortality inputs are summarized below and in Appendix A.

2.2.1 Demographic Inputs

Initial Population. The simulation begins with an initial population that reflects the sex, age, and tobacco use distribution (i.e., never, current, and former use of cigarettes and noncombusted tobacco products) of the U.S. population in 2021. This year was chosen because it was the most recent year for which all relevant data were available. The 2021 U.S. population size by sex and age were obtained from U.S. Census Bureau estimates (U.S. Census Bureau).

Births, Net International Migration, and Deaths. Projected births and net international migration in the simulation are derived from projections of birth, net international migrants, and population size produced by the U.S. Census Bureau for the U.S. population from 2021 through 2060 (U.S. Census Bureau). Birth and migration rates from 2061 through 2100 are projected using an exponential smoothing state space model (Hyndman et al., 2008a; Hyndman et al., 2008b). Immigrants entering the U.S. in the simulation are assigned tobacco use status based on estimates of tobacco use prevalence for recently arrived immigrants because of potential differences in tobacco use for immigrants and the U.S. population generally, such as lower cigarette smoking prevalence for female immigrants (Bosdriesz et al., 2013). Cigarette smoking prevalence (current and former use) for immigrants who had been in the U.S. less than five years is obtained from the 2014-2018 NHIS. We also use 2014-2018 NHIS data, which contains data for both e-cigarette and smokeless tobacco product use, to estimate current and former use of noncombusted tobacco products. Specifically, among male immigrants, current and former cigarette use prevalence were 15.2% and 12.9%, respectively; while current and former noncombusted tobacco use prevalence were 2.4% and 8.0%, respectively. Among female immigrants, current and former cigarette use prevalence were 3.9% and 6.3%, respectively; also current and former noncombusted tobacco use prevalence were 1.2% and 3.7%, respectively. We opted for not pooling 2018 and earlier data with 2019 and later data due to significant changes introduced in 2019 to NHIS data collection. Mortality is calculated based on tobacco use status as described below in Section 2.2.3.

Model Population Validation. Vugrin et al. (2015) previously showed that projections of the total U.S. population and annual mortality were similar to those of the Census Bureau (see Appendix C).

2.2.2 Tobacco Use Inputs

Initial Tobacco Use Population. Prevalence of tobacco product use among U.S. adults ages 18 years and over (accounting for all combinations of current, former, and never use for cigarettes and noncombusted tobacco products) were estimated from the 2020 NHIS data (National Center for Health Statistics, 2020) (see Appendix D). NHIS data collection was affected by the COVID-19 pandemic during 2020, with the survey mode of administration changed to telephone-only and then telephone-first

(Blumberg et al., 2021). NHIS weighting procedures were used to minimize any bias introduced by these changes in survey administration, but the possibility of bias still exists (Blumberg et al., 2021). According to NHIS data, the prevalence of current use of any commercial tobacco product among U.S. adults was 20.8% in 2019, 19.0% in 2020, and 18.7% in 2021 (Cornelius et al., 2023; Cornelius et al., 2022). The National Center for Health Statistics advises that these observed trends should be interpreted cautiously due to changes in survey methodology over time (Cornelius et al., 2022). In terms of the tobacco use definitions used in the model, current cigarette smokers had smoked at least 100 cigarettes in their lifetimes and currently smoked every day or some days, former smokers had smoked at least 100 cigarettes but not currently did not smoke at all, and never smokers had not smoked at least 100 cigarettes in their lifetimes. Current e-cigarette and smokeless tobacco users currently used those products every day or some days, former users had used those products at least once but currently did not use at all, and never users had never used the products at all.

Due to modifications in the fielding procedures of the 2021 National Youth Tobacco Survey (NYTS) as a result of the ongoing COVID-19 pandemic, comparisons between NYTS data for 2021 and other pre-pandemic and subsequent survey years may be limited (Gentzke et al., 2022).[2] Thus, 2020 NYTS data are used to estimate prevalence of exclusive cigarette smokers, exclusive noncombusted product users, and dual users for U.S. youth ages 9-17 years old for 2020 (see Appendix D, Table D1). Data collection for the 2020 NYTS was truncated because of school closures due to the COVID-19 pandemic, but nationally representative weighted estimates were obtained from collected data (Gentzke et al., 2020). Efforts were made in our analysis to capture regular use when available data permitted it because of the health risks associated with regular tobacco use. Current cigarette smoking reflects smoking 100 or more cigarettes in one's lifetime and smoking cigarettes on at least one day in the past 30 days. Current smokeless tobacco use reflects using on 20 or more days in the past 30 days for chewing tobacco, snuff, or dip or at least one day in the past 30 days for snus or dissolvable tobacco products; e-cigarette use reflects using on 20 or more days in the past 30 days; heated tobacco product use reflects using on 20 or more days in the past 30 days. The 2020 NYTS did not ask about oral nicotine product use.

Tobacco Use Transitions. Tobacco use transitions considered in the model include cigarette smoking initiation and cessation, noncombusted product initiation and cessation (treated as a single product class for e-cigarettes, smokeless tobacco, heated tobacco products, and oral nicotine products), and switching between product classes. Use transitions are allowed from one year to the next. Detailed information about the calculation of transition values is given in subsequent paragraphs, and Table I1 lists assumptions about transitions that are used in the model.

Smoking Initiation and Cessation. Projected age- and sex-specific smoking initiation and cessation rates for year 2021 are obtained from cigarette smoking histories for birth cohorts reconstructed from NHIS data (from 1965 through 2018) by Cancer Intervention and Surveillance Modeling Network (CISNET) researchers. Specifically, smoking initiation and cessation rates were estimated using age-period-cohort weighted-logistic regression models, following the same approach as presented in Holford et al. (2014), Holford et al. (2016), and Tam et al. (2018). Initiation rates represent

[2] 2021 National Youth Tobacco Survey, Office of Management and Budget (OMB) terms of clearance: "This collection is approved with the understanding that the results of the 2021 NYTS should not be directly compared to previous or subsequent years of data collection that primarily collect data on school campuses. Comparability will be compromised by the change in methods of survey administration and data collection."

a transition to current cigarette use (based on having smoked at least 100 cigarettes in one's life) with conditional probability that an individual who never smoked at the beginning of a year reports having begun to smoke by the end of that year. Cessation rates reflect successful smoking cessation for at least two years given that most relapse occurs during this period (Krall et al., 2002); therefore, transition probabilities for relapse behaviors are set to zero in the modeling simulations presented here. See Meza et al. (Meza et al., 2023) for details regarding the initiation and cessation definitions and mathematical approach used to fit the age-period-cohort models. In the baseline scenario, sex- and age-specific cigarette smoking initiation and cessation rates are assumed to remain constant throughout the projection period.

The CISNET initiation and cessation rates, although well validated and the most recent available, may not fully reflect recent changes in tobacco use patterns including decreases in cigarette smoking prevalence, especially among youth and young adults (Cornelius et al., 2022; Park-Lee et al., 2022). Sensitivity analyses described below were conducted to assess the effect of different assumptions about tobacco use trends.

NonCombusted Product Initiation and Cessation. Limited data are available to derive national up-to-date estimates of annual smokeless tobacco, heated tobacco product, oral nicotine product, and e-cigarette initiation and cessation rates. Recent analyses using PATH Study data (e.g., U.S. Department of Health and Human Services et al., 2021), provide data on initiation of ENDS from Wave 4 (2016-2017) to Wave 5 (2018-2019); however, those estimates are related to transitions from never use to ever use of a specific product at the current wave, rather than transitions to established use, as defined in the population model. Further, Brouwer et al. (2022) provides data on ENDS use initiation with different frequency of use thresholds (at least 1, 10, 20, and 30 days in the past 30 days) using PATH Study data, Waves 1-4 (2013-2017). Also, Brouwer et al. (2023) provides data on ENDS use initiation based on both established use and past 30-day use, using PATH Study data from Waves 2-4 (2015-2017) and Waves 4-5 (2017-2019). However, estimates from these papers do not account for transitions to smokeless tobacco, heated tobacco product, and oral nicotine product use, as defined in the population model. In the absence of up-to-date estimates of exclusive noncombusted product initiation rates from the published scientific literature, we scaled the sex- and age-specific smoking initiation rates from CISNET using youth (ages 9-17) prevalence estimates from the 2017-2020 NYTS, and young adults (ages 18-24) prevalence estimates from the 2020 NHIS. NYTS prevalence estimates for noncombusted product usecorrespond to frequent use, defined as use at least 20 days in the past 30 days.[3] Specifically, the ratio of exclusive noncombusted product use prevalence to cigarette smoking prevalence was used to generate exclusive noncombusted product initiation rates. Prevalence from the 2017-2020 NYTS and 2020 NHIS were also used to partition the CISNET smoking initiation rates into exclusive cigarette smoking, and dual cigarette and noncombusted product initiation. The computed scaling factors and the resulting initiation rates are presented in Appendix D (Tables D5 and D6). In the baseline scenario, it is assumed that sex- and age-specific noncombusted product initiation rates will remain constant until the end of the projection period, with no new product initiation after the age of 30 years. In sensitivity

[3] While past 30-day use is the conventional definition of current use of a tobacco product in the NYTS, we utilized the corresponding definition of frequent use (20 or more days of use in past 30 days) to correspond with initiation of regular use that is more closely associated with longer-term health outcomes. In this context, we scaled the initiation rates to reflect the initiation of regular, longer-term use. This approach is consistent with that for adult initiation to regular use and long-term cessation as defined by CISNET.

analyses, we examine the impact of varying assumptions for baseline trajectories of noncombusted tobacco product use.

We used the CISNET sex- and age-specific cigarette smoking cessation rates as cessation rates for all product categories. Cessation estimates for smokeless tobacco and e-cigarette users are limited, but an analysis of NHIS data found that lifetime quit ratios, calculated as the proportion of ever users who are former users, by age, were similar for cigarette smokers and smokeless tobacco users (data not shown).

Switching between Cigarettes and Noncombusted Tobacco Products. Researchers previously conducted and published a systematic review of published literature on transitions between cigarette and smokeless tobacco use in the U.S. (Tam et al., 2015). The review identified a limited number (n=6) of longitudinal studies in U.S. study populations that have been published since 2000. These studies exhibited considerable heterogeneity in terms of study design and tobacco use definitions. The available estimates (Zhu et al., 2009) indicate that switching completely from cigarettes to smokeless tobacco is rare among adults, although data for switching and transition to dual use in the U.S. are limited. Given the rise of e-cigarettes in the last few years (Boakye et al., 2022; Cullen et al., 2018; Wang et al., 2019), we assume that switching rates from cigarettes to noncombusted tobacco products are based primarily on transitions between cigarettes and e-cigarettes. Specifically, we used the switching rates, for age groups 12-14, 15-17, 18-24, 25-34, 35-54, and 55+, as presented in Brouwer et al. (2023), estimated for youth and adult participants in Waves 2-4 (years 2015-2017) and Waves 4-5 (years 2017-2019) of the PATH Study. From that study, one-wave transitions between exclusive cigarette use and exclusive ENDS use (averaged over the four waves) were 9.7%, 4.9%, 2.6%, 1.5%, 0.7%, and 0.5% for each age group, respectively. For youth (ages 9-17), since the switching data from the PATH Study were not based on recent survey years, and therefore may not represent switching patterns to contemporary ENDS devices, in the sensitivity analysis we assume an increase in switching in the baseline scenario. We also use the age-specific rates of transitioning from dual use to exclusive cigarette use or noncombusted tobacco product use presented in Brouwer et al. (2023). Uptake of noncombusted tobacco products in the product standard scenario is also allowed to occur at any age. We therefore examined the effect of different assumptions about e-cigarette initiation on noncombusted product initiation in sensitivity analyses, described below.

Cigarette Smoking Prevalence Validation. Vugrin et al. (2015) previously showed that projections of smoking prevalence using baseline inputs from the year 2000 were aligned closely with NHIS estimates through 2012 (see Appendix C, Figures C1 and C2). We updated the validation results by comparing U.S. adult cigarette smoking prevalence estimates from the baseline model scenario, as described in Apelberg et al. (2018), to published CDC's estimates for the period from 2015 to 2022. Results showed that baseline model outputs and CDC's estimates were closely aligned (see Appendix C, Figure C3).

2.2.3 Mortality Inputs

Never User Death Rates and Probabilities of Dying. Never user death rates form the basis of projections of mortality and tobacco-attributable mortality in the simulation. U.S. death rates from the 2019 vital statistics data are used for never user death rates at baseline, for ages less than 35 years (Xu et al., 2021), given that tobacco-attributable mortality is assumed to be minimal prior to this age (Adhikar et al., 2008). For ages 35 years and over at baseline, we estimated annual death rates from the 2019 NHIS-Linked Mortality Files (NHIS-LMF) data among never smoking participants in NHIS from 1997

through 2018 who were followed for mortality through linkage with the National Death Index from 2002 through 2019 (National Center for Health Statistics, 2019). Since smokeless tobacco use was assessed during some survey years (1998, 2000, 2005, 2010, 2012-2018), and e-cigarette use was only assessed during 2014-2018 (due to the recent introduction of this product), it was not possible to produce estimates of mortality among never users of cigarettes, smokeless tobacco, and e-cigarettes from 1997 through 2018. However, the majority of ever smokeless tobacco users are also ever smokers (Tomar et al., 2010), so we would expect only minimal differences in estimates for never smokers and estimates for never users of the three product classes. Appendix B, Table B2, shows deaths rates for never users estimated from the NHIS-LMF data. NHIS-LMF never user death rates are adjusted for low mortality in the NHIS's civilian non-institutionalized population, due to the exclusion of people in institutionalized settings such as long-term care institutions (e.g., nursing homes, hospitals for the chronically ill or physically or intellectually disabled, wards for abused or neglected children), persons in correctional facilities (e.g., prisons or jails, juvenile detention centers, halfway houses), and U.S. nationals living in foreign countries. The adjustment was done by using the ratio of U.S. death rates from the 2019 vital statistics data to NHIS-LMF death rates by sex and age (Xu et al., 2021). Appendix B, Table B3, show the ratios used for the adjustment. Never user death rates are projected for the period from 2022 through 2100 using mortality scaling factors obtained from the Lee-Carter mortality forecasting method (Lee & Carter, 1992; Hyndman, 2023; Villegas et al., 2018). Results for the mortality scaling factors are presented in Appendix B, Table B4. The resulting projected, adjusted never user death rates are then converted to probabilities of dying by sex and age using standard demographic methods (Preston et al., 2001).

Cigarette Smoking Mortality Relative Risks. Smoking mortality relative risks (RRs) for current and former smokers, as compared with persons who had never smoked, are estimated as hazard ratios (HRs) using Cox proportional hazard models with NHIS-LMF data from 1997 through 2018 NHIS participants followed for mortality through the end of 2019 (National Center for Health Statistics, 2019). HRs are estimated by sex and age group for current cigarette smokers and by sex, age group, and years since quitting for former smokers. Participants who reported pre-existing health conditions are excluded from the analyses. The HRs are estimated by tobacco-use status, sex, and age group, accounting for the data's complex survey design (Lin, 2000), and assuming a maximum 10-year follow-up period, under the assumption that tobacco-use status remained the same during the survival time. Models are fitted independently by sex and age group, and adjusted for race/ethnicity, educational attainment, poverty level, alcohol consumption, and body mass index (Salazar et al., 2021). The estimated HRs for current cigarette smokers are presented in Appendix B, Table B5. Also, the estimated HRs for former smokers, as a function of years since quitting, are presented in Appendix B, Figure B1.

Noncombusted Tobacco Mortality Relative Risks. Three prospective cohort studies with mortality follow-up informed assumptions about all-cause mortality risk among smokeless tobacco users in the U.S.: the First National Health and Nutrition Examination Survey (NHANES I), the American Cancer Society Cancer Prevention Study I (CPS-I), and Cancer Prevention Study II (CPS-II). The CPS-I and CPS-II studies were much larger than the NHANES study, with each enrolling over one million participants to study health behaviors and cancer risk (Henley, 2005). Analyses of these studies have examined mortality risk among male exclusive smokeless tobacco users compared with never tobacco users, controlling for demographic characteristics and other health behaviors. Since CPS-II was a more recent

cohort (beginning in 1982), we utilized these results here. In CPS-II, current use of chewing tobacco or snuff at baseline was associated with increased mortality risk (HR= 1.18, 95% Confidence Interval [CI] = 1.08-1.29) (Henley et al., 2005). No increased risk of mortality was observed among former smokeless tobacco users in CPS-II data (HR = 0.98, 95% CI = 0.85-1.13). In an analysis of people who switched completely from cigarette smoking to smokeless tobacco use compared with those who quit tobacco use entirely, the mortality risk was significantly elevated (HR = 1.08, 95% CI = 1.01-1.15) (Henley et al., 2007). For the model, we use a RR of 1.18 for current smokeless tobacco users and a RR of 1.00 for former smokeless tobacco users, compared with never tobacco users, and a RR of 1.08 for former cigarette smokers who subsequently use smokeless tobacco, compared with former smokers who subsequently do not use tobacco products. Given the limited time frame that e-cigarettes have been on the market, there are limited data on the long-term health risks of their use. As a result, we apply the same risks that are used for traditional smokeless tobacco to noncombusted product users generally in this analysis. In sensitivity analyses, we examine the impact of varied assumptions about the health risks of noncombusted tobacco products.

Tobacco User Probabilities of Dying. Mortality probabilities for current and former tobacco users are obtained by multiplying never user probabilities of dying (as described in the beginning of this subsection) by relative risk according to tobacco use status. In the main analysis, due to limited epidemiologic evidence of the health risks of dual use relative to cigarette smoking, we assume that dual users of cigarettes and smokeless tobacco maintain the same risk as cigarette only smokers. In a sensitivity analysis, we examine the impact of an increased mortality risk among dual users. For individuals switching from cigarettes to noncombusted product use, the RR for switching is multiplied by the RR of being a former smoker. The probability of dying is also constrained to be no larger than the risk for a current cigarette smoker of the same age and sex and to be no less than the risk for a current noncombusted tobacco product user of the same age and sex (see Appendix E for more details on the calculations used to generate mortality risks across all tobacco use states). The final projected probabilities of dying for each of the nine tobacco use states by age and sex are then multiplied in the model by the numbers of members of the relevant population subgroups to obtain the numbers of individuals surviving and dying during the time step.

2.3 Product Standard Scenario Data Inputs and Assumptions

As described in the background, a potential nicotine product standard is expected to impact the likelihood that current smokers will quit and non-smokers will become established, addicted smokers. In assessing the potential magnitude of impact on tobacco use and mortality, we compare the baseline scenario against scenarios in which the smoking cessation and smoking initiation rates in the population are influenced by a potential nicotine product standard. In addition, we examine the potential impact of smokers who quit and switch to a noncombusted product instead of quitting all tobacco completely, as well as the potential for continuing smokers to take up a noncombusted product and become dual tobacco users. We also examine the potential for those who do not initiate smoking (i.e., do not become established smokers) as a result of a potential nicotine product standard to take up a noncombusted product instead. In all the simulations presented in this document, we assumed that the potential nicotine product standard in the product standard scenario is introduced in 2027.

The values and ranges for the potential impact of a nicotine product standard on tobacco users and non-users were derived from the result of a formal expert elicitation conducted by Industrial

Economics, Incorporated (IEc) in 2018 through a contract with the FDA. These estimates supersede those collected in an initial expert elicitation conducted by IEc in 2015. The 2018 elicitation generally reconvened the same expert panel as 2015 and allowed them to update their estimates considering several studies (e.g., Donny et al. (2015) and Hatsukami et al. (2017)) on the effects of very low nicotine content (VLNC) cigarettes, as well as changes in use of tobacco products including ENDS (e.g., Jamal et al. (2017)). The 2015 elicitation methodology used to identify experts, develop the protocols, conduct the elicitations, and summarize the findings has been described in Apelberg et al. (2018). Additional details regarding the 2018 elicitation are provided in Appendix F in this document.

For the 2015 elicitation, IEc identified candidates from the fields of tobacco policy and tobacco science using a keyword search of the published literature. IEc then ranked the candidates based on their degree of influence using the Hirsch index (or h-index) and, in that order, recruited eight experts. Individuals were required to self-certify that they were free of any actual, apparent, or potential conflicts of interests before being deemed eligible to participate. In 2018, IEc contacted the eight panel members and formally invited them to participate in the updated elicitation. Seven of the original panel members agreed to participate and one member, who had since retired, declined. In addition to certifying their absence of any conflicts of interest, the returning panel members were instructed to refrain from reviewing the expert judgments from 2015 in order to avoid any influence from previous estimates.

The expert elicitations followed the same general procedures in 2015 and 2018. In each case, the elicitation process centered around three sessions conducted online by IEc using web conferencing software. In 2015, briefing books with key papers on the topics of interest as well as background data on tobacco use and policy were provided to the experts, who were asked to identify any other relevant information to share with the panel, for discussion in the initial session. In 2018, panel members discussed in an initial workshop a then recently-published FDA modeling analysis of potential population health effects of a nicotine product standard that incorporated findings from the 2015 expert elicitation (Apelberg et al., 2018), as well as other relevant recent research on the effects of low nicotine cigarettes and current tobacco product use. In the second and third sessions, detailed questionnaires were completed and reviewed independently by each expert with facilitation by IEc. The questions addressed by the experts were the anticipated impact of a nicotine product standard on:

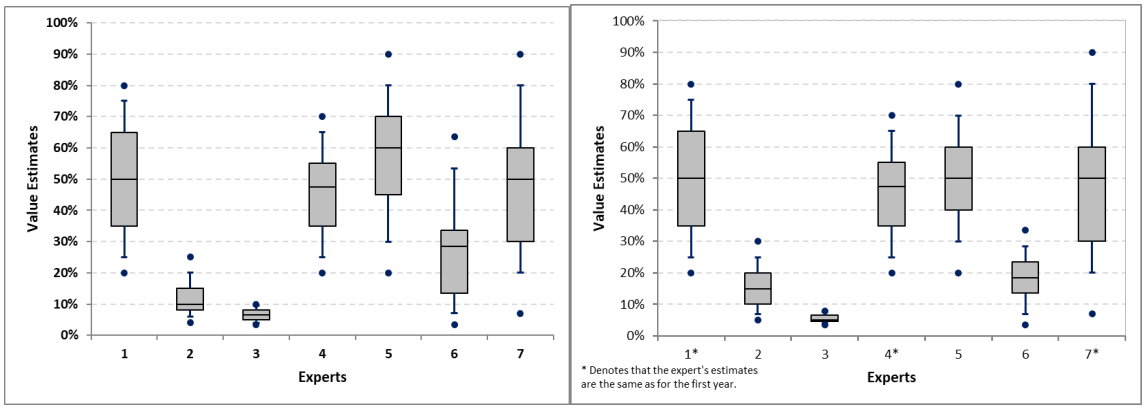
- cigarette smoking cessation rates;
- switching from cigarette smoking to use of non-covered tobacco products (i.e., premium cigars, waterpipe/hookah tobacco, smokeless tobacco, and e-cigarettes or other ENDS);
- dual use with non-covered tobacco product rates;
- cigarette smoking initiation rates; and
- non-covered tobacco product initiation rates.

Each expert was asked to provide his or her best estimates of expected impacts of the potential nicotine product standard. To characterize the uncertainty surrounding each expert's estimates, the protocol asks for estimates of seven values (minimum and maximum plausible values, and estimates of the 5^{th}, 25^{th}, 50^{th}, 75^{th} and 95^{th} percentile values), reflecting the expert's level of confidence (or uncertainty) about the true value of the parameter to be estimated. Experts were asked first about impacts in the year immediately following the potential product standard's implementation and then

about the impacts in the years following the first full year of implementation. Experts had the option of providing separate estimates of impacts for males and females for the initial and subsequent years. Switching, dual use, and initiation of non-covered products were broken out by product: e-cigarettes, smokeless tobacco, premium cigars, and waterpipe/hookah tobacco. For each question, experts were asked to provide the factors they considered pertinent to answering the question, including the studies and research findings most influential to informing their views and to rate their familiarity with the relevant literature. The elicitation process provided the experts with opportunities to interact and discuss divergent views in the initial sessions, from which each expert independently generated his or her estimates.

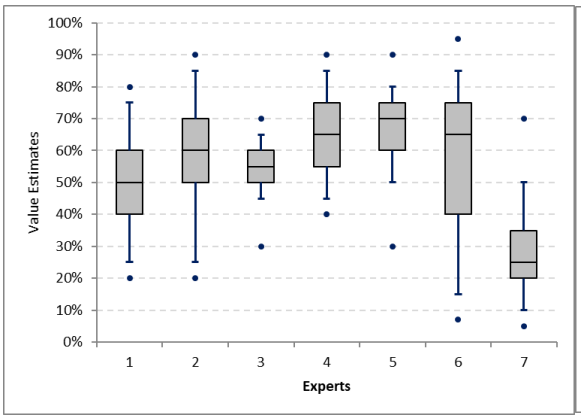
In general, estimates of the effects of a nicotine product standard on use behaviors such as smoking cessation, product switching, and smoking initiation were greater in magnitude in the 2018 expert elicitation than in the previous 2015 elicitation. For example, the median estimates of smoking cessation were 36% in the first year following implementation of a nicotine product standard and 34% in subsequent years in the 2018 elicitation, compared to 25% and 22%, respectively, in 2015. For product switching (from cigarettes to non-covered tobacco products), the median estimates were 56% and 58% in the first and subsequent years following implementation in the 2018 expert elicitation and 41% and 40% in 2015. Median estimates of reductions in smoking initiation were 63% and 65% in the first and subsequent years in the 2018 elicitation and 46% and 49% in 2015. In general, changes in the experts' estimates over time suggest a change in their opinion of the appeal of e-cigarettes as an alternative to other tobacco products including cigarettes. Calculations indicate that the absence of one of the experts in the updated elicitation did not have a substantial effect on the differences in the median estimates of parameter values provided by the experts. Overall, the experts' estimates indicate that the proposed product standard would introduce substantial changes in tobacco use behaviors which would result in substantial public health benefits.

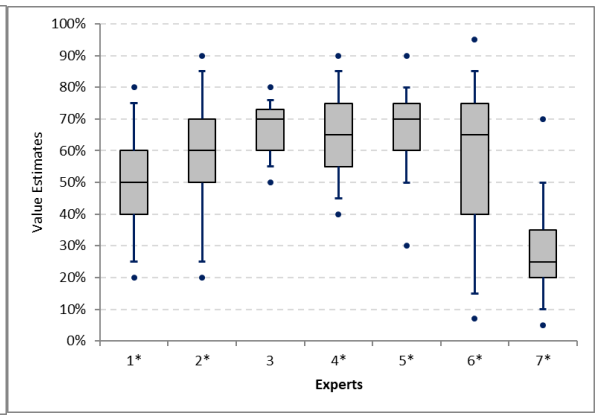
The behavioral transitions that were examined in the expert elicitation, as well as the values and ranges derived from the elicitation are summarized in Figures 2a-e below. The values and ranges that each expert provided for each of the five parameters for the first and subsequent years are provided in the IEc expert elicitation report, and in Appendix F in this document. The estimation of transition probabilities under the product standard scenario is described in Appendix G.



(i) First year (ii) Subsequent years

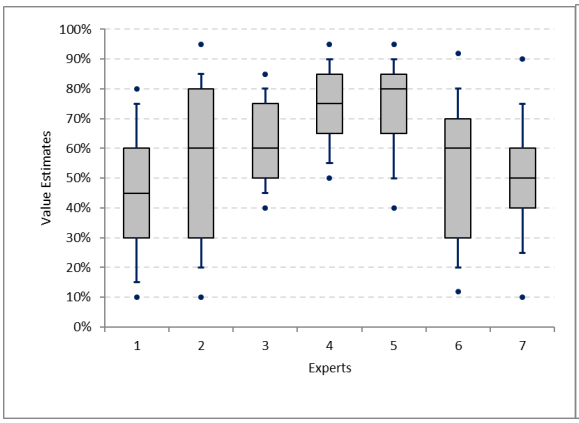
a. Percent of current smokers in the population who quit smoking in the first year after the proposed standard (i) and subsequent years (ii)

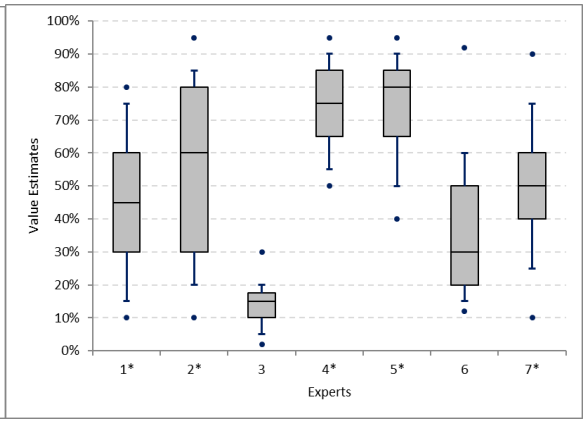




(i) First year (ii) Subsequent years

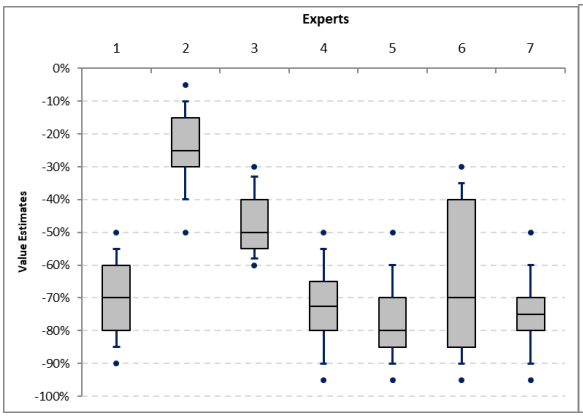
b. Percent of quitters in the population switching to non-covered tobacco products in the first year (i) and subsequent years (ii)

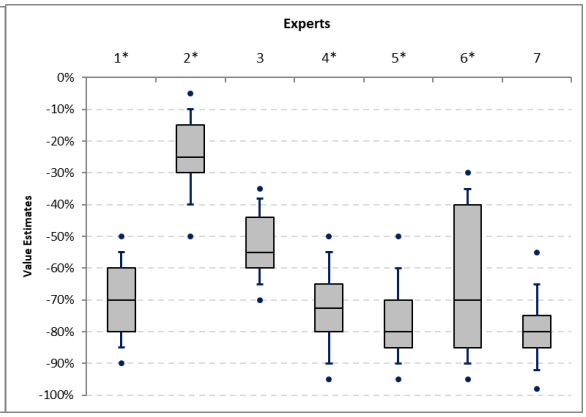




(i) First year (ii) Subsequent years

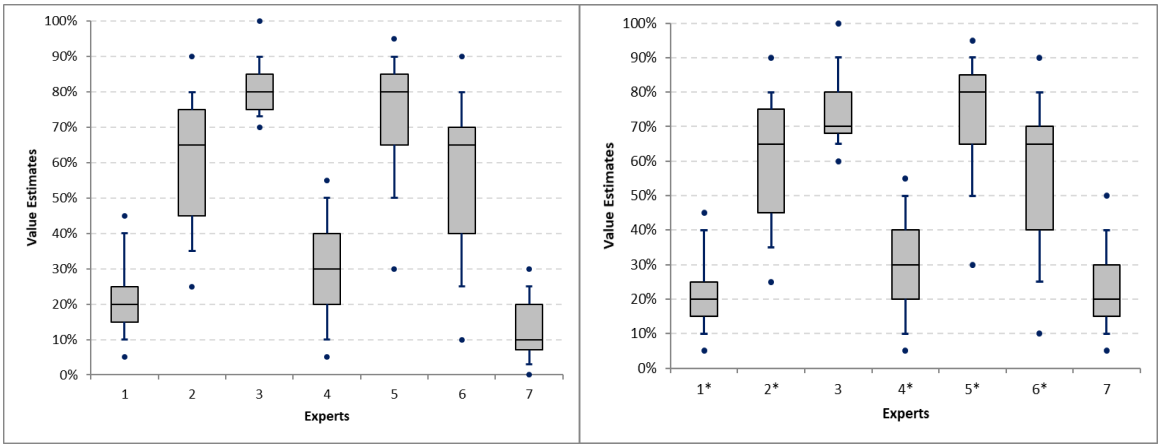
c. Percent of continuing smokers in the population who become dual users with non-covered tobacco products in the first year (i) and subsequent years (ii)





(i) First year (ii) Subsequent years

d. Percent reduction in baseline annual smoking initiation rates in the first year (i) and subsequent years (ii)



(i) First year (ii) Subsequent years

e. Percent of dissuaded smoking initiates in the population who initiate with non-covered tobacco products instead in the first year (i) and subsequent years (ii)

Figure 2. Behavioral Input Parameter Values Provided by 2018 Expert Elicitation Participants to Estimate the Impact of the Proposed Standard on Premature Morbidity and Mortality in the U.S.

For each of the five parameters, the expert elicitation produced seven estimates of the minimum and maximum, and 5th, 25th, 50th (median), 75th and 95th percentile values, one from each of the seven different experts. These input parameters were uniquely grouped and ordered by expert (for each of the 7 experts). That is, inputs from the same expert were grouped and formed a five by seven matrix. For each parameter of this matrix, 1000 sampling elements were sampled using the Latin hypercube sampling method and using the values of the minimum, 5th, 25th, 50th, 75th and 95th percentiles, and maximum. Using 1000 sampling elements for each of the five input parameters and by incorporating all other inputs of the model, 1000 simulations were conducted for each expert.

In simulating the effects of a nicotine product standard on population health, we assume that the risks from cigarette smoking do not appreciably change among those continuing to smoke after implementation of such a standard (other than through the potential for increased smoking cessation in the future). In the past, tobacco manufacturers have marketed "light" cigarettes as less harmful alternatives on the basis of lower machine-measured yields of nicotine or other constituents achieved through design features such as ventilation holes (Pollay & Dewhirst, 2002). However, rather than reduced exposure to constituents, it has been demonstrated that cigarette users could engage in compensatory smoking by modifying their use behaviors (e.g., blocking the ventilation holes with users' fingers and mouth) to compensate for this increase in ventilation and extract more nicotine from the products (Scherer, 1999). As a result, these products were designed to make them appear light to the user but could deliver as much nicotine as cigarettes with higher machine-measured nicotine yields.

In contrast to lower nicotine achieved through design features such as ventilation holes, the intention of a nicotine product standard would be to set a maximum nicotine content level in the tobacco filler of cigarettes and certain other combusted tobacco products. Unlike modifications such as ventilation holes that affect nicotine yield in smoke but can be overcome through user behavior,

reducing the nicotine content in the finished tobacco product places an absolute maximum limit on the amount of nicotine that can be extracted by the user from one cigarette. Multiple randomized controlled trials and clinical studies of VLNC cigarettes have demonstrated that while some transient compensatory smoking may occur following initial VLNC cigarette exposure, after continued use of VLNC cigarettes, smokers stop compensating (i.e., there are no sustained increases in cigarettes per day (CPD), CO exposure, or smoking topography compared to control conditions) (Benowitz et al., 2007; Benowitz et al., 2012; Buchhalter et al., 2005; Donny et al., 2007; Hatsukami et al., 2010; Hatsukami et al., 2013b; Hatsukami et al., 2013a; Walker et al., 2012). In fact, several studies have found reductions in cigarettes smoked per day and toxicant exposure resulting from the use of VLNC cigarettes (e.g., (Benowitz et al., 2012; Benowitz et al., 2007; Buchhalter et al., 2005; Donny et al., 2007; Hatsukami et al., 2013a; Hatsukami et al., 2013b; Hatsukami et al., 2010; Hatsukami et al., 2018; Walker et al., 2012).

As described in Apelberg et al. (2018) and presented as a consideration during the 2015 and 2018 Expert Elicitations, use of premium cigars and waterpipe/hookah tobacco are associated with very different patterns of use and economic cost (National Academies of Sciences, Engineering, and Medicine, 2022; Robinson et al., 2017); two factors that make it unlikely that cigarette smokers would quit cigarettes and switch to these products in large numbers in order to maintain their addiction. All of the experts in 2018 estimated that a large proportion of those switching from cigarettes would use e-cigarettes. In the main analysis, we assume all switching is to either e-cigarettes, heated tobacco products, smokeless tobacco, or oral nicotine products and use the noncombusted tobacco product RRs as described in Section 2.2.3. In the sensitivity analysis, we apply a higher mortality RR for use of noncombusted products. That analysis can suggest potential health impacts that may be observed if smokers switch to non-covered combusted products (i.e., premium cigars or waterpipe/hookah tobacco).

2.4 Incorporation of Uncertainty and Sensitivity Analyses

2.4.1 Uncertainty Through Monte Carlo Simulation

Given the inherent uncertainty associated with projecting the long-term impact of a future regulatory action, we conducted a range of analyses to examine the impact of uncertainty around key model inputs and assumptions on tobacco use prevalence and premature mortality. First, in the main analysis, we examined uncertainty in the behavioral responses to a potential nicotine product standard by conducting a Monte Carlo simulation using the distributions presented in Figure 2 (and in Appendix F). For the product standard scenario, a Latin hypercube sampling design with one thousand simulations was conducted for each set of expert-defined distributions, resulting in a total of seven thousand simulations. A further exploration of the resulting distributions indicated that most of the distributions appear to be skewed or skewed bimodal, while others appear to be symmetric. As a result, model output distributions could also present a skewed distribution pattern. The resulting model outputs were aggregated to create an overall set of output distributions, and distribution percentiles were calculated across all seven thousand simulations. Given the skewed distribution pattern in some model outcome distributions, the median value of the distribution is presented below as the main estimate and preferred measure of central tendency, as the mean is not usually in the middle of the distribution. Also, the 5th and 95th percentiles are presented as the lower and upper bounds, described below as the prediction range (PR).

2.4.2 Sensitivity Analyses

We conducted sensitivity analyses to assess the impact of specific data input assumptions, including those related to baseline trends in noncombusted product use, noncombusted product mortality risk, dual product use mortality risk, and switching to non-covered combusted products. Specifically, we conducted sensitivity analyses accounting for the following scenarios: (1) an increase in initiation of noncombusted tobacco product use among those who would otherwise not have used tobacco in the baseline scenario; (2) an increase in switching from cigarettes to noncombusted tobacco product use in the baseline scenario; (3) a decrease in smoking initiation in the baseline scenario; (4) an increase in smoking cessation in the baseline scenario; (5) the impact of using initiation and cessation rates for ENDS from PATH analyses as input model parameters at baseline; (6) lower and higher noncombusted tobacco product risk compared to baseline; (7) the impact of a varying baseline mortality risk associated with dual use of cigarettes and noncombusted tobacco products; (8) changes in baseline mortality rate projections; and (9) the potential impact of a nicotine product standard, accounting for the emergence of an illicit market for full nicotine content (FNC) cigarettes.

Initiation of e-cigarettes among youth and young adults has historically been on the rise, but recent data has suggested that youth use of e-cigarettes may have potentially peaked in 2019 and declined thereafter. According to results from the NYTS, frequent e-cigarette use defined as use at least 20 days in the past 30 days among middle school and high school students ages 9-17 rose from 2.9% in 2018 to 5.3% in 2019, then declined to 3.9% in 2020 and approximately 4.0% in 2022 (see (Cullen et al., 2018; Wang et al., 2019)(Cooper et al., 2022) for additional results). While noting the observed decrease in e-cigarette use prevalence since 2019, in a sensitivity analysis we also projected prevalence for exclusive cigarette smoking, exclusive noncombusted use, and dual use for the period 2021-2030 from NYTS data, assuming that exclusive noncombusted use and dual use would increase by 25% during the period 2021-2030 (see Appendix D, Table D2) because of the previous substantial increases in e-cigarette use among youth. This assumption could be conservative if prevalence of e-cigarette use remains about the same or decreases during the period. Those projections were used to compute scaling factors to estimate noncombusted product initiation rates (see Appendix D, Table D3). Noncombusted initiation was assumed to remain constant from 2031 until the end of the projection period.

To assess the impact of assumptions about current switching behavior, we conducted a sensitivity analysis in which switching rates increased by 50% and 100% in the baseline scenario. Current estimates of mortality risk for noncombusted product use are for smokeless tobacco use and are based on studies with a baseline assessment of use and an extended period of mortality follow-up, which may underestimate risks if some users quit during follow-up. We conducted sensitivity analyses in which smoking initiation rates decreased by 25% during the period 2021-2030, and smoking cessation increased by 10% in the baseline scenario. This assumption was used considering the decreased pattern in smoking prevalence in recent years. We also conducted sensitivity analyses considering initiation and cessation rates for ENDS, estimated from the PATH data Waves 2-4 (2015-2017) and Waves 4-5 (2017-2019), as presented in Brouwer et al. (2023). We explored the use of Brouwer's data as an alternative approach of the use of scaled smoking initiation rates for noncombusted tobacco product use; also, to explore the effect of using cessation rates for ENDS as an estimate of cessation for noncombusted tobacco products.

Estimates of mortality risk for e-cigarette use that are directly estimated from follow-up data are currently unavailable. We therefore conducted sensitivity analyses in which relative mortality risk for noncombusted product use was set at 1.1 and 1.3 (Henley et al., 2005). That is, assuming an average smoking mortality risk of 2.5 and a median risk of 1.18 for current users of noncombusted tobacco products, as compared with never smokers, then we assumed that the excess risk of using noncombusted tobacco products is 12% (=100x0.18/1.5) that of the excess risk associated with smoking cigarettes. Thus, the lower and upper excess risk for noncombusted products imply a range from 7% (=100x(1.1-1)/1.5) to 20% (=100x(1.3-1)/1.5) that of smoking excess risk for both genders.

In the baseline scenario, mortality risk from dual use of cigarettes and noncombusted tobacco products is assumed to be the same as cigarette smoking only. To relax this assumption, we conducted sensitivity analyses in which dual use mortality RRs in the baseline scenario were: 18% greater than the RR associated with smoking cigarettes (i.e., equal to the product of noncombusted and smoking RRs); dual use RR is the average of cigarette and noncombusted use RR; and dual use RR is equal to the noncombusted use RR. We also conducted a sensitivity analysis to examine the impact of assuming a decreased trend in mortality rates until 2060 using the Lee-Carter mortality estimates, and then keeping mortality rates constant after 2060. The key modeling assumptions, their scientific rationale, and the sensitivity analyses conducted are shown in Table 1. For the sensitivity analyses, all other parameter values are set to their values from the main analysis.

Table 1. Key Modeling Assumptions and Sensitivity Analyses Conducted to Examine Their Impact on Tobacco Use Prevalence and Mortality Projections.

Assumption	Rationale	Sensitivity Analysis
In the baseline scenario, initiation of noncombusted tobacco products is assumed to remain constant during the duration of the simulation.	While e-cigarette use remains popular among youth, recent trends indicate a decrease in prevalence of use among young people. Conservatively, we assume a constant level of noncombusted product initiation.	Examine the impact of increasing baseline rates of noncombusted product initiation by 25% during the period 2021-2030.
In the baseline scenario, switching from cigarettes to noncombusted tobacco products is based on epidemiological studies examining transitions from cigarettes to e-cigarettes.	It is assumed that switching from cigarettes to noncombusted products is highly dominated by transitions to e-cigarette use.	Examine the impact of an increase in switching (50% and 100% increase) from cigarettes to noncombusted product use per year in the baseline scenario.
In the baseline scenario, smoking initiation rates remain constant throughout the simulation period.	Although smoking prevalence has decreased in recent years, we assumed that smoking initiation remains constant with time, and changes in smoking prevalence are highly dominated by the increase in switching to noncombusted products.	Examine the impact of a 25% decrease in smoking initiation rate during the period 2021-2030.

In the baseline scenario, smoking cessation rates remain constant throughout the simulation period.	Although smoking prevalence has decreased in recent years, we assumed that smoking cessation remains constant during the simulation period, and that NHIS-derived cessation rates used in the model reflect recent changes in smoking cessation.	Examine the impact of a 10% increase in smoking cessation in the baseline scenario.
In the baseline scenario, smoking initiation rates were scaled to generate initiation rates for noncombusted tobacco products. Smoking cessation rates were used as cessation rates for noncombusted tobacco products.	Limited data are available to derive national up-to-date estimates of annual smokeless tobacco, heated tobacco product, oral nicotine product, and e-cigarette initiation and cessation rates.	Examine the impact of using initiation and cessation rates for ENDS, estimated from the PATH Study data for Waves 2-4 (2015-2017) and Waves 4-5 (2017-2019), as presented in Brouwer et al. (2023).
In the baseline scenario, mortality risks from the use of noncombusted tobacco products are assumed to be equal to the traditional smokeless tobacco all-cause mortality risks observed in CPS-II.	CPS-II reflects the largest U.S. cohort to examine all-cause mortality in relation to smokeless tobacco use. Risk may be underestimated due to fixed exposure and long follow-up period. Risks may be overestimated if the risks of e-cigarettes are lower than traditional smokeless products.	Examine the impact of lower (RR=1.1) and higher (RR=1.3) noncombusted tobacco product risk. These are the lower (7%) and higher (20%) relative excess risks of noncombusted tobacco products compared to cigarettes.
In the baseline scenario, mortality risk from dual use of cigarettes and noncombusted tobacco products is assumed to be the same as cigarette smoking only.	Limited epidemiologic studies examining long-term risk from dual product use. Changing patterns of cigarette smoking among dual users may influence risk.	Examine the impact of varying dual use RR considering: - Dual use RR is 18% greater than for cigarette smoking alone - Dual use RR is the average of cigarette and noncombusted use RRs - Dual use RR is equal to the noncombusted use RR
In the baseline scenario, never user death rates are projected for the period 2022- 2100 by using a Lee-Carter mortality forecasting method.	Lee-Carter method was used to project U.S. death rates from 2021 through 2100 by sex and age using observed U.S. death rates from years 1933-2020. Results show a decrease pattern over time.	Examine the impact of assuming a decreased trend in mortality rates until 2060 using the Lee-Carter mortality estimates, and then keeping mortality rates constant after 2060.

In the product standard scenario, cigarette smoking cessation rates are obtained from estimates from the expert elicitation.	The experts were selected based on their research productivity in the fields of tobacco science and tobacco policy and are thus knowledgeable about tobacco product use and use transitions.	Examine the impact of a doubling of smoking cessation rates in the product standard scenario based on results from clinical studies of the effects of VLNC cigarettes on smoking cessation.
In the product standard scenario, behavioral inputs obtained from expert elicitation assume regulatory compliance with the product standard.	The product standard would be national and comprehensive in scope and enforced by the U.S. government.	Examine the impact of alternative assumptions about use of FNC cigarettes (3.8%, 5.9%, and 21% of current cigarette smokers expected to quit FNC cigarettes due to the proposed product standard would not quit and would instead continue to smoke FNC cigarettes)

In addition to applying the experts' estimates of cigarette smoking cessation, we also examined a scenario in which the impact of the proposed product standard on smoking cessation is derived from clinical studies of VLNC cigarette use. Multiple studies of differing study designs, products, and outcomes provide evidence that VLNC cigarettes can facilitate smoking cessation among those interested in quitting, particularly when used with nicotine replacement therapy (NRT) (Becker et al., 2008; Donny et al., 2022; Hatsukami et al., 2013b; Hatsukami et al., 2010; Klemperer et al., 2019b; McRobbie et al., 2015; Rezaishiraz et al., 2007; Walker et al., 2012). Among smokers who want to quit, cessation rates appear to be similar to or greater than those observed with approved NRT, including the nicotine patch and lozenge. Among smokers who do not report an interest in quitting, VLNC cigarettes have been shown to encourage quitting intent and quit attempts (Benowitz, 2010; Benowitz et al., 2012; Donny et al., 2015; Walker et al., 2015). A systematic review of the efficacy of NRT for smoking cessation found a range in efficacy from 1.49 times control for nicotine gum to 2.48 times control for oral spray (Stead et al., 2012). We use the midpoint, a two-fold increase in cessation, as an alternative estimate of the long-term impact of the product standard on cessation. This estimate is very likely to be a lower bound because clinical studies of VLNC cigarettes have observed a high degree of non-compliance (i.e., participants returning to their usual brand of FNC cigarettes), estimated to be at least 60% in Benowitz et al. (2015) and 78% in Nardone et al. (2016) with biochemical verification. In contrast, once a nicotine product standard is in effect, smokers would be unable to legally buy FNC cigarettes. Because the results from clinical studies, although informative, do not reflect the real-world conditions and results that would likely occur with a product standard, we instead used the estimates provided in the expert elicitation as inputs in our main analysis.

Finally, we conducted sensitivity analyses to examine the potential unintended consequences of a nicotine product standard. Specifically, we examined the potential for an illicit market for FNC cigarettes to develop in response to the proposed product standard. In order to examine the potential impact of such an illicit market, we conducted a sensitivity analysis for the effects of diversion from

cessation to illicit trade, and initiation into illicit products, on the estimated benefits of a nicotine product standard. A previous simulation model developed by Tengs et al. (2005) evaluated the effects of a reduced nicotine standard and explicitly accounted for the emergence of a black market for FNC cigarettes by assuming a proportion of smokers would continue to purchase FNC cigarettes on the black market. We adopt a similar approach and assume that a specific proportion of smokers would divert to use of illicit FNC cigarettes.

Because a reduced nicotine product standard has not been implemented anywhere in the world, there is no empirical data on how illicit FNC cigarettes might dampen the benefits of a reduced nicotine standard. In the absence of such information, three types of data sources can inform the analysis: (1) estimates of the total size of the current illicit tobacco market; (2) survey data on levels of tax avoidance and evasion among U.S. smokers; and (3) levels of non-compliance in clinical studies of VLNC cigarettes. The following values are used to estimate the proportion of smokers likely to engage in use of illicit FNC cigarettes:

- We use 3.8% as a low-end estimate based on 2017 estimates of illicit trade volume in cigarettes from Euromonitor International (2018). This estimate excludes inter-state smuggling for purposes of tax avoidance. The Tengs et al. (2005) model previously used an estimate of the percent of low or untaxed illicit cigarettes on the total U.S. market to similarly represent the percent of smokers who would purchase FNC cigarettes on the illicit market.
- Using findings from the International Tobacco Control United States Survey (Cornelius et al., 2015), we estimate that 5.9% of U.S. smokers last purchased cigarettes from low-tax locations. We use this as a midpoint estimate for the proportion of cigarette smokers who may actively seek out illicit FNC cigarettes under a nicotine product standard.
- We use 21% as a high-end estimate based on the difference in non-compliance rates between reduced nicotine intervention groups (78%) and control groups assigned to FNC cigarettes (57%) in clinical trial data from Nardone et al. (2016) and Donny et al. (2015). Smokers had easy access to legal FNC cigarettes when the trial was conducted. The difference in non-compliance rates reflects the increased likelihood that smokers assigned to VLNC cigarettes would seek FNC cigarettes that are easily accessible. This estimate of 21% also represents the high-end of the range of illicit cigarette sales in the U.S. estimated in the National Research Council report (2015). This estimate reflected the methodology of the pack return survey by Fix et al. that found that 21% of cigarette smokers from a nationally representative survey returned cigarette packs for examination that did not have the appropriate tax stamp for their state of residence (2014). This 21% high-end estimate represents a highly unlikely upper bound because for such a high percentage of smokers to acquire FNC cigarettes, a convenient access to an illicit market would be needed, which is highly unlikely.

Using these percentages (3.8%, 5.9%, and 21%) as estimates of the proportion of smokers that may divert to use of FNC cigarettes under a proposed nicotine product standard, we adapt the main analysis and estimate the health benefits of a proposed nicotine product standard assuming each level of illicit trade. Specifically, we assume that 3.8%, 5.9%, and 21% of current cigarette smokers expected to quit FNC cigarette smoking due to the proposed nicotine product standard would not quit and would instead continue to smoke FNC cigarettes via illicit trade. The complement values, 96.2%, 94.1%, and 79%, were used as discount factors to adjust the cessation rates under the nicotine product standard

scenario. We incorporated changes in smoking initiation assuming that youth and young adults who would have initiated FNC cigarettes (in the absence of a rule) would seek to smoke FNC cigarettes via illicit trade. To do that, we use findings from an expert elicitation developed to gauge the impact of a menthol cigarette and cigar prohibition in the United States (Levy et al., 2021), which indicates that among people ages 12-24 who would have otherwise initiated menthol cigarette use, 2.6% would initiate illicit menthol cigarette use (experts' estimates ranged from 0% to 10%).

We also estimated the impact of increased initiation of noncombusted tobacco use among those who would otherwise not have used tobacco under the nicotine product standard. Due to potential increased manufacturer marketing of noncombusted products as a result of a nicotine product standard, consumers who would otherwise not have used tobacco may be more likely to take up a noncombusted tobacco product. Public perception of noncombusted products may also change as a result of a nicotine product standard, leading consumers who would otherwise have never used tobacco to perceive lower harms in using noncombusted products.

2.5 Outcome Metrics

In order to examine the impact of a potential nicotine product standard on population health, we examine a range of outcome metrics. They include prevalence of cigarette smoking, noncombusted tobacco use, dual smoking and noncombusted tobacco use, and any tobacco (cigarette smoking and/or noncombusted tobacco) use. We also calculate the number of smoking initiates, dissuaded initiates, and smoking quitters.

We also examine the effect of tobacco product use on health outcomes including tobacco-attributable mortality due to cigarette smoking and noncombusted tobacco use, life years lost or gained as a result of tobacco-attributable deaths or averted deaths, and changes in cigarette smoking morbidity, assessed as the difference in quality-adjusted life years (QALYs) lost due to smoking-attributable disease or illness. The number of life years lived by a population in a year is the number of individuals in the population for that year. The effect of cigarette smoking on morbidity is estimated using a quality-of-life approach developed by Jia and Lubetkin (2010). Reductions in quality-of-life due to smoking are assessed using EQ-5D index scores derived from Behavioral Risk Factor Surveillance System data for smokers and non-smokers (never and former smokers) by age. Jia and Lubetkin (2010) did not provide EQ-5D index scores for ages less than 18 years or noncombusted tobacco use, so we only estimate the effect of current smoking on morbidity for adults.

Model outcome metrics are calculated for the U.S. population over time. The methods used to estimate these metrics are described in detail in Appendix H of this document. Annual outcome metrics are summed over time to produce cumulative measures. Population health measures reflecting change due to the nicotine product standard are calculated as the difference between the baseline and product standard scenario for those measures. Individuals in the population are characterized by years of age, sex, and tobacco use status (never, former, and current cigarette smoking and noncombusted tobacco use), and metrics can be estimated for subgroups defined by combinations of these characteristics. As considered in Apelberg et al. (2018), to be conservative, we exclude any morbidity and mortality benefits accrued during the first three years after the implementation of the product standard from our cumulative estimates of tobacco-attributable mortality, life years gained, and morbidity outcomes.

3 Health Impact from Main Analysis

In the sections below, we present the main health impact analysis considering model inputs and assumptions as described in sections 2.2 and 2.3. A summary of all modeling assumptions and rationale is presented in Appendix I.

3.1 Changes in Tobacco Use

Figures 3a-d present the projected adult prevalence for current cigarette smoking overall, noncombusted tobacco use overall, dual use of both cigarettes and noncombusted tobacco, and use of any tobacco product, respectively, under the baseline and main product standard scenario. Compared to the previous Apelberg et al. (2018) publication, which relied on inputs and assumptions from a 2015 expert elicitation, e-cigarettes have increased in popularity over time, particularly among young people. However, more recent data indicate a decline in prevalence of use among young people. We conservatively estimate no increase in baseline projections for noncombusted tobacco and any tobacco product use relative to prior estimates. Also, as noted, in Section 2.3, median estimates of changes in tobacco use behaviors with a nicotine product standard such as smoking cessation tended to be greater in the 2018 expert elicitation than in the 2015 elicitation, leading to differences in estimates in the product standard scenario compared to previous results. Results for the product standard scenario are derived from the Monte Carlo simulation, incorporating uncertainty around the experts' estimates of behavioral responses to a potential nicotine product standard.

In the baseline scenario, cigarette smoking prevalence decreases from 12.5% in 2021 to 5.3% in 2050. Smoking prevalence declines immediately after the implementation of the standard in 2027 from 9.1% in the baseline scenario to a median of 4.5% (PR[4]: 0.3%, 8.8%) in the product standard scenario, due to the large increase in smoking cessation in the first year after implementation. In subsequent years, the difference in smoking prevalence between the scenarios would continue to grow due to sustained increases in cessation and decreases in initiation, relative to baseline. The projected smoking prevalence drops to 0.2% (PR: 0.1%, 2.7%) under the product standard scenario by 2050, compared to 5.3% under baseline. By 2100, smoking prevalence is estimated at 0.2% (PR: 0.1%, 1.9%) in the product standard scenario, compared to 4.6% under baseline.

[4] PR: Prediction range showing the 5th and 95th percentiles.

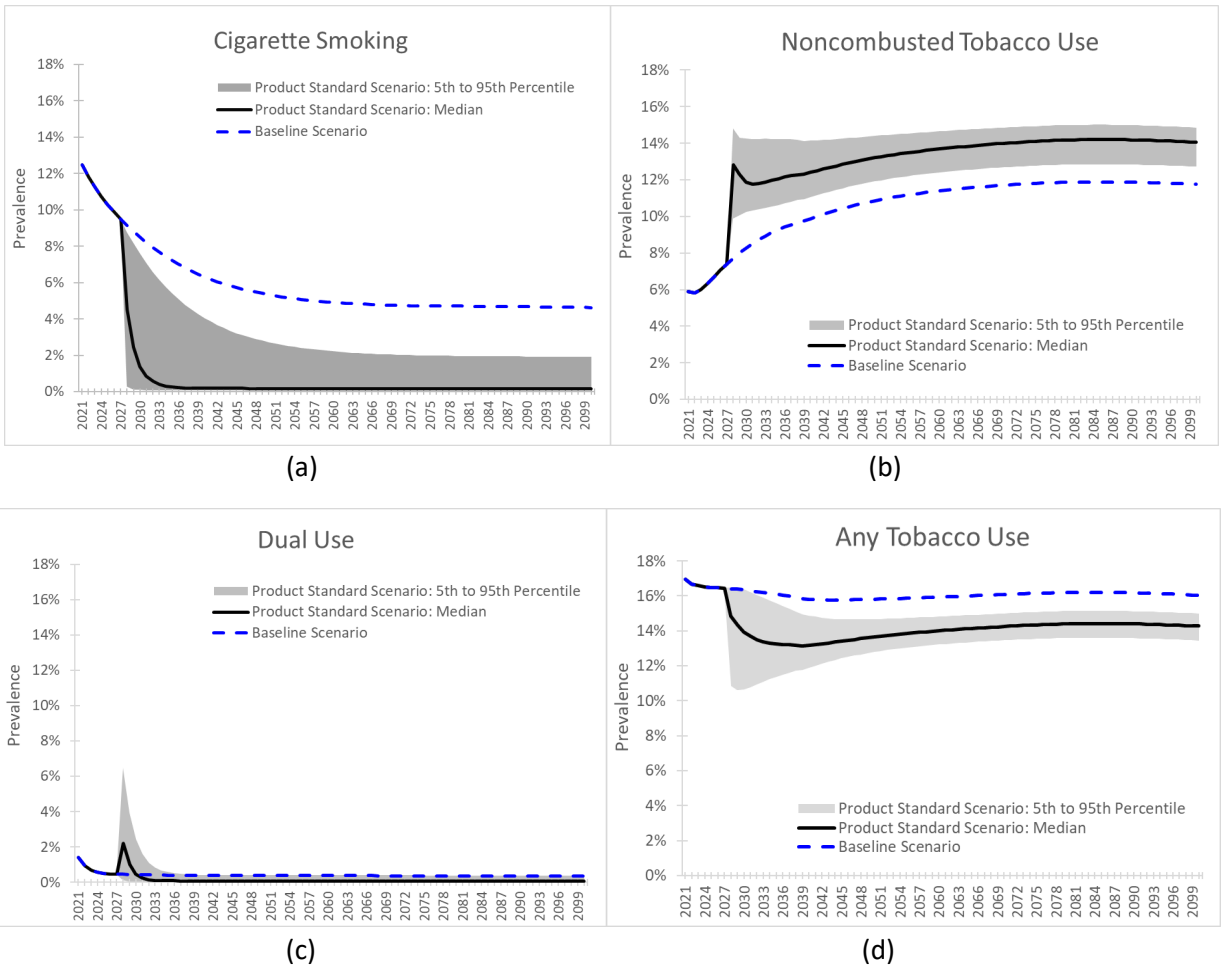


Figure 3. Projected Adult Prevalence of (a) Cigarette Smoking Overall (b) Noncombusted Tobacco Use Overall, (c) Dual Use of Cigarettes and Noncombusted Tobacco, and (d) Any Tobacco Use Under the Baseline and Product Standard Scenarios, from 2021 through 2100, as a Result of a Nicotine Product Standard Implemented in 2027.

Prevalence of noncombusted tobacco use overall increases in the baseline scenario from 5.9% in 2021 to 10.9% in 2050. Under the product standard scenario, concurrent with a dramatic reduction in cigarette smoking is an increase in noncombusted product use. Although it is assumed that noncombusted product initiation remains constant until the end of the projection period, noncombusted use continues to climb. This is because the number of new noncombusted tobacco users is much higher as compared with noncombusted quitters. That is, there are more current noncombusted tobacco users every year than noncombusted quitters, which causes an increase in noncombusted tobacco use prevalence throughout the simulation period. Adult noncombusted tobacco use increases from 7.7% in the baseline scenario to 12.8% (PR: 9.8%, 14.8%) in the product standard scenario within one year after the implementation of the policy (year 2028), due to the increase in switching from cigarette smoking and dual use as a result of a nicotine product standard. The prevalence of noncombusted tobacco use remains higher in the product standard scenario over time due both to increased uptake among smokers and increased initiation due to some dissuaded cigarette initiators taking up noncombusted products instead.

In the baseline scenario, prevalence of dual use of cigarettes and noncombusted products decreases from 1.4% in 2021 to 0.4% in 2050. Under the product standard scenario, dual use of cigarettes and noncombusted tobacco products increases immediately, since a greater proportion of continuing smokers take up noncombusted products than in the baseline, but this pattern does not continue over time with dual use prevalence reaching levels below 0.1% by 2035.

In the baseline scenario, any tobacco use prevalence does not vary much over time, decreasing from 17% in 2021 to 16% in 2050. Although the increase in noncombusted tobacco product use is larger than the decrease in smoking prevalence in the product standard scenario, overall tobacco use remains lower than in the baseline scenario.

3.1.1 Youth and Young Adults Who Do Not Become Smokers

Table 2 provides an estimated projection of the cumulative number of youth and young adults who do not become smokers as a result of implementation of a potential nicotine product standard over time (annual estimates are presented in Appendix J). Since a sustained decrease in smoking initiation rates is expected, the cumulative number of dissuaded smoking initiates would continue to increase over time. By 2100, we estimate that, as a result of the nicotine product standard, approximately 48 million youth and young adults (PR: 12.6, 64.1) who would have otherwise initiated smoking would not start smoking.

3.1.2 Additional Smokers Quitting

We estimate that approximately 13 million (PR: 0.8, 24.8) additional smokers from all ages are estimated to quit smoking within the first year of the proposed nicotine product standard's implementation, signifying a considerable gain over the estimated 1.6 million smokers that would have quit under the baseline scenario. The number of additional smokers quitting would increase to approximately 19.5 million (PR: 2.0, 21.4) within 5 years after implementation of a nicotine product standard, representing a gain of more than the 7.3 million quitters that would be anticipated under the baseline scenario (see Table 2). The distribution percentiles of the cumulative results indicate a skewed pattern, with median estimates closer to the 95th percentiles. A closer analysis of this pattern indicates that the 5th percentile estimates are related to lower percentage of current cigarette smokers that will quit smoking cigarettes following a nicotine product standard's implementation, as reported by two experts in the expert elicitation.

Table 2. Projected Number of Youth and Young Adults Who Would Not Initiate Smoking and Projected Cumulative Number of Net Quitters[a] (All Ages) Who Would Quit Smoking, as a Result of a Nicotine Product Standard Implemented in 2027.

Year/Period	Median	(5th, 95th Percentiles)
Cumulative Reduction in New Smokers (Millions)		
2028	1.3	(0.4, 1.7)
2030	2.6	(0.7, 3.4)
2040	8.6	(2.3, 11.5)

2050	14.8	(4.0, 19.8)
2060	21.1	(5.6, 28.3)
2070	27.5	(7.3, 37.0)
2080	34.1	(9.1, 45.9)
2090	40.8	(10.8, 54.9)
2100	47.6	(12.6, 64.1)
Cumulative Net Quitters[a] (Millions)		
Within 1st year (2027)	12.9	(0.8, 24.8)
Within 2 years (2027-2028)	17.5	(1.2, 24.1)
Within 3 years (2027-2029)	19.3	(1.6, 23.2)
Within 4 years (2027-2030)	19.8	(1.8, 22.3)
Within 5 years (2027-2031)	19.5[b]	(2.0, 21.4)

[a] Net quitters, defined as quitters in addition to baseline, is computed as: (# quitters under the nicotine product standard scenario) – (# quitters under baseline scenario)

[b] Cumulative net people who quit smoking declines slightly in year 5 of the simulation because there are more people who quit smoking in the baseline scenario compared with the product standard scenario. Since there are millions of fewer people smoking in the product standard scenario, eventually there are fewer people available to quit smoking compared to baseline.

3.2 Mortality and Morbidity Impact

Table 3 presents cumulative estimates of mortality and morbidity avoided among adults as a result of a nicotine product standard, for certain years in the simulation period. Annual estimates of cumulative avoided mortality and morbidity as well as cigarette smoking-attributable mortality with and without the product standard are presented in Appendix J. By 2060, we estimate that approximately 1.8 million deaths due to tobacco will be avoided (PR: 0.4, 2.0), rising to 4.3 million (PR: 1.6, 4.6) by the end of the century. The reduction in premature deaths attributable to the product standard would result in 19.6 million life years gained (PR: 3.6, 22.7) by 2060 and 76.4 million life years gained (PR: 26.5, 82.5) by 2100. In addition to the years of life gained due to reduced premature mortality from tobacco, the substantial reductions in smoking initiation and increases in smoking cessation will result in improvements in quality of life for those who quit or do not initiate smoking as a result of the product standard. Based on previously reported quality of life scores derived for smokers and non-smokers, stratified by age group (Jia et al., 2010), we estimate that a nicotine product standard would result in 24.0 million QALYs gained (PR: 10.1, 24.7) by 2060 due to reduced smoking morbidity. By 2100, this estimate is projected to increase to 53.1 million QALYs gained (PR: 27.5, 54.4) due to reduced smoking morbidity.

Table 3. Projected Number of Tobacco-Attributable Deaths Avoided, Life Years Gained, and QALYs Gained Due to Reduced Smoking Morbidity as a Result of a Nicotine Product Standard Implemented in 2027.

Year	Percentile	Cumulative Tobacco-Attributable Deaths Avoided (Millions)	Cumulative Life Years Gained (Millions)	Cumulative QALYs Gained Due to Reduced Smoking Morbidity (Millions)

2040	Median	0.4	2.0	9.6
	(5^{th}, 95^{th})	(0.1, 0.5)	(0.2, 2.7)	(2.7, 10.0)
2060	Median	1.8	19.6	24.0
	(5^{th}, 95^{th})	(0.4, 2.0)	(3.6, 22.7)	(10.1, 24.7)
2080	Median	3.1	47.4	38.2
	(5^{th}, 95^{th})	(1.0, 3.4)	(12.5, 52.5)	(18.5, 39.2)
2100	Median	4.3	76.4	53.1
	(5^{th}, 95^{th})	(1.6, 4.6)	(26.5, 82.5)	(27.5, 54.4)

4 Mortality Impact of Reduced Secondhand Smoke Exposure, Smoking-Related Perinatal Conditions, Smoking-Related Fires, and Use of Non-Premium Cigars and Pipe Tobacco

The overall public health benefits of a nicotine product standard are expected to be greater than those described above once we account for the impacts of reduced cigarette smoking on secondhand smoke exposure, smoking-related fires, and perinatal conditions in addition to the impacts of reduced use of other combusted tobacco products. Below, we estimate additional mortality benefits of a potential nicotine product standard using results from the model-derived attributable mortality projections along with information about the relative mortality burden attributable to cigarette smoking and secondhand smoke exposure, smoking-related perinatal conditions, smoking-related fires, non-premium cigar use, and pipe tobacco use.

Estimation of the mortality benefits of a nicotine product standard from reduced secondhand smoke exposure, smoking-related perinatal conditions, smoking-related fires, and use of non-premium cigars and pipe tobacco used a consistent post-processing approach. The general estimation approach relied on scaling the estimate of 437,400 deaths annually attributable to direct cigarette smoking from 2005-2009 (U.S. Department of Health and Human Services, 2014), according to the number of deaths attributed to each of the following causes in published estimates for the U.S.: secondhand smoke exposure, smoking-related perinatal conditions, smoking-related fires, and use of non-premium cigars and pipe tobacco. That ratio was then applied to the model derived projected changes in avoided tobacco-attributable deaths under the main product standard scenario (Table 3) in order to project the number of avoided deaths over time from each of these five causes (i.e., secondhand smoke exposure, smoking-related perinatal conditions, smoking-related fires, non-premium cigar use, and pipe tobacco use). Deaths averted from smoking-related perinatal conditions and fires may be initially underestimated because mortality benefits for these causes may be more immediate than for tobacco-attributable deaths generally, which are not counted in the model in the first three years after implementation of the product standard. With the exception of deaths from use of non-premium cigars, the ratios of deaths from each cause to U.S. direct cigarette smoking-attributable deaths for 2005-2009 were held constant throughout the projection period. These ratios could change over time, particularly

for deaths from use of non-premium cigars and pipe tobacco, because changes in use patterns and resulting health effects of these products and cigarettes could differ over time.

4.1 Mortality Impact of Secondhand Smoke Exposure

The impacts of a nicotine product standard on mortality due to secondhand smoke exposure were estimated by first calculating the ratio of secondhand smoke (41,280 deaths; (U.S. Department of Health and Human Services, 2014)) to primary smoking-attributable deaths. Estimates of deaths in the U.S. due to secondhand smoke exposure were published in the 2014 Surgeon General's Report on the health effects of smoking (U.S. Department of Health and Human Services, 2014) and were obtained from estimates of nonsmokers' exposure to secondhand smoke and published relative risks of coronary heart disease and lung cancer for secondhand smoke exposure (Max et al., 2012). That value, 9.4%, was then applied to the projections of tobacco-attributable deaths avoided yielding an estimate of approximately 183,400 deaths (PR: 40,800, 204,600) due to secondhand smoke exposure avoided by 2060, rising to approximately 427,800 deaths avoided (PR: 160,000, 457,600) by the end of the century (Table 4).

4.2 Mortality Impact of Smoking-Related Perinatal Conditions

Cigarette smoking is responsible for approximately 1,000 deaths from perinatal conditions annually including over 600 deaths from prenatal conditions and 400 deaths from sudden infant death syndrome (SIDS). Estimates of U.S. perinatal mortality were also published in the 2014 Surgeon General's Report (U.S. Department of Health and Human Services, 2014), based on relative risks for the associations between prenatal smoking and pre-term related deaths and SIDS (Dietz et al., 2010). The impacts of a nicotine product standard on perinatal mortality were estimated by first calculating the ratio of perinatal deaths (1,013 deaths; (U.S. Department of Health and Human Services, 2014)) to primary smoking-attributable deaths. That value, 0.2%, was then applied to the projections of tobacco-attributable deaths avoided yielding an estimate of approximately 4,500 perinatal deaths (PR: 1,000, 5,000) avoided by 2060, rising to approximately 10,500 deaths avoided (PR: 3,900, 11,200) by the end of the century (Table 4). Given that decreases in cigarette smoking prevalence under a nicotine product standard will have immediate, rather than lagged impacts on fetal health and the health of newborn children, we expect avoided smoking-attributable perinatal deaths to accrue more rapidly than the estimates presented here.

4.3 Mortality Impact of Smoking-Related Fires

To estimate the impact of a nicotine product standard on the number of deaths caused by smoking-related fires, we applied the average of 590 deaths annually from 2012-2016 from home structure fires started by smoking materials reported by Ahrens (2019). These smoking materials include cigarettes, pipes, cigars, and undetermined smoking material, which are assumed to be mostly lit tobacco products. We calculated the ratio of smoking-related fire deaths to cigarette smoking-attributable deaths to be approximately 0.1% and applied that value to the projections of avoided tobacco-attributable deaths, yielding an estimate of approximately 2,600 deaths (PR: 600, 2,900) due to

smoking-related fires avoided by 2060, rising to approximately 6,100 deaths avoided (PR: 2,300, 6,500) by the end of the century (Table 4).

Table 4. Projected Number of Tobacco-Attributable Deaths Avoided for Secondhand Smoke, Smoking-Related Perinatal Conditions and Smoking-Related Fires as a Result of a Nicotine Product Standard Implemented in 2027.

Year	Percentile	Cumulative Secondhand Smoke Attributable Deaths Avoided	Cumulative Perinatal Deaths Avoided	Cumulative Smoking-related Fire Deaths Avoided
2040	Median	39,800	1,000	600
	(5^{th}, 95^{th})	(4,400, 49,200)	(100, 1,200)	(100, 700)
2060	Median	168,300	4,100	2,400
	(5^{th}, 95^{th})	(36,900, 188,300)	(900, 4,600)	(500, 2,700)
2080	Median	294,300	7,200	4,200
	(5^{th}, 95^{th})	(87,200, 320,200)	(2,100, 7,900)	(1,200, 4,600)
2100	Median	409,100	10,000	5,800
	(5^{th}, 95^{th})	(153,000, 437,600)	(3,800, 10,700)	(2,200, 6,300)

4.4 Mortality Impact of the Use of Non-Premium Cigars

To estimate the impacts of a potential nicotine product standard on avoided deaths attributable to smoking cigars other than premium cigars, we used estimates of premature deaths attributable to regular cigar smoking from Nonnemaker et al. (2014). Nonnemaker et al. estimated deaths from regular cigar smoking in the U.S. in 2010 using cigar smoking prevalence and relative risk data. Given that Nonnemaker et al. included all cigar types in their estimate of 9,246 premature deaths and considering that we have not included premium cigars in the analysis, we estimated the fraction of deaths attributable to cigar products other than premium cigars. We estimate that among established (ever used fairly regularly) current (every day or some day) cigar smokers in Wave 4 of the PATH Study, approximately 80% reported smoking non-premium cigars (i.e., filtered cigars, cigarillos, traditional non-premium cigars) and approximately 20% reported smoking traditional premium cigars based on cigar type and usual brand information using a classification methodology described previously (Corey et al., 2014) and subsequently updated (National Academies of Sciences, Engineering, and Medicine, 2022). On that basis, 80% * 9,246 deaths = 7,397 deaths annually are attributed to using non-premium cigars. This 80% figure for non-premium cigars is an approximation because some traditional premium cigar smokers in the PATH Study may have been established users of other cigar types, and it may be an underestimate of the mortality risk of non-premium cigars because the use patterns and health effects of premium cigars may differ from those of other cigar types.

Adult cigar smoking has historically remained stable. Data from the NHIS over 2000-2015 have shown that prevalence of current established cigar smoking has remained generally stable at around

2.3% among U.S. adults aged 18 years and older (Rostron et al., 2019a). Adult (aged 26 years or older) cigar use also remained relatively stable in NSDUH data for 2011 and 2019 and did not significantly change (4.2% in 2011 to 4% in 2019) (Substance Abuse and Mental Health Services Administration (SAMHSA), 2020). Incorporating this relatively stable trend in adult cigar use and assuming that adult cigar use is the main driver of cigar-attributable deaths in the close future, we assume that non-premium cigar-attributable mortality would remain constant at 7,397 cigar-attributable deaths through 2065 (or roughly the time at which cigar users aged 26 and older in 2021 would reach age 70 and older) at baseline.

However, as youth and young adult cigar smoking has declined in recent years, we adopt a different trend in baseline cigar-attributable mortality in the further future (after 2065). In our estimates of the ratio of baseline cigar to cigarette smoking-attributable deaths, we took into consideration that prevalence of cigar smoking among adults has remained relatively stable over time, whereas youth use has declined. NHIS estimates have shown that prevalence of current established cigar smoking remained generally consistent at around 2.3% among US adults aged 18 years and older from 2000 to 2015 (Rostron et al., 2019a). In contrast, prevalence of current cigar smoking among high school youth decreased from 11.6% in 2011 (2013) to 2.8% in 2022 (Park-Lee et al., 2022) according to NYTS data. Past month cigarette smoking and cigar use were both statistically significantly lower in young adults (aged 18-25 years) between 2011 and 2019 in NSDUH data, although the absolute decline in cigar use was less than the decline in cigarette use (33.5% in 2011 compared to 17.5% in 2019 for cigarettes; 10.9% in 2011 compared to 7.7% in 2019 for cigars) (Substance Abuse and Mental Health Services Administration (SAMHSA), 2020). Recent changes in youth and young adult cigar use are likely to impact later trends in cigar-attributable mortality. According to data from the PATH Study, young adult (aged 18-24 years) past 30-day cigar use declined from 15.7% during Wave 1 from 2013-2014 to 11.0% during Wave 5 from 2018-2019, representing a 30% relative decline in prevalence (United States Department of Health and Human Services, 2021b). Additionally, data from the PATH Study Waves 3 and 5 indicates that cigar use among young adults aged 18 years declined from 7.2% to 3.9%, implying a steeper decline of approximately 45% in more recent years within this smaller age cohort (internal CTP analysis). We use these two data points to estimate the decrease in cigar smoking among young people because both provide relevant information from a national survey that is specific to tobacco use and average them to produce an estimate of (30% + 45%)/2 = 37.5%. To obtain baseline non-premium cigar-attributable mortality from 2066 through the end of the modeling period (2100), we assume non-premium cigar-attributable mortality will eventually follow the observed relative decline in cigar use among young adults as they reach older ages. Specifically, we assume that non-premium cigar smoking-attributable deaths among youth initiators will decrease on average by 37.5% over 40 years (from 2078 to 2117)[5]. That is, the cigar smoking-attributable deaths will decrease on average to (100% – 37.5%) * 7,397 ≈ 4,600 deaths over the period 2078-2117. Assuming a linear decrease in cigar smoking-attributable mortality from 2065 to 2117 and an average of approximately 4,600 deaths over the period 2078-2117, implies non-premium cigar smoking-attributable mortality will decline linearly from 7,397 in 2065 to approximately 4,390 deaths in 2100. We assume a linear decrease for simplicity and because

[5] For youth, we assume that initiation occurs by the age of 18, followed by a cigar smoking-attributable death 52 years later. We then assume cigar use initiation occurs during 2025-2064 (40-year period), and cigar smoking-attributable deaths begin to occur a year after the period from 2025 + 52 = 2077 through 2064 + 52 = 2116; that is, over the period 2078-2117.

trends for cigar use considered in this post-processing strategy come from a short interval (PATH Study data, Waves 1 to 5, and Waves 3 to 5.

We then calculated the ratio of non-premium cigar smoking-attributable deaths to projected cigarette-attributable deaths over time in the baseline scenario, and applied these values to the projections of avoided cigarette smoking -attributable deaths (from exclusive cigarette smoking and dual use of cigarettes and noncombusted tobacco products due to the higher risks of cigarettes) in the nicotine policy scenario (Table 3). Using this approach, we estimated that by 2060 approximately 54,800 (PR: 13,200, 60,500) deaths due to non-premium cigar use would be avoided, rising to approximately 215,700 (PR: 91,600, 225,800) deaths avoided by 2100 (see Table 5).

Similar estimates were calculated accounting for the effects of a product standard prohibiting characterizing flavors other than tobacco in cigars on deaths averted from non-premium cigar smoking by the nicotine product standard. These estimates reduced baseline non-premium cigar-attributable deaths in a phased-in manner reaching a constant reduction of 780 deaths averted after 30 years. These estimates and results are presented in detail in section 6.2 of this document.

4.5 Mortality Impact of the Use of Pipe Tobacco

To estimate the impacts of a nicotine product standard on avoided deaths attributable to pipe tobacco smoking we used the estimate of 1,095 premature deaths provided by Nelson et al. (1996). Nelson et al. estimated U.S. deaths attributable to pipe smoking among men, who represented almost all U.S. pipe smokers at the time, in 1991. We calculated the ratio of pipe tobacco to cigarette attributable deaths to be 0.3% and applied that value to the projections of avoided tobacco-attributable deaths yielding an estimate of approximately 4,500 deaths (PR: 1,000, 5,000) due to pipe tobacco smoking avoided by 2060, rising to approximately 10,900 deaths avoided (PR: 4,100, 11,600) by the end of the century (see Table 5).

Table 5. Projected Number of Tobacco-Attributable Deaths Avoided for Non-Premium Cigar and Pipe Tobacco Use as a Result of a Nicotine Product Standard Implemented in 2027.

Year	Percentile	Cumulative Non-Premium Cigar Attributable Deaths Avoided	Cumulative Pipe Tobacco-Attributable Deaths Avoided
2040	Median	8,900	1,100
	(5^{th}, 95^{th})	(1,000, 11,000)	(120, 1,300)
2060	Median	54,800	4,500
	(5^{th}, 95^{th})	(13,200, 60,500)	(1,000, 5,000)
2080	Median	134,700	7,800
	(5^{th}, 95^{th})	(46,000, 144,100)	(2,300, 8,500)
2100	Median	214,700	10,900
	(5^{th}, 95^{th})	(91,600, 225,800)	(4,100, 11,600)

It should be noted that these estimates do not take into account the possibility that transitions to noncombusted tobacco product use in response to the proposed nicotine product standard could lead to some deaths from other causes, specifically deaths due to secondhand exposure, perinatal conditions, and fires. For example, e-cigarette use and malfunction has been linked to fires, burns, and explosions that have caused serious injuries (Rossheim et al., 2019). We do not attempt to quantify the additional deaths from these causes that could result from transitions to noncombusted tobacco use because of the current lack of data on the population health effects of noncombusted products for these causes. It is expected that the population health impact of transitions to noncombusted product use for these causes would be less than the current impact of cigarette smoking. For example, the U.S. Fire Administration reported that there were no deaths from e-cigarette fires or explosions in the U.S. from 2009 to 2016 (McKenna Jr., 2017), although some deaths from this cause may have occurred since then.

5 Sensitivity Analyses

In addition to the main analyses concerning projected death and disability, we examined the sensitivity of modeled results to underlying assumptions related to baseline product use projections and mortality risk estimates. These sensitivity analyses accounted for the following: an increase in noncombusted tobacco product initiation; different assumptions related to people who smoke cigarettes switching to noncombusted tobacco products per year; a decrease in cigarette smoking initiation; lower and higher noncombusted tobacco product mortality risk compared to baseline; different assumptions for dual product use mortality risk; and changes in baseline mortality rate projections. We also conducted sensitivity analysis to assess the potential impact of a substantial illicit market for FNC cigarettes. The results of these sensitivity analyses are presented below.

5.1 Baseline Parameter Assumptions

Any effort to project the impact of a policy action on the population will necessarily require assumptions to simplify the complexity of human behaviors in the real world. In the main analysis, we account for uncertainty in the potential behavioral responses to a nicotine product standard. In this section, we examine the sensitivity of modeled results to underlying assumptions related to baseline product use projections and mortality risk estimates. Table 6 presents results from the simulation under different assumptions of the rate at which cigarette smokers switch to non-covered combusted tobacco products per year (as described in Table 1). In general, changes to baseline inputs of noncombusted product use trajectories and health risks had minimal impact on cigarette smoking prevalence and attributable morbidity and mortality, and the nicotine product standard still resulted in substantial public health benefits. Assuming increasing initiation rates for noncombusted product use until year 2030 implies that the number of tobacco users will be higher under the baseline and nicotine product standard scenarios, with a higher proportion being noncombusted tobacco users. In terms of mortality RR, we applied a RR of 1.18 for noncombusted tobacco users as compared with never smokers (i.e., the risk of death associated with noncombusted tobacco use is assumed to be 1.18 times greater than the risk of death associated with never using tobacco products). Thus, as explained in Section 2.4, this assumption implies that noncombusted product excess risk is 12% that of the excess risk associated with cigarette smoking.

As shown in Table 6, varying baseline input parameter values had very small effect on estimates of the potential population health effects of a nicotine product standard. Assuming a 25% decrease in cigarette smoking initiation during the period from 2021 to 2030 resulted in modest decreases in smoking prevalence and health benefits, in particular, reductions in morbidity due to smoking, by 2100 compared to main scenario. Similarly, assuming a 10% increase in smoking cessation also resulted in small decreases in morbidity due to smoking, as compared with the main scenario. Increases in baseline complete switching to noncombusted tobacco product use resulted in small decreases in smoking prevalence and health benefits in terms of life years gained and reduced smoking morbidity by 2100 compared to the main scenario. Using initiation and cessation rates for ENDS, from Brouwer et al. (2023) resulted in a slight increase in public health benefits compared to the main scenario. For example, by year 2100, cumulative tobacco-attributable deaths avoided, cumulative life years gained, and cumulative QALY gained increase by 3.4%, 3.8%, and 0.8%, respectively. Using Brouwer's initiation rates for ENDS only, resulted in almost no change compared to the main scenario. For example, by year 2100, cumulative tobacco-attributable death avoided, cumulative life years gained, and cumulative QALY gained decrease by 0.3%, 0.2% and 0.2%., respectively. Different assumptions about baseline relative risks also produced modest changes in differences in life years gained.

Sensitivity analyses were also conducted examining assumptions about the potential effect of the nicotine product standard on smoking cessation. In addition to the modeling results obtained through expert-derived inputs, we also generated projections based on results from clinical studies of VLNC cigarette use and cessation. Based on these studies, we applied a two-fold increase in all age and gender-specific cessation rates (estimates ranged from 6.4% to 19.8%), as compared to the baseline cessation rates (ranged from 3.2% to 9.9%), as an alternative estimate of the long-term impact of the proposed product standard on cessation, while maintaining the median of the expert-derived values for the other parameters (as described in Section 2.3 in this document). The projected health impacts assuming a two-fold increase in cessation based on results from clinical studies fell within the range of results obtained from the expert-derived inputs (see Table 6).

Table 6. Impact of Varying Baseline Assumptions on Projected Smoking Prevalence and Avoided Mortality and Morbidity by 2100. Median (5^{th}, 95^{th} Percentiles) Estimates.

Scenario	Projections Through Year 2100			
	Cigarette Smoking Prevalence (%)	**Cumulative Tobacco-Attributable Mortality Avoided (Millions)**	**Cumulative Life Years Gained (Millions)**	**Cumulative QALYs Gained from Reduced Smoking Morbidity (Millions)**
Main scenario	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	76.4 (26.5, 82.5)	53.1 (27.5, 54.4)
Baseline noncombusted tobacco product trajectory				
Increased noncombusted initiation	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	76.5 (26.7, 82.5)	53.1 (27.5, 54.4)
50% increased complete switching	0.13 (0.06, 1.7)	4.2 (1.7, 4.5)	74.9 (28.6, 80.7)	51.9 (29.0, 52.9)

100% increased complete switching	0.12 (0.06, 1.5)	4.2 (1.8, 4.4)	73.6 (30.3, 79.0)	50.8 (30.2, 51.6)
Baseline smoking initiation trajectory				
25% decrease in smoking initiation during the period 2021-2030	0.13 (0.1, 1.6)	4.1 (1.5, 4.4)	72.9 (24.3, 79.0)	45.2 (22.9, 46.4)
Baseline smoking cessation				
10% increase in smoking cessation	0.15 (0.1, 1.8)	4.0 (1.5, 4.3)	70.9 (24.9, 76.4)	50.1 (26.3, 51.2)
Baseline noncombusted initiation and cessation rates from PATH				
Using ENDS initiation rates from Brouwer et al. (2023)	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	76.2 (26.3, 82.4)	53.0 (27.5, 54.3)
Using ENDS initiation and cessation rates from Brouwer et al. (2023)	0.2 (0.1, 1.9)	4.5 (1.7, 4.8)	79.3 (27.6, 84.9)	53.5 (28.0, 54.8)
Baseline noncombusted mortality relative risk (RR)				
Higher RR than main scenario (RR=1.3)	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	75.0 (26.0, 81.4)	53.1 (27.5, 54.4)
Lower RR than main scenario (RR=1.1)	0.2 (0.1, 1.9)	4.4 (1.6, 4.7)	77.2 (26.9, 83.2)	53.1 (27.5, 54.4)
Baseline dual use RR				
Dual use RR is 18% greater than for cigarette smoking	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	75.9 (25.0, 82.4)	53.1 (27.5, 54.4)
Dual use RR is the average of cigarette and noncombusted use RR	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	77.0 (28.6, 82.6)	53.1 (27.5, 54.4)
Dual use RR is equal to the noncombusted use RR	0.2 (0.1, 1.9)	4.3 (1.6, 4.6)	77.6 (30.7, 82.7)	53.1 (27.5, 54.4)
Baseline mortality rate projections				
Keep mortality rates constant starting at 2060	0.2 (0.1, 2.0)	4.7 (1.9, 5.1)	77.9 (28.2, 83.9)	53.0 (27.4, 54.2)

5.2 Potential Unintended Consequences

The main analysis did not consider the potential impact of a substantial illicit market for FNC cigarettes. Thus, we estimated the impact of diversion from cessation to illicit trade by assuming that a proportion of smokers would continue to purchase FNC cigarettes on the black market, as well as the impact of allowing youth and young adults to initiate into illicit FNC cigarette use. As described in Section 2.4, we generated three potential illicit trade estimates—developed by referencing the scientific literature—with which to calculate proportions of smokers diverted to use of illicit FNC cigarettes, and proportions of never users who would have otherwise initiated FNC cigarettes (in the absence of a rule), to adjust the smoking cessation and initiation rates under the proposed nicotine product standard. Table 7 provides a range of possible impacts to the number of net quitters (quitters in addition to the baseline scenario), tobacco-related mortality, and morbidity, assuming three illicit trade impact scenarios. Increasing the assumed proportion of people who smoke who may divert to the use of illicit FNC cigarettes (3.8%: low-end estimate, 5.9%: midpoint estimate, and 21.0%: high-end estimate), and allowing youth and young adults (who would have otherwise initiated FNC cigarette use) to initiate into illicit FNC cigarette use (0%, 2.6%, and 10%) under the proposed nicotine standard, resulted in reductions in the projected cumulative net quitters following the implementation of the nicotine product standard policy (Table 7). However, even in the case of significant diversion to FNC cigarettes, the number of people projected to quit smoking remains substantial.

Additionally, changes in smoking initiation and cessation under the proposed nicotine product standard across the three illicit trade impact scenarios resulted in reductions in the projected cumulative attributable morbidity and mortality outcomes following the implementation of the policy (Table 7). It is noteworthy that significant benefits in terms of reduced morbidity and mortality are realized as a result of this product standard, even in a scenario in which greater proportions of the smokers are assumed to divert to use of illicit FNC cigarettes.

Table 7. Projected Health Benefits as a Result of the Proposed Nicotine Product Standard implemented in 2027 Under Three Illicit Trade Scenarios. Median (5^{th}, 95^{th} Percentiles) Estimates.

Period/Year	**Illicit Trade Impact Scenarios**			
	Main scenario (No Impact)	**Low Impact[a]**	**Medium Impact[b]**	**High Impact[c]**
Cumulative Number of Net Quitters (Millions)				
Within 1st year (2027)	12.9 (0.8, 24.8)	12.4 (0.7, 24.6)	12.1 (0.7, 24.4)	9.9 (0.3,22.6)
Within 5th year (2027-2031)	19.5 (2.0, 21.4)	19.3 (1.7, 21.3)	19.2 (1.5, 21.4)	18.1 (0.3, 21.4)
Cumulative Tobacco Attributable Deaths Avoided (Millions)				
2040	0.4 (0.1, 0.5)	0.4 (0.04, 0.5)	0.4 (0.04, 0.5)	0.4 (0.01, 0.5)
2060	1.8 (0.4, 2.0)	1.8 (0.4, 2.0)	1.8 (0.3, 2.0)	1.7 (0.1, 2.0)
2080	3.1	3.1	3.1	3.0

	(1.0, 3.4)	(0.8, 3.4)	(0.8, 3.4)	(0.4, 3.3)
2100	4.3 (1.6, 4.6)	4.3 (1.5, 4.6)	4.3 (1.4, 4.6)	4.2 (0.9, 4.5)
Cumulative Life Years Gained (Millions)				
2040	2.0 (0.2, 2.7)	2.0 (0.1, 2.7)	2.0 (0.1, 2.7)	1.8 (0.01, 2.6)
2060	19.6 (3.6, 22.7)	19.4 (3.2, 22.6)	19.3 (3.0, 22.6)	18.4 (1.2, 22.0)
2080	47.4 (12.5, 52.5)	47.1 (11.4, 52.4)	46.9 (10.7, 52.3)	45.3 (5.3, 51.5)
2100	76.4 (26.5, 82.5)	76.0 (24.6, 82.3)	75.8 (23.4, 82.2)	73.9 (13.7, 81.3)
Cumulative QALYs Gained from Reduced Smoking Morbidity (Millions)				
2040	9.6 (2.7, 10.0)	9.6 (2.5, 10.0)	9.5 (2.4, 10.0)	9.2 (1.5, 9.9)
2060	24.0 (10.1, 24.7)	24.0 (9.6, 24.7)	23.9 (9.2, 24.7)	23.4 (6.5, 24.6)
2080	38.2 (18.5, 39.2)	38.2 (17.7, 39.2)	38.0 (17.0, 39.2)	37.3 (12.6, 39.0)
2100	53.1 (27.5, 54.4)	53.0 (26.6, 54.4)	52.8 (25.5, 54.3)	51.9 (19.3, 54.1)

[a] Low Impact: 3.8% people who smoke would divert to use illicit FNC cigarettes, and 0% youth and young adults would initiate illicit FNC cigarettes

[b] Medium Impact: 5.9% people who smoke would divert to use illicit FNC cigarettes, and 2.6% youth and young adults would initiate illicit FNC cigarettes

[c] High Impact: 21.0% people who smoke would divert to use illicit FNC cigarettes, and 10.0% youth and young adults would initiate illicit FNC cigarettes

In the main modeling analysis, we account for people who would have initiated cigarette smoking and initiated use of a noncombusted tobacco product instead as a result of the product standard. It is also possible that there could be increased initiation of noncombusted tobacco product use among those who would otherwise not have used tobacco under the product standard, for example, due to increased marketing of noncombusted products as a result of the policy or changes in public perceptions of the harms of noncombusted products. In a sensitivity analysis, starting at 2027 (year of the proposed nicotine standard implementation), we assumed a 20% increase in the initiation of noncombusted tobacco products among those who would otherwise have not used tobacco. Table 8 provides the projected impacts on tobacco-related mortality and morbidity through the year 2100. Compared with the main results, a 20% increase in initiation of noncombusted tobacco use had minimal impacts given the substantial reduction in adverse health effects projected under a potential nicotine product standard. It is important to note that, because we only have data on the effect of cigarette smoking (and not noncombusted product use) on quality of life, in the projections, QALYs gained from reduced smoking morbidity are not affected by increasing noncombusted product use initiation.

Table 8. Impact of Increased Initiation of Noncombusted Tobacco Products as a Result of the Proposed Nicotine Product Standard Implemented in 2027 on Projected Smoking Prevalence and Tobacco-Attributable Mortality and Morbidity by 2100. Median (5^{th}, 95^{th} Percentiles) Estimates.

Scenario	Projections Through Year 2100			
	Noncombusted Tobacco Use Prevalence (%)	Cumulative Tobacco-Attributable Mortality Avoided (Millions)	Cumulative Life Years Gained (Millions)	Cumulative QALYs Gained from Reduced Smoking Morbidity (Millions)
Main scenario	14.1 (12.7, 14.9)	4.3 (1.6, 4.6)	76.4 (26.5, 82.5)	53.1 (27.5, 54.4)
20% increased initiation of noncombusted products	15.4 (14.0, 16.1)	4.3 (1.6, 4.6)	75.9 (26.1, 82.1)	53.1 (27.5, 54.4)

6 Health Impact Accounting for Other Tobacco Product Standards

In 2022, FDA issued proposed product standards to prohibit menthol as a characterizing flavor in cigarettes (87 FR 26454, May 4, 2022) and to prohibit all characterizing flavors (other than tobacco) in cigars (87 FR 26396, May 4, 2002). If finalized, these rules are anticipated to reduce overall youth initiation and increase cessation among individuals who smoke cigarettes and cigars. We ran an adjusted simulation to model the impacts of a nicotine product standard on population health after first taking into account the behavioral impact of these rules, assuming that they would be finalized and implemented before a nicotine product standard went into effect. In this adjusted model, we utilized estimates of the likely population health impact of these rules, quantified in peer-reviewed publications and discussed in the proposed rules, to adjust the baseline inputs for initiation of combusted and noncombusted products, as well as cessation of combusted products and likelihood of switching to noncombusted products to incorporate the impact of the final rules on this proposed nicotine product standard.

6.1 Potential Impact Accounting for a U.S. Prohibition of Menthol Cigarettes

We quantified the potential impact of a menthol cigarette product standard on the U.S. population (87 FR 26454, May 4, 2022), assuming that the implementation of a rule prohibiting menthol affects baseline model input parameters associated with smoking initiation, smoking cessation, noncombusted product initiation, and switching from cigarettes to noncombusted products. To avoid confusion with the main analysis baseline scenario, we called this new scenario a "menthol product standard baseline scenario." First, we assumed that the menthol product standard is implemented in 2025, two years before the implementation of a potential nicotine product standard in 2027. Changes in tobacco use behaviors due to the implementation of a menthol product standard (primarily for would-be and current menthol smokers) were derived from a peer-reviewed, published expert elicitation that was developed to assess the impact of a menthol product standard on smoking initiation and cessation, and on noncombusted use (Levy et al., 2021). Specifically, 11 experts were asked to estimate transitions regarding current smoking and noncombusted use patterns under a menthol product standard, including becoming an illicit menthol cigarette user for young people who would have initiated menthol cigarette use; switching to non-menthol cigarettes (including HTPs), smokeless

tobacco, or e-cigarettes; or quitting use of all tobacco products. We used the results of the expert elicitation (finalized in September 2020) to compute scaling factors that were used to scale smoking initiation and cessation rates, as well as switching and noncombusted product initiation. People who currently smoke non-menthol cigarettes were assumed to be unaffected by the menthol product standard. Details regarding the calculation of scaling factors, considering the expert elicitation data, can be found in Appendix K of this document.

In the menthol product standard baseline scenario, baseline smoking initiation and noncombusted initiation rates were adjusted starting in 2025 (i.e., year of menthol product standard implementation) until the end of the simulation period. Also, baseline smoking cessation and complete switching (from cigarettes to noncombusted products) were adjusted only at the first year of the menthol product standard implementation. After the first year, when a sudden increase in smoking cessation and complete switching was incorporated, the remaining people who smoke became users of non-menthol or illicit menthol cigarettes, subject to the cessation and complete switching rates for people who smoke non-menthol cigarettes, as implemented in Levy et al. (Levy et al., 2023). We conducted the analysis considering the mean values of the expect elicitation data presented in (Levy et al., 2021). Specifically, we scaled the baseline transition rates to account for a decrease in cigarette smoking initiation, an increase in noncombusted product initiation, and an increase in smoking cessation and switching.

Table 9 presents the impact of the nicotine product standard using baseline assumptions adjusted for the effect of the proposed menthol cigarette product standard for years 2040, 2060, 2080, and 2100. In general, changes to baseline inputs of initiation and cessation of cigarettes, as well as switching to noncombusted products as a result of the implementation of the proposed menthol cigarette product standard slightly reduced projected smoking prevalence and avoided mortality and morbidity, compared to the main analysis results. Specifically, we estimated that by 2060, approximately 1.6 million deaths due to tobacco will be avoided (PR: 0.4, 1.7), rising to approximately 3.4 million (PR: 1.1, 3.6) by 2100. These estimates are approximately 11% and 21% less than the corresponding estimates that do not account for the potential impact of a menthol product standard. The reduction in premature deaths as a result of the nicotine product standard would result in 17.9 million life years gained (PR: 3.4, 20.4) by 2060, raising to 60.6 million life years gained (PR: 19.2, 65.3) by 2100. These estimates represent approximately a 9% and 21% reduction compared with the corresponding estimates under the main analysis.

Table 9. Impact of Proposed Nicotine Product Standard Implemented in 2027 on Projected Smoking Prevalence and Avoided Mortality and Morbidity from Main Analysis (Unadjusted Baseline Scenario) and Adjusted Menthol Product Standard Scenario Implemented in 2025. Median (5^{th}, 95^{th} Percentiles) Estimates.

Year	Unadjusted Baseline Scenario	Menthol Adjusted Scenario
Cigarette Smoking Prevalence (%)		
2040	0.2 (0.07, 4.0)	0.1 (0.06, 2.8)
2060	0.2 (0.07, 2.2)	0.1 (0.05, 1.4)

2080	0.2 (0.06, 2.0)	0.1 (0.05, 1.3)
2100	0.2 (0.06, 1.9)	0.1 (0.05, 1.2)
Cumulative Tobacco-Attributable Deaths Avoided (Millions)		
2040	0.4 (0.1, 0.5)	0.4 (0.1, 0.5)
2060	1.8 (0.4, 2.0)	1.6 (0.4, 1.7)
2080	3.1 (1.0, 3.4)	2.6 (0.7, 2.8)
2100	4.3 (1.6, 4.6)	3.4 (1.1, 3.6)
Cumulative Life Years Gained (Millions)		
2040	2.0 (0.2, 2.7)	2.0 (0.2, 2.6)
2060	19.6 (3.6, 22.7)	17.9 (3.4, 20.4)
2080	47.4 (12.5, 52.5)	40.6 (10.3, 44.5)
2100	76.4 (26.5, 82.5)	60.6 (19.2, 65.3)
Cumulative QALYs Gained from Reduced Smoking Morbidity (Millions)		
2040	9.6 (2.7, 10.0)	7.8 (2.1, 8.1)
2060	24.0 (10.1, 24.7)	17.5 (7.0, 17.9)
2080	38.2 (18.5, 39.2)	26.1 (11.9, 26.6)
2100	53.1 (27.5, 54.4)	34.9 (17.0, 35.7)

6.2 Potential Impact on Non-Premium Cigar Mortality Accounting for Flavored Cigar and Menthol Cigarette Product Standards

On May 4, 2022, FDA also issued a proposed product standard that would prohibit characterizing flavors (other than tobacco) in cigars (87 FR 26396, May 4, 2002). It is estimated that such a standard would prevent 780 deaths due to cigar smoking in the U.S. each year (Rostron et al., 2019b). A post-processing analysis of cumulative non-premium cigar-attributable deaths avoided was conducted to account for the effects of such a product standard, considering the adjustments to projected cigarette-attributable deaths in the baseline and nicotine product standard scenarios due to the menthol cigarette product standard. For the purpose of this analysis, we assumed both rules—the menthol cigarette and flavored cigar product standards—would be implemented in 2025. Specifically,

we assumed that the avoided cigar-attributable deaths expected to result from the flavored cigar rule begin to occur two years after the rule's effective date (2027) and would increase in a phased-in manner over a 30-year period (from 2026 to 2055). We then assumed a full mortality benefit of 780 avoided deaths would continue after 30 years, with a constant benefit of 780 deaths avoided until year 2064. We also assume avoided deaths will increase from 780 in 2064 to 1,120 in 2100. Details regarding the calculation of avoided cigar-attributable deaths due to the proposed flavored cigar standard can be found in Appendix L of this document.

The estimated deaths averted by a flavored cigar product standard were subtracted from baseline non-premium cigar deaths in the U.S. each year to produce yearly estimates for non-premium cigar deaths with a flavored cigar standard. We used these estimates to calculate a ratio of baseline non-premium cigar to baseline cigarette-attributable deaths for each year in the projection period. We then applied those ratios to the projections of avoided cigarette-attributable deaths, adjusted for the effects of the menthol cigarette product standard in the baseline and nicotine standard scenarios, to estimate non-premium cigar-attributable deaths under the nicotine policy scenario.

Table 10 presents estimates of the impact of the nicotine product standard implemented in 2027, using baseline assumptions adjusted for the effect of the proposed flavored cigar and menthol cigarette product standards implemented in 2025. We estimate that by 2060, in the U.S., approximately 45,600 deaths (PR: 11,100, 49,700) due to non-premium cigar use will be averted, rising to approximately 164,000 deaths avoided (PR: 65,000, 172,100) by 2100. In general, these estimates are approximately 17% and 24% less than the corresponding estimates that do not account for the potential impact of a product standard prohibiting characterizing flavors (other than tobacco) in cigars.

Table 10. Projected Number of Tobacco-Attributable Deaths from Non-Premium Cigar Use Avoided for as a Result of a Nicotine Product Standard Implemented in 2027 From the Main Analysis and With Adjustment for Flavored Cigar and Menthol Cigarette Product Standards Implemented in 2025.

Year	Percentiles	Cumulative Non-Premium Cigar-Attributable Deaths Avoided from Main Analysis	Cumulative Non-Premium Cigar-Attributable Deaths Avoided with Flavored Cigar and Menthol Cigarette Standards
2040	Median	8,900	8,000
	(5^{th}, 95^{th})	(1,000, 11,000)	(1,000, 9,500)
2060	Median	54,800	45,600
	(5^{th}, 95^{th})	(13,200, 60,500)	(11,100, 49,700)
2080	Median	134,7000	107,700
	(5^{th}, 95^{th})	(46,000, 144,100)	(35,000, 114,500)
2100	Median	214,700	164,000
	(5^{th}, 95^{th})	(91,600, 225,800)	(65,000, 172,100)

7 Conclusion

In this analysis, we estimate the impact of a potential nicotine product standard for cigarettes and certain other combusted tobacco products, including cigarettes, cigarette tobacco, RYO tobacco, cigars (other than "premium" cigars), and pipe tobacco on population health in the U.S. using a computational model that accounts for population dynamics and transitions between cigarette smoking and use of noncombusted tobacco products (i.e., smokeless tobacco, e-cigarettes and other ENDS, heated tobacco products, and oral nicotine products). Such a product standard would be based on FDA's authority to establish a tobacco product standard under section 907 of the Federal Food, Drug, and Cosmetic Act as amended by the Family Smoking Prevention and Tobacco Control Act (2009) and would be promulgated through the rulemaking process. In addition to the direct effects of cigarette smoking on the health of smokers, we use the modeled projections to also estimate the impacts on deaths from secondhand smoke exposure, perinatal outcomes, and smoking-related fires, as well as non-premium cigar and pipe smoking.

This document outlines the framework and the methodology of the computational model and describes the source of the data inputs that informed creation of the baseline for the population health model. This document also describes the application of this population health model to a hypothetical policy scenario restricting nicotine levels in cigarettes and certain other combusted tobacco products to be minimally addictive or nonaddictive. In general, sensitivity analyses related to changes to the baseline inputs of noncombusted product use trajectories as well as to mortality risks for noncombusted product and dual use had minimal impacts on smoking prevalence and attributable mortality and morbidity. The largest impacts were observed when accounting for the potential of an illicit market, which reduced the health benefits of the proposed nicotine product standard. However, even after incorporating a range of illicit trade impacts, substantial reductions in morbidity and mortality were still observed. Overall, this analysis demonstrates that a nicotine product standard would be expected to result in significant reductions in smoking prevalence and premature death from tobacco, and improvements in health-related quality of life.

Results in this analysis are similar to those in a previous published analysis conducted by FDA using estimates from the earlier 2015 expert elicitation (Apelberg et al., 2018), although there are some differences due to changes in tobacco use and estimates from the expert elicitation process over time. In terms of outcome measures, the previous analysis found that, over a 50-year period following the implementation of a nicotine standard in 2020, there would be a median value of 20.2 million fewer cigarette smoking initiates in the U.S. by 2070, whereas the current analysis found a median of 32.1 million dissuaded smoking initiates by 2077 (with the nicotine standard implemented in 2027). This difference is largely attributed to updated expert opinion (2018 vs 2015 Expert Elicitation) which provided higher estimates for the percentage reduction in smoking initiation due to the nicotine standard, leading to a larger number of dissuaded initiates compared to the Apelberg et al. (2018) publication. The previous analysis also estimated that there would be a median value of 4.2 million fewer tobacco-attributable deaths by 2070 resulting in a gain of 54.4 million more life years. The current analysis, in comparison, estimated that there would be a median of 2.9 million tobacco-attributable deaths averted by 2077 resulting in 43.1 million life years gained as a result of the nicotine product standard. The decrease in tobacco-attributable deaths averted and life years gained compared with the Apelberg et al. (2018) analysis is largely due to lower CISNET smoking initiation rates and lower smoking prevalence at baseline in year 2021 (current analysis) compared to 2015 (previous analysis).

That decrease is also associated with higher switching rates (from cigarettes to noncombusted tobacco use) at baseline in the current analysis compared to the data used in the previous analysis. Results from both analyses are generally comparable to those from an earlier simulation that modeled a proposal from the American Medical Association to gradually reduce the nicotine content of cigarettes, which estimated that a total of 157 million QALYs would be gained from reduced mortality and morbidity due to smoking over a 50-year period through 2053 (Tengs et al., 2005).

Since the 2018 expert elicitation, new results have been published from multiple studies and analyses evaluating reduced or VLNC cigarette use. Much of the recent literature is reviewed and synthesized in Donny et al. (2022), but highlighted findings from some of the new literature related to this modeling approach are also summarized here. In general, results from studies published after 2018 are consistent with those published prior to 2018. For example, new studies have demonstrated similar use behaviors (i.e., cigarette consumption, puff topography) between FNC and VLNC cigarettes (Branstetter et al., 2019; Denlinger-Apte et al., 2020; Faulkner et al., 2019; Smith et al., 2020; Tidey et al., 2019; White et al., 2022) or lower relative use associated with VLNC cigarettes (Smith et al., 2019; Tidey et al., 2019). Klemperer et al. (2019a) and Smith et al. (2019) found that switching from FNC to VLNC cigarettes did not promote complete cessation among participants in two clinical trials; however, clinical studies that assessed the abuse liability of VLNC cigarettes have generally found lower ratings of positive subjective effects (Branstetter et al., 2019; Cassidy et al., 2018; Chukwueke et al., 2020; Smith et al., 2020; Streck et al., 2020; Tidey et al., 2019), reductions in nicotine dependence (Klemperer et al., 2019b; Klemperer et al., 2019c; Shiffman et al., 2019) or no change in nicotine dependence (Smith et al., 2019; Tidey et al., 2019) following extended use of VLNC cigarettes, consistently greater choice for higher-nicotine content cigarettes than VLNC cigarettes in concurrent-choice studies (Perkins et al., 2020a, 2020b; Streck et al., 2020), and greater hypothetical purchasing of FNC than VLNC cigarettes (Cassidy et al., 2019; Kaplan et al., 2022; Streck et al., 2020). Together, these findings demonstrate lower abuse liability of VLNC than FNC cigarettes, which would likely result in reduced likelihood of users transitioning to regular use and reductions in nicotine dependence severity among established users. Regarding illicit purchasing of FNC cigarettes, some studies estimated that 19-36% of combusted cigarette users might be interested in trying to purchase FNC cigarettes illicitly (Hall et al., 2019; Patel et al., 2019), and illicit FNC cigarettes might serve as weak substitutes for legal VLNC cigarettes in a subset of combusted cigarette users, but ENDS availability may reduce demand for both VLNC and illicit FNC cigarettes (Dolan et al., 2023). When considered together, the results from studies published since 2018 support the conclusions and assumptions from the 2018 expert elicitation, as the data primarily indicate that VLNC cigarettes have lower abuse liability than FNC cigarettes, switching to VLNC cigarettes does not result in lasting compensatory use behaviors, and the interest in or likelihood of trying to purchase illicit FNC cigarettes is low and potentially mitigated by the availability of alternative noncombusted tobacco products.

Limitations. There are several limitations of the present analysis that should be noted. First, although cigarette smoking inputs are derived from large, nationally representative sources and the population model has been previously demonstrated to replicate estimates of smoking prevalence for the U.S. population, more limited data are available for noncombusted tobacco products. As a result, certain simplifying assumptions were necessary to incorporate the impact of switching to or initiating the use of noncombusted tobacco products on population health. For example, cigarette smoking initiation rates were scaled to generate similar rates for noncombusted tobacco product use, thus implying that age and gender patterns for noncombusted product use are similar to those for cigarette smoking. Other assumptions were made about the future trajectory of noncombusted tobacco product

use and risk associated with dual tobacco product use. We conducted various sensitivity analyses to examine the impact of these assumptions on the reductions in morbidity and mortality. Across all sensitivity analyses, a nicotine product standard would have a substantial impact on public health in terms of reductions in smoking prevalence, premature death from tobacco, and improved health-related quality of life.

Second, we were not able to specifically capture the wide variety of tobacco product use in this analysis. In the expert elicitation, transitions to non-cigarette tobacco products were asked about in terms of smokeless tobacco, e-cigarettes or other ENDS, waterpipe/hookah tobacco, and premium cigars. Consistent with estimates from the 2018 expert elicitation that transitions to waterpipe and premium cigar use will be minimal following implementation of a nicotine product standard, noncombusted products were assumed to constitute all non-covered tobacco use in this analysis. We considered smokeless tobacco, e-cigarette, heated tobacco product, and oral nicotine product use together as a single noncombusted tobacco product category in the model because this approach was computationally more feasible. We also applied mortality risks for smokeless tobacco use to noncombusted product use generally because we lacked mortality data for e-cigarettes, heated tobacco products, and oral nicotine products. We also examined the potential effects of lower and higher mortality risks for noncombusted products in sensitivity analyses. The expert elicitation also did not specifically consider transitions to heated tobacco product or oral nicotine product use, given that these products were not marketed in the U.S. at that time. However, current use of these products in the U.S. is limited with one analysis of 2019 TUS-CPS data finding that ever use of heated tobacco products was 1.6% among U.S. adult smokers (Azagba et al., 2021).

Third, due to the more limited data available for non-cigarette combusted products and the limitations of a two-product model, we used the model-derived attributable mortality projections as the basis for projecting avoided mortality due to use of other combusted products (i.e., non-premium cigars and pipe tobacco) with published estimates of mortality from these exposures for the U.S. This approach assumes that initiation and cessation of non-premium cigars and pipe tobacco will follow the projected trajectories (under the baseline and product standard scenarios) for cigarette smoking. We also assume that the reductions in cigarette smoking that ultimately lead to lower attributable mortality will be similar for other combusted tobacco products. In addition, the estimate of deaths attributable to non-premium cigar products assumes the mortality burden of non-premium (versus premium) cigars can be partitioned according to usual cigar type. Finally, the estimates of U.S. pipe tobacco-attributable deaths used in the analysis are from 1991 and may overestimate current mortality from pipe tobacco because pipe smoking prevalence among U.S. adult men in NHIS decreased from 14.1% in 1965 to 2.0% in 1991 and was at 1.2% for all pipes including waterpipes in 2021 (Cornelius et al., 2023; Nelson et al., 1996). The 1991 mortality estimates are the most recent published estimates of pipe tobacco-attributable mortality for the U.S., and we note that the absolute mortality burden of pipe tobacco smoking was relatively low compared to other combusted tobacco product use even then at an estimated 1095 deaths among U.S. men per year. We also use the projections for avoided attributable mortality to estimate the deaths due to secondhand smoke exposure, perinatal conditions, and smoking-related fires due to limited data, generally in the form of estimates of mortality from these causes for the U.S. population, for these causes of mortality. We do not consider any additional deaths from these causes that could result from switching to noncombusted products in the product standard scenario.

Fourth, although we assessed the potential for reduced smoking morbidity through the application of a self-reported quality of life measure, comparable information was not available for morbidity from noncombusted tobacco product use and was, therefore, not assessed. Therefore, the overall impact on morbidity may be overestimated because noncombusted tobacco product use morbidity was not included. In addition, quality of life scores were available only for smokers and non-smokers, rather than former and never smokers separately, which may have influenced the estimated timing of morbidity benefits.

Fifth, there may be other future population-level policies that could impact the inputs and assumptions of this model (e.g., changes in tobacco use behaviors, prevalence rates, as well as changes in the tobacco market and regulatory policies). We note that future implementation of other potential tobacco product standards, such as those restricting menthol in cigarettes and characterizing flavors (other than tobacco) in cigars, would necessitate adjustments to our modeling inputs and assumptions. Varying key modeling assumptions to account for potential changes in tobacco use behaviors due to the impact of regulatory policies with overlapping time horizons could be used in future applications of the model to layer the impact of regulatory policies.

Sixth, prevalence of use of various tobacco products has changed significantly in recent years, and it is not entirely known if these trends will intensify, remain essentially the same, or change direction. For example, cigarette smoking prevalence has generally steadily declined, especially among youth, whereas youth e-cigarette use prevalence has both increased and decreased over time. We used the best and most recent data available on these trends and have incorporated sensitivity analysis in the model to consider the effects of different assumptions about future product use. Similarly, the most recent expert elicitation was conducted in 2018 and does not reflect trends in tobacco product use since that time.

Seventh, it is assumed that the nicotine product standard will be implemented in 2027, that the required reduction in nicotine levels will be immediate, and that the standard will be comprehensively enforced. Any deviation from these assumptions could result in different outcomes.

Eighth, population estimates are presented for the U.S. population as a whole and not for subgroups defined by characteristics such as age, gender, race, ethnicity, socioeconomic status, and mental health status.

Finally, projecting the impact of future actions on behavior over the long-term will be inherently uncertain. Although an objective and rigorous process was used to identify experts and elicit their informed opinions on potential behavioral responses to a nicotine product standard, their estimates are ultimately subjective and presumably somewhat imperfect. Estimates from the experts exhibited a certain amount of variability as seen in Figure 2, and estimates from the same experts sometimes varied between the 2015 and 2018 elicitations. These differences could be the result of changes in the experts' opinions concerning the potential appeal and use of specific tobacco products, especially e-cigarettes, over time as well as additional research on the effects of VLNC cigarettes. A related issue is that the expert elicitation was completed in 2018 and was based of the state of the science on VLNC cigarettes and tobacco product use and trends available at that time. More recent data and studies could impact expert opinion. Lastly, although we have incorporated uncertainty in predicted behavioral responses through a Monte Carlo analysis and examined the impact of key modeling assumptions through individual sensitivity analyses, the analysis was not able to capture all possible sources of uncertainty. For example, the combined effect of variation in multiple baseline parameter values was not assessed in this analysis, although variation of individual parameter values had minimal effect on model projections

as seen in Table 6. Overall, the ranges of estimates produced through these analyses all resulted in projections of substantial health benefits to the population as a whole, even if any particular estimate may be uncertain.

Other Public Health Impacts. The estimates of public health benefits in this analysis are likely to be conservative, since our analysis does not account for the full range of impacts that smoking has on public health in the U.S.

First, although we estimated the impact of the proposed standard on self-reported quality of life, this may not capture the full breadth and depth of smoking-attributable morbidity. Tobacco smoke exposure can cause immediate and long-term adverse health effects (U.S. Department of Health and Human Services, 2014). Cigarette smoking "has been causally linked to diseases of nearly all organs of the body, to diminished health status, and to harm to the fetus" (U.S. Department of Health and Human Services, 2014). Each year, an estimated 480,000 persons in the U.S. die from smoking; the U.S. Surgeon General has reported that for every person that dies from smoking, about 30 individuals will suffer from at least one smoking-related disease (U.S. Department of Health and Human Services, 2014). One study estimated that individuals are living with 14.0 million major smoking-related conditions in the U.S., including more than 7.4 million cases of chronic obstructive pulmonary disease, nearly 2.3 million heart attacks, 1.8 million cases of diabetes, nearly 1.2 million stroke events, more than 300,000 cases of lung cancer, and nearly 1 million cases of other smoking-attributable cancers (i.e., bladder, cervix, colon/rectum, kidney, larynx, mouth, tongue, lip, throat, pharynx, stomach) (Rostron, Chang, & Pechacek, 2014). Cigarette smoking, in addition to causing disease, can diminish overall health status leading to higher risks for surgical complications, including wound healing and respiratory complications, increased absenteeism from work, and greater use of health care services (U.S. Department of Health and Human Services, 2014). In 2018, cigarette smoking cost the U.S. more than $600 billion, including more than $240 billion in healthcare spending (Shrestha et al., 2022; Xu et al., 2021), nearly $185 billion in lost productivity from smoking-related illnesses and health conditions (Shrestha et al., 2022), nearly $180 billion in lost productivity from smoking-related premature death (Shrestha et al., 2022; U.S. Department of Health and Human Services, 2014), and $7 billion in lost productivity from premature death from secondhand smoke exposure (Max et al., 2012; U.S. Department of Health and Human Services, 2014). Increased smoking cessation, reduced cigarette consumption and lower progression to regular use will reduce both mortality from smoking, as well as the enormous burden of cigarette smoking-attributable diseases in the U.S.

Second, the estimated impacts to public health do not include the morbidity reductions associated with reduced exposure to secondhand smoke among infants and children. Analysis of NHANES data found that approximately half of all U.S. children aged 3-18 years were exposed to cigarette smoke regularly at home or other locations that still permit smoking in the period from 1999 to 2010 (Quinto et al., 2013). Also, an study using NYTS data reported that, in 2019, 25.3% and 23.3% of students were exposed to home and vehicle secondhand smoke, respectively (Walton et al., 2020). Exposure to cigarette smoke among children and adolescents can trigger asthma attacks and lead to more frequent respiratory infections compared to those not exposed to smoke (U.S. Department of Health and Human Services, 2014).

Third, lower prevalence of cigarette smoking and reduced cigarette consumption will decrease the occurrence of fire injuries and damages caused by smoking materials, including cigarettes and other lighted tobacco products. From 2012-2016, an estimated 18,100 home structure fires in the U.S. were caused by smoking materials on average each year (Ahrens, 2019). Reductions in smoking as a result of

a nicotine product standard are likely to lead to not only fewer fatalities (described above) but also reductions in the more than 1,130 injuries, and more than $476 million in direct property damages annually resulting from smoking-attributable home structure fires (Ahrens, 2019).

Fourth, these projections did not include the potential health benefits associated with smokers cutting down on the number of cigarettes smoked as a result of a nicotine product standard. Quitting cigarette smoking entirely clearly leads to the greatest reductions in disease risk and duration of smoking has been shown to be a greater driver of disease risk than frequency of use (U.S. Department of Health and Human Services, 2010). Although some studies have not found evidence of lower disease risk after cutting down on cigarettes (Benhamou et al., 1989; Godtfredsen, 2002; Godtfredsen et al., 2003; Godtfredsen et al., 2002; U.S. Department of Health and Human Services, 2010) others have shown that substantial reductions in cigarette consumption can lead to some reductions in disease risk, especially for lung cancer, compared to those who continued to smoke at non-reduced levels (Chang et al., 2021). Such studies have found decreased risk of lung cancer deaths (Tverdal et al., 2006) and decreased risk of incident lung cancer among smokers reducing cigarette consumption (Godtfredsen et al., 2005; Song et al., 2008). As described above, studies of VLNC cigarettes in smokers have shown that their use results in reductions in cigarettes smoked per day and exposure to toxic constituents among individuals who continue to smoke, which may reduce smoking-related disease risks. Consequently, additional public health benefits may be observed among those who continue to smoke cigarettes after a nicotine product standard is in place.

Finally, these estimates do not account for improvements in health disparities that could result from a nicotine product standard, including reductions in cigarette smoking for groups such as individuals with low socioeconomic status or mental health conditions that have smoking prevalence levels that are higher than the national average (Cornelius et al., 2022).

Overall, this analysis has found that a potential nicotine product standard would have substantial benefits for the U.S. public health. Results indicate that the product standard would produce an immediate and substantial reduction in cigarette smoking prevalence, resulting in an estimated 20 million additional individuals quitting smoking within five years and almost 48 million fewer smoking initiates by 2100. These reductions in smoking would lead to over 4 million fewer tobacco-attributable deaths, almost 77 million additional years of life, and over 53 million additional QALYs due to reduced smoking-related morbidity. The product standard would also produce substantial public health benefits from reductions in mortality from non-premium cigar and pipe tobacco use as well as deaths from secondhand smoke exposure, smoking-related perinatal conditions, and smoking-related fires.

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Appendix A: Baseline Data Inputs and Sources

Table A1. Description of Baseline Input Parameters and Data Sources Used in the Analysis.

Model Component	Model Parameter	Data Source and Notes
Initial Population	Population distribution by sex and age	Data were obtained from U.S. Census National Population Estimates for 2021. Annual Estimates of the Resident Population by Single Year of Age and Sex for the United States: April 1, 2020, to July 1, 2021 (NC-EST2021-AGESEX-RES) Source: https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html
	Tobacco use status (combinations of current, former, and never use for cigarettes and noncombusted products) by sex, age, and time since cessation (for cigarettes only)	Data were obtained from the 2020 National Health Interview Survey (NHIS) data for adults (ages 18 years and older) and the 2020 National Youth Tobacco Survey (NYTS) for youth (ages less than 18 years old). NYTS and NHIS data were used to partition smoking prevalence into prevalence of 1) exclusive cigarette smoking, 2) dual cigarette and noncombusted product use, 3) exclusive noncombusted product use, and 4) no tobacco use for baseline year. Sources: NHIS: https://www.cdc.gov/nchs/nhis/2020nhis.htm NYTS: https://www.cdc.gov/tobacco/data_statistics/surveys/nyts/data/index.html
Births	Annual births by sex	Annual births by sex were derived from projections produced by the U.S. Census Bureau for the years 2021-2060 based on the 2010 Census. Births for the years 2061-2100 were projected using an exponential smoothing state space model. Source: https://www.census.gov/data/datasets/2017/demo/popproj/2017-popproj.html (Dataset: Projected Births by Sex, Race, and Hispanic Origin for the United States: 2016 to 2060)
Net International Migration	Annual net migration by sex	Annual net migration by sex was derived from projections produced by the U.S. Census Bureau for the years 2021-2060 based on the 2010 Census. Migration estimates for the years 2061-2100 were projected using an exponential smoothing state space model. Source: https://www.census.gov/data/datasets/2017/demo/popproj/2017-popproj.html (Dataset: Projected Net International Migration by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: 2016 to 2060)

Model Component	Model Parameter	Data Source and Notes
	Immigrant age distribution	Data were obtained from U.S. Census Bureau, 2016-2020 American Community Survey 5-Year Estimates. Table S0502: Selected Characteristics of the Foreign-Born Population by Period of Entry into the United States. Source: https://data.census.gov/cedsci/table?q=foreign-born&tid=ACSST5Y2020.S0502
	Immigrant smoking prevalence by sex	Data were obtained from the 2014-2018 NHIS. Cigarette smoking prevalence (for current and former use) was calculated for immigrants to the U.S., ages 18 years and older, who had been in the U.S. less than five years. Source: https://www.cdc.gov/nchs/nhis/index.htm The 2014-2018 NHIS contains data for both cigarettes and noncombusted tobacco use. We opted for not pooling 2018 and earlier data with 2019 and later data due to significant changes introduced in 2019 to NHIS data collection. https://nhis.ipums.org/nhis/userNotes_2019_NHIS_Redesign.shtml https://blog.popdata.org/pooling-years-of-nhis-data/
	Immigrant noncombusted prevalence by sex	Data were obtained from the 2014-2018 NHIS. Noncombusted tobacco use prevalence (for current and former use) was calculated for immigrants to the U.S., ages 18 years and older, who had been in the U.S. less than five years. Source: https://www.cdc.gov/nchs/nhis/index.htm
Deaths	Never smoker death rate by sex and age (used for never tobacco users in model)	U.S. death rates estimates from the 2019 National Vital Statistics Reports were used for never cigarette smokers ages less than 35 years, given that smoking-attributable mortality is low at these ages. Never smoker death rates for ages 35 years and over were estimated from the 2019 NHIS-LMF data for NHIS Sample Adult Questionnaire participants from 1997 through 2018, followed for mortality through linkage with the National Death Index until 2019. Sources: https://www.cdc.gov/nchs/data/nvsr/nvsr70/nvsr70-08-508.pdf https://www.cdc.gov/nchs/data-linkage/mortality-public.htm

Model Component	Model Parameter	Data Source and Notes
	Mortality adjustment factor by sex and age	NHIS-LMF never smoker death rates were adjusted for low mortality in the NHIS's civilian non-institutionalized population by multiplying the rates by the ratio of U.S. Vital Statistics death rates divided by NHIS-LMF death rates by sex and age. Source: National Vital Statistics Report, Deaths: Final Data for 2019, Table 2 https://www.cdc.gov/nchs/data/nvsr/nvsr70/nvsr70-08-508.pdf
	Mortality scaling factor	Mortality scaling factors for 2021-2100 were calculated from U.S. death rates projections for the same period, using Lee-Carter Method (Lee & Carter, 1992) and historic U.S. death rates from years 1933-2020 available from the Human Mortality Database. Source: https://www.mortality.org/Country/Country?cntr=USA
	Relative risk by sex, age, smoking status, and age at cessation for former smokers	HRs were estimated from the 2019 NHIS-LMF data (National Center for Health Statistics, 2019). Source: https://www.cdc.gov/nchs/data-linkage/mortality-public.htm
	Relative risk for smokeless tobacco users	HRs calculated from American Cancer Society Cancer Prevention Study II (CPS-II) data for current smokeless tobacco users (Henley et al., 2005) and former cigarette smokers who subsequently initiated smokeless tobacco use (Henley et al., 2007).
Cigarette Smoking Transition Behaviors	Sex and age-specific initiation rate	Cigarette smoking initiation rates were derived by CISNET researchers, based on smoking histories for birth cohorts reconstructed from NHIS data (from 1965 through 2018). See Tam et al. (2018) for details regarding the methods used to estimate the initiation and cessation rates.
	Sex and age-specific cessation rate	Cigarette smoking cessation rates were derived by CISNET researchers, based on smoking histories for birth cohorts reconstructed from NHIS data (from 1965 through 2018). See Tam et al. (2018) for details regarding the methods used to estimate the initiation and cessation rates.
	Sex and age-specific relapse rate	Set to 0
Noncombusted Transition Behaviors	Sex and age-specific initiation rate	Prevalence of current cigarette, smokeless and e-cigarette use from 2017-2020 NYTS and 2020 NHIS are used to scale smoking initiation rates to obtain initiation rates for exclusive cigarette use, exclusive noncombusted use and dual cigarette and noncombusted use (see Appendix D).
	Sex and age-specific cessation rate	Smoking cessation rates are used for cessation from noncombusted products.

Model Component	Model Parameter	Data Source and Notes
	Sex and age-specific switching rate	One-year switching rates from cigarettes to noncombusted tobacco products for age groups 12-14, 15-17, 18-24, 25-34, 35-54, and 55+, were obtained from Brouwer et al. (2023), estimated for youth and adult participants in Waves 2-4 (2015-2017) and Waves 4-5 (2017-2019) of the PATH Study. Rates for females and males are equal.
	Sex and age-specific rates from dual use to exclusive cigarette/noncombusted tobacco product use	Data obtained from Brouwer et al. (2023) for age groups 12-14, 15-17, 18-24, 25-34, 35-54, and 55+, estimated for youth and adult participants in Waves 2-4 (2015-2017) and Waves 4-5 (2017-2019) of the PATH Study. Rates for females and males are equal.
	Sex and age-specific relapse rate	Set to 0

Appendix B: Calculation of Population Size in Dynamic Population Model

Let $A = \{0,1,\cdots,G-1,G^{+}\}$ be the set of ages, where $G^{+} = \{G, G+1, G+2, \cdots\}$ (G = 100 in the current implementation), $S = \{male, female\}$ be the set of sexes, and *U* be the set of all possible tobacco product use states considered in the model, $U = \{NN, CN, FN, NC, CC, FC, NF, CF, FF\}$[6] for two tobacco products. Equations 1 through 5 provide a mathematical representation of the model. Table B1 defines key model parameters and variables. Given that much of the data necessary to develop parameters is provided on an annual basis, time steps are generally taken to be one-year increments, and parameters and variables are defined and described accordingly. A different sized time step could certainly be used[7], and interpretation of parameter and variable definition would need to change accordingly.

$$Pop(0, s, u_{never}, t_{i+1}) = b(s, t_{i+1}) + m(0, s, u_{never}, t_{i+1}) \quad (1)$$

$$Pop(0, s, u, t_{i+1}) = 0, u \neq u_{never} \quad (2)$$

$$Pop(a+1, s, u, t_{i+1}) = \sum_{x \in U} Pop(a, s, x, t_i) \times p(x \to u | a+1, s, x, t_{i+1}) \times [1 - p(death | a+1, s, u, t_{i+1})] + m(a+1, s, u, t_{i+1}), a = 0, \cdots, G-1 \quad (3)$$

$$(G^{+}, s, u, t_{i+1})$$

$$= \sum_{x \in U} Pop(G-1, s, x, t_i) \times p(x \to u | G, s, x, t_{i+1}) \times [1 - p(death | G, s, u, t_{i+1})] = + \sum_{x \in U} Pop(G^{+}, s, x, t_i) \times p(x \to u | G^{+}, s, x, t_{i+1}) \times [1 - p(death | G^{+}, s, u, t_{i+1})] + m(G^{+}, s, u, t_{i+1}) \quad (4)$$

$$p(death | a, s, u, t_i) = RR(a, s, u, t_i) \times p(death | a, s, u_{never}, t_i). \quad (5)$$

Equations 1-5 describe how subpopulations are tracked. The number of newborns (age 0) is determined solely by births and migration of infants less than age 1 (Equation 1), and all newborns are assumed to have never used any of the tobacco products (Equation 2). For older ages (Equations 3 and 4), the size of a subpopulation is calculated by determining the number of people from the previous year who transition into a particular subpopulation and do not die, and the number of net international migrants entering or leaving the subpopulation.

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[6] First letter denotes cigarette use status, and second letter denotes non-combusted tobacco product use status. N = never, C = current, and F = former. These nine tobacco use states are the use states presented in Figure 1. For example, *NN* = Never/Never, *CN* = Current/Never, and *FC* = Former/Current.

[7] In its most general form, the model can use any specified time step for which appropriate parameters can be determined. In practice, annual time steps are most commonly used.

The model assumes that the all-cause mortality proportion for a subpopulation is the product of the all-cause mortality relative risk (RR) for this subpopulation and the base mortality probability of dying for never users of any of the N tobacco products by sex and age (Equation 5). Because use of any tobacco product is assumed to have no protective effect (relative to never use), all RRs are greater than or equal to 1.

Table B1. Model Parameters and Variables

Parameter	Description	Input Parameter or Output Variable
$Pop(a, s, u, t_i)$	Number of individuals of age *a*, sex *s*, and tobacco use status *u* at year t_i. The population at year t_0 is defined to be the initial population.	For *i* = 0, input For *i* > 0, output
$p(x \rightarrow u \mid a+1, s, x, t_{i+1})$	Annual proportion of individuals of age *a+1*, sex *s*, and tobacco use status *x* that transition to tobacco use status *u* in the time interval $(t_i, t_{i+1}]$. When *x = u*, this parameter represents the rate at which individuals maintain and do not change their tobacco use status.	Input
$p(death \mid a, s, u, t_{i+1})$	Annual proportion of individuals with age *a+1*, sex *s*, and tobacco use status *u* that die in the time interval $(t_i, t_{i+1}]$	Input
$b(s, t_{i+1})$	Number of births of sex *s* during the time interval $(t_i, t_{i+1}]$	Input
$m(a, s, u, t_{i+1})$	Number of net international migrants of age *a*, sex *s*, and tobacco use status *u* entering/leaving the population during the time interval $(t_i, t_{i+1}]$	Input

Table B2. Never Smoker Deaths Rates Per 100,000 for NHIS 1997-2018 Sample Participants with Mortality Follow-up period 2002-2019, by Sex and Age Groups.

Age Group	Males		Females	
	Death Rate	Standard Error	Death Rate	Standard Error
35-44	174.8	8.6	98.9	5.6
45-54	281.9	10.9	210.9	8.1
55-64	565.3	17.2	416.2	13.7
65-74	1309.7	36.9	981.2	22.0
75-84	3919.2	80.2	2906.2	43.1
85+	12903.8	222.8	10829.2	103.0

Table B3. Ratio of 2019 US National Vital Statistics Death Rates to 2002-2019 Overall NHIS-LMF Death Rates, by Sex and Age Groups.

Age Group	Death Rates per 100,000		Ratio
	Overall NHIS-LMF Rate	2019 National Vital Statistics Rate	
	Males		
35-44	218.0	257.0	1.18
45-54	444.1	490.0	1.10
55-64	975.2	1111.9	1.14
65-74	2155.7	2178.6	1.01
75-84	5332.4	5074.1	0.95
85+	14419.2	14229.6	0.99
	Females		
35-44	129.7	141.6	1.09
45-54	307.4	297.3	0.97
55-64	636.9	669.8	1.05
65-74	1449.6	1402.0	0.97
75-84	3766.5	3710.9	0.99
85+	11475.2	12666.1	1.10

Mortality Scaling Factors

The model projects never-smoker death rates from 2021 through 2100 using mortality scaling factors obtained from the Lee-Carter mortality forecasting method (Lee et al., 1992) with Poisson errors, as implemented in the R packages "demography" version 2.0 (Hyndman, 2023) and "StMoMo" version 0.4.1 (Villegas et al., 2018). The Lee-Carter method was used to project U.S. death rates from 2021 through 2100 by sex and age using observed U.S. death rates from years 1933-2020, available from the Human Mortality Database. Mortality scaling factors by sex and age were calculated as the ratio of projected rates for 2021-2100 to the projected rates for 2021. These scaling factors were then applied to the never-smoker death rates to produce projected never-smoker death rates by sex and age for years 2021-2100. Table B2 shows the estimated mortality scaling factors for years 2024 and 2030-2100 (by 10-year intervals).

Table B4. U.S. Mortality Scaling Factors Obtained from the Lee-Carter Mortality Forecasting Method, by Sex, Age, and for years 2024 and 2030-2100 (by 10-year intervals).

Sex	Age	Years								
		2024	**2030**	**2040**	**2050**	**2060**	**2070**	**2080**	**2090**	**2100**
Female	0	0.920	0.779	0.590	0.447	0.339	0.256	0.194	0.147	0.111
	1-4	0.923	0.787	0.603	0.462	0.354	0.272	0.208	0.160	0.122
	5-9	0.930	0.804	0.632	0.496	0.389	0.306	0.240	0.188	0.148
	10-14	0.947	0.849	0.708	0.590	0.492	0.410	0.342	0.285	0.237
	15-19	0.964	0.897	0.794	0.704	0.624	0.552	0.489	0.434	0.384
	20-24	0.970	0.913	0.825	0.746	0.674	0.610	0.551	0.498	0.450
	25-29	0.972	0.918	0.836	0.760	0.692	0.629	0.573	0.521	0.474
	30-34	0.970	0.914	0.827	0.748	0.676	0.612	0.554	0.501	0.453
	35-39	0.967	0.904	0.809	0.723	0.647	0.578	0.517	0.462	0.413
	40-44	0.965	0.898	0.796	0.706	0.626	0.556	0.493	0.437	0.388
	45-49	0.966	0.901	0.803	0.715	0.637	0.567	0.505	0.450	0.401
	50-54	0.966	0.903	0.806	0.719	0.642	0.573	0.511	0.456	0.407
	55-59	0.968	0.908	0.815	0.732	0.658	0.591	0.531	0.477	0.428
	60-64	0.967	0.903	0.807	0.720	0.643	0.574	0.513	0.458	0.409
	65-69	0.966	0.901	0.802	0.714	0.636	0.566	0.504	0.448	0.399
	70-74	0.965	0.898	0.797	0.707	0.627	0.557	0.494	0.438	0.389
	75-79	0.963	0.894	0.789	0.696	0.615	0.543	0.479	0.423	0.373
	80-84	0.968	0.906	0.813	0.729	0.653	0.586	0.525	0.471	0.422
	85+	0.974	0.924	0.847	0.776	0.711	0.651	0.596	0.546	0.501
Male	0	0.919	0.777	0.587	0.443	0.335	0.253	0.191	0.144	0.109
	1-4	0.929	0.801	0.627	0.490	0.383	0.300	0.234	0.183	0.143
	5-9	0.928	0.799	0.623	0.485	0.378	0.295	0.230	0.179	0.140
	10-14	0.943	0.840	0.691	0.569	0.469	0.386	0.318	0.262	0.216
	15-19	0.967	0.904	0.809	0.723	0.647	0.578	0.517	0.462	0.413
	20-24	0.978	0.934	0.866	0.803	0.745	0.690	0.640	0.593	0.550
	25-29	0.986	0.959	0.915	0.873	0.833	0.795	0.758	0.724	0.691
	30-34	0.986	0.959	0.915	0.873	0.833	0.795	0.758	0.723	0.690
	35-39	0.979	0.939	0.875	0.816	0.761	0.709	0.661	0.616	0.574
	40-44	0.971	0.916	0.831	0.754	0.684	0.621	0.563	0.511	0.464
	45-49	0.967	0.905	0.809	0.724	0.648	0.580	0.519	0.464	0.415
	50-54	0.964	0.897	0.795	0.705	0.625	0.554	0.491	0.435	0.386
	55-59	0.964	0.895	0.791	0.699	0.618	0.546	0.482	0.426	0.377
	60-64	0.961	0.889	0.780	0.684	0.600	0.526	0.461	0.405	0.355
	65-69	0.961	0.887	0.777	0.681	0.596	0.522	0.457	0.401	0.351
	70-74	0.963	0.894	0.789	0.696	0.615	0.542	0.479	0.423	0.373
	75-79	0.967	0.903	0.807	0.720	0.643	0.575	0.513	0.458	0.409
	80-84	0.972	0.919	0.837	0.762	0.694	0.632	0.576	0.524	0.477
	85+	0.979	0.939	0.876	0.817	0.762	0.711	0.663	0.618	0.576

Table B5. Mortality Hazard Ratios for Current Cigarette Smokers, as Compared with Never Smokers, Estimated Using Cox Proportional Hazard Models with NHIS-LMF Data for Years 1997-2018.

Age Group	Males		Females	
	HR	95% CI	HR	95% CI
35-44	**1.62**	(1.37, 1.92)	**2.17**	(1.78, 2.64)
45-54	**2.09**	(1.82, 2.4)	**2.30**	(1.98, 2.68)
55-64	**2.57**	(2.28, 2.9)	**2.61**	(2.32, 2.94)
65-74	**2.66**	(2.4, 2.95)	**2.90**	(2.64, 3.19)
75-84	**2.16**	(1.96, 2.39)	**2.67**	(2.47, 2.9)
85+	**1.49**	(1.25, 1.77)	**1.47**	(1.31, 1.65)

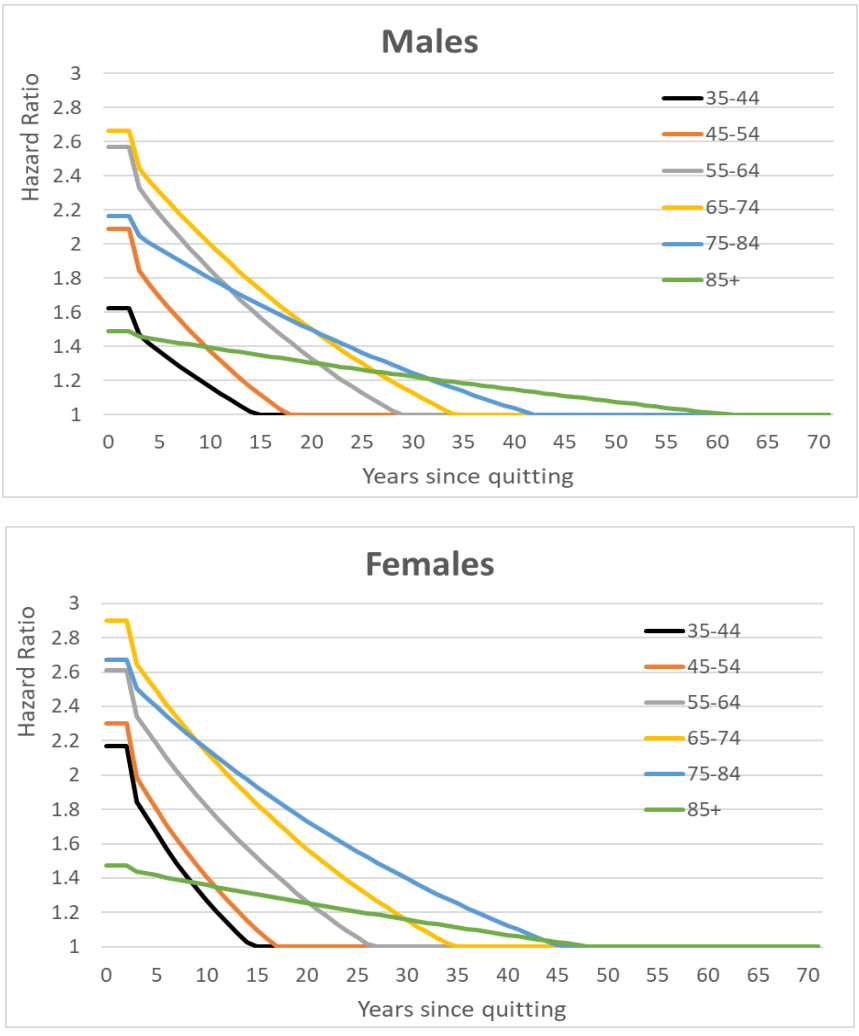

Figure B1. Estimated Hazard Ratios for Former Smokers as a Function of Years Since Quitting Using Cox Proportional Hazard Models with NHIS-LMF Data for Years 1997-2018, for Females and Males, and by Age Groups.

Appendix C: Model Validation

The model used in this document was validated by comparing results from baseline scenarios of the model and published estimates and projections for the U.S. population. The model projections are similar to the U.S. national estimates and projections for population size, deaths, cigarette smoking prevalence, and smoking-attributable mortality (SAM), as summarized below.

Comparisons of Population and Mortality Projections

We compared U.S. population and mortality projections from the baseline scenario of the model with these from U.S. Census Bureau for the period from 2021 to 2060. Figure C1 (a) presents U.S. Census Bureau and model projections for the total U.S. population from 2021 until 2060. The two sets of estimates are close, and the relative percentage difference in a given year between the two estimates is less than 1% for years 2021-2058, and is about 1% for 2059 and 2060. Figure C1 (b) presents the mortality projections from the model and U.S. Census Bureau from 2021 to 2060. The model estimates are initially lower than the Census projections, but model and Census projections of deaths converge to a difference of less than 1% by 2060.

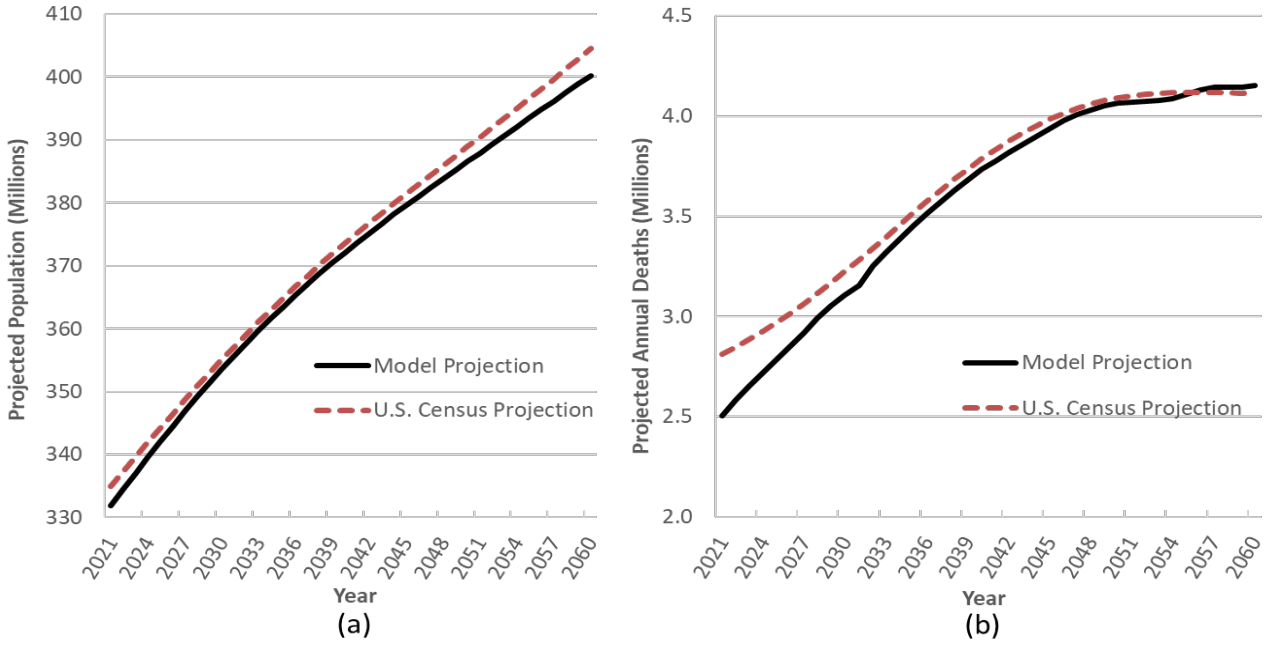

Figure C1. U.S. Total Population (a) and Mortality (b) Projections from the Model and U.S. Census Bureau for the Period 2021-2060.

Comparison of Smoking Prevalence

Vugrin et al. (2015) compared U.S. adult cigarette smoking prevalence estimates from the baseline model to estimates from the NHIS for the period from 2000 to 2012. NHIS estimates were used by the Centers for Disease Control and Prevention (CDC) as estimates of smoking prevalence for the U.S. population. Figure C2 shows model projections from 2000 to 2050 and the CDC's observed estimates from 2000 to 2012 for smoking prevalence among U.S. adults (ages 18 years and older). The model estimates for 2000-2012 are comparable in magnitude to the CDC's estimates and show a similar decline over time (Figure C2 (a)). Similarly, for U.S. adult smoking prevalence by sex (Figure C2 (b)) or by age

group (Table C1), the model projections and the CDC's estimates are comparable in magnitude and show similar decreases over time.

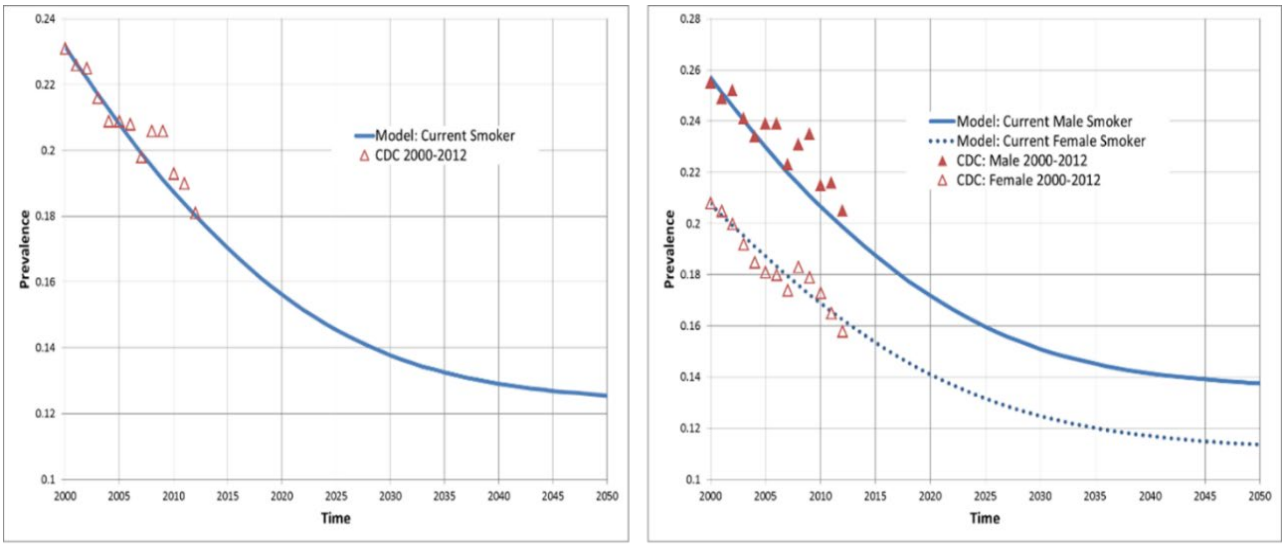

Figure C2. Model Projections from 2000 to 2050 and CDC's Estimates from 2000 to 2012 for U.S. Adult Smoking Prevalence (a) and Categorized by Sex (b). Source: Vugrin et al. (2015), Appendix S3.

Table C1. U.S. Smoking Prevalence by Age from Model Projections and CDC's Estimates.

Year	Estimated by	Age (years)				
		18-44	45-64	65-74	75+	65+
2000	Model	0.270	0.240	0.129	0.058	0.095
	CDC	0.267	0.237	NA	NA	0.096
2005	Model	0.245	0.213	0.125	0.052	0.088
	CDC	0.241	0.219	0.111	0.058	NA
2010	Model	0.227	0.189	0.116	0.039	0.079
	CDC	0.215	0.211	0.130	0.051	NA

*Data sources: CDC (2014)[8] and Vugrin et al. (2015) Appendix S3. In 2000 and 2001, the CDC reported smoking prevalence for ages 65 years and older. In 2003, the CDC changed the reporting format to report smoking prevalence for ages 65 to 74 years, and 75 years and older. NA = not available.

To validate the model with recent prevalence data, we compared U.S. adult cigarette smoking prevalence estimates from the baseline model scenario, as described in Apelberg et al. (2018), to estimates from the CDC for the period from 2015 to 2022. Both the model projection and CDC's

[8] Centers for Disease Control and Prevention (2014) NCHS Vital Health Statistics Series 10. Data From the National Health Interview Survey. Numbers 215, 218, 222, 225, 228, 232, 235, 240, 242, 249, 252, and 256.

estimates show that smoking prevalence is declining over time. Also, the model projection trend and estimates are comparable to the CDC's estimates (Figure C3).

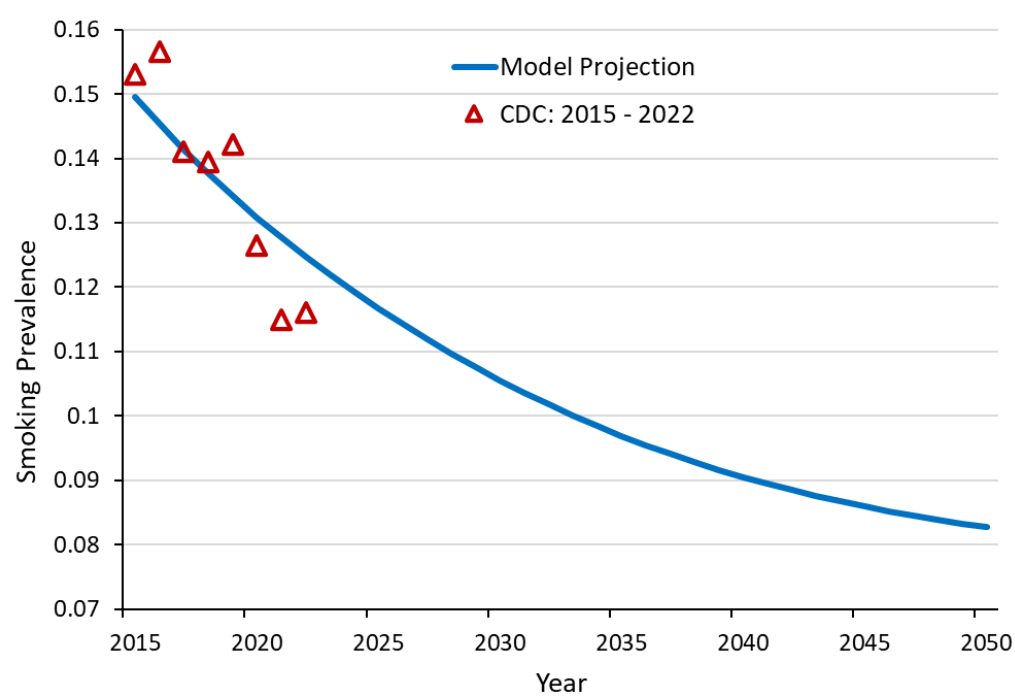

Figure C3. Model Projections from Apelberg at al. (2018) for the period from 2015 to 2050 and CDC's Estimates from 2015 to 2022 for U.S. Adult Smoking Prevalence.

Smoking-Attributable Mortality

Vugrin et al. (2015) validated the model using estimates of cigarette SAM and the smoking-attributable fraction of deaths (SAFD) in the U.S. population. Baseline model estimates presented in Vugrin et al. (2015) and the CDC for the period from 2000 to 2009 are comparable. Table C2 presents SAM estimates from the model and from the CDC (Centers for Disease Control and Prevention, 2008; U.S. Department of Health and Human Services, 2014) for the years 2000 to 2004, and 2005 to 2009. Since the model estimates SAM from all-cause mortality while the CDC estimates SAM for a set of smoking-related causes, the methods used to estimate SAM are not exactly the same. Regardless of this difference, the two sets of estimates are generally consistent. The model estimates an average of 416,000 annual smoking-attributable deaths in the U.S. from 2000 to 2004, which is consistent with the CDC's estimate of 392,000 annual smoking-attributable deaths during this period. Similarly, the model and the CDC's estimates of annual smoking-attributable deaths in the U.S. from 2005 to 2009 are comparable.
Table C2 also shows estimated SAFD for the U.S., which is calculated by dividing the number of smoking-attributable deaths by the total numbers for an age group in a time period. Model estimates are again comparable to the CDC's estimates and the SAFD estimated using a variety of estimation methods (Table 4 in Fenelon and Preston (2012)).

Table C2. Cigarette Smoking-Attributable Mortality (SAM) and Smoking-Attributable Fraction of Deaths (SAFD) for Adults Ages 35 Years and Older.

	Total SAM	Average Annual SAM[+]	Average Annual SAFD

Year	Model	CDC*, **	Model	CDC	Model	CDC++, +++
2000-2004	2,080,000	1,960,000	416,000	392,000	0.18	0.17
2005-2009	1,950,000	2,190,000	390,000	438,000	0.16	0.19

*Data Sources: U.S. Department of Health and Human Services (2014) and Vugrin et al. (2015), Appendix S3.
** Since model projections of SAM do not include deaths from secondhand smoking exposure, residential fires and perinatal deaths, the CDC's estimates in this table do not include these deaths.
+Average Annual SAM = (Total SAM)/5.
++Average Annual SAFD = (SAM in 5-year period)/ (Total number of deaths in 5-year period).
+++Data source for total number of deaths: CDC Wonder Online Databases (2013) Detailed Mortality: About Underlying Cause of Death, 1999-2010.

Appendix D: Estimation of Tobacco Use Prevalence and Initiation Rates for Cigarettes and Noncombusted Products

Youth Baseline Tobacco Use Prevalence

The 2020 National Youth Tobacco Survey (NYTS) data for U.S. middle and high school students are used to estimate prevalence of current tobacco product use by sex and age groups (Table D1). For example, according to 2020 NYTS data, 4.55% of U.S. male youth were exclusive noncombusted tobacco product users; 0.18% of U.S. male youth were exclusive cigarette smokers; and 0.57% of U.S. male youth were dual cigarette and noncombusted product users.

Table D1. Prevalence of Current Tobacco Product Use, by Sex and Age Group from, 2020 NYTS Used for Baseline Youth Prevalence.

	Exclusive cigarette smoking (no noncombusted use) % (95% CI*)	**Dual cigarette and noncombusted use** % (95% CI*)	**Exclusive noncombusted use (no cigarette smoking)** % (95% CI*)	**No cigarette smoking and no noncombusted use** % (95% CI*)
Sex				
Males	0.18 (0.07-0.44)	0.57 (0.32-1.01)	4.55 (3.77-5.47)	94.70 (93.61-95.62)
Females	0.17 (0.08-0.33)	0.42 (0.21-0.83)	3.72 (2.93-4.72)	95.69 (94.46-96.66)
Males (year)				
9 - 13	0.04 (0.01-0.21)	0.04 (0.01-0.22)	1.16 (0.76-1.76)	98.77 (98.15-99.18)
14 - 15	0 (NA)	0.62 (0.31-1.25)	3.82 (2.99-4.89)	95.55 (94.28-96 .55)
16 - 17	0.54 (0.21-1.40)	1.21 (0.56-2.56)	9.71 (8.07-11.65)	88.54 (86.18-90.54)
Females (year)				
9 - 13	0.12 (0.02-0.65)	0.03 (0.01-0.19)	1.05 (0.71-1.53)	98.80 (98.21-99.20)
14 - 15	0.02 (0.00-0.24)	0.31 (0.11-0.87)	4.30 (3.02-6.10)	95.36 (93.32-96.80)
16 - 17	0.37 (0.18-0.76)	1.00 (0.52-1.92)	6.54 (5.07-8.41)	92.09 (89.81-93.90)

Notes: Cigarette smoking reflects smoking ≥ 100 cigarettes in lifetime and smoking cigarettes ≥ 1 day in the past 30 days; noncombusted use refers to use of smokeless tobacco, e-cigarettes, and/or heated tobacco products; smokeless tobacco use reflects using on ≥ 20 days in the past 30 days for chewing tobacco, snuff, or dip, or ≥ 1 day in the past 30 days for snus or dissolvable tobacco; e-cigarette use reflects using on ≥ 20 days in the past 30 days; heated tobacco product use reflects using on ≥ 20 days in the past 30 days.
*CI=confidence interval; 95% CI was estimated by modified Wilson approach for complex surveys.

Projected Tobacco Use Prevalence to Compute Noncombusted Product Initiation for Sensitivity Analysis

The 2017-2020 NYTS data are used as baseline data to project tobacco use prevalence for the period 2021-2030 to calculate scaling factors for noncombusted product initiation rates. Prevalence for cigarette use is projected to remain at the same level in subsequent years as was observed in baseline (see Table D2). E-cigarette use may continue to increase in the future, so scaling factors in these years are calculated in a manner that allowed for increases in noncombusted product use. Specifically, prevalence of use for product categories including e-cigarette use are projected to increase by 25% between baseline and 2030 as shown in Table D2. The baseline and projected prevalence projections are used to scale the sex- and age-specific smoking initiation rates used in the model for exclusive

cigarette, exclusive noncombusted, and dual cigarette and noncombusted use. For example, the ratio of youth exclusive noncombusted product use prevalence to cigarette smoking prevalence from the 2017-2020 NYTS was used to generate exclusive noncombusted product initiation rates at baseline. In this case, the scaling factors for males would be 0.41% / 1.42% = 28.87% for exclusive smokers, 1.01% / 1.42% = 71.13% for dual cigarette and noncombusted product users, and 4.58% / 1.42% = 322.54% for exclusive noncombusted users, where 1.42% is the male cigarette smoking prevalence at baseline. Initiation scaling factors for subsequent years are calculated in the same manner as described for baseline year. Table D3 shows the computed scaling factors for baseline and for the period 2021-2030. Product use prevalence and initiation rates were projected to remain constant in years after 2030.

Table D2. Youth Baseline Prevalence from 2017-2020 NYTS and Projected Current Tobacco Product Prevalence (%) for the Period 2021-2030.

	Current cigarette smoking	Current exclusive cigarette smoking	Current exclusive noncombusted[a] use	Current dual cigarette and noncombusted use
Females				
Baseline	0.89	0.40	3.12	0.50
Projected				
2021	0.89	0.38	3.20	0.51
2022	0.89	0.37	3.28	0.52
2023	0.89	0.36	3.36	0.53
2024	0.89	0.35	3.43	0.55
2025	0.89	0.33	3.51	0.56
2026	0.89	0.32	3.59	0.57
2027	0.89	0.31	3.67	0.58
2028	0.89	0.30	3.75	0.60
2029	0.89	0.28	3.82	0.61
2030	0.89	0.27	3.90	0.62
Males				
Baseline	1.42	0.41	4.58	1.01
Projected				
2021	1.42	0.38	4.70	1.04
2022	1.42	0.36	4.81	1.06
2023	1.42	0.33	4.93	1.09
2024	1.42	0.31	5.04	1.11
2025	1.42	0.28	5.16	1.14
2026	1.42	0.26	5.27	1.16
2027	1.42	0.23	5.38	1.19
2028	1.42	0.21	5.50	1.21
2029	1.42	0.18	5.61	1.24
2030	1.42	0.15	5.73	1.26

[a] Noncombusted products included in NYTS from 2017-2019 were smokeless tobacco and e-cigarettes. Heated tobacco products were also asked about in NYTS in 2020. Noncombusted products in model projections from 2021-2030 include these products as well as oral nicotine products.

Table D3. Scaling Factors Used to Compute Noncombusted Product Use Initiation for Sensitivity Analysis.

Year	Exclusive cigarette smoking	Exclusive noncombusted product use	Dual use of cigarettes and noncombusted product
Females			
Baseline	0.44	3.49	0.56
Projected			
2021	0.43	3.58	0.57
2022	0.42	3.67	0.58
2023	0.40	3.76	0.60
2024	0.39	3.84	0.61
2025	0.37	3.93	0.63
2026	0.36	4.02	0.64
2027	0.35	4.11	0.65
2028	0.33	4.19	0.67
2029	0.32	4.28	0.68
2030	0.30	4.37	0.70
Males			
Baseline	0.29	3.23	0.71
Projected			
2021	0.27	3.31	0.73
2022	0.25	3.40	0.75
2023	0.23	3.48	0.77
2024	0.22	3.56	0.78
2025	0.20	3.64	0.80
2026	0.18	3.72	0.82
2027	0.16	3.80	0.84
2028	0.14	3.88	0.86
2029	0.13	3.96	0.87
2030	0.11	4.04	0.89

Adult Baseline Tobacco Product Prevalence

2020 National Health Interview Survey (NHIS) data were used to produce estimates of tobacco use among adults ages 18 years and older, accounting for all combinations of current, former, and never use for cigarettes and noncombusted tobacco products. Table D4 shows the breakdown of U.S. adult tobacco prevalence from NHIS data by sex, age, and product category type.

Table D4. Adult Baseline Tobacco Product Use Prevalence, % (95% Confidence Interval) from 2020 NHIS.

	Tobacco Product Use Category								
	CC	**CF**	**CN**	**FC**	**FF**	**FN**	**NC**	**NF**	**NN**
Males									
Age (years)									
18-24	4.3 (2.9-6.4)	3.5 (2.3-5.2)	1.4 (0.7-3.1)	2.4 (1.5-3.8)	2.9 (1.9-4.2)	0.3 (0.1-1.0)	8.5 (6.5-11.0)	22.2 (19.0-25.9)	54.5 (50.4-58.7)
25-34	3.1 (2.3-4.1)	9.2 (7.5-11.1)	3.9 (2.9-5.2)	5.3 (4.2-6.7)	8.7 (7.4-10.3)	4.2 (3.2-5.6)	4.8 (3.7-6.0)	15.1 (13.2-17.1)	45.7 (43.1-48.4)
35-44	3.2 (2.4-4.2)	6.9 (5.7-8.3)	7.1 (5.7-9.0)	4.8 (3.8-6.1)	10.4 (9.0-11.9)	9.9 (8.5-11.5)	2.3 (1.7-3.2)	7.5 (6.4-8.7)	47.9 (45.4-50.4)
45-54	1.8 (1.2-2.6)	6.6 (5.4-7.9)	7.1 (5.7-8.7)	3.7 (2.8-4.8)	8.7 (7.4-10.2)	11.1 (9.6-12.8)	3.2 (2.4-4.3)	9.0 (7.7-10.4)	48.8 (46.2-51.5)
55-64	0.6 (0.3-1.1)	5.3 (4.5-6.3)	9.8 (8.5-11.2)	2.3 (1.7-3.1)	8.8 (7.5-10.2)	18.9 (17.1-20.7)	1.6 (1.1-2.3)	6.0 (5.1-7.2)	46.6 (44.3-48.9)
65-74	0.5 (0.2-1.0)	3.9 (3.0-5.0)	8.1 (6.7-9.7)	2.2 (1.6-3.0)	7.8 (6.6-9.2)	33.0 (30.8-35.3)	0.7 (0.4-1.3)	2.7 (2.1-3.6)	41.1 (38.9-43.4)
75-84	0.4 (0.1-2.2)	2.0 (1.2-3.3)	4.4 (3.1-6.0)	2.0 (1.2-3.2)	10.2 (8.3-12.5)	42.0 (38.7-45.3)	0.7 (0.3-1.6)	1.7 (1.0-2.9)	36.6 (33.4-40.1)
85+	0 (NA)	0.1 (0.0-1.1)	3.8 (1.8-7.9)	2.1 (0.9-5.2)	4.2 (2.6-6.6)	45.9 (40.2-51.8)	0 (NA)	1.5 (0.6-3.7)	42.3 (36.6-48.3)
Females									
Age (years)									
18-24	1.1 (0.5-2.1)	2.8 (1.7-4.4)	1.7 (0.8-3.3)	1.5 (0.8-2.8)	1.7 (0.9-3.3)	1.6 (0.7-3.4)	4.5 (3.0-6.6)	13.9 (11.5-16.8)	71.3 (67.6-74.7)
25-34	0.9 (0.5-1.5)	5.4 (4.4-6.7)	4.1 (3.2-5.2)	1.8 (1.2-2.5)	5.1 (3.9-6.6)	4.4 (3.5-5.5)	1.9 (1.3-2.7)	9.4 (8.1-10.9)	67.0 (64.5-69.4)
35-44	0.9 (0.6-1.4)	6.0 (4.9-7.3)	5.9 (4.8-7.1)	1.5 (1.1-2.2)	5.5 (4.4-6.7)	9.6 (8.4-10.9)	0.3 (0.2-0.6)	2.9 (2.3-3.7)	67.4 (65.0-69.6)
45-54	1.2 (0.7-1.9)	6.6 (5.3-8.1)	6.4 (5.2-7.7)	1.7 (1.2-2.6)	3.8 (2.9-4.8)	12.5 (11.0-14.1)	0.4 (0.2-0.9)	2.4 (1.6-3.6)	65.2 (62.6-67.8)
55-64	0.6 (0.3-1.1)	5.1 (4.3-6.1)	8.7 (7.5-10.0)	1.3 (0.9-1.9)	3.5 (2.8-4.3)	21.5 (19.7-23.3)	0.5 (0.2-1.3)	1.1 (0.7-1.5)	57.9 (55.7-60.0)
65-74	0.4 (0.2-0.8)	3.2 (2.4-4.3)	6.9 (5.9-8.2)	0.4 (0.2-0.7)	2.2 (1.7-2.9)	26.0 (24.2-27.9)	0.2 (0.0-0.6)	0.4 (0.2-0.7)	60.2 (58.0-62.3)
75-84	0.1 (0.0-0.4)	0.9 (0.5-1.6)	4.8 (3.6-6.4)	0.3 (0.1-0.7)	1.0 (0.6-1.7)	32.7 (30.2-35.3)	0 (NA)	0.3 (0.1-0.7)	59.9 (57.2-62.6)
85+	0 (NA)	0.1 (0.0-0.6)	0.9 (0.4-2.1)	0 (NA)	0.7 (0.2-2.2)	24.2 (20.3-28.6)	0.2 (0.0-1.0)	0.7 (0.2-2.3)	73.3 (68.8-77.4)

Abbreviations: N=never use, C=current use, and F=former use. First letter denotes cigarette use status, and second letter denotes noncombusted tobacco product use status.

Notes: Current cigarette users reported smoking at least 100 cigarettes in their lifetime and smoking cigarettes every day or some days at the time of interview. Former cigarette smokers reported smoking at least 100 cigarettes in their lifetime and not currently smoking cigarettes. Never cigarette smokers had not smoked at least 100 cigarettes in their lifetime. Current noncombusted tobacco users reported ever using e-cigarettes or smokeless tobacco (including chewing tobacco, snuff, dip, snus, or dissolvable tobacco) and using e-cigarettes or smokeless every day or some days at the time of interview. Former noncombusted tobacco users reported ever using e-cigarettes or smokeless tobacco products and currently not using e-cigarettes or smokeless tobacco. Never noncombusted tobacco users had never used e-cigarettes and smokeless tobacco.

Initiation Rates for Cigarettes and Noncombusted Products

We generated sex- and age-specific initiation rates for exclusive cigarette use, exclusive use of noncombusted tobacco products, and dual use by scaling the smoking initiation rates from CISNET using prevalence estimates from the 2017-2020 NYTS (for youth ages 9-17) and the 2020 NHIS (for young adults ages 18-30). Specifically, the ratio of exclusive noncombusted product use prevalence to cigarette smoking prevalence was used as scaling factor to generate exclusive noncombusted product initiation rates. Similarly, the ratio of exclusive cigarette/dual use to cigarette smoking prevalence was used as scaling factor to generate initiation rates for exclusive cigarette/dual use, respectively. Table D5 shows the prevalence data and computed scaling factors, and Table D6 shows the computed sex- and age-specific initiation rates.

Table D5. Prevalence for Youth and Young Adult from 2017-2020 NYTS and 2020 NHIS Data, and Estimated Scaling Factors.

	Prevalence (%)			Scaling Factor		
	Exclusive cigarette smoking	**Exclusive noncombusted use**	**Dual cigarette and noncombusted use**	**Exclusive cigarette smoking**	**Exclusive noncombusted use**	**Dual cigarette and noncombusted use**
Female						
9-17	0.40	3.12	0.50	0.44	3.49	0.56
18-24	1.67	4.49	1.08	0.61	1.63	0.39
Male						
9-17	0.41	4.58	1.01	0.29	3.23	0.71
18-24	1.44	8.48	4.31	0.25	1.47	0.75

Table D6. Estimated sex- and age-specific annual rates of initiation for exclusive cigarette use, exclusive use of noncombusted tobacco products, and dual use.

Age	**Initiation for exclusive cigarette use**		**Initiation for exclusive use of noncombusted tobacco**		**Initiation for dual use**	
	Female	**Male**	**Female**	**Male**	**Female**	**Male**
9	0.04%	0.05%	0.29%	0.52%	0.05%	0.12%
10	0.07%	0.07%	0.53%	0.84%	0.08%	0.19%
11	0.12%	0.12%	0.95%	1.36%	0.15%	0.30%
12	0.22%	0.19%	1.70%	2.19%	0.27%	0.48%
13	0.37%	0.31%	2.92%	3.55%	0.47%	0.78%
14	0.60%	0.51%	4.75%	5.72%	0.76%	1.26%
15	0.89%	0.77%	6.98%	8.68%	1.11%	1.91%
16	1.12%	1.04%	8.86%	11.65%	1.41%	2.57%
17	1.19%	1.17%	9.39%	13.18%	1.49%	2.91%
18	1.48%	0.98%	3.98%	5.80%	0.96%	2.95%
19	1.20%	0.83%	3.22%	4.88%	0.77%	2.48%
20	0.89%	0.63%	2.39%	3.69%	0.58%	1.88%

21	0.63%	0.44%	1.69%	2.61%	0.41%	1.33%
22	0.46%	0.32%	1.23%	1.87%	0.29%	0.95%
23	0.34%	0.23%	0.90%	1.36%	0.22%	0.69%
24	0.25%	0.17%	0.68%	1.02%	0.16%	0.52%
25	0.20%	0.13%	0.53%	0.79%	0.13%	0.40%
26	0.16%	0.11%	0.42%	0.62%	0.10%	0.31%
27	0.13%	0.08%	0.34%	0.50%	0.08%	0.25%
28	0.10%	0.07%	0.28%	0.41%	0.07%	0.21%
29	0.09%	0.06%	0.23%	0.34%	0.06%	0.17%
30	0.07%	0.05%	0.20%	0.29%	0.05%	0.15%

Appendix E: Calculation of Mortality Risk by Tobacco Use State

Table E1 lists assumptions and calculations used to combine individual product relative risk (RR) values (i.e., RRs for smoking and RRs for noncombusted product use). RR values for smoking were taken from hazard ratios that were estimated for 1997-2018 NHIS Sample Adult Questionnaire participants followed for mortality through linkage with the National Death Index through the end of 2019 (National Center for Health Statistics, 2019). RR values for noncombusted product users are based on HRs for current users of smokeless tobacco (HR = 1.18, 95% CI = 1.08-1.29) reported by Henley et al. (2005), and this value is used for all individuals (male and female) who are aged 35 years or older. The RRs for former noncombusted tobacco product users is assumed to be 1. All individuals less than 35 years old, regardless of tobacco product use state, are assigned an RR value of 1.

With the exception of the former cigarette smoker/current noncombusted tobacco product user (FC in Table E1) product use state, the RRs are the maximum of the relevant smoking and noncombusted product RRs. Following the results observed by Henley et al. (2007) for individuals who switched from cigarettes to smokeless tobacco, FC individuals are assigned RRs that are 8% higher than RRs for former smokers, as long as that quantity does not exceed the RR for current smokers or is not less than the RR for current noncombusted product users.

Table E1. Relative risk (RR) Scenario Assumption

Tobacco Use Status*	Relative Risk Calculation	Interpretation
NN	RR = 1	NN is the state for individuals who never used either group of tobacco products. Individuals in this state have the minimum relative risk value, RR = 1.
CN	RR= RR for current smoker	CN is the state for current smokers who never used noncombusted tobacco products. Individuals in this state are assumed to have RR values equal to current smokers.
FN	RR = RR for former smoker	FN is the state for former smokers who never used noncombusted tobacco products. Individuals in this state are assumed to have RR values equal to former smokers.
NC	RR = RR for current smokeless tobacco user	NC is the state for current users of noncombusted tobacco products who have never smoked cigarettes. The relative risk is assumed to be equal to the median relative risk values for smokeless tobacco users reported by Henley et al. (2005).
CC	RR = max [RR for current smoker, RR for current user of noncombusted tobacco products]	CC is the state for dual users. RR for dual use is the maximum of the individual product RRs. Since the RR for current smokers is higher than the RR for current users of noncombusted products, the RR for dual use is assumed to be equal to the RR for current smokers.

FC	RR = max{min[1.08*RR for former smokers, RR current smokers],RR for current noncombusted use}	FC is the state for former smokers who are current users of noncombusted tobacco products. Using the results of Henley et al.'s (2007) study, the RR for this state is 8% higher than the RR for the FN (individuals who quit cigarettes but do not use noncombusted products) as long as: - 8% above the RR for former smokers is not larger than the RR for current smokers. If not, RR is set to that for current smokers; - 8% above the RR for former smokers is not less than the RR for current noncombusted tobacco product users. If not, RR is set equal to that for current noncombusted use.
NF	RR = 1	NF is the state for former users of noncombusted tobacco products who never smoked cigarettes. It is assumed that the relative risk for this state is equal to RRs for individuals who never used either group of tobacco products, i.e., RR = 1.
CF	RR = RR for current smoker	CF is the state for current smokers who are former users of noncombusted tobacco products. These individuals are assigned an RR equal to current smokers' RR since that value is equivalent to using the maximum value of current smoker RR (≥1) and former noncombusted tobacco product user RR (=1).
FF	RR = RR for former smoker	FF is the state for former smokers and former users of noncombusted tobacco products. The individuals retain the RR from the highest risk behavior, i.e., smoking.

*First letter denotes cigarette use status, and second letter denotes use of noncombusted tobacco product use status. N=never, C=current, and F=former.

Appendix F: Expert Elicitation on the Behavioral Impacts of a Potential Nicotine Product Standard

Background

In March 2018, FDA issued an Advance Notice of Proposed Rulemaking (ANPRM) seeking public comment for consideration in developing a potential nicotine standard (83 FR 11818, March 16, 2022). In conjunction with the nicotine ANPRM, FDA asked Industrial Economics, Incorporated (IEc) to reconvene the panel of experts consulted in 2015 to consider, once again, the behavioral impacts of a potential nicotine product standard. FDA's interest in revisiting the elicitation was motivated by recognition that a number of factors that might influence the experts' judgments had changed since the initial elicitation was conducted. For example:

- The literature on clinical trials using reduced nicotine content (RNC) cigarettes had expanded, providing additional information on how smokers may respond to such products.

- The U.S. market for e-cigarettes and other electronic nicotine delivery systems (ENDS) had continued to evolve, reflecting both changes in the range of products available and consumers' familiarity with them. National surveys showed changes in the use of ENDS, either alone or in combination with other forms of tobacco. This information was potentially relevant in assessing the extent to which implementation of a nicotine standard might make ENDS an attractive alternative to combusted tobacco products.

FDA's decision to reconvene the panel and revisit the elicitation was designed to give the experts an opportunity to update their estimates of the behavioral impacts of the potential product standard in light of this new information. As a secondary objective, it was also designed to give FDA an opportunity to solicit the experts' thoughts on the implications of limiting the scope of a potential product standard to a narrower set of combusted tobacco products that would include cigarettes, cigarette tobacco, and RYO tobacco. As in the first instance, the purpose of the elicitation was to generate individual estimates that reflected the diverse opinions of the experts instead of producing a consensus estimate from the group as a whole. These estimates were then used to provide a range of inputs that FDA could use in modeling.

Methodology

Parameters of Interest

Given the structure of the health effects simulation model, FDA requires information on the effect of a potential nicotine product standard on five parameters: (1) cigarette smoking cessation; (2) switching from cigarettes to non-covered tobacco products (i.e., premium cigars, waterpipe/hookah tobacco, e-cigarettes or other ENDS, and smokeless tobacco); (3) initiation of the use of non-covered tobacco products by those who continue to use cigarettes (i.e., "dual use"); (4) cigarette smoking initiation; and (5) initiation of the use of non-covered tobacco products by those who otherwise would have become cigarette users. In the previous elicitation, IEc and FDA together developed five elicitation variables, as defined below:

1. **Cigarette cessation variable**: The percentage of current cigarette smokers that will quit smoking cigarettes following a nicotine product standard's implementation.

2. **Product switching variable**: Among current cigarette smokers who quit smoking following implementation of a nicotine product standard, the percentage that will switch completely to non-covered tobacco products.

3. **Dual use variable**: Among current cigarette smokers who continue to smoke after a nicotine product standard is implemented, the percentage that will become dual users of cigarettes and non-covered tobacco products.

4. **Cigarette initiation variable**: The percentage change in cigarette initiation rates with the potential standard in place, relative to initiation rates prior to a nicotine product standard's implementation.

5. **Non-covered product initiation variable**: The percentage of those who would have become cigarette smokers if not for the potential standard who will instead initiate the use of non-covered tobacco products.

For each of the five parameters listed above, the elicitation was designed to obtain estimates of expected impacts of a potential nicotine product standard both in the first year of its implementation and in all subsequent years (i.e., an annual average impact for all years after the first year of the potential standard's implementation). In addition, for the three parameters that address non-covered products (i.e., the parameters related to product switching, dual use, and initiation of the use of non-covered tobacco products), the elicitation seeks both an overall estimate of the value of the parameter and an estimate of the distribution of use among each of the four categories of non-covered tobacco products. For example, the elicitation first asks experts to estimate the overall rate at which current cigarette smokers would transition to dual use of cigarettes and non-covered tobacco products; it then asks experts to estimate what percentage of those who transition to dual use would use (1) premium cigars, (2) waterpipe/hookah tobacco, (3) smokeless tobacco, or (4) e-cigarettes.

To characterize the uncertainty surrounding each expert's estimates, the protocol asks for estimates of seven values, reflecting the expert's level of confidence (or uncertainty) about the true value of the parameter to be estimated. The protocol describes these values to the respondent as follows:

- Your minimum and maximum values.
- Your 5th and 95th percentile values.
- Your 25th and 75th percentile values.
- Your 50th percentile value.

IEc instructed the experts to provide estimates in the order shown above, beginning with the minimum and maximum and working inward to the median estimate. This was done to avoid any anchoring that might take place if the experts were to begin with their "best" estimate (i.e., the median), and then adjust from there in estimating the remaining values. Studies have found that the anchoring process, which is the tendency to use an initial piece of information as a starting point and then make adjustments to form subsequent estimates, can lead to biased estimates from adjustments that are insufficiently large (O'Hagan et al. 2006). Evidence of bias from anchoring and adjustment has been observed even when anchors are arbitrary.

Identifying and Recruiting the Experts

IEc began the recruiting process by extending formal invitations to the eight members of the 2015 panel. The letter of invitation provided an overview of the purpose of revisiting the original elicitation and the

structure of the elicitation process. It also noted important conditions for participation, including the need to enter into a non-disclosure agreement before confidential information could be shared; the need to certify to the absence of any conflicts of interest; and, to avoid anchoring on previous estimates, the importance of refraining from reviewing the judgments the experts had provided in 2015. As with the original elicitation, the invitation noted that the members of the panel would be identified in IEc's report, but that their responses to the elicitation would be provided to CTP on an anonymous basis.

Shortly after emailing invitations to the members of the original expert panel, IEc contacted them by phone to solicit their participation. All but one of the eight members of the original panel agreed to take part; the eighth, now retired, declined the invitation. Table F1 lists the members of the reconstituted panel, which includes three individuals identified as experts in tobacco science, two identified as experts in tobacco policy, and two identified as experts in both areas. The experts' input was anonymized such that FDA received estimates from the experts below without knowing which expert provided each set of estimates.

Table F1. Members of the Expert Panel

Name	**Affiliation**
Dr. David Abrams	Professor Department of Social and Behavioral Sciences College of Global Public Health New York University
Dr. K. Michael Cummings	Professor Department of Psychiatry and Behavioral Sciences College of Medicine Medical University of South Carolina
Dr. Geoffrey T. Fong	Professor Department of Psychology Faculty of Arts University of Waterloo
Dr. Andrew Hyland	Chair Department of Health Behavior Division of Cancer Prevention and Population Sciences Roswell Park Comprehensive Cancer Center
Dr. Raymond Niaura	Professor Department of Social and Behavioral Sciences College of Global Public Health New York University
Dr. Jennifer O'Loughlin	Professor Department of Social and Preventive Medicine School of Public Health University of Montreal
Dr. Gilles Paradis	Professor and Chair Department of Epidemiology, Biostatistics, and Occupational Health Faculty of Medicine McGill University

Training the Experts

As part of the expert elicitation process, it is essential to explain to the experts how their judgments will be used and why those judgments are important (O'Hagan et al., 2006). It is also necessary to train the experts in the elicitation approach, specifically, to familiarize them with the process of creating calibrated judgments or characterizing their knowledge and uncertainty in probabilistic terms. According to best practice guidelines, this training should include: (1) an introduction to probability and probability distributions; (2) information about common judgment heuristics and biases, including advice about how to avoid them; and (3) practice elicitation questions for which the true answer can be found but is unlikely to be known by any of the experts. Because all of the experts who participated in this elicitation had undergone extensive training in these three areas during the previous elicitation, IEc elected not to repeat the training process. Instead, during the pre-elicitation workshop, IEc and FDA explained the motivation for the current elicitation – i.e., to update the estimates from the previous elicitation to reflect recent developments in the academic literature and to obtain the experts' input on the potential impacts of an alternative product standard – and established the importance of the elicitation for FDA. In addition, IEc reinforced the importance of the assumptions and definitions employed in the elicitation protocol and reiterated its request that the panelists refrain from reviewing the responses and estimates they provided during the 2015 elicitation. The panelists affirmed that they had not reviewed their previous responses and agreed not to do so for the duration of the exercise.

The Elicitation

The last stage of the elicitation process is the elicitation of expert opinion itself. For this elicitation, we broke this stage into three steps:

1. Conduct separate web conference interviews with each expert to complete the elicitation protocol.

2. Provide each expert with a summary of his or her individual responses to the elicitation questions and verify that we have characterized their thoughts accurately.

3. Ask the experts to review the elicitation protocol once more and provide IEc with any revisions to their initial responses within approximately one week of receiving their individual summaries.

IEc conducted web conference interviews with each of the seven experts independently. IEc asked each expert to spend several hours prior to the interview reading through the protocol and thinking through his or her answers. In order to make the best use of the experts' time, IEc requested that they try to answer the questions about the studies and research findings that influenced their thinking before the interview. The interviews were led by one of two senior members of IEc's staff, each of whom had extensive experience in expert elicitation and was familiar with the relevant literature on nicotine and tobacco control. Directing the interview included reading the protocol instructions and questions aloud and answering any requests for clarification. As the expert answered each question, a second IEc staff person entered his or her response into the shared copy of the protocol, giving the expert an opportunity to confirm that the answer was captured fully and accurately. If there was any ambiguity in the expert's response, the lead interviewer would attempt to clarify it through the use of probing questions. Similarly, if an expert's response suggested potential overconfidence, the lead interviewer would encourage the expert to elaborate upon the rationale underlying his or her estimates.
At the conclusion of the interviews, IEc invited the experts to provide comments on the elicitation protocol (including whether or not the background information and elicitation questions were

sufficiently clear) and the elicitation process in general. All experts responded that they found the background information satisfactory and the elicitation questions clear.

After all seven elicitation interviews were completed, IEc created presentations for each expert that summarized all of the answers they provided to the questions in the elicitation protocol. Each expert reviewed the summary of his or her responses and informed IEc of any corrections or revisions he or she wished to make. These revisions generally concerned elaboration on the relevant scientific literature or clarification of the rationale underlying the expert's quantitative estimates. In several cases, however, IEc raised specific questions with the experts concerning the estimates they had provided, noting potential inconsistencies in responses or possible misinterpretations of a question. For example, IEc reached out to Expert 3 to inquire about an apparent inconsistency in the expert's response to Question 1; in this case, as in others, the expert responded by providing a revised set of estimates. In other instances, the expert responded by clarifying his or her rationale. These changes were incorporated into the individual summary presentations. IEc then shared the revised presentation with the expert responsible to confirm that it accurately reflected his or her views.

Results

Question 1: Cigarette Cessation

All seven experts believed that a nicotine product standard would increase the cigarette smoking cessation rate in the year immediately following its implementation. The experts cited several reasons for this conclusion, including the likelihood that smokers would find VLNC cigarettes less satisfying than regular cigarettes and that alternative tobacco products containing more satisfying levels of nicotine would serve as desirable substitutes.

Three of the seven experts believed that the magnitude of the effect of a potential nicotine product standard on cigarette smoking cessation rates would be the same during subsequent years as in the year immediately following implementation. Overall, the experts' median estimates of the percentage of current cigarette smokers who would quit smoking cigarettes in the year immediately following implementation of a nicotine standard ranged from 6.5 to 60 percent; their median estimates of the cessation rate for subsequent years ranged from 5 to 50 percent. Tables F2 and F3 show the experts' estimates.

Question 2: Product Switching

All seven experts believed that some portion of those who quit smoking cigarettes would initiate use of one or more non-covered products during the year immediately following a nicotine product standard's implementation. The reasons given for this response included the fact that many who would quit smoking cigarettes would be looking for alternative sources of nicotine, that the use of alternative tobacco products by former cigarette smokers is common even in the absence of a nicotine product standard, and that e-cigarettes in particular are a popular alternative to cigarettes for smokers who are trying to quit.

Six experts believed that the rate of product switching by former cigarette users would be the same during the year immediately following implementation of a nicotine product standard and in subsequent years. The reasons provided for this response included a lack of data available to justify different estimates, coupled with the large uncertainty in estimating product switching rates and the possibility that switch rates could either increase (e.g., if alternative products become more suitable substitutes) or decrease over time (e.g., if the subset of smokers who would find it easiest to quit using cigarettes were removed from the smoking population by the end of Year 1). One expert believed that the magnitude of

the effect would be greater in subsequent years. This expert reasoned that, because those who find it easiest to quit will do so in the first year, the remaining pool of smokers would likely be more heavily addicted to nicotine and would be more likely to turn to alternative sources of nicotine to aid their quit attempts. Tables F4 and F5 show the experts' estimates.

Question 3: Dual Use

All seven experts believed that some portion of those who continue smoking cigarettes following implementation of a nicotine product standard would initiate use of a non-covered tobacco product. The experts expected that at least some of those who continue to use cigarettes would be motivated to supplement the diminished nicotine that they would be receiving from VLNC cigarettes through the use of non-covered products. They also noted that the difference between transitioning to dual-use and completely switching to non-covered products may depend on how long it takes cigarette smokers to find an alternative product that they find satisfying, as well as their awareness of the potential harms posed by the use of non-covered products relative to cigarettes.

Five experts believed that the magnitude of a nicotine product standard's effect on dual use would be the same in subsequent years as in the year immediately following implementation of the product standard. These experts cited a lack of evidence suggesting that the pattern of dual use would change over time, as well as large uncertainties in estimating dual-use initiation rates. The remaining two experts believed that the effect of a nicotine product standard on dual use initiation rates would be lower in subsequent years. They reasoned that most of those inclined to engage in dual use will begin to do so relatively quickly, and that smokers who have "survived" while using only VLNC cigarettes throughout the first year are likely to be less nicotine dependent, and therefore less likely in subsequent years to seek other sources of nicotine. Tables F6 and F7 show the experts' estimates.

Question 4: Initiation of Cigarette Use

All seven experts believed that a nicotine product standard would reduce cigarette smoking initiation rates in the year immediately following its implementation. To support this view, the experts cited reductions in the addictive potential and appeal of cigarettes after implementation of such a product standard, as well as the likelihood of diminished satisfaction with their use. These factors might contribute both to lower rates of experimentation and to lower rates of transition from experimentation to regular use, leading to decreased initiation.

Five experts believed that the magnitude of a nicotine product standard's effect on initiation of cigarette use would be the same in subsequent years as in the year immediately following standard's implementation. These experts reasoned that VLNC cigarettes should impact each new cohort of youth experimenters equally, leading to the same effect on initiation rates from year to year. They also noted that the biological effects of the standard would be the same in subsequent years, meaning lower nicotine levels would continue to be less reinforcing and result in lower initiation rates. The remaining two experts believed that the magnitude of the effect on initiation rates would be greater in subsequent years. These experts expected that initial reductions in the prevalence of cigarette smoking would reduce the social factors that contribute to initiation, leading to a "snowball effect" that would cause initiation rates to decline further in subsequent years. These two experts stated that the social norm of non-smoking would strengthen with time, further reducing smoking initiation rates in subsequent years. Tables F8 and F9 show the experts' estimates.

Question 5: Initiation of Non-Covered Product Use

All seven experts believed that some portion of those the potential standard would deter from becoming cigarette smokers would initiate use of a non-covered tobacco product in the year immediately following a nicotine product standard's implementation. The primary reason cited for this conclusion was what one expert referred to as the shared liability model; i.e., that young people who are inclined to take risks will do so regardless of changes in the range of risky options available to them. The experts reasoned that at least some of these individuals might turn away from VLNC cigarettes to experiment with tobacco products, like e-cigarettes, that would contain higher levels of nicotine. The experts also noted that a portion of young people are likely to experiment with tobacco products (as well as other products, such as marijuana and alcohol) for social reasons or for purposes of self-medication (e.g., those with attention deficit disorder); these individuals might be deterred from initiating the use of VLNC cigarettes and instead initiate the use of non-covered products. In further support of this reasoning, the experts noted that the variety of noncombusted tobacco products available – particularly with respect to e-cigarettes – is large and growing, which makes it more likely that those inclined to experiment with non-covered tobacco products would be able to find a product they would initially enjoy, and to which they might eventually become addicted. More generally, the experts noted that youth are already using noncombusted tobacco products, especially e-cigarettes, and found it reasonable to conclude that some of those deterred from initiating use of cigarettes would see non-covered tobacco products as a possible alternative.

Five experts believed that the percentage of those deterred from initiating cigarette use who would instead initiate the use of non-covered products would be the same during subsequent years as in the year immediately following implementation of the potential product standard. These experts reasoned that fundamental changes in the cohort of experimenting youth are unlikely from year to year, and that one therefore could expect the potential standard to have the same effect on initiation of non-covered tobacco products in subsequent years as in the first year. In contrast, Expert 3 believed that in subsequent years a smaller percentage of those deterred from becoming cigarette smokers would initiate the use of non-covered products, on the grounds that shifting social norms would dampen experimentation with all forms of tobacco. Expert 7 came to the opposite conclusion – i.e., that a greater percentage of those deterred from becoming cigarette smokers would initiate the use of non-covered products – reasoning that innovation by the tobacco industry would in the future lead to the introduction of non-covered products that young people would find more attractive. Tables F10 and F11 show the experts' estimates.

Discussion

The 2018 expert elicitation produced quantitative, probabilistic estimates of the impact of potential nicotine product standard on transitions in the use of covered and non-covered tobacco products. The elicitation built upon the previous elicitation on this subject, conducted in 2015. The elicitation did not seek to elicit a consensus estimate from the expert panel. The absence of consensus is clearly reflected in the results. For certain parameters, IEc observed some agreement among a subset of the experts (e.g., five experts indicated, for their median estimate, that a nicotine product standard would reduce smoking initiation rates by 70 to 80 percent, both in the year immediately following implementation and in subsequent years). In general, however, the experts' estimates differed, both with respect to their median values and the range of uncertainty surrounding those estimates.

This elicitation followed well-established practices in the field of expert elicitation, designed to produce well-calibrated estimates with minimal bias. The process was largely based on that employed in 2015 for FDA's initial elicitation on the behavioral impacts of a potential nicotine product standard. All of the experts participated in that initial elicitation, and thus were familiar with the focus of the elicitation and

the process of providing probabilistic judgments. The elicitation protocol was in large part an adaptation of the 2015 protocol. Similarly, the pre-elicitation workshop, like the workshops conducted in 2015, was designed to provide the experts an opportunity to review the relevant scientific literature and share their views, particularly with respect to recent research on the impact of using cigarettes with reduced nicotine content, trends in e-cigarette use, or trends in the dual use of tobacco products, all of which might have a direct bearing on their estimates of the behavioral impacts of a potential nicotine product standard. The feedback received from the experts indicates that the protocol was clear and that the experts had little difficulty correctly interpreting or responding to the questions. On a practical note, the web conferencing software employed to support the workshops and the elicitation interviews worked well; remote participation, including the use of the collaboration site for sharing of the protocol, literature, and workshop presentations, was generally seamless.

While the overall process was quite similar to that employed in 2015, it differed in some potentially important respects. For example:

- The 2018 update was conducted with only seven of the eight original members of the panel.

- The 2018 process featured a single pre-elicitation workshop. In contrast, the process employed in 2015 included two pre-elicitation workshops and a post-elicitation workshop, at which the members of the panel reviewed and discussed their initial estimates. Following the third workshop, the experts were given the opportunity to revise their initial estimates; six of the eight did so.

The potential impact of these differences is unclear. From an analytic perspective, it would have been preferable to conduct the elicitation with all eight members of the original panel. This would have permitted us to present a comparison of the estimates each expert provided in 2015 to his or her estimates in 2018. We are unable to present this type of comparison, since doing so would make it possible to identify the estimates provided in 2015 by the missing member of the panel. At the same time, we do not believe that the reduction in the size of the panel had a substantial effect on the range of perspectives provided or on the quality of the group's interactions. As they did in 2015, the members of the panel offered highly informed perspectives on the role of nicotine in cigarette smoking initiation and cessation, as well as current trends in the use of various tobacco products – both those that would be covered by a potential nicotine product standard and those that would not.

Table F2. Cessation in the First Year - Final Elicited Estimates of the Percentage of Cigarette Smokers Who Would Quit Smoking in the First Year of a Nicotine Product Standard*

Value	**Expert**						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Max	80	25	10	70	90	63.5	90
95th	75	20	9.5	65	80	53.5	80
75th	65	15	8	55	70	33.5	60
50th	50	10	6.5	47.5	60	28.5	50
25th	35	8	5	35	45	13.5	30
5th	25	6	4	25	30	7	20
Min	20	4	3.5	20	20	3.5	7

*Elicitation protocol asks, "During the year immediately following the potential product standard's implementation, what is your estimate of the true percentage of current cigarette smokers in the U.S. (as represented in the health effects simulation model) who would quit smoking cigarettes?"

Table F3. Cessation in Subsequent Years – Final Elicited Estimates of the Percentage of Cigarette Smokers Who Would Quit Smoking in the Subsequent Years*

Value	Expert						
	1§	2	3	4§	5	6	7§
Max	80	30	8	70	80	33.5	90
95th	75	25	7.5	65	70	28.5	80
75th	65	20	6.5	55	60	23.5	60
50th	50	15	5	47.5	50	18.5	50
25th	35	10	4.5	35	40	13.5	30
5th	25	7	4	25	30	7	20
Min	20	5	3.5	20	20	3.5	7

*Elicitation protocol asks, "For the years following the first full year of the potential product standard's implementation, what is your estimate of the true percentage of cigarette smokers in the U.S. who would quit smoking cigarettes each year (i.e., the true average annual cessation rate for cigarette smoking in the U.S.)?"
§Denotes that the expert's estimates are the same as for the first year.

Table F4. Switching in the First Year – Final Elicited Estimates of the Percentage of Quitters Who Would Initiate Use of Non-Covered Products in the First Year of a Nicotine Product Standard*

Value	Expert						
	1	2	3	4	5	6	7
Max	80	90	70	90	90	95	70
95th	75	85	65	85	80	85	50
75th	60	70	60	75	75	75	35
50th	50	60	55	65	70	65	25
25th	40	50	50	55	60	40	20
5th	25	25	45	45	50	15	10
Min	20	20	30	40	30	7	5

* Elicitation protocol asks, "For the year immediately following the potential product standard's implementation, what is your estimate of the true percentage of those who quit smoking cigarettes who, in that same year, would initiate use of one or more non-covered tobacco products?"

Table F5. Switching in Subsequent Years – Final Elicited Estimates of the Percentage of Quitters Who Would Initiate Use of Non-Covered Products in Subsequent Years*

Value	Expert						
	1§	2§	3	4§	5§	6§	7§
Max	80	90	80	90	90	95	70
95th	75	85	76	85	80	85	50
75th	60	70	73	75	75	75	35
50th	50	60	70	65	70	65	25
25th	40	50	60	55	60	40	20
5th	25	25	55	45	50	15	10
Min	20	20	50	40	30	7	5

*Elicitation protocol asks, "For the years following the first full year of the potential product standard's implementation, what is your estimate of the true percentage of those who quit smoking cigarettes in a given year who, in that same year, would initiate use of one or more non-covered tobacco products?"
[§]Denotes that the expert's estimates are the same as for the first year.

Table F6. Dual Use in the First Year – Final Elicited Estimates of the Percentage of Those Who Continue to Smoke Who Would Initiate Use of Non-Covered Products in the First Year of a Nicotine Product Standard*

Value	Expert						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Max	80	95	85	95	95	92	90
95th	75	85	80	90	90	80	75
75th	60	80	75	85	85	70	60
50th	45	60	60	75	80	60	50
25th	30	30	50	65	65	30	40
5th	15	20	45	55	50	20	25
Min	10	10	40	50	40	12	10

*Elicitation protocol asks, "For the year immediately following the potential product standard's implementation, what is your estimate of the true percentage of those who continue to smoke cigarettes who, in that same year, would become dual users of cigarettes and one or more non-covered tobacco products?"

Table F7. Dual Use in Subsequent Years – Final Elicited Estimates of the Percentage of Those Who Continue to Smoke Who Would Initiate Use of Non-Covered Products in Subsequent Years*

Value	Expert						
	1[§]	**2[§]**	**3**	**4[§]**	**5[§]**	**6**	**7[§]**
Max	80	95	30	95	95	92	90
95th	75	85	20	90	90	60	75
75th	60	80	17.5	85	85	50	60
50th	45	60	15	75	80	30	50
25th	30	30	10	65	65	20	40
5th	15	20	5	55	50	15	25
Min	10	10	2	50	40	12	10

* Elicitation protocol asks, "For the years following the first full year of the potential product standard's implementation, what is your estimate of the true percentage of those who continue to smoke cigarettes who, in a given year, would become dual users of cigarettes and one or more non-covered tobacco products?"
[§]Denotes that the expert's estimates are the same as for the first year.

Table F8. Change in Initiation in the First Year – Final Elicited Estimates of the Percentage Change in Annual Cigarette Smoking Initiation Rates Caused by a Nicotine Product Standard in its First Year*

Value	Expert						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Max	-90	-50	-60	-95	-95	-95	-95
95th	-85	-40	-58	-90	-90	-90	-90
75th	-80	-30	-55	-80	-85	-85	-80
50th	-70	-25	-50	-72.5	-80	-70	-75
25th	-60	-15	-40	-65	-70	-40	-70
5th	-55	-10	-33	-55	-60	-35	-60

Min	-50	-5	-30	-50	-50	-30	-50

*Elicitation protocol asks, "For the year immediately following the potential product standard's implementation, what is your estimate of the true percentage change in annual cigarette smoking initiation rates the potential product standard would cause, relative to baseline rates?"

Table F9. Change in Initiation in Subsequent Years – Final Elicited Estimates of the Percentage Change in Annual Cigarette Smoking Initiation Rates Caused by a Nicotine Product Standard During Subsequent Years*

Value	**Expert**						
	1§	**2§**	**3**	**4§**	**5§**	**6§**	**7**
Max	-90	-50	-70	-95	-95	-95	-98
95th	-85	-40	-65	-90	-90	-90	-92
75th	-80	-30	-60	-80	-85	-85	-85
50th	-70	-25	-55	-72.5	-80	-70	-80
25th	-60	-15	-44	-65	-70	-40	-75
5th	-55	-10	-38	-55	-60	-35	-65
Min	-50	-5	-35	-50	-50	-30	-55

*Elicitation protocol asks, "For the years following the first full year of the potential product standard's implementation, what is your estimate of the true percentage change in annual cigarette smoking initiation rates the potential product standard would cause, relative to baseline rates?"
§Denotes that the expert's estimates are the same as for the first year.

Table F10. Initiation of Non-Covered Products in the First Year – Final Elicited Estimates of the Percentage of Those Deterred from Becoming Cigarette Smokers Who Would Instead Initiate Use of Non-Covered Tobacco Products in the First Year of a Nicotine Product Standard*

Value	**Expert**						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Max	45	90	100	55	95	90	30
95th	40	80	90	50	90	80	25
75th	25	75	85	40	85	70	20
50th	20	65	80	30	80	65	10
25th	15	45	75	20	65	40	7
5th	10	35	73	10	50	25	3
Min	5	25	70	5	30	10	0

*Elicitation protocol asks "consider those who, in the year immediately following implementation, you believe the standard would deter from becoming cigarette smokers. What is your estimate of the true percentage of these individuals who, in that same year, would instead initiate use of one or more non-covered tobacco products?"

Table F11. Initiation of Non-Covered Products in Subsequent Years – Final Elicited Estimates of the Percentage of Those Deterred from Becoming Cigarette Smokers Who Would Instead Initiate Use of Non-Covered Tobacco Products During Subsequent Years*

Value	**Expert**						
	1§	**2§**	**3**	**4§**	**5§**	**6§**	**7**
Max	45	90	100	55	95	90	50
95th	40	80	90	50	90	80	40
75th	25	75	80	40	85	70	30
50th	20	65	70	30	80	65	20

25th	15	45	68	20	65	40	15
5th	10	35	65	10	50	25	10
Min	5	25	60	5	30	10	5

*Elicitation protocol asks "consider those who, in each year following the first full year of implementation, you believe the standard would deter from becoming cigarette smokers. What is your estimate of the true percentage of these individuals who, in the year they are deterred from becoming cigarette smokers, would instead initiate use of one or more non-covered tobacco products?"

§Denotes that the expert's estimates are the same as for the first year.

Appendix G: Estimation of Transition Probabilities Under the Product Standard Scenario

Table G1 shows a description of the parameters used in model simulations for a potential nicotine product standard. Values and distributions for each parameter were determined using an expert elicitation process. The values provided by each expert can be found in Appendix F. The Greek letters serve as variable names in subsequent equations.

Table G1. Behavioral Input Parameters Used to Estimate the Impact of a Nicotine Product Standard on Premature Morbidity and Mortality in the U.S.

Description of Parameters
$\alpha(t)$: Fraction of current smokers who quit smoking as a result of a nicotine product standard
$\beta(t)$: Fraction of quitters switching to noncombusted products
$\gamma(t)$: Fraction of continuing smokers who become dual product users
$\delta(t)$: Fraction reduction in annual smoking initiation rates
$\varepsilon(t)$: Fraction of dissuaded smoking initiates who initiate with noncombusted tobacco products instead

For each year in the simulation at or beyond the implementation of a nicotine product standard (i.e., $t \geq 2027$), each transition probability shown in Figure G1 (denoted by letters a, b, ⋯, p) is computed as follows:

$$a(t,pol) = \big(1-\delta(t)\big)\varepsilon(t)b(t,base) + \big(1-\delta(t)\big)e(t,base) + a(t,base)$$

$$b(t,pol) = \delta(t)b(t,base)$$

$$c(t,pol) = \delta(t)c(t,base)$$

$$d(t,pol) = d(t,base)$$

$$e(t,pol) = \delta(t)e(t,base)$$

$$f(t,pol) = \alpha^*(t)\big(1-\beta(t)\big),$$
$$where\ \alpha^*(t) = \min\{\alpha(t)\big(f(t,base) + g(t,base)\big), 1\}$$

$$g(t,pol) = \alpha^*(t)\beta(t)$$

$$h(t,pol) = \delta(t)h(t,base)$$

$$i(t,pol) = \delta(t)i(t,base)$$

$$j(t,pol) = (1-\alpha^*(t))\gamma(t)$$

$$k(t,pol) = k(t,base)$$

$$l(t,pol) = \begin{cases} \alpha^*(t)\big(1-\beta(t)\big), & t = 2027 \\ \alpha^*(t), & t = 2028,\cdots,2100 \end{cases}$$

$$m(t,pol) = \big(1-\alpha^*(t)\big)\big(p(t,base) + m(t,base)\big)$$

$$n(t,pol) = \alpha^*(t)(1 - p(t,base) - m(t,base))$$

$$o(t,pol) = o(t,base)$$

$$p(t,pol) = \alpha^*(t)(p(t,base) + m(t,base))$$

$$prob(CF \to CC) = \begin{cases} (1-\alpha^*(t))\gamma(t), & t = 2027 \\ 0, & t = 2028,\cdots,2100 \end{cases}$$

$$prob(CF \to FC) = \begin{cases} \alpha^*(t)\beta(t), & t = 2027 \\ 0, & t = 2028,\cdots,2100 \end{cases}$$

Note that explicit notation for age and sex is suppressed since the calculation is identical for each age and sex. Further, note that "*a*" in these calculations refers to transition *a* in Figure G1 (NN to NC)[9] and is not intended to represent the age index variable as in previous sections.

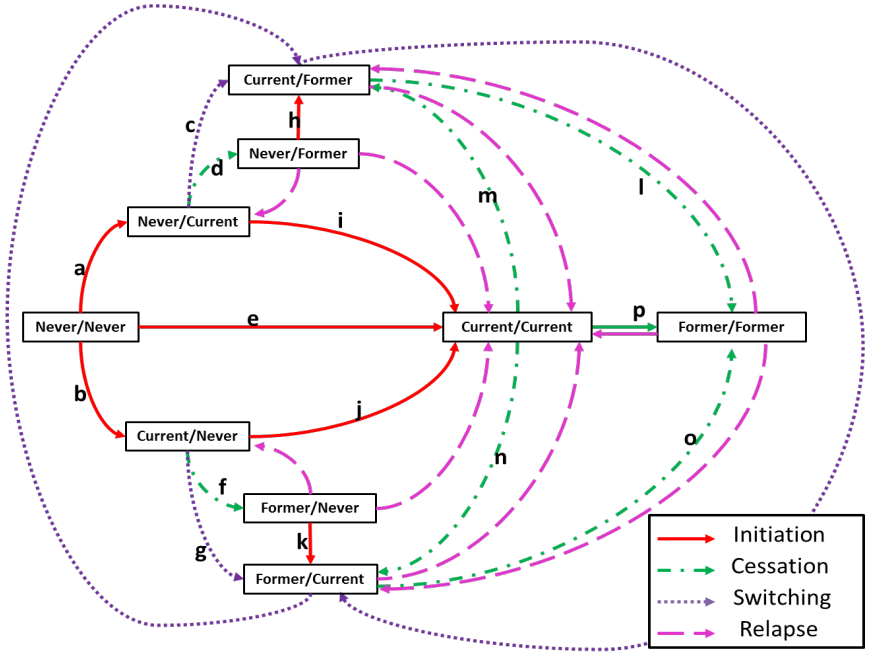

Figure G1. Tobacco Use Status Transitions for a Two-Product Model Formulation. Transition behaviors (illustrated by directed edges) are categorized into four groups: initiation, cessation, switching, and relapse. Nine possible use states are represented as boxes in which the first and second terms correspond to use of the first and second products, respectively. In this analysis, the first and second products represent cigarettes and noncombusted tobacco products, respectively.

[9] First letter denotes cigarette use status, and second letter denotes noncombusted tobacco product use status. N=never, C=current, and F=former.

Appendix H: Estimation of Outcome Metrics

To examine the impact of a potential nicotine product standard on population health, we examine a range of outcome metrics, including changes in tobacco use prevalence, smoking initiates and quitters, and morbidity and mortality in the U.S. population over time. The approach to estimating these outcome measures is described below.

Tobacco Use

Prevalence of individuals with certain tobacco use status (U_1) at time t among a subpopulation with ages in subset (A_1) and sexes in the subset (S_1) is calculated as follows:

$$prev(A_1, S_1, U_1, t) = \frac{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U_1} Pop(a, s, u, t)}{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U} Pop(a, s, u, t)}, A_1 \subset A, S_1 \subset S, U_1 \subset U, \quad (6)$$

where:

- $Pop(a, s, u, t)$ is the size of the subpopulation where "a" is age, "s" is sex, and "u" is tobacco use status at time t;
- $A = \{0, 1, 2, \cdots, 100+\}$ is the set of
- $S = \{m, f\}$ is the set of sexes; and
- $U = \{NN, CN, FN, NC, CC, FC, NF, CF, FF\}$[10] is the set of all tobacco use status.

Note that prevalence for any specific single tobacco product as well as prevalence for simultaneous dual use of both tobacco products is specified by constructing the appropriate subset of tobacco use states (U_1 specified in Equation 6). For example, dual use can be specified by $U_1 = \{CC\}$; current use of the first product can be specified by $U_1 = \{CN, CC, CF\}$; and current use of the second product can be specified by $U_1 = \{NC, CC, FC\}$. Also, the adult subpopulation can be specified by $A_1 = \{18,19, \cdots, 100+\}$, and the male subpopulation can be specified by $S_1 = \{m\}$.

The following are examples of computing prevalence if we designate cigarettes as the first product and noncombusted tobacco products as the second product:

a. Current adult smoking prevalence for both sexes at time t is calculated as:

$$prev(A_1, S_1, U_1, t) = \frac{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U_1} Pop(a, s, u, t)}{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U} Pop(a, s, u, t)}, \quad (7)$$

where $A_1 = \{18,19, \cdots, 100+\}, S_1 = \{m, f\}, U_1 = \{CN, CC, CF\}$.

b. Current adult noncombusted tobacco use prevalence for both sexes is calculated as:

$$prev(A_1, S_1, U_1, t) = \frac{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U_1} Pop(a, s, u, t)}{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U} Pop(a, s, u, t)}, \quad (8)$$

where $A_1 = \{18,19, \cdots, 100+\}$, $S_1 = \{m, f\}$, $U_1 = \{NC, CC, FC\}$.

[10] First letter denotes cigarette use status, and second letter denotes noncombusted tobacco product use status. N=never, C=current, and F=former.

c. Current adult dual use prevalence for both sexes is:

$$prev(A_1, S_1, U_1, t) = \frac{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U_1} Pop(a, s, u, t)}{\sum_{a \in A_1} \sum_{s \in S_1} \sum_{u \in U} Pop(a, s, u, t)}, \quad (9)$$

where $A_1 = \{18,19, \cdots, 100+\}, S_1 = \{m, f\}, U_1 = \{CC\}$.

The size of the population (the number of people) can also be computed. The following are some examples:

a. The size of the subpopulation of all individuals who have quit smoking (using the first product) at some point in the past up to time t and including time t is:

$$former\ smokers(t) = \sum_{a \in A} \sum_{s \in S} \sum_{u \in U_1} \sum_{q=0}^{70+} Pop(a, s, u, q, t), U_1 = \{FN, FC, FF\}, \quad (10)$$

where: q = 0 indicates an individual who quit less than 1 year ago, q = 1 indicates an individual who quit between 1 and 2 years ago, …, q =69 indicates an individual who quit between 69 and 70 years ago, and q =70+ indicates an individual who quit more than 70 years ago. In the model, smoking cessation is tracked from 0 to 70 years where the final subgroup (70+) includes all those individuals who have quit 70 or more years ago.

b. The number of individuals who quit smoking in a year is calculated as:

$$\begin{aligned} &new\_quitters(t) \\ &= \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = CN, t) \times [p(CN \to FN | a, s, u = CN, t) + p(CN \to FC | a, s, u = CN, t)] \\ &+ \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = CC, t) \times [p(CC \to FC | a, s, u = CC, t) + p(CC \to FF | a, s, u = CC, t)] \\ &+ \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = CF, t) \times [p(CF \to FF | a, s, u = CF, t) + p(CF \to FC | a, s, u = CF, t)] \end{aligned} \quad (11)$$

where:

- $new\_quitters(t)$ = the number of people that quit smoking cigarettes in year t[11]; and
- $p(CX \to FY | a, s, u = CX, t)$ = the probability in year t that an individual with age=a, sex=s, and tobacco product use state CX (X=N, C, or F) transitions to tobacco product use state FY (Y=N, C, or F).

The first, second, and third lines of the calculation in Equation 11 indicate the number of people who quit cigarettes in year t and were never, current, and former noncombusted users in year t, respectively.

[11] Note that the number of people who quit in year t does not include the probability of death term. Consequently, the number of people who quit in year t and do not die will be less than the number of quitters.

c. The number of individuals who initiate smoking in a year is calculated as:

$$
\begin{aligned}
&new\_initiates(t) \\
&= \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = NN, t) \times [p(NN \rightarrow CN | a, s, u = NN, t) + p(NN \rightarrow CC | a, s, u = NN, t)] \\
&+ \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = NC, t) \times [p(NC \rightarrow CC | a, s, u = NC, t) + p(NC \rightarrow CF | a, s, u = NC, t)] \\
&+ \sum_{a \in A} \sum_{s \in S} Pop(a, s, u = NF, t) \times [p(NF \rightarrow CF | a, s, u = NF, t)]
\end{aligned} \tag{12}
$$

where:

- $new\_initiates(t) =$ the number of people that initiate smoking cigarettes in year t[12]; and
- $p(NX \rightarrow NY | a, s, u = NX, t) =$ the probability in year *t* that an individual with age=*a*, sex=*s*, and tobacco product use state NX (X=N, C, or F) transitions to tobacco product use state CY (Y = N, C, or F).

The first, second, and third lines of the calculation in Equation 12 indicate the number of people who initiate cigarettes in year t and were never, current, and former noncombusted users in year *t*, respectively.

The cumulative number of people who quit smoking as a result of the policy between years *t*0 and *t*1 is calculated as:

$$
\sum_{t=t0}^{t1} new\_quitters(t, base) - new\_quitters(t, pol), \tag{13}
$$

where:

- $new\_quitters(t, base)$ = the number of cigarette smokers that quit in year *t* under the baseline scenario; and
- $new\_quitters(t, pol)$ = the number of cigarette smokers that quit in year *t* under the product standard scenario.

The cumulative number of dissuaded smokers from the policy between years *t*0 and *t*1 is calculated as:

$$
\sum_{t=t0}^{t1} new\_initiates(t, base) - new\_initiates(t, pol), \tag{14}
$$

where:

- $new\_initiates(t, base)$ = the number of people that initiate cigarette smoking in year *t* under the baseline scenario; and

[12] Note that the number of people that initiate in year *t* does not include the probability of death term. Consequently, the number of people that initiate in year *t* and do not die will be less than the number of new initiates.

- $new\_initiates(t, pol)$ = the number of people that initiate cigarette smoking in year *t* under the product standard scenario.

Mortality

The mortality effects of tobacco use are also assessed on an annual and cumulative basis. Tobacco-attributable mortality on an annual basis is estimated as:

$$AD(t) = \sum_{a \in A} \sum_{s \in S} \sum_{x,u \in U} Pop(a,s,x,t-1) \times p(x \to u|a,s,x,t) \times [RR(a,s,u,t) - 1] \times p(death|a,s,u_{never},t)$$

where:

- $AD(t)$ = the number of tobacco-attributable deaths in year *t*;
- $p(x \to u|a,s,x,t)$ = the probability that an individual with age *a*, sex *s*, and tobacco use state *x* transitions to tobacco use state *u* in year *t*;
- $RR(a,s,u,t)$ = the relative risk in year *t* for an individual with age a, sex s, and tobacco use state *u*; and
- $p(death|a,s,u_{never},t)$ = the annual proportion of individuals with age *a*, sex *s*, and who have never used either cigarettes or noncombusted tobacco products that die in year *t.*

Annual tobacco-attributable deaths can be summed over time to estimate the cumulative number of premature deaths that are attributable to tobacco use.

Morbidity

In the model, the morbidity impact of cigarette is assessed using a quality-of-life approach developed by Jia and Lubetkin (2010). Reductions in quality-of-life due to cigarette smoking are assessed using EQ-5D index scores derived from the Behavioral Risk Factor Surveillance System data for smokers (*sk*) and non-smokers (*nsk*) by age (*a*):

$$morb(t) = \sum_{a \in A_1} \sum_{s \in S} \sum_{u \in U_1} \left(x_a^{nsk} - x_a^{sk}\right) Pop(a,s,u,t), A_1 = \{18,19,\cdots,100+\}, U_1 = \{CN, CC, CF\}, \quad (16)$$

where:

- $morb(t)$= the quality-adjusted life years for adults lost due to smoking morbidity in year *t*;
- x_a^{nsk}= the EQ-5D index scores for non-smokers (never and former smokers) with age *a*; and
- x_a^{sk}= the EQ-5D index scores for current smokers with age *a*.

Jia and Lubetkin (2010) do not provide EQ-5D index scores for youth (ages less than 18 years); therefore, the model only estimates morbidity impact for adults 18+.

The difference in morbidity estimates between the policy and baseline scenarios in year *t* ($Difference_{morb}(t)$) is calculated using the $morb(t)$ outputs from each scenario as

$$Difference_{morb}(t) = baseline_{morb}(t) - policy_{morb}(t), \quad (17)$$

where:

- $baseline_{morb}(t)$ = the $morb(t)$ output in the baseline scenario in year *t*; and
- $policy_{morb}(t)$ = the $morb(t)$ output in the product standard scenario in year *t*.

Quality-adjusted life years (QALYs) gained from reduced smoking morbidity by year *T* is given by the cumulative sum of the differences from years 1 to *T* as

$$\text{QALYs} = \sum_{t=1}^{T} Difference_{morb}(t). \quad (18)$$

Life years

The life years lived by a population within a specified age range in year *t* ($lifeyears(t)$) is the number of individuals in the population that year for the specified age group. In the model it is calculated for the whole population that includes all age groups as:

$$lifeyears(t) = \sum_{a \in A} \sum_{s \in S} Pop(a, s, t), \qquad A = \{0, 1, 2, \cdots, 100+\}, S = \{m, f\}. \quad (19)$$

The difference in $lifeyears(t)$ between the policy and baseline scenarios in year *t,* $Difference_{lifeyears}(t)$, computed using $lifeyears(t)$ outputs from each scenario is

$$Difference_{lifeyears}(t) = policy_{lifeyears}(t) - baseline_{lifeyears}(t), \quad (20)$$

where:

- $baseline_{lifeyears}(t)$ = the $lifeyears(t)$ output in the baseline scenario in year *t*; and
- $policy_{lifeyears}(t)$ = the $lifeyears(t)$ output in the product standard scenario in year *t.*

Life years gained by year *T* is given by the cumulative sum of the differences from years 1 to *T* as

$$LifeYear_{gained} = \sum_{t=1}^{T} Difference_{lifeyears}(t). \quad (21)$$

Appendix I: Summary of Modeling Assumptions

Table I1. Summary of Modeling Assumptions and Rationale Used to Examine the Potential Impact of the Proposed Nicotine Product Standard.

Modeling Assumption	Rationale
General Inputs	
Potential product standard applies to cigarettes, cigarette tobacco, RYO tobacco, non-premium cigars, and pipe tobacco	These are the combusted products that smokers would be most likely to switch to in order to sustain addiction
Product standard implemented in 2027	This year reflects current timeline
Demographic Inputs	
Noncombusted tobacco product prevalence for immigrants arriving in the U.S. is set to 0	Azagba and Shan (2021) found low prevalence of e-cigarette use among immigrants
Tobacco Use Transition Inputs	
Transition probabilities for smoking relapse are set to 0	CISNET smoking cessation rates are based on successful cessation for at least two years
Sex- and age-specific cigarette smoking and noncombusted product initiation and cessation rates remain constant during the projection period in the baseline scenario with no new product initiation after the age of 30 years	The trajectories of future product initiation and cessation are uncertain, and product initiation after age 30 is limited
Noncombusted product initiation rates are obtained by scaling CISNET smoking initiation rates based on smoking and noncombusted product use prevalence data from NYTS and NHIS	Limited data on noncombusted product initiation are available from national health surveys
CISNET sex- and age-specific smoking cessation rates are used as cessation rates for noncombusted product use	Limited data on noncombusted product cessation are available from national health surveys
Initiation and cessation of cigarette and noncombusted products are independent of one another for youth	Limited data on product use transitions are available for youth
Mortality Inputs	
U.S. death rates from vital statistics data are used for never user death rates for ages less than 35 years	Tobacco-attributable mortality is commonly assumed to be minimal before this age (Centers for Disease Control and Prevention, 2008)

Tobacco use status is assumed to remain the same during mortality follow-up period in estimating mortality hazard ratios from NHIS-LMF data	Tobacco use information is obtained at baseline in NHIS and not updated
Mortality risks for smokeless tobacco users are used for noncombusted product users generally	Specific mortality risks for e-cigarette users are generally not available
Dual users of cigarettes and noncombusted products have the same mortality risks as cigarette smokers	Limited data are available on mortality risks for dual users
Mortality risks for individuals who have switched from cigarette smoking to noncombusted product use cannot be higher than those of current smokers and lower than those of current noncombusted product users	Switching to noncombusted product use, which has lower risk as a category than smoking, should not increase mortality risk and should have at least the risk of noncombusted product use generally
Product Standard Scenario Inputs	
Smoking mortality risks are the same in the baseline and product standard scenarios	Clinical studies have not found increased cigarette consumption as measured by CPD with VLNC cigarettes
Values and ranges for the potential impact of a nicotine product standard on tobacco users and non-users were derived from the result of a formal expert elicitation conducted in 2018	Experts provided estimates considering information from several studies (e.g., Donny et al. (2015); Hatsukami et al. (2017)) on the effects of VLNC cigarettes, as well as changes in use of tobacco products including ENDS (e.g., Jamal et al. (2017))

Appendix J: Additional Results from Main Analysis

The population model provides annual estimates for number of Individuals who would not Initiate smoking as a result of a nicotine product standard implemented in 2027. Figure J1 shows those projections.

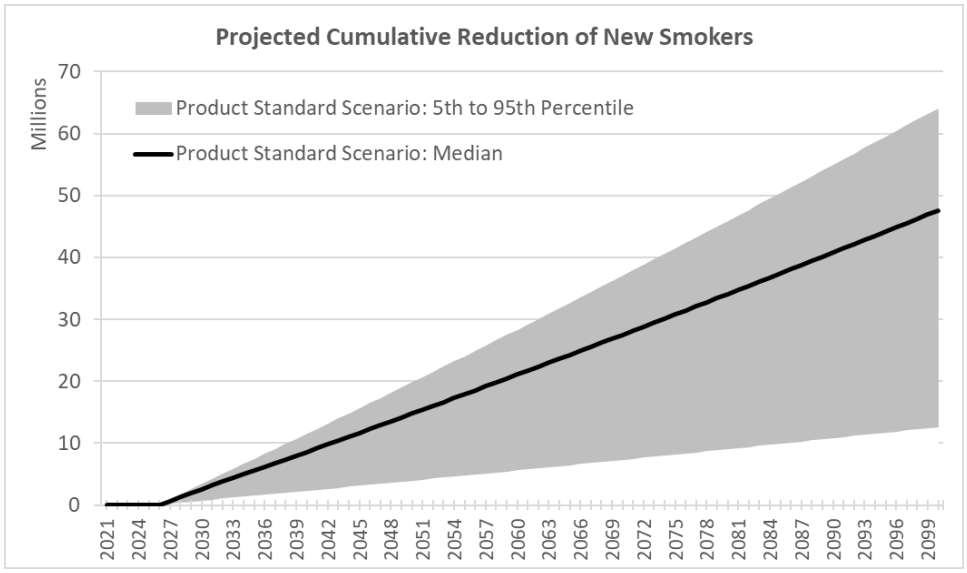

Figure J1. Projected Cumulative Reduction in New Smokers as a Result of a Nicotine Product Standard Implemented in 2027 for the Period 2021-2100.

The population model also provides annual estimates for mortality and morbidity, for the period 2021-2100, as shown in the below figures and tables.

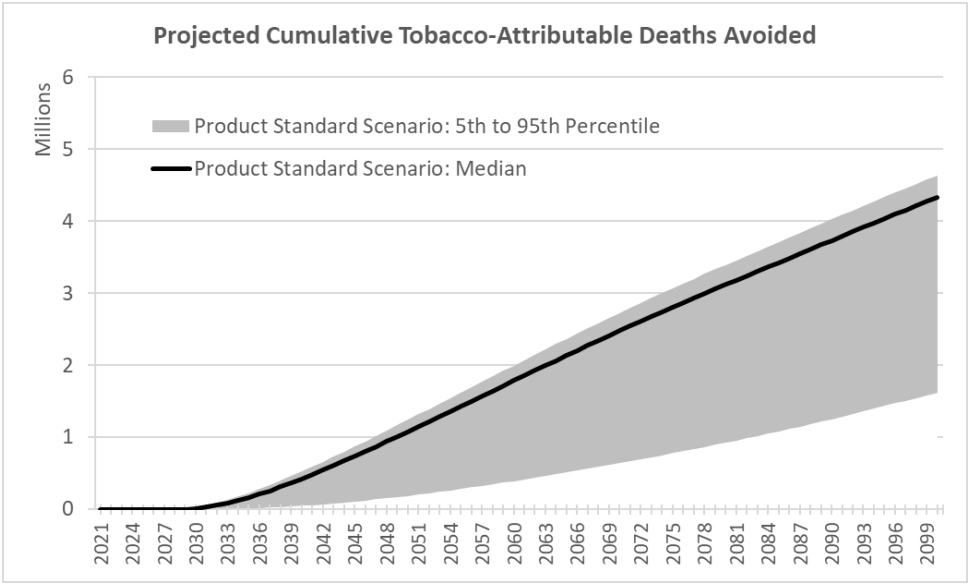

Figure J2. Projected Cumulative Tobacco-Attributable Deaths Avoided as a Result of a Nicotine Product Standard Implemented in 2027.

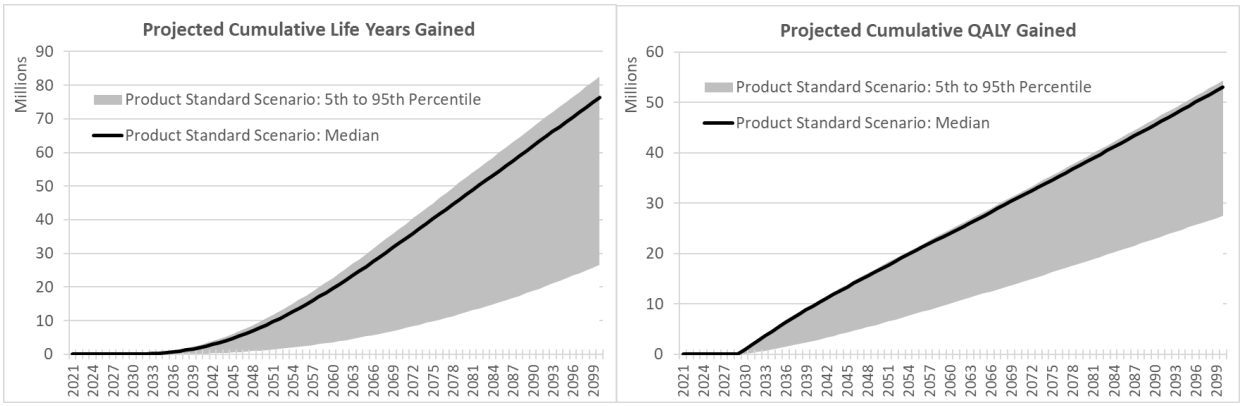

Figure J3. Projected Cumulative Life Years Gained and QALYs Gained Due to Reduced Smoking Morbidity as a Result of a Nicotine Product Standard Implemented in 2027.

Table J1. Annual Estimates of Tobacco-Attributable Deaths Under Baseline and Nicotine Standard Scenarios.

Year	Baseline Scenario	Nicotine Standard Scenario (Median Estimates)
2030	390,138	377,159
2040	324,731	267,254
2050	237,090	167,622
2060	165,340	94,168
2070	122,852	54,961
2080	96,347	34,532
2090	87,510	26,235
2100	85,173	25,758

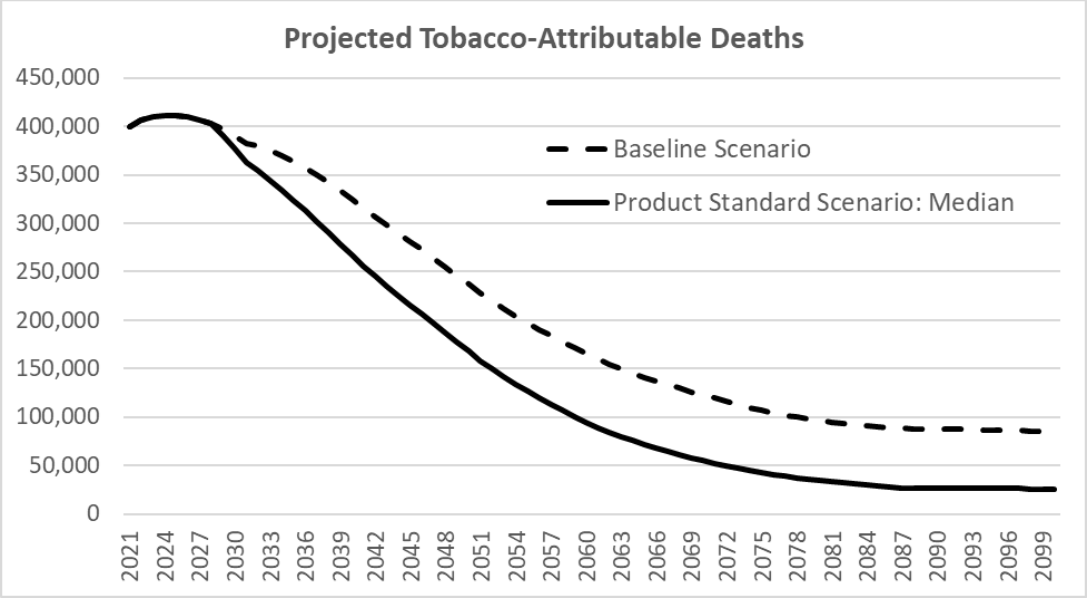

Figure J4. Projected Tobacco-Attributable Deaths Under Baseline and Nicotine Product Standard Scenarios (Median Estimates) for the Period 2021-2100.

Table J2. Annual Estimates of Cigarette Smoking-Attributable Deaths Under Baseline and Nicotine Product Standard Scenarios.

Year	Baseline Scenario		Proposed Nicotine Standard Scenario (Median estimates)	
	Exclusive Cigarette Use	Dual Use	Exclusive Cigarette Use	Dual Use
2030	253,724	134,374	169,926	205,192
2040	190,505	131,718	104,274	160,443
2050	121,144	112,560	52,923	110,968
2060	74,387	86,980	23,392	66,075
2070	51,141	66,997	12,301	36,852
2080	37,766	52,957	7,059	20,342
2090	33,041	47,840	5,896	11,773
2100	31,210	46,988	5,727	10,716

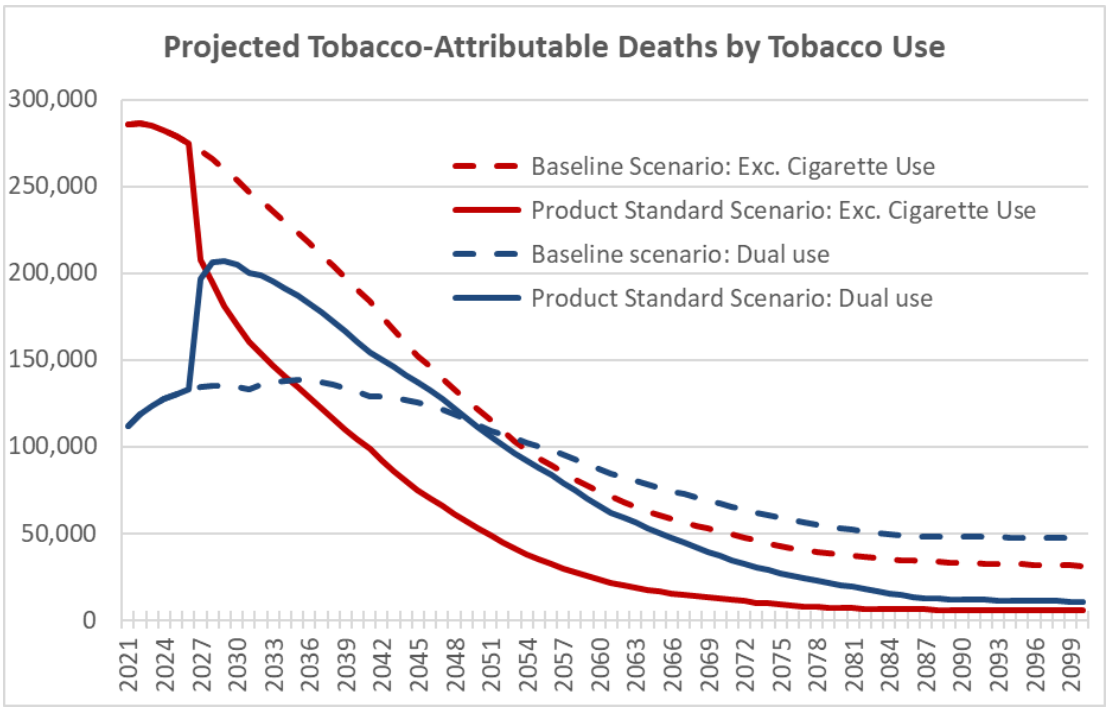

Figure J5. Projected Tobacco-Attributable Deaths for Exclusive Cigarette and Dual Users Under Baseline and Nicotine Product Standard Scenarios (Median Estimates) for the Period 2021-2100.

Appendix K: Changes in Baseline Inputs for a Potential Menthol Product Standard Impact Analysis

Scaling Factor to Adjust Smoking Cessation

Under the baseline scenario, the overall smoking cessation rate, at age a, for menthol and non-menthol smokers, can be estimated as

$$Cess_a = NonMentholCess_a \times (1 - MentholProp_a) + MentholCess_a \times MentholProp_a, \quad (22)$$

where $MentholProp_a$ denotes the proportion of menthol smokers among all smokers at age a, and $MentholCess_a$ and $NonMentholCess_a$ denote the menthol and non-menthol cessation rates, respectively. Let $RatioCess_a$ be the ratio of menthol to non-menthol cessation rates at age a, then Equation 22 can be rewritten as

$$Cess_a = NonMentholCess_a \times (1 - MentholProp_a + RatioCess_a \times MentholProp_a). \quad (23)$$

Following Levy et al. (2021), as well as previous studies (Mills et al., 2021; Schneller et al., 2020; Villanti et al., 2017) showing that cessation rates are lower among menthol than non-menthol smokers, we set $RatioCess_a = 0.8$ for all ages and both genders.

Under the menthol product standard baseline scenario, we assume an increase in smoking cessation (I_{Cess}) among current menthol smokers due to the menthol product standard implementation; thus, the overall smoking cessation rate can be adjusted as follows

$$Cess_a^{Ban} = NonMentholCess_a \times (1 - MentholProp_a + RatioCess_a \times MentholProp_a \times (1 + I_{Cess})). \quad (24)$$

From Equations 23 and 24, the adjusted smoking cessation rate, $Cess_a^{Ban}$, can be rewritten as

$$Cess_a^{Ban} = Cess_a \times SF_a^{Cess}, \quad (25)$$

where SF_a^{Cess} denotes the scaling factor used to adjust the baseline smoking cessation rate at the first year of the menthol product standard implementation, calculated as

$$SF_a^{Cess} = \frac{1 - MentholProp_a + RatioCess_a \times MentholProp_a \times (1 + I_{Cess})}{1 - MentholProp_a + RatioCess_a \times MentholProp_a}. \quad (26)$$

After the first year of the menthol product standard, when a sudden increase in smoking cessation is incorporated, the remaining smokers will become non-menthol or illicit menthol cigarette users, subject to the cessation rates for non-menthol smokers (Levy et al., 2023). The proportion of menthol smokers among all smokers, for different age groups, was calculated from PATH data Wave 5 (2018-2019) (United States Department of Health and Human Services, 2021a). The increase in cessation for menthol smokers was calculated from an expert elicitation, as described in Levy et al. (2021). Eleven experts provided estimates of changes in menthol smoking cessation due to the menthol product standard. The mean experts' responses were used to calculate scaling factors to adjust the baseline smoking cessation rates under the menthol product standard baseline scenario. Table K1 shows the

computed scaling factors used in our simulations to adjust the overall smoking cessation rates during the first year of the menthol product standard implementation.

Table K1. Scaling factors to adjust baseline smoking cessation rates under the menthol product standard baseline scenario.

Age Group	Proportion of Menthol Smokers	Mean Increase in Cessation Among Menthol Smokers Due to the Menthol Product Standard[a]	Scaling Factor[b] (SF_a^{Cess})
15-17	0.54	1.3	1.63
18-24	0.46	1.3	1.53
25-30	0.39	1.3	1.44
30+	0.39	0.8	1.27

[a] Increase in cessation is measured as the ratio of net increment in menthol smoking cessation to menthol smoking cessation at baseline.
[b] Computed from Equation 26.

Scaling Factor to Adjust Switching from Smoking to Noncombusted Product Use

Under the baseline scenario, and following a similar rationale as presented in Equations 22 and 23, the switching rate from menthol and non-menthol cigarettes to noncombusted product use, at age *a,* can be written as

$$Switch_a = NonMentholSwitch_a \times (1 - MentholProp_a + RatioSwitch_a \times MentholProp_a), \quad (27)$$

where $RatioSwitch_a$ denotes the ratio of menthol to non-menthol switching at age a. Following Levy et al. (2023), we set $RatioSwich_a = 0.9$ for all ages and both genders.

Under the menthol product standard baseline scenario, we assume an increase in switching (I_{Switch}) among current menthol smokers who would transition to noncombusted product use due to the menthol product standard implementation. Thus, the switching rate defined in Equation 27 can be adjusted as

$$Switch_a^{Ban} = Switch_a \times SF_a^{Switch}, \quad (28)$$

where SF_a^{Switch} denotes the scaling factor used to adjust the baseline switching rate at the first year of menthol product standard implementation

$$SF_a^{Switch} = \frac{1 - MentholProp_a + RatioSwitch_a \times MentholProp_a \times (1 + I_{Switch})}{1 - MentholProp_a + RatioSwitch_a \times MentholProp_a}. \quad (29)$$

The increase in switching rates under the menthol product standard baseline scenario was calculated from an expert elicitation, as described in Levy et al. (2021). Table K2 shows the computed scaling factors considering a mean increase in switching reported by the experts.

Table K2. Scaling factors used to adjust baseline switching from smoking to noncombusted product use under the menthol product standard baseline scenario.

Age Group	Proportion of Menthol Smokers	Mean Increase in Switching Among Menthol Smokers Due to the Menthol Product Standard[a]	Scaling Factor[b] (SF_a^{Switch})
15-17	0.54	1.8	1.93
18-24	0.46	1.8	1.78
25-30	0.39	1.8	1.66
30+	0.39	0.8	1.29

[a] Increase in switching is measured as the ratio of net increment in switching under the menthol product standard to baseline switching.
[b] Computed from Equation 29.

Scaling Factor to Adjust Smoking Initiation

Under the menthol product standard baseline scenario, smoking initiation at age *a*, for people through age 30, can be written as follows:

$$Init_a^{Ban} = Init_a \times SF_a^{Init}, \quad (30)$$

where:

$$SF_a^{Init} = (1 - MentholProp_a + MentholProp_a \times PropDivertedNonMenthol\,), \quad (31)$$

$Init_a$ denotes the baseline smoking initiation rate at age a, and $PropDivertedNonMenthol$ denotes the proportion of would-be menthol smokers who would be diverted to non-menthol smoking (including illicit menthol cigarette use). SF_a^{Init} denotes the scaling factor used to adjust the baseline smoking initiation rate. As before, we use the expert elicitation data from Levy et al. (2021) to get information regarding $PropDivertedNonMenthol$. Table K3 shows the computed scaling factors considering experts' mean responses on proportion diverted to non-menthol smoking.

Table K3. Scaling factors used to adjust baseline smoking initiation under the menthol product standard baseline scenario.

Age Group	Proportion of Menthol Smokers	Proportion Diverted to Non-Menthol Smoking Due to the Menthol Product Standard[a]	Scaling Factor[b] (SF_a^{Init})
15-17	0.54	0.36	0.65
18-24	0.46	0.36	0.70
25-30	0.39	0.36	0.75

[a] Mean experts' responses on proportion diverted to non-menthol smoking due to the menthol product standard.
[b] Computed from Equation 31.

Scaling Factor to Adjust Noncombusted Initiation

Under the menthol product standard scenario, noncombusted smoking initiation at age *a*, for people through age 30, can be written as follows:

$$NonCombInit_a^{Ban} = NonCombInit_a + Init_a \times SF_a^{NonCombInit}, \quad (32)$$

where:

$$SF_a^{NonCombInit} = (MentholProp_a \times PropDivertedNonComb), \quad (33)$$

$NonCombInit_a$ denotes the baseline noncombusted smoking initiation rate at age a, and $PropDivertedNonComb$ denotes the proportion of would-be menthol smokers who would be diverted to noncombusted tobacco use (including smokeless tobacco, e-cigarettes, and heated tobacco products). $SF_a^{NonCombInit}$ denotes the scaling factor used to adjust the baseline noncombusted smoking initiation rate. As before, we use the expert elicitation data from Levy et al. (2021) to get information regarding $PropDivertedNonComb$. Table K4 shows the computed scaling factors for considering experts' mean responses on proportion diverted to noncombusted use.

Table K4. Scaling factors used to adjust baseline noncombusted initiation under the menthol product standard baseline scenario.

Age Group	Proportion of Menthol Smokers	Proportion Diverted to Noncombusted Use Due to Menthol Product Standard[a]	Scaling Factor[b] ($SF_a^{NonCombInit}$)
15-17	0.54	0.20	0.11
18-24	0.46	0.20	0.09
25-30	0.39	0.20	0.08

[a] Mean experts' responses on proportion diverted to noncombusted tobacco product use (including smokeless tobacco, e-cigarettes, and heated tobacco products) due to the menthol product standard.
[b] Computed from Equation 33.

Appendix L: Estimation of Cigar-Attributable Deaths Due to a Proposed Cigar Flavored Standard

Table L1 shows the estimated number of avoided cigar-attributable deaths expected to result from the implementation of the flavored cigar product standard. To allow for a gradual phase-in of health effects, we assume that avoided premature deaths begin to occur two years after the rule's effective date (2024). Knoke et al. (Knoke et al., 2008) assume, given the biology of lung cancer, that the risk of death from lung cancer would begin to decrease two or more years following smoking cessation. A meta-analysis by Reitsma et al. (Reitsma et al., 2020) which assessed data from 49 prospective cohort studies, generally supports this assumption. To estimate the timing of the impact of the final rule, we use research on the rate at which excess mortality from cigarette smoking declines after smoking cessation. Knoke et al. (Knoke et al., 2008) estimate that excess mortality from lung cancer for cigarette smokers who quit before developing cancer, relative to those who continue to smoke, scales down by an exponential factor that depends on the number of years since the smoker has quit and their age at quitting. They estimate this factor as:

$$e^{-(0.274-0.00279\times\text{age at smoking cessation})\times(\text{years since quitting}-2)} \quad (34)$$

To apply this factor to avoided cigar-attributable premature deaths, we assume 40 years as the average age at quitting. Using household survey data of U.S. adults over 18 years of age, Schauer et al. (Schauer et al., 2015) showed that the average quitting age of 40 years did not change over time between 1997 and 2012. We also assume that quitting occurs immediately, meaning that years since quitting equals the number of years since the rule has taken effect. Subtracting the estimated factor from one for a given year after the rule takes effect provides an estimate of the share of avoided cigar-attributable premature deaths that will have occurred by that year. After year 30, we assume that the full mortality benefit for baseline exclusive cigar smokers of 780 will be realized.

Table L1. Estimates of the annual baseline avoided cigar-attributable deaths as a result of the proposed cigar flavored product standard.

Year	Years Since Quitting Equal to Years After Effective Date of Rule	Scale Down Factor[a] (%)	Cigar Flavored Rule Impact Phase-in: 1-Scale Down Factor (%)	Annual Baseline Avoided: Phase-in x Avoided Deaths[b]
2025	1	-	-	-
2026	2	-	-	-
2027	3	85.0%	15.0%	117
2028	4	72.3%	27.7%	216
2029	5	61.4%	38.6%	301
2030	6	52.2%	47.8%	373
2031	7	44.4%	55.6%	434
2032	8	37.7%	62.3%	486
2033	9	32.1%	67.9%	530
2034	10	27.3%	72.7%	567
2035	11	23.2%	76.8%	599
2036	12	19.7%	80.3%	626
2037	13	16.8%	83.2%	649

2038	14	14.2%	85.8%	669
2039	15	12.1%	87.9%	686
2040	16	10.3%	89.7%	700
2041	17	8.8%	91.2%	712
2042	18	7.4%	92.6%	722
2043	19	6.3%	93.7%	731
2044	20	5.4%	94.6%	738
2045	21	4.6%	95.4%	744
2046	22	3.9%	96.1%	750
2047	23	3.3%	96.7%	754
2048	24	2.8%	97.2%	758
2049	25	2.4%	97.6%	761
2050	26	2.0%	98.0%	764
2051	27	1.7%	98.3%	767
2052	28	1.5%	98.5%	769
2053	29	1.2%	98.8%	770
2054	30	1.1%	98.9%	772
2055	31	0.0%	100.0%	780
…	…	…	…	…
2064	40	0.0%	100.0%	780

[a] Scale down factor was computed using the exponential function described in Equation 34. (Knoke et al., 2008).
[b] Phase-in x Avoided Deaths = (1 – Scale Down Factor)*780.

Table L2 shows additional estimates of avoided cigar-attributable deaths from year 2064 to 2100. Specifically, for years 2064 to 2078 we assume a linear trend increase in avoided deaths from 780 in 2064 to 1,123 deaths in 2078. We then assume that during the period 2079-2091 that number of avoided deaths will remain constant at 1,123. Finally, we also assume that for the period 2092-2100 the number of avoided deaths will be 1,120.

Table L2. Additional estimates of the annual baseline avoided cigar-attributable deaths as a result of the proposed cigar flavored product standard, for the period 2064-2100.

Year	Annual Baseline Avoided Cigar-Attributable Deaths Due to the Cigar Flavored Rule
2064	780
2065	805
2066	829
2067	854
2068	878
2069	903
2070	927
2071	952
2072	976

2073	1,001
2074	1,025
2075	1,050
2076	1,074
2077	1,099
2078-2091	1,123
2092-2100	1,120