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A DISCRETE EVENT SIMULATION MODEL TO ESTIMATE POPULATION LEVEL HEALTH AND ECONOMIC IMPACTS OF SMOKING CESSATION INTERVENTIONS

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ABSTRACT

We design and develop a predictive model that estimates health and economic outcomes associated with smoking cessation interventions using discrete-event simulation (DES). Outcomes include estimates of sustained abstinence from smoking, quality of life years gained, cost of treatment, additional health-related morbidity due to long-term effects of smoking (e.g. lung cancer, stroke), and cost-effectiveness of the various smoking cessation options. Interventions assessed include nicotine replacement therapy (patch or gum,), oral medication (bupropion and varenicline), and abstinence without pharmacologic assistance. The DES approach allows us to account for heterogeneity of patients and dynamic changes in disease progression. Results show that even a single quit attempt can be cost-effective over the patients' lifetime. Furthermore, based on the incremental cost-effectiveness ratios, varenicline dominates other treatments at 10 years, 30 years, and over the lifetime. Understanding the comparative effectiveness and cost of alternative smoking cessation strategies can improve clinical and patient decision-making.

1 INTRODUCTION

According to the US Surgeon General, active cigarette smoking remains a major public health concern despite numerous FDA regulations, highly publicized litigation efforts against major tobacco companies, and considerable evidence documenting the health risks of smoking (US DHHS 2014). Several studies have demonstrated that tobacco use is the leading cause of preventable deaths in the US (Mokdad et al. 2004; CDC 2002). Among Americans, cigarette use is responsible for about 480,000 deaths/year, and on average, smokers die 10 years earlier than nonsmokers (Jha et al. 2013). More than 16 million people in the US suffer from smoking-caused illness (CDC 2014). Despite the medical dangers, smoking prevalence remains quite high at 18% of the US adult population in 2012 (CDC 2014). Although 70% of smokers want to quit, long-term smokers experience significant difficulty breaking the habit and overcoming nicotine addiction (CDC 2011a).

Multiple smoking cessation therapies and interventions have been developed since the early 1960s to aid smokers in quitting; however, more than 45 million adults in the US continue to smoke cigarettes (CDC 2011a). Even with pharmacologic intervention, recidivism is extremely high (CDC 2011b). Numerous unsuccessful pharmacotherapy attempts may be costly and result in economic and emotional hardship due to repeated failures and feelings of guilt (Ranney et al. 2006). Smoking-related medical expenses and productivity loss cost the US approximately $289 billion each year (DHHS 2014).

Multiple types of smoking cessation therapies (e.g., varenicline, bupropion, nicotine replacement therapy [NRT], counseling) have been assessed individually or in combination using decision tree and Markov models, and studies of these interventions have generally found smoking cessation to be cost-effective (Jackson et al. 2007; Neilson and Fiore 2000; McGhan and Smith 1996; Fiscella and Franks 1996; Cromwell et al. 1997; Orme et al. 2001; Gilbert et al. 2004; Cornuz et al. 2006; Howard et al. 2008). Previous studies have assessed the effects of smoking cessation on disease incidence, although estimates were not generalizable to the US population (Hoogenveen et al. 2008) or were obtained from Markov cohort structures, which can be limited in that they do not account for individual-level heterogeneity (Howard et al. 2008; Hoogenveen et al. 2008). One DES model (Xenakis et al. 2011) measured smoking cessation abstinence and relapse one year after a treatment attempt using clinical trial data comparing varenicline to bupropion or placebo, but changes in lifetime smoking behavior and smoking-related illness were not evaluated. More recently, Getsios et al (2013) use DES to model individual quit attempts and lifetime risk of diseases is determined and quality of life and cost is assigned, rather than being modeled explicitly. We use DES to measure and compare the impact of different pharmacologic and non-pharmacologic smoking cessation interventions (NRT, Varenicline, bupropion, non-pharmacologic-assisted [i.e., cold turkey]) on lifetime smoking-related disease prevalence (chronic obstructive pulmonary disease [COPD], lung cancer, myocardial infarction [MI], stroke), mortality, quality of life, and costs at the US population level. A meta-analysis of 1-year continuous abstinence rates (CARs) was conducted to estimate intervention efficacy.

We employ DES for several reasons. First, to assess cost-effectiveness of various smoking cessation therapies, DES evaluates individuals progressing through the model in sequential order based upon individual-level variation in demographic characteristics (e.g., age, gender), smoking-related disease risk, treatment adherence, and relapse. The dynamic framework of DES allows for changes in characteristics over time as events occur (e.g., age increases, disease severity changes). Transition probabilities in a DES model can be functions of individual-level attributes (e.g., disease risk can depend on gender and smoking status, mortality risk can depend on the amount of time since disease diagnosis). Each event simultaneously accounts for potential disease-related outcomes and costs based on important risk factors such as age, gender, smoking status, and disease history (e.g. adverse/acute events such as a stroke or myocardial infarction [MI]). In comparison, a Markov cohort model for smoking cessation (e.g., Howard et al. 2008) describes a homogeneous group of individuals transitioning through pre-defined health states over time where risks of smoking-related disease or death are calculated as the expected portion of the simulated population. Another benefit of modeling smoking cessation using DES is that the system behavior is a summary of each individual's unique clinical history allowing us to examine health and economic outcomes at both the individual and aggregate population levels.

This manuscript describes the development and verification of a DES model to estimate health and economic outcomes associated with US smokers' actions and responses to different smoking cessation interventions after making a one-time quit attempt, along with resulting smoking-related co-morbidities over a lifetime.

2 SIMULATION MODEL

This section describes the development of a DES model to estimate health and economic outcomes for a US cohort of smokers exposed to alternative pharmacologic and non-pharmacologic smoking cessation interventions while considering multiple smoking-related co-morbid conditions. First, we describe the flow of the simulation model and structural assumptions. Next, we discuss simulation input parameters (underlying population characteristics, smoking cessation intervention efficacy and recidivism, co-morbidity and mortality risk). Data extrapolation methods for multiple data sources (US Census, Centers for Disease Control and Prevention [CDC], peer-reviewed literature, *Red Book*) are explained. We then discuss how we measured health and economic impacts at the US population level.

2.1 Model Structure

ARENA version 13.5 (Rossetti 2010) was used to build the simulation model. Figure 1 provides a high-level view of the simulation model structure. First, a cohort of smokers with US demographic characteristics (gender and age structure of smoking adults) is created. All smokers are considered healthy (i.e., without smoking-related co-morbidity) at baseline. Upon entry into the simulation, 100 percent of smokers make one smoking cessation attempt using a pharmacotherapy (NRT, varenicline, bupropion) or non-pharmacologic-assisted approach (cold turkey), or smokers do not attempt to quit smoking (denoted by the broken line in Figure 1). Intervention success is evaluated, according to trial-based efficacy evidence (explained in Section 2.2) at the end of year one at which time individuals either successfully quit smoking or remain smokers with no additional quit attempts. Former smokers (i.e., successful quitters) have a risk of smoking relapse. Both former and current smokers (i.e., individuals who never successfully quit smoking or those who relapsed) carry annual smoking-related health (lung cancer, COPD, stroke, MI) and death risks as well as non-disease-specific all-cause mortality risk. Attributes of individuals (e.g., age, smoking cessation intervention and co-morbidity costs, health state utility values [refer to Section 2.3]) are updated periodically. Aggregate population-level measurements of smoking prevalence, incidence of relapse, smoking cessation intervention effectiveness, death from smoking-related conditions, smoking cessation intervention cost, and cost of managing a smoking-related illness are output. The underlying cohort is based on the age- and gender-specific distribution of smokers ages 18-70 derived from US Census population tables and US smoking prevalence estimates from the National Center of Health Statistics (NCHS 2013).

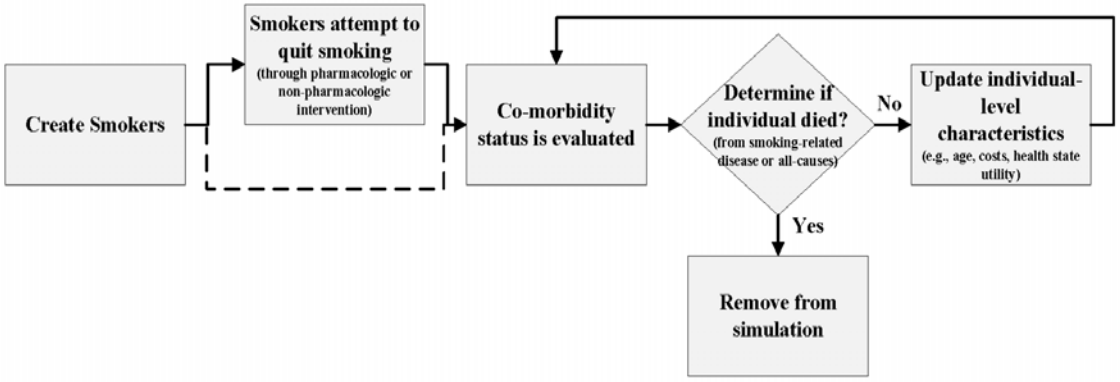


Figure 1: High-level schematic of simulation flow.

2.2 Model Parameters

2.2.1 Efficacy of smoking cessation interventions

Smoking cessation intervention efficacy is measured using continuous abstinence rates (CARs; defined as continuous smoking abstinence since treatment) at one year. Reported efficacy rates for smoking cessation interventions are highly variable; therefore, we calculated a weighted average of effect estimates from various studies to obtain a single estimate of the summary effect size across studies. After reviewing the medical literature, we included 16 studies which were from US populations and reported CAR. CARs across studies per intervention were combined and we computed the weighted average CAR for NRT (13.3%), bupropion (18.4%), varenicline (20.7%), and non-pharmacologic-assisted (4.4%) to estimate intervention success at one year (Table 1, Panel A). The probability of abstinence at one year is estimated from the CARs.

2.2.2 Recidivism

Using published literature, we estimate the likelihood of recidivism after 2 years (16.5%), 3-5 years (9.7%), 6-10 years (4.3%), and ≥11 years (0.6%) in those who successfully quit smoking (Table 1, Panel B). Former smokers are assumed to relapse according to an annual probability based upon the total time abstinent; that is to say, the longer a former smoker has remained abstinent from smoking, the more likely he/she is to continue to refrain. Based on Gilpin, Pierce, and Farkas (1997), although the risk of relapse diminishes significantly over time, no former smoker is ever completely immune to the potential for relapse.

Table 1: Intervention efficacy and recidivism.

A. Intervention efficacy rates[a] at 1 year	
Intervention	**CAR**
NRT	0.133 (0.031 - 0.540)
Bupropion	0.184 (0.063 - 0.303)
Varenicline	0.207 (0.144 - 0.346)
Non-pharmacologic	0.044 (0.040 - 0.130)
B. Probability of recidivism[b]	
Years since quit smoking	**Proportion relapsed**
1-2	0.165 (0.09-0.24)
2-5	0.097 (0.024-0.17)
5-10	0.043 (0.005-0.08)
≥10	0.006 (0.001-0.01)

CAR, continuous abstinence rate; NRT, nicotine replacement therapy

[a]Defined as treatment-specific, CO2-verified, CAR over a one-year time period, i.e. during trial follow-up.

[b]Defined as non-treatment-specific, prolonged abstinence beyond 12 months.

2.2.3 Smoking Related Illnesses

Although smoking is a risk factor for numerous non-communicable diseases and adverse events, we chose to focus on lung cancer, chronic obstructive pulmonary disease (COPD), stroke, and myocardial infarction (MI), for two reasons. First, these four conditions represent significant epidemiologic and economic burdens to American society (US DHHS 2014) and second, good data exist on the probabilities and outcomes for these disease states in a smoking population. Diseases are either present/absent with the possibility of acute exacerbation or improvements in condition. Individuals with lung cancer and COPD are assumed to live with the disease until death. Stroke and MI are modeled as acute events and individuals may have multiple events over a lifetime. Additionally, individuals may develop one or more smoking-related conditions. Estimates of lung cancer, COPD, stroke, and MI were determined by the literature and considered to be dependent upon demographic attributes (e.g., age, gender) and the individual's smoking characteristics (current or former smoker, time since quitting).

Annual lung cancer risk by age, gender, and smoking status were derived from Bain et al. (2004). Lung cancer incidence rates per 100,000 person years for different smoking start age groups in current

smokers were combined and weighted according to light and heavy cigarette use. The combined rates were converted to annual rates (dividing by 100,000) which were used to estimate the annual probability of developing lung cancer. For former smokers, risk estimates were further stratified by time from quitting groups.

An individual may develop different levels of COPD (mild, moderate, or severe). In the absence of good data about COPD transitions between mild, moderate, and severe disease, we assumed that people diagnosed with COPD were diagnosed with mild, moderate, and severe disease according to proportions in the literature and that they remain in those "states" until death. Individuals living with COPD are at risk of COPD exacerbations (minor or major). Annual incidence of COPD exacerbation is modeled for each COPD level by applying the binomial probability distribution. For example, the exacerbation rate per annum for mild disease of 0.79 is converted to an annual probability of 0.5462 [$1\text{-}e^{(0.79)}$]. We assume a maximum of 4 possible COPD exacerbations annually. Since the expected value, $E(x)$, of a binomial distributed random variable is the product of the number of trials [(n); 4] and the proportion of success [(p), COPD exacerbation] we compute the likelihood of independent COPD exacerbations to be 0.1366. Next, we determine how many major exacerbations occurred using the binomial distribution formula and given the annual number of COPD exacerbations and the percentage of minor exacerbations.

Each year, individuals are subject to risk of stroke based on gender and smoking status. To estimate stroke risk, age-standardized rate of stroke per 100,000 person-years (Kelly et al. 2008) were converted to annual probabilities. Risk of first and subsequent strokes is assumed to be the same (i.e., stroke risk is independent of the number of previous strokes).

Risk of MI is dependent on smoking status following Hsia et al. (2004). Weighted 4.5 year probabilities of MI (stratified by current and former smoker) were translated to annual probabilities.

2.2.4 Mortality

We model two causes of death, disease-specific mortality and all-cause mortality, which allowed us to account for death from both smoking-related diseases of interest and death from natural causes. Disease-specific mortality risks are estimated from published case-fatality rates (defined as the proportion of individuals with a disease who die from the disease during a given time period). Information is not available for smoking status-adjusted case fatality rates. Since the incidence rates for disease have been adjusted by smoking status, there is no reason to think that once diagnosed with the disease of interest, smokers should have differential risk of death than non-smokers. Thus, once individuals have the disease of interest, we assume their prognosis is similar.

Mortality assumptions for each smoking-related condition (lung cancer, COPD, stroke MI) differ according to the epidemiology of the specific condition. For example, risk of death from lung cancer depends on gender, age (<50 or ≥50), and number of years an individual has lived with lung cancer (Howlader et al. 2013). Individuals with COPD who have at least one major COPD exacerbation (regardless of mild, moderate, or severe COPD) during a year are at risk of death from COPD during that year. Post-stroke mortality is only possible the year of the stroke event. By contrast, individuals are at risk of death from MI for five years following an MI event and risk varies by gender and time since MI. If a subsequent MI occurs at any time during the 5-years, the 5-year risk period starts over. Two data sources were combined (Parikh et al. 2009; Vaccarino et al. 2001) to estimate MI-related death risks. First, the distribution of deaths from MI at 2 years by gender and age groups from Vaccarino et al. (2001) was used to estimate a case fatality weight for males and females. Then, using case fatality rates at 1 year and 5 years since MI (Parikh et al. 2009), we obtain cumulative case fatality rates for years 1 through 5 assuming a linear increase over time. The gender-specific weights were then applied resulting in case fatality estimates by gender and time since MI (up to 5 years). All case fatality rates were converted to annual probabilities of mortality.

We used life tables from the Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS) on age-specific, gender-specific, all-cause mortality in the American population to estimate non-disease-specific death. The CDC/NCHS data on all-cause mortality in the American population include deaths from diseases we are interested in tracking in the model (i.e. lung cancer, COPD, stroke, MI) but also include data on "healthy" nonsmokers. We expect the incidence of death due to lung cancer, COPD, stroke, and MI to be lower in the healthy, nonsmoking population. As an example of the data used, Table 2 shows the inputs that were used for COPD in the simulation.

Table 2: COPD simulation inputs.

Smoking status	**Lifetime probability of developing COPD**[b] (Pelkonen et al. 2008)		
Current smoker	0.32		
Former smoker[a]	0.13 (0.12-0.14)		
Disease severity	**Percent who develop each COPD disease severity** (Wilson, Devine, and So, 2000)	**Exacerbation frequency per annum** (Spencer et al. 2005)	**Percent of minor exacerbations** (Spencer et al. 2005)
Mild	70.34 (68-73)	0.79	94
Moderate	19.33 (19-20)	1.22	93
Severe	10.33 (8-13)	1.47	90
COPD case fatality rate (Hoogendoorn et al. 2011)			
After a major exacerbation	15.6%		

COPD, chronic obstructive pulmonary disease
[a]We assume a former smoker carries the same risk as a non-smoker.
[b]Converted lifetime rate to annual probability using sex-specific life expectancy tables for smokers at 50 years; former smokers group denominator calculated using the average life expectancy between current smokers and general population.

2.2.5 Costs

Costs of smoking cessation interventions and smoking-related illnesses are accrued over time. *Red Book* (PDR, 2010) costs are used for pharmacologic interventions; for NRT, the costs are weighted based on the usage proportion of gum, patch and lozenges and their recommended use for intermediate smokers. Zero cost is associated with the non-pharmacologic-assisted (i.e., cold turkey) option. The cost of a smoking cessation intervention is a one-time cost paid in year one. Annual cost of living with each co-morbidity and adverse event costs were derived from the literature. All costs were inflated to 2010 $US using the Consumer Price Index inflation calculator. An annual discount rate of 3.0 percent was applied to all economic outcomes. Table 3 shows lung cancer costs used, as an example.

2.2.6 Smoking Cessation Intervention Effectiveness

Smoking cessation intervention effectiveness is measured in quality-adjusted life years (QALYs) which quantifies disease burden in terms of both quality of life (i.e., value of living in a particular state of health) and quantity of life (i.e., number of years alive or time of death). The amount of time spent in a particular health state is weighted by a health state utility score which attempts to reduce multi-dimensional health outcomes to a single representation or measure of health. Health state utility scores represent the severity

of a disease relative to perfect health and are scaled between 0 (indicating death) and 1 (indicating perfect health).

Table 3: Costs of treating lung cancer

Lung cancer, phase-specific costs (Kutikova et al. 2005)	**Cost**
Initial treatment phase (5.7 mos)	$13,759.00
Secondary treatment phase (7.4 mos)	$4,468.00
Terminal treatment phase (5.6 mos)	$11,249.00
% receiving terminal treatment only (no initial treatment)	9%
% receiving secondary treatment after failing initial treatment	29%
% receiving terminal treatment immediately after failing initial treatment	27%

Health state utility values associated with smoking-related conditions in our model are drawn from peer-reviewed literature. We incorporate gender- and age-specific utility values, where possible. We assume that current smokers in good health have a slightly lower utility than former smokers in good health and that quality of life decreases with age, in accordance with the literature (Fiscella and Franks 1996). The simulation differentiates between utilities to be applied short-term at the time of the complication (e.g., acute events such as stroke) and those to be applied long-term in subsequent cycles for more chronic conditions (e.g., lung cancer).

Individuals with lung cancer are assumed to have a reduced health state utility value (utility = 0.5) from the time of diagnosis until simulation termination or death (whichever occurs first). For individuals who have COPD, baseline health state utility values are assigned based on the COPD level (mild, moderate, severe). When a COPD exacerbation occurs, the COPD health state utility is weighted to reflect a 3 month decrement in health, and the decrement amount is based on the number and type (minor or major) of COPD exacerbations. Health state utility scores for a stroke are decremented when the stroke occurs, but improvements in condition are taken into account by allowing the health state utility to be modified for post-exacerbation improvements over time. For example, individuals who have suffered a stroke are considered to have a history of stroke, which is an improvement over the actual stroke event itself, and patients who have suffered more than one stroke are considered to have a history of multiple strokes. Individuals who experience MI are assigned a short-term (1 year) health state utility of 0.857 when the event occurs.

Main outcomes were total and average per person costs, number of clinical events and QALYs. Aggregate QALY over an individual's lifetime is the sum of all QALYs associated with different health states over the lifetime of the individual (i.e., for each year of life in each health state, the relative/weighted health state utility value of that year in that health state). A QALY discount rate of 3.0 percent is applied annually.

3 RESULTS

Cohorts of 100,000 smokers each were simulated to receive one of the five smoking cessation interventions (NRT, bupropion, varenicline, non-pharmacologic-assisted, no intervention) with outcomes followed annually over a horizon of 10 years, 30 years, and over the remaining lifetime, yielding 20 experiments. For each experiment, we obtained 95% confidence intervals (CIs) around the mean output from 30 replications. To reduce variance between experiments, the same random number stream is used for the same purpose across all runs (Stout and Goldie 2008). Table 4 shows results for all interventions, including total cost and QALYs (for 100,000 individuals) and per person costs and QALYs. Note that these are cumulative over the time period, such that for NRT over 10 years, this means the average QALYs per person were 6.77 over ten years. If all people were alive after ten years, this would be about

.67 QALY per year per person, QALYs are zero after death, thus we cannot provide QALYs in a per year per person unit. A step-wise comparison of treatments was conducted. Interventions were ranked by increasing effect and compared to each other sequentially. Table 5 shows the results of the incremental cost effectiveness ratios (ICERs) at 10 years and lifetime. In addition, results show that compared to baseline, varenicline was the most cost-effective at all three time points.

Table 4: Cost and outcomes of treatments at 10 years and lifetime

Treatment	Total Cost	Average Cost per person	Total QALY	Average QALY per person
NRT				
10 years	$1,501,894,815	$15,019	677,396.37	6.77
Lifetime	$7,231,168,614	$72,312	1,476,107.10	14.76
Bupropion				
10 years	$1,494,518,864	$14,945	678,349.63	6.78
Lifetime	$7,213,409,259	$72,134	1,479,146.64	14.79
Varenicline				
10 years	$1,500,281,141	$15,003	678,753.43	6.79
Lifetime	$7,219,640,290	$72,196	1,480,012.41	14.80
Non-pharmacologic				
10 years	$1,484,420,114	$14,844	675,323.34	6.75
Lifetime	$7,243,805,101	$72,438	1,470,603.32	14.71
No Treatment				
10 years	$1,491,221,940	$14,912	674,519.21	6.75
Lifetime	$7,273,359,128	$72,734	1,467,323.19	14.67

Table 5: Incremental Cost-Effectiveness Ratio Results of Comparing Treatments

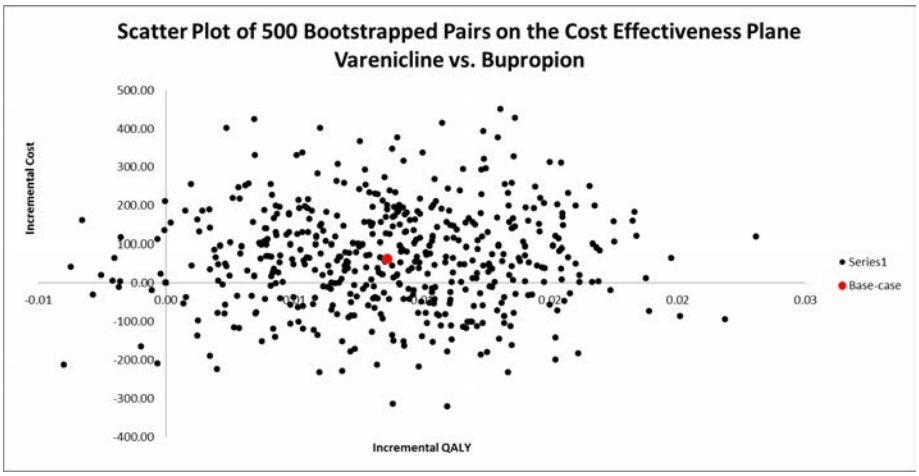
Treatment	Average Cost per person	Average QALY per person	Incremental Cost	Incremental QALY	ICER	Decision
10 year ICER Results						
No Treatment	$ 14,912	6.745				
Non-pharmacologic-assisted	$ 14,844	6.753	$ 68	-0.008	-$8,459	Dominant
NRT	$ 15,019	6.774	$ (175)	-0.021	$8,430	Tradeoff
Bupropion	$ 14,945	6.783	$ 74	-0.010	-$7,738	Dominant
Varenicline	$ 15,003	6.788	$ (58)	-0.004	$14,270	Tradeoff
Lifetime ICER Results						
No Treatment	$ 72,734	14.673				
Non-pharmacologic-assisted	$ 72,438	14.706	$ 296	-0.033	-$9,010	Dominant
NRT	$ 72,312	14.761	$ 126	-0.055	-$2,296	Dominant
Bupropion	$ 72,134	14.791	$ 178	-0.030	-$5,843	Dominant
Varenicline	$ 72,196	14.800	$ (62)	-0.009	$7,197	Tradeoff

Notes: Compared cost of interventions for 5 treatment arms. Ranked strategies by increasing QALY & compared cost-effectiveness between the lowest QALY with the strategy that has the next highest QALY

QALY, Quality-Adjusted Life Year; ICER, Incremental Cost-Effectiveness Ratio; NRT, Nicotine Replacement Therapy

An uncertainty analysis between the two most cost-effective treatments, varenicline and bupropion, was also conducted. These results are shown in Figure 2; the SE quadrant indicates vareniclene dominates bupropion in 14.6% of cases while the NE quadrant indicates vareniclene is more effective but more expensive in 83.7% of cases.

Figure 2: Cost-effectiveness plane of Vareniclene versus Bupropion at lifetime



In addition to the cost-effectiveness analysis, the simulation allows us to conduct a comparative analysis of the treatments in terms of the prevalence and mortality of smoking related conditions. For example, Table 6 shows the simulated incidence of smoking-related conditions.

Table 6: Simulated Incidence of comorbidities, 10 years and lifetime

Treatment	Percent who developed at least one smoking-related condition	Percent who had atleast one MI event	Percent who had at least one Stroke	Percent who developed Lung Cancer	Percent who developed COPD
NRT					
10 years	16.51	4.37	5.69	3.37	3.86
Lifetime	61.07	14.24	18.04	31.06	12.40
Bupropion					
10 years	16.38	4.34	5.64		3.81
Lifetime	60.88	14.21	18.03	30.91	12.30
Varenicline					
10 years	16.34	4.33	5.65	3.34	3.78
Lifetime	60.79	14.16	17.99	30.90	12.25
Non-pharmacologic					
10 years	16.69	4.40	5.72	3.42	3.95
Lifetime	61.42	14.34	18.10	31.30	12.56
No Treatment					
10 years	16.79	4.42	5.72	3.45	4.01
Lifetime	61.70	14.37	18.15	31.46	12.76

4 CONCLUSION

While the QALYs gained on a per person basis are small, note that treatments are cost saving over a lifetime, which make them appealing to policy makers, who usually deal with trading off cost for QALYs. Furthermore, extrapolation of average per person costs and QALYs to the full population of US smokers who desire to quit smoking indicates that if 32.2 million smokers attempted a single treatment of vareniclene, the potential lifetime savings are $17.3Billion, with 11.9Million QALYs gained. It is critical

for policymakers and insurers to encourage smoking cessation and consider providing incentives for smoking cessation as early as possible and for clinicians and patients to engage in shared decision making about which treatment strategy would be best for the patient in terms of long-term abstinence, overall resources invested, and cumulative health risks avoided over time. Although the estimates resulting from this model will be specific to the associated clinical process being modeled, many of the modules created for this study are generic and can easily be transferred to other disease models. It is believed that this model will aid decision makers in recognizing the impact that preventative-care initiatives will have, and to evaluate possible alternatives.

One limitation of the model is that we do not consider costs associated with extended life due to avoiding mortality from smoking-related diseases. Including these costs is a potential area for future work.

The use of a DES model presented several advantages over other methodologies, such as Markov or decision tree models. We are able to incorporate heterogeneity of individuals as well as disease structure and timing. Furthermore, it provides a framework for further incorporating individual behavior or reaction to interventions, as is one of our planned extensions.

In particular, we are currently incorporating a choice model, informed by national survey data, so that smokers will choose their intervention based on individual-level attributes (clinical and socio-demographics) and product-level attributes (e.g. cost, side-effects). This will not only allow us to assess preferences for smoking cessation approaches, but will also allow us to estimate the current costs of smoking, as well as the benefits of different policies that affect product attributes, such as taxes.

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