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Estimating the Health Impacts of Tobacco Harm Reduction Policies: A Simulation Modeling Approach

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With adult smoking prevalence rates declining too slowly to reach national objectives, opinion leaders are considering policies to improve tobacco-related outcomes by regulating the composition of cigarettes to be (1) less harmful and/or (2) less addictive. Because harm reduction efforts may actually encourage higher cigarette consumption by promoting a safer image, and addictiveness reduction may increase the harmfulness of cigarettes by encouraging compensatory smoking behaviors, policymakers must consider the tradeoffs between these two approaches when proposing legislation to control cigarette content. To estimate health impacts, we developed a dynamic computer model simulating changes in the age- and gender-specific smoking behaviors of the U.S. population over time. Secondary data for model parameters were obtained from publicly available sources. Population health impacts were measured as change in smoking prevalence and the change in cumulative quality-adjusted life-years (QALYs) in the U.S. population over 75 years. According to the risk-use threshold matrix generated by the simulation, modifying cigarettes to reduce their harmfulness and/or addictiveness could result in important gains to the nation's health. Addictiveness reduction efforts producing a 60% improvement in smoking behavior change probabilities would produce a net gain in population health at every plausible level of increase of smoking-related harm that was modeled. A 40% reduction in smoking-related harm would produce a net QALY gain at every level of behavior change considered. This research should prove useful to policymakers as they contemplate giving the FDA the authority to regulate the composition of cigarettes.

KEY WORDS: Harm reduction; QALYs; reduced nicotine cigarettes; risk-use equilibrium; system dynamics

1. INTRODUCTION

Cigarette smoking is now widely acknowledged as the single leading preventable cause of death in the United States.[1] Smoking causes more fatalities each year in this country than AIDS, alcohol, cocaine, heroin, homicide, suicide, motor vehicle crashes, and fires combined.[2]

Although numerous policies have been implemented to reduce tobacco use with varying degrees of success, smoking prevalence in the United States continues to exceed 20%. In fact, given that in 1995, 25% of the adult population were smokers, and in 2002, 23% smoked,[3] the rate of decline has not been at a sufficient pace to achieve the Healthy People 2010 objective of reducing smoking prevalence among adults to 12% or less.[4,5] Although 70% of current smokers

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report wanting to quit and 34% actually try to quit each year, only 10% of those who attempt to quit succeed for even one year.[6]

Opinion leaders who wish to see an acceleration in the decline of smoking prevalence have taken a renewed interest in supplementing current efforts with policies to change the composition of cigarettes to reduce tobacco-related harm further.[7] The Institute of Medicine, for example, has produced a comprehensive report making a case for *harm reduction*, defined as efforts to reduce the mortality and morbidity risk of smoking without completely eliminating tobacco use.[6] The American Medical Association, on the other hand, advocates an *addictiveness reduction* approach, which calls for a reduction in the amount of nicotine found in cigarettes to reduce smoking prevalence.[8]

The notion of harm reduction is not a new one, although most previous efforts toward this end have been more cosmetic than substantive. "Low tar" cigarettes, introduced in the 1950s, were essentially "safer image" products rather than being truly less hazardous in any meaningful sense.[9,10] Researchers have suggested that, at a minimum, harmful additives such as acetaldehyde and pyridine, included to enhance nicotine's addictive effects, can be removed from cigarettes.[11] In addition, companies may be able to remove or reduce some of the major classes of carcinogenic substances such as the nitrosamines, aldehydes, polycyclic aromatic hydrocarbons (PAHs), and trace heavy metals. Reduced exposure to toxins may result in reduced harm, although no direct scientific evidence of this exists at present.

Farone[12,13] has suggested that the Environmental Protection Agency (EPA) might extend its current maximum allowable exposure levels to cigarettes. Cigarettes contain known carcinogens that, if found at the same level elsewhere in the environment, would be considered in violation of current EPA standards. For example, a single unfiltered cigarette contains 100 μg of formaldehyde, 120 μg of arsenic, and 1400μg of acetaldehyde, even though the EPA requires that daily exposure to these chemicals not exceed 40 μg, 0.06 μg, and 90 μg, respectively.

Though reduced-toxin cigarettes have a certain obvious appeal, detractors express concern that when the population perceives cigarettes to be safer, tobacco use may increase.[14] The experience with filter cigarettes and low tar cigarettes offers evidence that the public will consume a seemingly safer product in lieu of avoiding tobacco use entirely.[10,15] However, a cigarette that is truly safer, and not merely promoting a "safer image," would have the potential to reduce the excess mortality and morbidity experienced by those who continue to smoke and those exposed to second-hand smoke.

Unlike reduced-toxin cigarettes, the addictiveness reduction approach does not improve the safety of smoking, but seeks to reduce the prevalence of smoking by making the behavior less habit-forming. Based on the criteria of the World Health Organization,[16] the U.S. Surgeon General,[17] and the American Psychiatric Association,[18] nicotine is a dependence-producing drug. Reducing the nicotine level in cigarettes would prevent smokers from maintaining their dependence on the substance.[19] It is the compulsion for nicotine that exposes smokers to toxins in cigarettes—the carcinogens, teratogens, and carbon monoxide—that cause most smoking-induced diseases.

Faced with reduced levels of nicotine in their cigarettes, many smokers may quit. However, scientific evidence with low-yield cigarettes indicates that those who continue to smoke may compensate for the loss of nicotine by smoking more cigarettes[7] or smoking each cigarette to a shorter butt length.[20,21] Such compensatory smoking behaviors may increase exposure to the harmful components of cigarette smoke and may offset some of the improvements in population health resulting from lower smoking prevalence.

Another unintended consequence of reducing nicotine levels is that demand for higher-nicotine cigarettes may encourage the smuggling of cigarettes into the United States. There are ways to reduce smuggling of cigarettes but it will be impossible to completely curtail the black market, and the availability of cigarettes with high levels of nicotine would dilute the effects of limiting the nicotine content of cigarettes.

Policies to modify the composition of cigarettes to reduce the public health burden of smoking may employ reducing toxins, eliminating nicotine, or a combination of both. There is a complex interaction among different variables for any of these policy choices. The harm reduction approach may actually increase the number of addicted smokers by promoting an image that cigarettes are safe, and the addictiveness reduction approach may encourage compensatory smoking behaviors that cause more harm to those who continue smoking despite reduced nicotine levels. Because improving the safety of cigarettes on one dimension may make them more dangerous on the other, policymakers must consider the impacts of changing the composition of cigarettes on both aspects simultaneously.

This article employs a dynamic simulation modeling approach to produce a risk-use threshold matrix reporting estimates of the long-term population health consequences of a range of tobacco regulation policies that manipulate the contents of cigarettes to impact their harmfulness and addictiveness. In our previous work, we presented population health impacts of reducing toxins in cigarettes(22) (reducing harm while increasing prevalence) and health impacts of reducing nicotine in cigarettes(23) (lowering addictiveness while worsening smoking-related harm). Here, we revisit those tradeoffs and expand our scope to include scenarios in which modifying cigarette composition increases harmfulness and addictiveness simultaneously, and scenarios in which both aspects decrease simultaneously. Additionally, we extend the simulation period from 50 to 75 years to ensure all potential smokers are exposed to the impacts of modified cigarettes so that the total cumulative health effects are captured in the model, and we compare these effects over multiple time points.

In the next section, we describe the inputs and assumptions that govern our model, and our methods for calibrating and running the simulation to produce estimates of long-term cumulative population health outcomes. We then summarize these outcome estimates for a range of plausible scenarios and, finally, we discuss the interpretation of these results and some limitations of our work.

2. METHODS

Levy *et al.*(24) provide a review of several models that have been developed to simulate tobacco control policies. To estimate the anticipated population health gains or losses from a hypothetical federal policy modifying cigarettes to reduce their addictiveness, harmfulness, or both, we developed a computer simulation model using Vensim.(25) This is a flexible model that has been used to explore several tobacco control policies.(22,23,26–28) The model estimates births, deaths, aging, net migration, and smoking status distributions for the population over the next 75 years. Ultimately, the simulation calculates the anticipated cumulative long-term public health gains or losses assuming different patterns of tobacco use and levels of harm associated with smoking. The model schematic is given in Fig. 1.

To start the present simulation, we initialized the model with the number of people in the U.S. population in the year 2003. We divided the population into cohorts according to gender, initial age,(29) and smoking status (current, former, or never smoker),(30–32) and simulated annual transitions over 75 years using change probabilities that vary by age, gender, smoking status, and year. The number of live births for each year, for example, is computed by multiplying the number of women in each age cohort by the corresponding age-specific fertility rate. Similarly, the number of deaths each year is computed by multiplying the number of people of each combination of age, gender, and smoking status by that group's respective mortality probability,(33,34) and taking the sum across all groups for each year. Net migration rates reflect changes due to people moving in and out of the population for each gender and age group.(33,35)

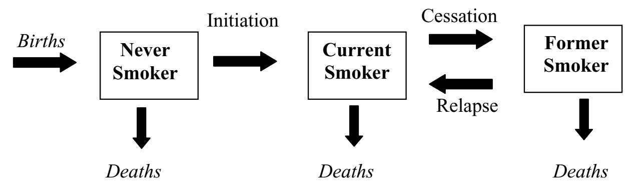


Fig. 1. Model schematic.

The population is divided into three smoking status categories based on their smoking behavior participation—*never smokers*, who have smoked less than 100 cigarettes in their lifetime, *current smokers*, who have smoked 100 or more cigarettes in their lifetime and have smoked in the past 30 days, and *former smokers*, who have smoked 100 or more cigarettes in their lifetime, but none in the past 30 days. Every member of the initial population is assigned to one of these three smoking status categories according to external prevalence estimates.(30,36,37)

For every year that follows, the number of never smokers within each age by gender group is multiplied by the corresponding age- and gender-specific initiation probability to determine how many people leave the never smoker category to join the current smoker category. The number of current smokers (by age and gender group) is multiplied by group-specific cessation probabilities to obtain the number of individuals subtracted from the current smoker group and added to the former smoker group. Similarly, the number of former smokers (by age and gender group) is multiplied by group-specific relapse probability to indicate how many former smokers will become current smokers again. Age- and gender-specific initiation, cessation, and relapse probabilities were derived from multiple sources.(35,37,38)

In our model, gains or losses in an individual's health are measured with quality-adjusted life-years (QALYs). The QALY measure, recommended by the U.S. Task Force on Cost-Effectiveness in Health and Medicine,[39] combines improvements in length of life and health-related quality of life into a single measure. Quality of life data for current, former, and never smokers of various ages and genders were obtained from the Quality-of-Well-Being Scale (Kaplan, 1999, personal communication).

Current smokers have lower health-related quality of life than former smokers, who have lower health-related quality of life than never smokers. For example, the QOL values for males in the 40- to 44-year age group are 0.82, 0.88, and 0.90 for current, former, and never smokers, respectively. The QOL values for females in the same age group and smoking status are 0.83, 0.87, and 0.88, respectively. Health-related quality of life values decrease as age increases.

We estimated mortality hazard functions using mortality data for each gender[29] and smoking status[33] and built those into the model to simulate improvements in length of life and QALYs. Because we are not evaluating the future benefits of an action against present costs, we did not discount our projected results.

2.1. Model Calibration

To ensure the accuracy of the model, we calibrated it against reliable external estimates of (1) smoking prevalence (never, current, and former), (2) population size (by age and gender), and (3) life expectancy (by age, gender, and smoking status). We compared each model output with reliable existing external estimates, and then made adjustments to select model parameters to improve correspondence. We repeated this exercise until all model outputs were within 3% of corresponding external estimates.

To calibrate smoking prevalence, we started the model in 1995, loading it with historical data. We then ran the model forward and observed the predicted prevalence of current smokers, former smokers, and never smokers in every year from 1995 to 2003. We corrected discrepancies in never smoker prevalence by changing the initiation rate and discrepancies in current and former smoker prevalence by changing cessation and relapse rates. As an example, our model estimated that 23.6% of the adult population would be current smokers in 2000, while 22.5% would be former smokers, and 53.9% never smokers. These estimates compared favorably to estimates from the National Health Interview Survey,[40] which reported prevalence as 23.2%, 22.2%, and 54.6%, respectively.

To calibrate population size, we ran the model forward through the year 2075. We compared population counts for years 2025, 2050, and 2075 with U.S. Census middle series projections for those years.[29] To improve the correspondence between model estimates and Census projections, we made slight increases to fertility and decreases to mortality. In the end, model estimates of population size for both genders and all age groups differed from Census projections by less than 1% for the future years 2025, 2050, and 2075 (for all years, $R^2 = 0.99$).

Finally, we compared the simulated life expectancy of current, former, and never smokers to external estimates from the American Academy of Actuaries[41] and Hatton Financial,[42] revising mortality rates to improve correspondence. Life-expectancy estimates vary by age and gender, but as one example, the model estimated that a 45-year-old female never smoker would live 39.37 additional years and a female current smoker of the same age would live 33.94 additional years. These life-expectancy estimates compare favorably with insurance industry estimates of 39.33 and 33.89 years, respectively.

2.2. Modeling Harm Modification

Whether cigarettes can be made safer by removing carcinogens and other hazardous substances is still an open question. Tobacco use may increase but those who choose to smoke may live longer because the incidence of fatal cancers and other diseases may decline, and may enjoy a higher quality of life due to lower incidence of smoking-related disability.

We estimated the QALY gains or losses by modifying the differential between current smokers and never smokers for both mortality and morbidity. In response to evidence suggesting that the premature death of approximately one-half of cigarette smokers can be attributable to smoking,[43] we considered the maximum improvement to be 50%. However, because the degree of any improvement is uncertain, we simulated hypothetical reductions in the differential in mortality and morbidity between current smokers and never smokers by amounts ranging from 0% to 50%. Similar adjustments were made in the differential between never smokers and former smokers in mortality and morbidity risk.

We also considered the possibility that changes in the content of cigarettes, or other changes in the social and policy contexts of tobacco use, may result in compensatory smoking behaviors (e.g., consuming more cigarettes per day,[10] increasing puff volume per cigarette[19,20]) that make smoking even more harmful than in the status quo. Therefore, we also modeled outcomes assuming that the differential mortality and morbidity risks for smokers versus never smokers increase by between 0% and 50%. In total, we model scenarios assuming 11 levels of harm modification, in 10% increments from −50% to +50% change (−50%, −40%, −30%, . . . , 30%, 40%, 50%).

For example, the mortality risk for a 40-year-old male smoker is 0.0052 and for a never smoker of the same age and gender is 0.0022, for a mortality risk differential of 0.0030. An intervention that reduces smoking attributable harm by 20%, therefore, would be assumed to reduce the risk differential to 0.0006 (0.0030 × 20%), resulting in no change in the mortality risk for never smokers, but a reduction of mortality risk for current smokers to 0.0046 (0.0052 − 0.0006). A 20% increase in smoking-attributable health risk, on the other hand, would raise the group-specific mortality to 0.0058 (0.0052 + 0.0006).

Smoking-attributable morbidity was computed in a similar fashion using age- and gender-specific quality of life (QOL) scores. If a male smoker is assigned a QOL score of 0.845 for his 40th year of life, and a male never smoker gets a QOL of 0.880 for the same year, the differential would be 0.035. Under the same 20% harm reduction scenario, the QOL differential would reduce by 0.007 (0.035 × 20%), leaving the never smoker's QOL the same, but raising the QOL for a 40-year-old current smoker to 0.852 (0.845 + 0.007). Increasing the harm of smoking by 20% would lower the same group's QOL to 0.838 (0.845 − 0.007). Similar calculations were performed for all modeled outcome scenarios for every age and gender group.

We also considered that at the time of any change in federal policy to regulate cigarette content, considerable irreparable damage would already have been done to the health of people who had been smoking for some time, even if they immediately began to smoke reduced-toxin cigarettes. To simulate this, we assumed that the improvement in the survival prospects of current smokers would be in proportion to the amount of time they smoked reduced-toxin versus regular cigarettes. We used the number of years that had passed since each smoker was 18 years old (i.e., current age −18) as a proxy for this amount of time, which is a reasonable assumption considering that 89% of smokers begin smoking before 18 years of age.[32] We modeled any change in the mortality of smokers as a function of age and, as the simulation progressed over the 75 years, as a function of time since cigarette content regulations were introduced. We estimated reductions in the mortality and morbidity of former smokers in the same fashion.

2.3. Modeling Addictiveness Modification

We evaluated the health implications of efforts to reduce the likelihood of smoking to reach addictive levels by reducing nicotine contents in cigarettes.

Changes in population smoking behavior are modeled via three mechanisms. First, we assume that reducing the addictiveness of tobacco would reduce the probability of initiating smoking for every age and gender. Second, we assume the probability of cessation, which also varies by age and gender, would increase. And third, we assume former smokers of every age and gender would have a decreased probability of relapse.

Additionally, we consider the possibility that changes in the social and policy contexts of smoking behavior (such as promoting an image of "safer" cigarettes) could actually increase the probability of becoming a smoker. For this reason, we also modeled the outcomes of a worsening of the addictiveness of cigarettes by assuming initiation and relapse probabilities increase, and cessation probability decreases.

In every case, we assume that all three behavior change probabilities are adjusted by the same factor in each addiction risk modification scenario. For example, in the status quo condition, a 25-year-old female has an initiation probability of 0.0078 if she is a never smoker, a cessation probability of 0.0123 if she is a current smoker, and a relapse probability of 0.0107 if she is a former smoker. If we assume that addictiveness improves by 10% for the population, this initiation probability would decrease to 0.0070, cessation rate would rise to 0.0135, and relapse rate would fall to 0.0096. If addictiveness worsens by 10%, the age and gender group-specific initiation rate would instead rise to 0.0086, cessation rate would fall to 0.0111, and relapse rate would increase to 0.0118. In the interest of thoroughness, we present outcome estimates for a broad range of plausible behavior change probability values in increments of 10% from −80% to +80%.

2.4. Producing a Matrix of Plausible Outcomes

The population-level effects of modifying the composition of cigarettes have never been observed. Therefore, it is not possible to estimate accurately the change in smoking behavior or change in mortality following a federal mandate to alter the content of cigarettes in any specific way. Instead, we simulated various levels of change in both smoking behavior and mortality to estimate a range of possible health outcomes.

After running a model assuming no change in policy (status quo), we simulated each hypothetical change in mortality and morbidity combined with a change in tobacco use behavior over a 75-year period to provide a matrix of plausible outcomes. For the first six years of the model run, we assume no changes in behavior or smoking-related health risks to account for lag time between when a policy regulating the content of cigarettes is introduced and when it is acted upon.

For each model run, we estimated the total cumulative QALYs that would be expected to accrue to the entire U.S. population over that period, and estimated the adult smoking prevalence for the population at the endpoint. We then calculated the difference in QALYs between status quo and policy model runs to estimate the long-term changes in population health that would be anticipated due to modified cigarette content. Results are presented in Tables I and II.

For every behavior scenario simulated, we estimated a "break-even point," that is, the level of tobacco-related health risk modification that would result in zero net change in QALYs for that level of behavior change. Break-even points were computed by fitting a regression line to predict net QALYs from the level of change in smoking-related health risk for each of the 11 simulated behavior change scenarios. We determined the break-even point by solving for the level of change in smoking-related health risk that produces zero net QALYs in the resulting regression equation within each behavior change scenario.

3. RESULTS

Table I presents the cumulative change in QALYs (in millions) accrued by the population over the course of the 75-year simulation period assuming different net effects of changing the composition of cigarettes. The row headings (behavior change) indicate the net percentage change in initiation, cessation, and relapse probabilities from the status quo. Positive values indicate changes in these probabilities that would reduce the number of smokers in the population, and negative values indicate changes that increase smoking prevalence. For example, the values presented in the row labeled "20%" provide the incremental accumulation of QALYs for each level of change in smoking-related health risk assuming that initiation probabilities for never smokers of every age and gender decrease by 20%, cessation probabilities of ever smokers increase by 20%, and relapse probabilities of former smokers decrease by 20%. Similarly, the "−30%" row presents the outcomes of initiation and relapse probabilities increasing by 30% and cessation probability decreasing by 30%. The "0%" row represents no change from the status quo in smoking behavior change probabilities. For simplicity's sake, behavior changes that produce a net reduction in population smoking prevalence (represented in rows with positive headings) will be referred to as "improved," and behavior changes that produce a net increase in population smoking prevalence will be referred to as "worsened."

The column headings of Table I (change in smoking-related health risk) indicate the net percentage change in the excess mortality and morbidity risk for ever smokers (current and former smokers) of every age and gender. The outcomes presented in columns with positive headings reflect a reduction in smoking-related mortality and morbidity risk, such that the "50%" column reflects excess health risk for current smokers is cut in half. Negative column headings indicate the assumption that smoking is even more hazardous than it is in the status quo. For example, the "−50%" column presents the net accumulated QALYs for each level of behavior change assuming the excess risk for mortality and morbidity for current smokers increases by 50%. The column labeled "0%" gives outcomes assuming no change from status quo in excess health risk. Again, to simplify the discussion of these probability changes, we refer to changes that reduce the excess health risk for smokers as "improved" and changes that increase the excess health risk for smokers as "worsened."

The cumulative net QALYs accrued over the 75-year period assuming various levels of behavior change and smoking-related health risk can be read from Table I by finding the cell of the table that corresponds with the row and column headings of interest. For example, if the excess smoking-attributable health risk improves by 20% and smoking behavior change probabilities worsen by 30%, the population would accrue a net positive 13 million QALYs (reported

Table I. Cumulative Change in Quality-Adjusted Life-Years (in millions) over 75 Years Depending on the Change in the Smoking-Related Health Risk and the Change in Tobacco Use Behavior

		Change in Smoking-Related Health Risk										
		(<- Worse)						(Improve ->)				
		−50%	−40%	−30%	−20%	−10%	0%	10%	20%	30%	40%	50%
Behavior Change	(Improve –>)	80%										
	80%	122	152	183	215	248	281	315	350	385	422	460
	70%	75	108	141	175	210	245	281	318	356	395	435
	60%	30	64	99	135	172	210	248	287	327	369	411
	50%	−16	21	58	96	135	174	215	256	299	342	387
	40%	−62	−23	16	57	98	139	182	226	270	316	363
	30%	−107	−66	−25	17	60	104	149	195	242	290	340
	20%	−152	−109	−66	−22	24	70	117	165	214	264	316
	10%	−197	−152	−107	−61	−13	35	84	134	186	239	293
	0%	−242	−196	−148	−100	−50	0	51	104	158	213	269
(<– Worse)	−10%	−287	−239	−189	−139	−87	−35	19	74	130	187	246
	−20%	−333	−282	−230	−178	−124	−70	−14	43	102	161	223
	−30%	−378	−325	−272	−217	−162	−105	−47	13	73	136	199
	−40%	−424	−369	−313	−257	−199	−140	−80	−18	45	110	176
	−50%	−470	−413	−355	−296	−236	−175	−113	−49	17	84	152
	−60%	−516	−457	−397	−336	−274	−211	−146	−80	−12	58	129
	−70%	−562	−502	−440	−377	−312	−247	−180	−111	−41	31	105
	−80%	−609	−547	−483	−417	−351	−283	−214	−143	−70	5	81

at the intersection of the "+20%" column and the "−30%" row). If smoking-related health risks worsened by 30%, however, and behavior change probabilities only improved by 20%, the population would accrue a net negative 66 million QALYs (reported at the intersection of the "−30%" column and the "20% row).

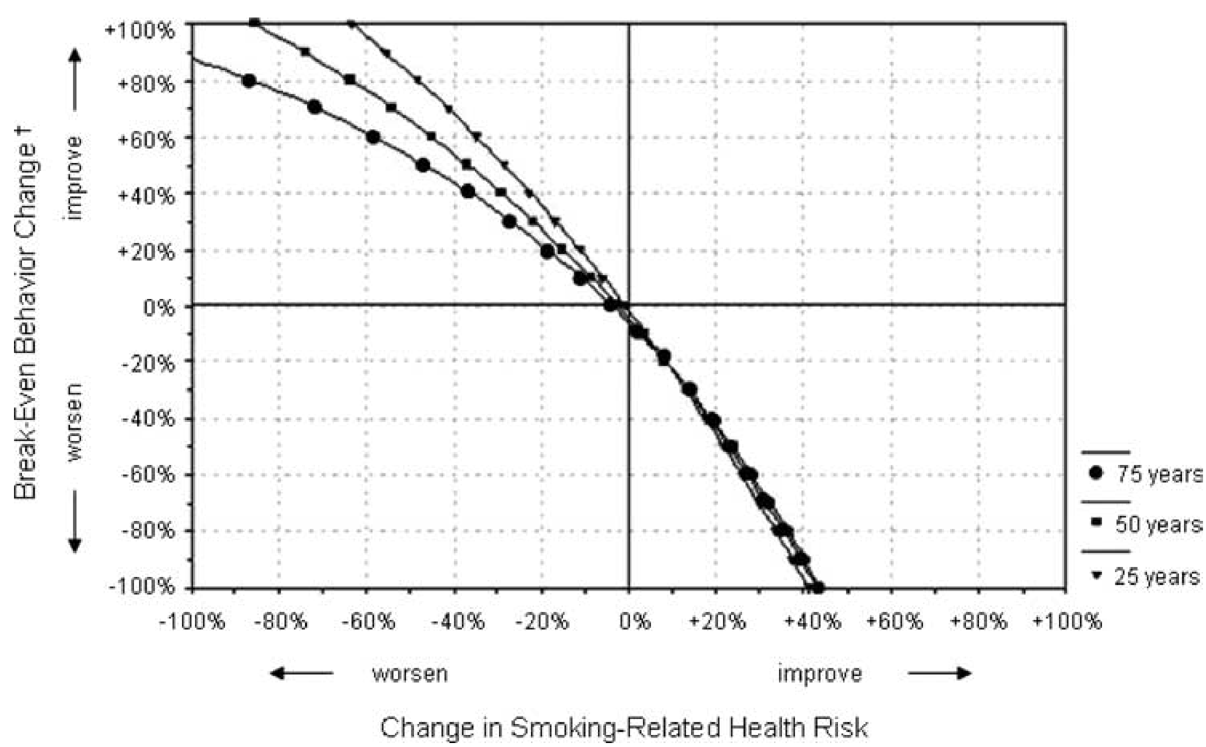
Table II employs a format similar to Table I to present the smoking prevalence at the end of 75 years assuming varying levels of smoking-related health risk and behavior change. For example, if cigarettes are safer such that the excess health risk for ever smokers is worsened by 30% (in the "−30%" column) and if behavior change probabilities improve by 20% (in the "+20%" row), then the prevalence of current smokers would decrease from a status quo level of 22.3% to 17.0% of the population after 75 years.

Fig. 2 plots the "break-even" points in terms of cumulative QALYs for each outcome scenario—that is, the level of behavior change that would be necessary to offset a given percentage of change in smoking-related health risk to produce a net change in total accumulated QALYs of zero. For example, for a 75-year simulation, to offset the decline in QALYs produced by a 40% worsening of smoking-attributable health risk (represented in the figure at the "−40%" point on the *x*-axis), behavior change would have to improve by approximately 40%. The net increase in cumulative QALYs associated with a 10% improvement in smoking-related health risk (the "10%" point on the *x*-axis) would be completely negated by a worsening in behavior change of around 20%. Any scenario that can be represented above the plotted curve would result in a net gain in QALYs and scenarios below the curve would cause a net loss in QALYs.

Fig. 2 also compares the cumulative QALY break-even functions for three time points: 25, 50, and 75 years after implementing a policy change to alter the composition of cigarettes. For scenarios in which the health risks associated with smoking improve (represented on the right half of the figure), the amount that behavior change probabilities must worsen to offset the health benefits of harm reduction remains approximately constant for all time points. In scenarios where smoking becomes more harmful (the left half of the figure), the relative impact of behavior change over harm reduction on population health increases as time goes by. For example, after 25 years, a 50% improvement in behavior change probabilities would be necessary to cancel out the cumulative health declines following a 30% worsening of smoking-related harm. After 75 years, however, only a slightly more than 30% improvement in behavior change would be sufficient to offset the health

Table II. Estimated Prevalence of Current Smokers in 75 Years Depending on the Change in the Smoking-Related Health Risk and the Change in Tobacco Use Behavior

		Change in Smoking-Related Health Risk										
		(<- Worse)						(Improve ->)				
Behavior Change		−50%	−40%	−30%	−20%	−10%	0%	10%	20%	30%	40%	50%
(Improve −>)	80%	4.4	4.4	4.4	4.5	4.5	4.5	4.5	4.5	4.5	4.6	4.6
	70%	6.3	6.3	6.3	6.3	6.4	6.4	6.4	6.4	6.5	6.5	6.5
	60%	8.2	8.2	8.3	8.3	8.3	8.4	8.4	8.5	8.5	8.5	8.6
	50%	10.2	10.3	10.3	10.4	10.4	10.4	10.5	10.5	10.6	10.7	10.7
	40%	12.4	12.4	12.4	12.5	12.5	12.6	12.7	12.7	12.8	12.9	12.9
	30%	14.5	14.6	14.7	14.7	14.8	14.8	14.9	15.0	15.1	15.1	15.2
	20%	16.8	16.9	17.0	17.0	17.1	17.2	17.2	17.3	17.4	17.5	17.6
	10%	19.2	19.3	19.3	19.4	19.5	19.6	19.7	19.8	19.9	20.0	20.1
	0%	21.8	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8
(<− Worse)	−10%	24.2	24.3	24.3	24.4	24.5	24.7	24.8	24.9	25.0	25.1	25.3
	−20%	26.8	26.9	27.0	27.1	27.2	27.3	27.5	27.6	27.7	27.9	28.0
	−30%	29.5	29.6	29.7	29.8	30.0	30.1	30.2	30.4	30.5	30.7	30.8
	−40%	32.3	32.4	32.5	32.7	32.8	33.0	33.1	33.3	33.4	33.6	33.8
	−50%	35.2	35.3	35.5	35.6	35.8	35.9	36.1	36.2	36.4	36.6	36.8
	−60%	38.2	38.4	38.5	38.7	38.8	39.0	39.2	39.3	39.5	39.7	39.9
	−70%	41.3	41.5	41.6	41.8	42.0	42.1	42.3	42.5	42.7	42.9	43.2
	−80%	44.5	44.7	44.9	45.0	45.2	45.4	45.6	45.8	46.0	46.3	46.5



†Break-Even Behavior Change is the amount by which behavior change probabilities must be altered to offset the cumulative health impacts of a given change in smoking-related health risk to produce zero net accumulation of QALYs compared to the status quo. For example, the net increase in cumulative QALYs associated with a 10% improvement in smoking-related health risk (the +10% point on the *x*-axis) would be completely negated by a worsening in behavior change of around 20% (the −20% point on the *y*-axis). Any scenario that can be represented above the plotted curve would result in a net gain in QALYs and scenarios below the curve would cause a net loss in QALYs.

Fig. 2. Break-even behavior change probability to offset change in the smoking-related health risk (25, 50, and 75 year simulations).

detriment produced by the same 30% worsening in the harmfulness of smoking. This is because the annual health benefits of reducing the addictiveness of cigarettes increases with each passing year.

4. DISCUSSION

Efforts to reduce the public health burden of smoking by changing the composition of cigarettes involves tradeoffs between making cigarettes less hazardous and making smoking less attractive. Detractors fear that a harm reduction approach will encourage smoking by promoting the impression that cigarettes are safer than they actually are.(15) Reducing nicotine, on the other hand, may reduce smoking prevalence but invite more harmful compensatory smoking practices for those who do not quit.(44)

The value of computer simulation is that it offers a way to combine all concerns and the best available data into a model to estimate the likely cumulative impact on population health over the long term. Prior work includes that of Sumner(45) who modeled the impact of replacing cigarettes with nicotine inhalers and Kozlowski *et al.*(46) who discussed the risk–use equilibrium. Our work differs from prior research as we quantify the gain in population health that might be expected for a given level of tobacco risk and use. Because we cannot predict exactly how changing the composition of cigarettes will impact their addictiveness or their harmfulness, we have, instead, produced a risk-use threshold matrix for a range of smoking-related health risk and behavior change scenarios that decisionmakers can use to evaluate several interventions. The range of plausible scenarios can be narrowed as more data on the outcomes of modifying cigarettes become available.

Numerous mechanisms other than directly manipulating the level of toxins in cigarettes can impact smoking-related health risk. Compensatory smoking associated with reduced nicotine levels, which we have already mentioned, or substituting low-nicotine cigarettes with other harmful tobacco products would worsen the health risks associated with tobacco use. The persistence of high-toxin cigarettes via the black market may dilute the improvement in mortality risk associated with mandating lower toxin levels. Improved medical treatment of smoking-related disease would reduce the health risk of smoking, independent of the content of cigarettes. Similarly, behavior change may be impacted by mechanisms other than altering nicotine content. Other anti-smoking interventions such as education programs, increased taxes, and improved control of youth access to cigarettes may also improve initiation, cessation, and relapse rates in the population. On the other hand, as mentioned before, promoting a safer image for cigarettes may actually encourage tobacco use. Although this article discusses policies to regulate the content of cigarettes, the risk-use threshold matrix presented can be used to evaluate the long-term health effects of any intervention that impacts some combination of the addictiveness and/or harmfulness of cigarettes.

The upper-left quadrant of the matrix (Table I) represents any scenario in which smoking prevalence declines (e.g., by lowering nicotine levels or restricting the supply of cigarettes through stricter access control laws) but the harmfulness of smoking increases (e.g., from compensatory smoking, or an increased demand for less safe tobacco products through black markets and other means). The upper-right quadrant describes scenarios in which smoking becomes simultaneously less attractive (e.g., reducing smoking participation with higher excise taxes) and less harmful (e.g., if the same taxes also reduce the number of cigarettes consumed by those who continue to smoke). Values in the lower-right quadrant reflect situations in which smoking becomes more prevalent (e.g., by promoting an image that cigarettes are safer) but less harmful (e.g., reduced toxin cigarettes or improved treatment of smoking-related disease). Values in the lower-left quadrant reflect increases in both the prevalence and harmfulness of smoking (e.g., increased smoking participation and consumption due to effective marketing by tobacco companies).

When the impact of an intervention is well understood on one of the two change axes, but not on the other, the risk-use threshold matrix can be used to conduct sensitivity analyses to determine a plausible range of impacts. For example, if a strong consensus exists that a proposed policy will create a 30% improvement in smoking behavior, but its impact on the harm experienced by those who continue to smoke is unknown, a base case assuming no impact on harmfulness could be found in the cell on the +30% row and the 0% column. Moving to the right within the same row would provide outcome estimates assuming a net reduction in smoking-related harm, whereas moving to the left would provide outcome estimates assuming the harmfulness of smoking increases.

It is anticipated that some cigarette smokers, when faced with reduced nicotine, will switch to other products, for example, pipes, cigars, chew, or snuff, to satisfy their craving for nicotine. Policymakers might be well advised to mandate nicotine reductions, not just in cigarettes, but in all tobacco products sold in the United States, thus minimizing switching behavior. Moreover, to eliminate any risk due to compensatory smoking, it is important to reduce nicotine contents to nonaddictive levels.

As nicotine is reduced to nonaddictive levels, there will likely be a sharp increase in the number of smokers who want to quit. Many will visit their physicians seeking nicotine replacement therapy to aid cessation or relief from withdrawal symptoms. Treatment offered by health care professionals will be invaluable in ensuring the mandate's success.

Some caveats will aid the reader in interpreting our results. We compare policy changes with a status quo scenario, where no change in tobacco use is expected to occur. In reality, absent any mandate, tobacco use may increase or decrease. We decided that assuming no change in the status quo offered a clear baseline against which different policy changes might be compared.

We have assumed an equal change in initiation, cessation, and relapse when modifying smoking-related behaviors. There are circumstances in which some aspects of behavior are affected more than others; for example, initiation is affected by a greater or less extent than is cessation. Our goal was to develop general risk-use trade-off curves that can be used to evaluate several policy options, so we assume equal change.

Particular toxins are associated with particular health consequences, and the extent to which cessation reverses or stops the damage varies by disease. We have not modeled any particular disease; instead, we present this work as a what-if analysis. For example, if it was feasible to make cigarettes safer such that excess mortality difference among never and current smokers can be reduced by 30% and it results in a worsening of smoking behavior by 20%, the result will be a gain of 102 million QALYs over 75 years.

The simulation model only takes into account the health impacts of modifying the harmfulness or addictiveness of cigarettes on smokers; it does not consider the health impacts on the nonsmoking population. Reducing the exposure (with fewer people smoking and cigarettes containing fewer harmful substances) will produce additional health benefits to those exposed to second-hand cigarette smoke.

We have not explicitly modeled the black market. Instead, by considering a range of behavior change we are indirectly accounting for the black market. For example, if the reader believes that only 50% behavior change is possible because the black market will dilute the impacts of policy, and if 40% behavior change is anticipated as a result of introducing reduced nicotine cigarettes, then the 20% behavior change column in Table I would apply ($40\% \times 50\% = 20\%$).

Researchers have identified that there are peer, norm-induced, and/or social contagion aspects of cigarette use. Thus, if the prevalence of smoking declines, that in and of itself might reduce rates of initiation. Such feedback effects are not considered in this model. Nicotine reduction may reduce smoking, and if there are peer and norm-induced effects that are strong, the model might be underestimating the health benefits of nicotine reduction relative to toxin reduction.

Our research also gives insight into the future research directions that are needed. Most importantly, it will be essential to understand the relationship between any decrease in particular toxins and the reduction in disease and mortality that might occur.[6] Also important to assess are the synergistic effects of the components of tobacco smoke.

We hope that the thresholds presented in this article will prove useful as scientists move forward in examining the technical feasibility of producing a reduced toxin and reduced nicotine cigarette and policymakers contemplate giving the Food and Drug Administration the authority to regulate tobacco.

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