Online Supplement:
Simulation Model Structure and Data

Model Structure

The population dynamics model projects the changing sizes of subpopulations of smokers, MRTP users, dual users, former users, and never-users over a long time horizon (Figure S1). It simulates individual tobacco product use histories and deaths in annual steps, for a random sample from a population. Each transition probability is assumed constant for each individual given age, sex, and tobacco use history. For example, the probability that a 60-year-old, male, pack-a-day, lifetime cigarettes-only smoker dies at age 60 is a constant, but this probability changes with age and depends on that individual's level of cigarettes per day (CPD) and years smoking.
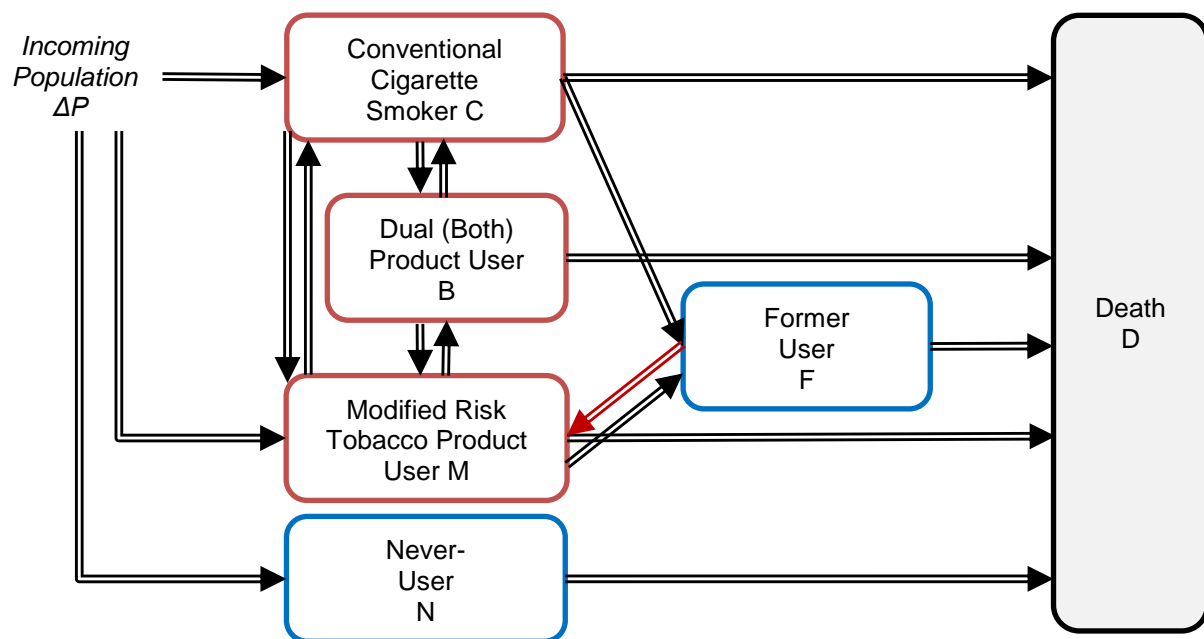

Figure S1. Model diagram
Each box represents a possible status and each arrow a possible transition for each simulated individual. The red F-M arrow is the only form of relapse allowed, and is allowed only for former smokers (a case of special interest); otherwise, cessation is assumed to be permanent.

Initial Population and Growth

The initial population was specified by the total population count in the first year, together with the proportions of this population at each age from 18 to 99 and 100+, for men and women separately (166

proportions totaling 100%). These were based on population data from the US Census Bureau.[1] The initial year was set to 2012, before e-cigarettes were expected to have a substantial effect on smoking prevalence in the US. Smoking status was categorized as current, former, or never-smoker. Proportions of the initial population with each of these statuses were specified in three age groups: 18-25, 26-64, and 65+, separately for each sex (18 proportions), based on 2012 National Survey on Drug Use and Health (NSDUH) survey data.[2] Given an age and sex simulated from the population distribution, the age group was determined, and the initial smoking status was drawn using the status proportions for that age group and sex. Current and former smokers were further assigned an average CPD level, and former smokers were assigned a number of years since quitting. Population growth was specified not by birth rates, since 0-17 year olds were not modeled, but by the annual sizes of the new 18-year-old subpopulation as projected by the US Census Bureau.[1]

Initiation and Cessation

The rate of initiation to cigarette use was taken as the cigarette smoking prevalence percentage at age 18, plus any increases at ages 19 and 20. Increases after age 20 were excluded because they were largely lost at ages in the late 20s (presumably due to early cessation). Initiation thus defined was modeled to decline linearly based on 2002-2009 NSDUH data. This assumption fitted the full 2002-2012 data reasonably well. However, for projection beyond 2012 in the cigarettes-only scenario without a new product, the 2012 initiation rates were used and were held fixed for simplicity, as were smoking cessation rates.

Holford et al.,[3] using 1965 to 2009 National Health Interview Survey (NHIS) data and various assumptions, estimated cessation rates over time (birth cohort) and age. Substantially higher cessation rates were found for women than men and for older ages than younger ages. These results were modeled as exponential increases in cessation rate with age for each sex, for the most recent birth cohort provided, 1970. Holford et al. defined cessation as smoking abstinence for at least two years, but to avoid complex modeling of relapses, the model here assumes that smoking cessation is permanent. Therefore it is plausible that cessation rates based on Holford et al. are too high for permanent cessation, and indeed in the model calibration, cessation rates were "tuned" down to fit smoking prevalence data by sex and age group over the calibration period.

Mortality Rates

All-cause mortality rates were modeled by age group, sex, and smoking status. Background all-cause mortality for never-smokers, and relative risks (RRs) of death for smokers, by age group and sex were taken from Thun et al.,[4] who reported on "contemporary cohorts" of 956,756 subjects with mean age 66 years but excluding ages <55 (Table S1). USDHHS[5] provided RR for 35-54 year old men and women (Table S2), and never-smoker death rates for 35-54 year old men and women, not supplied in either reference, were taken from Woloshin et al.[6] Death rates were then adjusted to approximate those of the US Census Bureau's 2012-2060 population projections.

Effects on death rates of changes in RR (such as after quitting) were accounted for as described in the paper. For both current and former smokers, the effects of average CPD on mortality were accounted for by adjustments to these curves. The CPD level for each smoker was assumed constant until a smoker quits or reduces CPD due to addition of a new product, and was a uniform random draw within the smoker's CPD category. This category was selected based on the proportion of smokers in each CPD category, by sex (Figure S2). ER was adjusted for CPD with a logarithmic function as described in the paper, based on data from several sources (Table S3).

Calibration/Validation and Projections

The model was calibrated with US Census Bureau population data[7,8] and projections,[1] as well as NSDUH data on smoking prevalence and CPD from 2002-2009,[2] reserving 2010-2012 data for validation. NSDUH was selected over NHIS for smoking prevalence and CPD data, as it has a larger sample size, has a higher response rate, and is potentially less biased with in-person interviewing on both licit and illicit substances[9]. NSDUH provided annual smoking prevalence and CPD data over 2002-2012 by sex and the following age groups: age 18, 19, 20, 21, 22-23, 24-25, 26-29, 30-34, 35-49, 50-64, and ≥65. CPD levels are grouped as <1, 1, 2-5, 6-15, 16-25, 26-35, and >35 CPD; for modeling, the first two CPD groups were combined. Current smokers were defined as those smoking within the last 30 days *and* having smoked at least 100 cigarettes smoked over one's lifetime.

Though projections from 2002 were in reasonable agreement with data through 2012 (Figure S3), for maximum accuracy in future projections, 2012 data were used in place of projections from 2002. Projections were made to 2060, with cigarettes only and with both products (Figure S4).

Table S1. Mortality rates per 100,000 and relative risks with confidence intervals, age 55+
From Thun et al. 2013, Table S2 (5 contemporary cohorts, 2000-2010).

Age	Never-Smoker Men	Never-Smoker Women	Current Smoker Men	Current Smoker Women	Relative Risk Men	Relative Risk Women	Relative Risk 95% CI Men	Relative Risk 95% CI Women
55-59	299	265	1102	705	3.7	2.7	3.1-4.4	2.2-3.1
60-64	530	361	1795	1069	3.4	3.0	3.1-3.7	2.7-3.2
65-69	826	577	2880	1799	3.5	3.1	3.3-3.7	2.9-3.3
70-74	1356	913	4424	2789	3.3	3.1	3.1-3.4	2.9-3.2
75-79	2323	1552	6078	4119	2.6	2.7	2.5-2.8	2.5-2.8
80-84	4340	2902	10278	6629	2.4	2.3	2.1-2.6	2.1-2.5
85+	10522	6274	18698	12178	1.8	1.9	1.4-2.2	1.7-2.3

Table S2.   Relative risks by smoking status, sex, and age 35+

From USDHHS 2014, Table 12.3. Note: 35-54 year old results supplement Table S1; for older ages Table S1 is used because of its more detailed age groups and inclusion of never-smoker rates. Never-smoker rates for 35-54 year olds from Woloshin (2008)[6] are 250 for males and 195 for females per 100,000 (10-year mortality risks for 35-year-olds averaged with 45-year-olds from Figures 2 and 4 of that paper).

	Current Smoker		Former Smoker	
Age	Men	Women	Men	Women
35-54	2.55	1.79	1.33	1.22
55-64	2.97	2.63	1.47	1.34
65-74	3.02	2.87	1.57	1.53
≥75	2.40	2.47	1.41	1.43

Table S3.   Relative risks by cigarettes per day (CPD) and sex

(a) From Thun et al. 2013, Table S3

CPD	Men	Women
<10	2.21	2.27
10-19	2.60	2.69
20-39	3.33	3.48
40+	4.08	4.41

(b) From Bjartveit et al. 2005, Table 3

CPD	Men	Women
1-4	1.57	1.47
5-9	1.94	1.90
10-14	2.36	2.29
15-19	2.66	2.97
20-24	3.19	3.14
25+	3.42	2.61

(c) From Thun et al. 1997, Appendices 16-17

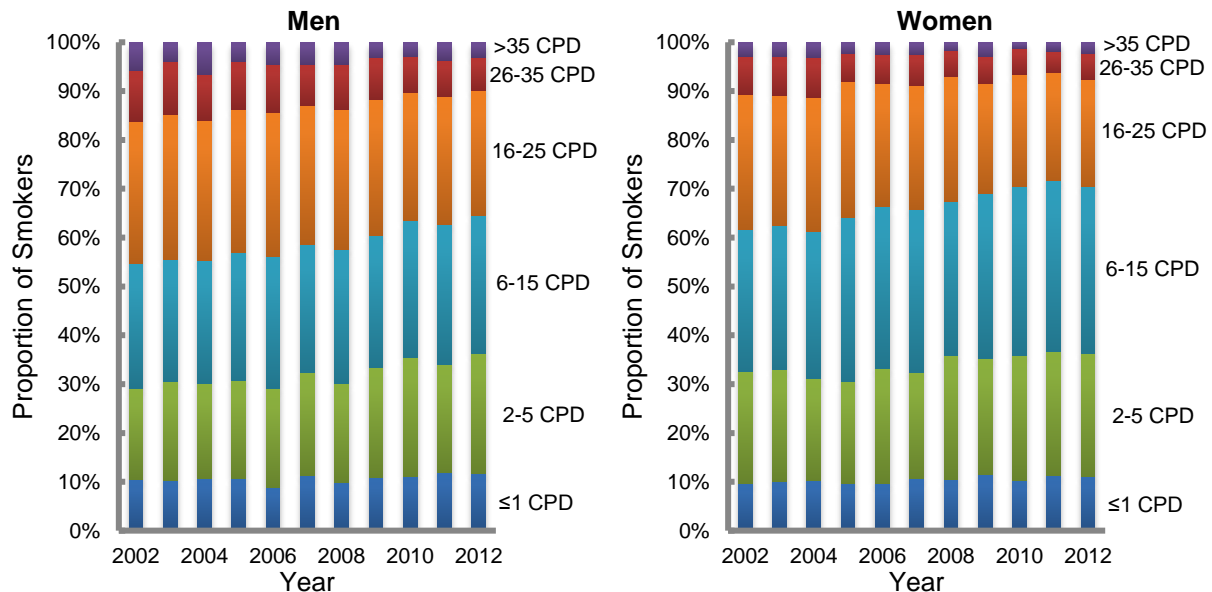| | | Years Smoking | | | | | | | |
| | | Men | | | | Women | | | |
CPD	Age	20-29	30-39	40-49	50+	20-29	30-39	40-49	50+
1-19	50-59	2.0	3.0	3.3		1.5	1.7	2.0	
1-19	60-69	1.6	1.9	2.2	3.2	1.4	1.5	2.1	2.9
1-19	70-79	1.2	1.7	1.7	2.3	1.1	1.8	1.4	1.9
20	50-59	2.0	2.9	4.8	11.4	1.7	2.3	3.0	
20	60-69	1.9	1.8	2.8	4.3	1.9	2.3	2.6	4.3
20	70-79	2.2	1.3	1.9	2.5	1.4	1.9	1.9	2.4
21-39	50-59	2.1	2.7	4.3		1.6	2.6	3.6	
21-39	60-69	2.0	1.7	2.6	4.4	1.7	1.7	2.9	3.9
21-39	70-79		1.8	1.8	2.5	4.0	1.5	1.9	2.3
40	50-59	2.5	3.2	4.8	13.5	2.0	3.0	4.1	
40	60-69	0.9	2.2	3.0	4.0	1.0	2.2	3.0	4.7
40	70-79		1.5	2.4	2.6	2.7	2.5	2.0	2.8
41+	50-59	2.4	3.2	5.8		2.4	3.4	4.7	
41+	60-69		2.0	2.9	3.9		1.5	4.4	2.9
41+	70-79			1.6	2.5		6.1	1.9	1.4

Figure S2. Proportions of smokers in CPD categories over 2002-2012 by sex
Source: NSDUH[2]. Model uses 2012 data. Data are adjusted for days per month smoked (data not shown).
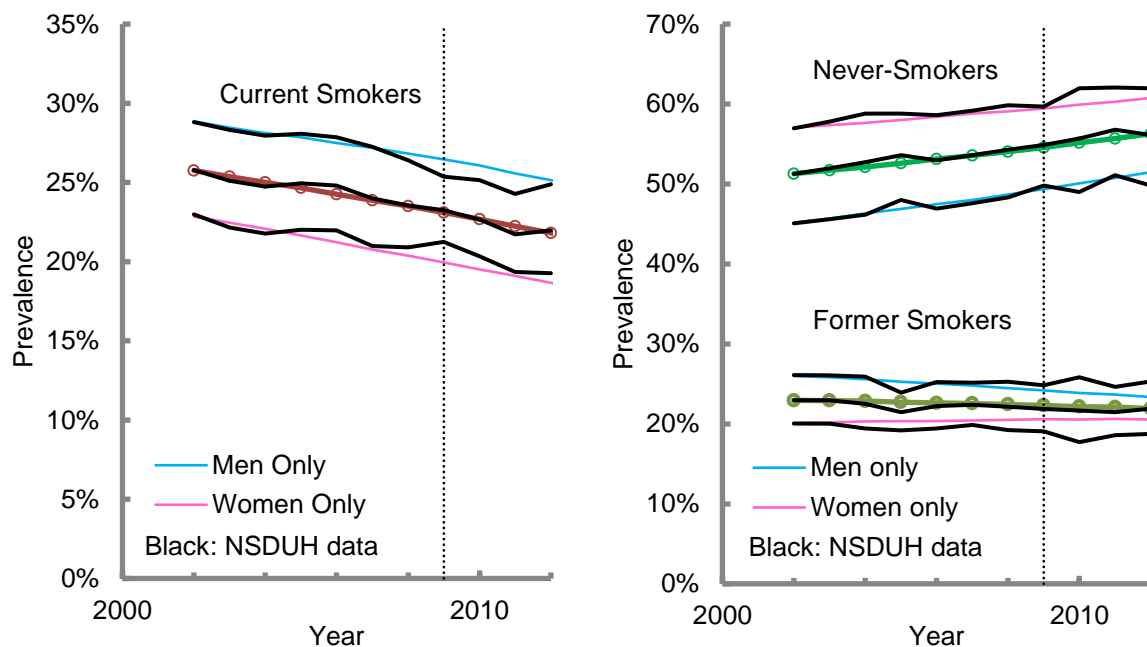
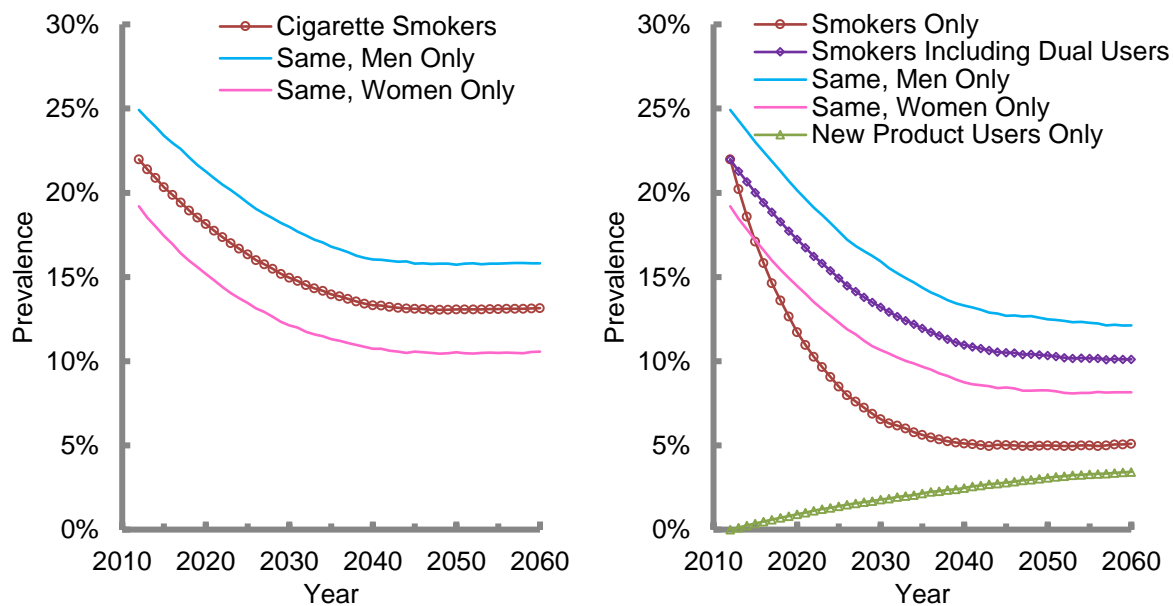**Figure S3. Model calibration (2002-2009) and validation (2010-2012) with prevalence by smoking status and sex**

Figure S4. Comparison of base-case cigarettes-only and two-product prevalence projections

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