Module 6 : Research

6.5 Population Modelling and Analysis

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1. SUMMARY

Population modeling shows that the introduction of *IQOS* products will contribute to the reduction of smoking-related harm by offering adult smokers a less risky alternative. We evaluated the public health impact of *IQOS* products on smoking-attributed deaths between ages 30-79 due to four major smoking-related diseases: (i) lung cancer, (ii) chronic obstructive pulmonary disease, (iii) ischaemic heart disease and (iv) stroke between 2024 and 2080.

Our findings indicate that *IQOS* products will prevent about 50,000 smoking-related deaths for each percentage point of population prevalence that it reaches in 10 years after its introduction. For example, if the population prevalence of *IQOS* grows to 5% and stays steady until 2080, it leads to the reduction of 225,000 smoking-attributed deaths and 2.2 millions of years life saved (YLS).

2. APPROACH

The Population Health Impact Model (PHIM) was used to model and analyze the public health impact of *IQOS* products in the U.S. This model relies on estimating transition probabilities between product categories such as combusted cigarettes, e-cigarettes and heat-not-burn products. As *IQOS* products are currently not marketed in the U.S., we used evidence from the Population Assessment of Tobacco and Health (PATH) Study for transitions between never, current and former of tobacco- and nicotine-containing products and former. In our baseline Conversion scenario, we assumed that there were the same probabilities of transition between combusted cigarettes and *IQOS* combusted cigarettes as between combusted cigarettes and e-cigarettes. In sensitivity analyses, we relaxed this assumption and assumed a higher likelihood to switch from combusted cigarettes to *IQOS* products.

3. METHODOLOGY

PMP S.A. developed the PHIM[1] to estimate the reduction in the number of smoking-attributable deaths (SADs) and in years of lives saved (YLS) following the introduction of an MRTP. It was originally described by Weitkunat et al. (2015) and has subsequently been used in a number of publications to model the effect of introducing an MRTP into the United States (Djurdjevic et al. 2018, Lee et al. 2017), Japan (Lee et al. 2018), Sweden (Djurdjevic et al. 2019), and Germany (Rytsar et al. 2022a, Rytsar et al. 2022b). It has also been used to estimate mortality reduction in the United States if conventional cigarettes (CCs)

[1] See *IQOS* 2.4 MRTPA submitted on 5 Dec 2016, Section 7.4 Executive Summary: Population Health Impact Model studies and Appendix Report PHIM (Population Health Impact Model) System, Simulation and Sensitivity Analysis Report, Version 1.1, August 2016.

were largely replaced by e-cigarettes (Lee et al. 2022), and is among a number of modelling approaches considered in a recent review (Lee et al. 2021).

The basic method involves two components, the Prevalence (P-) component and the Epidemiologic (E-) component. The P-component starts in a specified year with a population of a given sex and age range with a defined distribution of CC smoking. The population is then followed over discrete time intervals (year) under both a "Reference Scenario" and several different "Alternative Scenarios" using estimated transition probabilities (TPs), which estimates the probability of changing product use in an interval. In the Reference Scenario, the set of products is introduced, and the distribution of product use statuses in the population is updated at each interval based on TPs which allow for switching between products as well as for initiation, quitting or re-initiation of each product considered. Each Alternative Scenario introduces either a new product or a tobacco control policy. These can be introduced separately or in combination and PHIM generates a complete product use history for each Scenario for the follow-up period.

The E-component then uses the histories to estimate age-specific relative risks (RRs) compared to never users for each follow-up year for each of four diseases: lung cancer (LC), chronic obstructive pulmonary disease (COPD), ischemic heart disease (IHD) and stroke. These four diseases are estimated to contribute 66% of all SADs (Weitkunat et al. 2015). The estimation involves a negative exponential model (NEM), allowing for multiple changes in product use, the NEM being described and justified elsewhere (Lee et al. 2015, Lee et al. 2017). The model estimates the excess risk (RR−1) of the given disease at each year of age from the excess risk of the previous year, together with knowledge of changes in product use during that year. The model requires estimates for each disease of the RR for continued smoking and the half-life (H) of quitting. H denotes the time required from quitting for the excess risk (RR−1) to halve. It also requires estimates of the excess risk of exclusive new product use relative to exclusive smoking (F), sometimes referred to as the "effective dose". In line with Martin et al. (2018), we assumed that the effective dose of heat-not-burn products such as IQOS is 20% of combusted cigarettes.

The product-related deaths are estimated for each Scenario based on (a) the average RR for each disease, (b) population counts and (c) national mortality estimates by sex, age group and time period. Number of years of life lost (YLL) before age 75 years are then estimated using the method of Gardner and Sanborn (1990) based on the assumption that deaths in each age group have a mean age of death at the midpoint of the corresponding range. Note that in the above, population estimates for future years are taken from national population projections, while death rates by disease for future years are estimated by applying the method of Osmond and Gardner (1982) to the corresponding data reported for earlier years.

This approach estimates numbers of SADs and number of YLL in each Scenario. The difference between the Reference and Alternative scenarios provides the effect of introducing new product(s) or/and tobacco control measures as estimated by the drop in deaths (DD) or number of years of life saved (YLS).

The most recent version, PHIM v8.2 is used in this study. It incorporates the following updates pertinent to this analysis:

- allows for up to 10 groups, giving more flexibility in coping with multiple products
- allows or a probabilistic version in which a set of Markov states is defined, based on all the combinations of single years of age and smoking status (including time quit for ex-smokers). Each of these states is assigned a probability based on National Statistics of population and smoking habits, with the sum of the probabilities of all the states being 1. The population values in the output are generated by considering each age, summing the probabilities for each state relating to the age and multiplying the answer by the population with that age, the population being taken from National Statistics with 5-year age values divided by 5.

3.1. Modeling approach

This study aims to quantify the population health effects of the marketing authorization of *IQOS* products and measure it in the change in SADs and YLS after the introduction of *IQOS* products to the U.S.

PHIM represents interaction between combusted cigarettes, e-cigarettes (ECIGs) and *IQOS* products. All models run from 2010 to 2080, with ECIG introduced from 2010 and *IQOS* products in 2024. (Figure 1)

Figure 1. Modeling plan
Observed data for PHIM covers the period of 2000 to 2020, the models run from 2010 to 2080, the year when their public health impact is evaluated.

The public health impact of *IQOS* products is estimated as the difference between SADs and YLS in the Reference Scenario with CC and ECIG and the Alternative Scenario with CC, ECIG and *IQOS* products.

3.2. Data

3.2.1. Population-level data

All data are for the U.S. and are sex and age specific. The baseline year is 2010, with follow-up for 50 years in one-month periods. Males and females are considered separately in all applications. The initial population is aged 10-79 years. At each year of follow-up, a new set of 10-year olds is included, equivalent to the initial sample of 10-year olds, and those aged 79 years drop out of follow-up[2].

The population data are from the estimates on the United Nation website, consisting of estimates for observed years and "medium variant" projections for future years up to 2100.

The mortality data come from the WHO's Mortality Database website for years up to 2017, with data for subsequent years estimated using the age-period-cohort model of Osmond and Gardner (1982a) as described in Appendix 7.1.

Five-year estimates of CC smoking prevalence for periods from 1996-2000 up to 2016-2020 were obtained based on the US survey series provided by the National Survey on Drug Use and Health (NSDUH) and the National Health Interview Surveys (NHIS) for years up to 2018.

For the purposes of estimating SADs, the estimates of RR and H were as given in Table 5 of Lee et al. (2017).

3.2.2. Transition probabilities between nicotine-use states

The transition rates between CC, ECIG and their dual uses were estimated from the PATH study for Adults (ages 18+) using the methodology developed by Brouwer et al. (2022). As usage of e-cigarette flavors were not recorded in PATH Wave 1, we analyzed Waves 2-5 using the R code for Weighted Multistate Markov Models available on the website of Center for the Assessment of Tobacco Regulations and estimated transition rate ratios by age. See Appendix 7.2 of this document for further details.

[2] The age of 79 is taken as the highest age as cause of death certification is not considered reliable at older ages (Weitkunat et al. 2015).

Because of inconsistencies between cigarette and e-cigarette use definitions between the PATH Adult and Youth samples[3], we restricted our data source to the Adult sample and assumed that 15-19 year-olds had the same transition probabilities as 20-24 year-olds and 10-14 year-olds were 1/3 as likely to initiate any product use than 20-24 year-olds.

3.3. Scenarios

To shed light on the population health impact of *IQOS* products, we compared the Reference scenario (CC and ECIG on the market) with an Alternative scenario in which *IQOS* products are introduced. To assess variations to that Alternative, we also conducted sensitivity analyses by accounting for a wide range of *IQOS* products uptake.

3.3.1. Reference scenario

In the Reference scenario, there are only combusted cigarettes and e-cigarettes. This scenario describes the current state of the combusted cigarette and e-cigarette market on the United States and forecasting the current use of these products estimates the SADs due to CC and ECIG in the absence of *IQOS* products until 2080. Dual use of products is accounted for.

3.3.2. Conversion scenario

In the Conversion scenarios, *IQOS* products are introduced as an additional product in 2024. This scenario provides a point-estimate for the population health impact of *IQOS* products based on assumptions explained in Appendix 7.3. The main assumption regarding switching in the Conversion scenario is that the probability to switch to *IQOS* from CC and from *IQOS* to CC is the same as to E-CIG from CC and from E-CIG to CC, respectively. We relaxed this assumption in sensitivity analyses and investigated the population health impact of *IQOS* products under a wider range of switching probabilities. For a more expanded list of analyses, see Report PHIM (Population Health Impact Model) System, Simulation and Sensitivity Analysis Report, Version 1.1, August 2016 in our original MRTPA submission[4].

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[3] Established adult smokers or e-cigarette users are those who have smoked at least 100 cigarettes in their lifetime, and currently smoke every day or some days and ECIG users – respondent who has ever used an e-cigarette, has used fairly regularly, and uses every day or some days. In the case of youth, smokers or e-cigarette users are those who have ever smoked a cigarette (used ECIG) and have smoked (used) in the past 30 days. The Youth definition of smoker or e-cigarette user, especially in the case of former smokers, would yield biased results compared with the adult sample.

[4] *IQOS* 2.4 MRTPA submitted on 5 Dec 2016, Section 7.4 Executive Summary: Population Health Impact Model studies and Appendix Report PHIM (Population Health Impact Model) System, Simulation and Sensitivity Analysis Report, Version 1.1, August 2016

4. RESULTS

PHIM first forecasts product-use prevalences and then based on the number of future smokers, e-cigarette and *IQOS* users, it estimates the population health impact of these products.

4.1. Expected product-use prevalences

The Reference scenario forecasts the prevalence of CC, ECIG and Dual (CC + ECIG) until 2080. In this scenario, CC use levels-off around 10% for both males and females around 2030 for females and around 2060 for males. Exclusive e-cigarette use reaches a population prevalence of about 3% for both males and females and dual CC and ECIG use has a population prevalence of about 1% in the whole forecast interval. These estimates align well with observed CC and ECIG prevalence data coming from the Center for Disease Control and Prevention (CDC), National Survey on Drug and Health (NSDUH), National Health Interview Survey (NHIS), Mayer et al (2020) and Boakye et al (2022). (Figure 2)

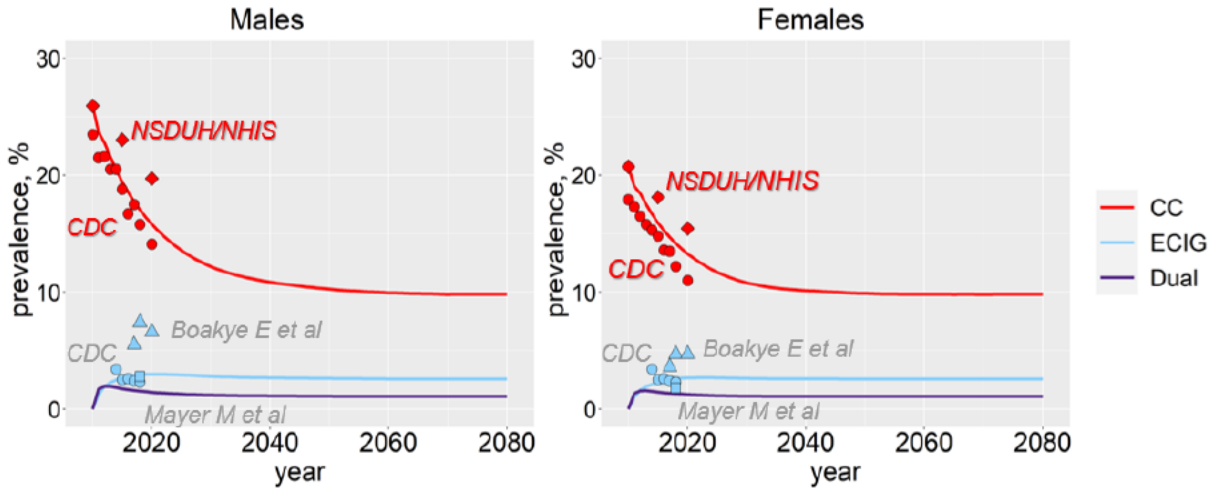

Figure 2. CC, ECIG and Dual (CC + ECIG) prevalence forecast in the Basic scenario. *2010-2080*
The solid lines denote the modeled values, the red dots correspond to the Center for Disease Control and Prevention (CDC) combusted cigarette estimates, the red diamonds relate to the CC prevalence from the National Survey on Drug and Health (NSDUH) and National Health Interview Survey (NHIS). The blue dots are e-cigarette prevalence data coming from CDC, the blue squares are from Mayer et al (2020) and the blue triangles are from Boakye et al (2022).

In the Alternative scenario, *IQOS* product enter market in 2024. As the primary source of *IQOS* users is assumed to be CC smokers, the prevalence of CC drops after the introduction of *IQOS* products. As e-cigarette and *IQOS* users are assumed to be independent groups who do not switch to the other product group, the introduction of *IQOS* products only changes e-cigarette prevalence through CC smokers. (Figure 3)

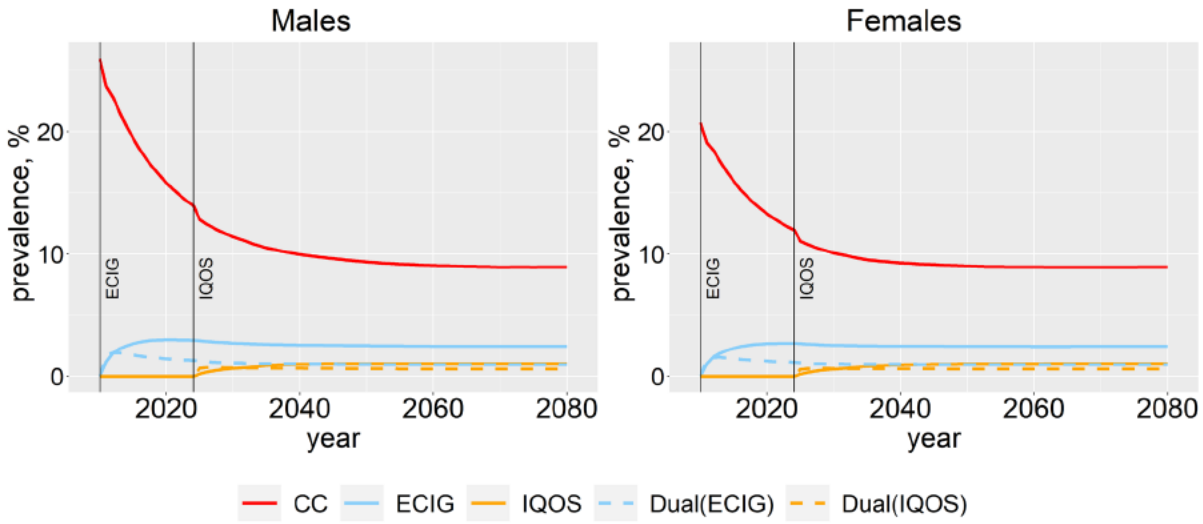

Figure 3. CC, ECIG, Dual (CC + ECIG), IQOS and Dual (CC + IQOS) prevalence forecast in the Alternative scenario. *2010-2080*

Note that the exact redistribution of CC to *IQOS* is dependent on the assumption of the future market share of the product and the one on Figure 3 corresponds to the assumptions in Appendix 7.3.

4.2. Reduction in smoking-attributed deaths

To understand the expected population health impact of *IQOS* products in terms of reduction in smoking-attributed deaths, we created sensitivity analyses around the population prevalence everyof *IQOS* use starting from the Conversion scenario.

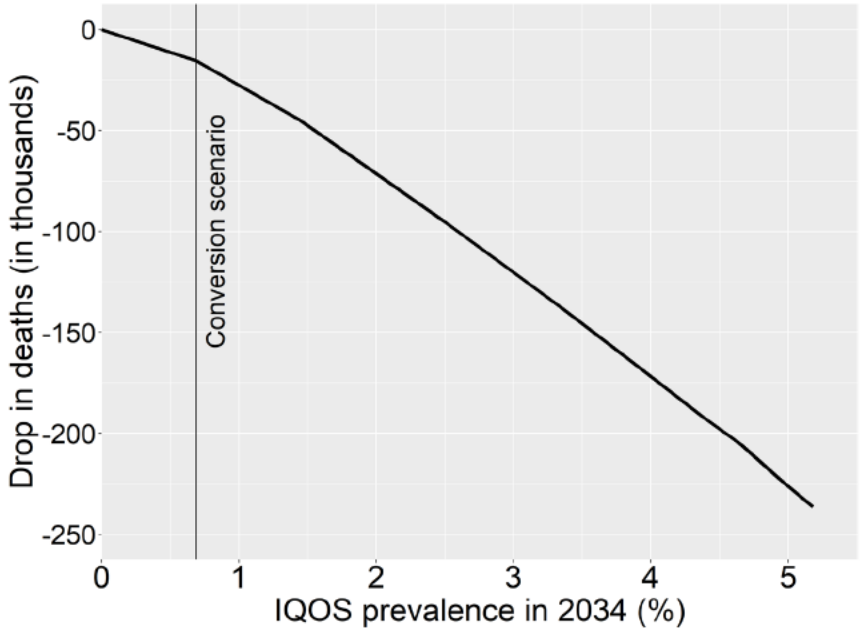

Figure 4. Sensitivity analyses for *IQOS* population prevalence and reduction in smoking-attributed deaths
The figure shows the population prevalence of *IQOS* in 2034, 10 years after its introduction and the number of smoking-attributed deaths prevented between ages 30 and 79 until 2080 from the four major smoking-related diseases: lung cancer, COPD, ischaemic heart disease and stroke.

As Figure 4 shows, for each percentage point increase in population prevalence of *IQOS* use, the smoking-attributed deaths from lung cancer, COPD, ichaemic heart disease and stroke between ages 30-79 decrease by about 50,000 and this decrease slightly accelerates by each additional percentage point. Under the Conversion scenario, with about 0.7% of population prevalence of *IQOS* use in 2034, the drop in deaths amounts to 15,519 with 0.2 million of YLS while at 5% of population prevalence, the drop in deaths reaches 225,000 with 2.2 million of YLS

5. DISCUSSION

IQOS product offer a public health benefit for the population as a whole as it shifts the distribution of tobacco-use towards a less harmful product from combusted cigarettes. As we do not have direct evidence of consumer behavior in the U.S., we used data from PATH and modeled behavior of smokers with respect to *IQOS* products relatively to e-cigarettes. As *IQOS* is a more similar product to combusted cigarettes than e-cigarettes are, we conducted sensitivity analyses to explore the public health impact of *IQOS* products by increasing the likelihood of switching to *IQOS* products from combusted cigarettes starting from the rates of switching to e-cigarettes.

The Conversion scenario assumes conservatively that the probability of switching from combusted cigarettes to *IQOS* products is the same as switching from combusted cigarettes to e-cigarettes as it can be observed in PATH data. However, due to the similarity of heat-not-burn products such as *IQOS* products and combusted cigarettes (Sutanto 2020), the probability of switching from combusted cigarette to *IQOS* products may be higher than from combusted cigarettes to e-cigarettes.

Our sensitivity analyses investigate the increasing the likelihood of switching from combusted cigarettes to *IQOS* products compared with the baseline switching rate which is equivalent to switching from combusted cigarettes to e-cigarettes. At this baseline level, the population prevalence of *IQOS* is under 0.7% and the drop in smoking-attributed deaths is 15,519 with 0.2 millions of YLS. If smokers were three times more likely to switch to *IQOS* products than e-cigarettes, the population prevalence of *IQOS* use would reach 2% in 2034 and there would be a reduction of 71,880 smoking-attributed deaths and 0.7 million of YLS by 2080. (Figure 4 and Figure 5).

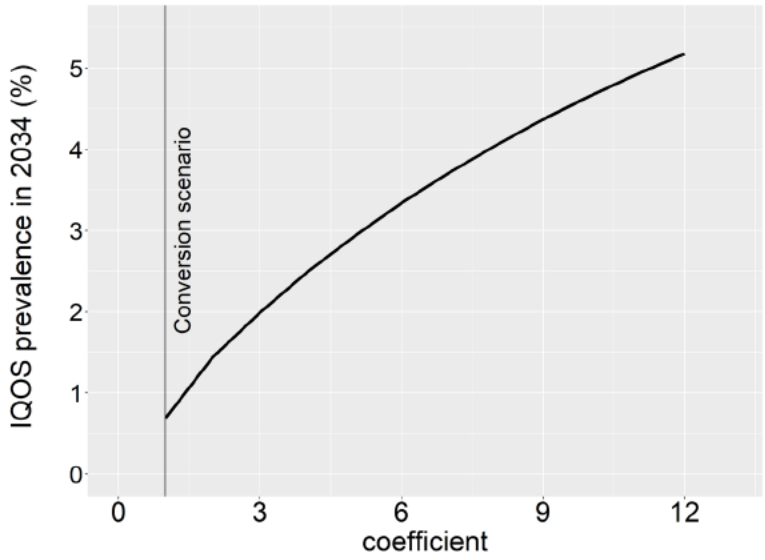

Figure 5. Sensitivity analyses for *IQOS* population prevalence and the multiplier coefficient for increasing switching from combusted cigarettes to *IQOS*

Each unit of coefficient denotes the likelihood to switch from combusted cigarettes to *IQOS* products by being equal to coefficient times the probability to switch from combusted cigarettes to e-cigarettes and the likelihood to switch from *IQOS* products to combusted cigarettes is equal to the probability to switch from e-cigarettes to combusted cigarettes divided by the same coefficient. As this coefficient increases, the population of prevalence of IQOS also increases.

If smokers are 12 times more likely to switch to *IQOS* products from combusted cigarettes than to e-cigarettes, the population prevalence of *IQOS* use reaches 5.18% (Figure 5) and the reduction in smoking-attributed deaths 237,000 and 2.3 millions of YLS (Figure 4). At this point, the population prevalence of combusted cigarettes decreases to about 5% as well (Figure 6).

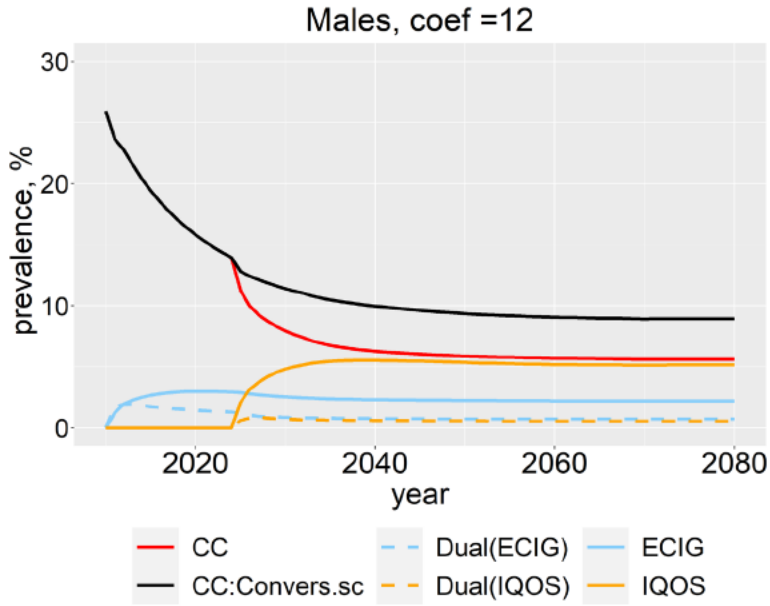

Figure 6. Sensitivity analyses: Population prevalence of CC, ECIG and *IQOS* at high switching from CC to IQOS

Among males, the population prevalence of *IQOS* reaches 5% and the population prevalence of combusted cigarettes drops to 5% as well when switching from combusted cigarettes to *IQOS* products is 12 times greater than switching from combusted cigarettes to e-cigarettes.

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7. APPENDIX

7.1. Modelling disease rate patterns by period and age using the Osmond and Gardner method

Mortality trends are often portrayed as a matrix, with age groups in rows and time periods in columns that show rates based on number of deaths and person-years at risk. Where age groups and time periods are equal, diagonals of increasing age and period relate to "cohorts" born around the same year. Interest often centers on whether trends result from period or cohort effects. However, knowing that two of the age, period, or cohort factors defines the third, there is no unique best-fitting solution to the model.

In 1982, Osmond and Gardner (1982a, 1982b) recommended an approach based on the relative success of the three two-variable sub-models.

The method involves fitting a model where the logged rates are expressed as linear functions of the individual age, period, and cohort parameter logs. This involves minimizing a weighted function of the squares of the residuals while constraining the period and cohort values, so that their averages are kept at unity. This raises an identifiability problem, since the logical association between age, period, and cohort values leads to either an infinite set of possible solutions or minima. Given any one solution, another can be obtained by adding or subtracting successive shift quantity multiples to each logged age, period, and cohort value. Thus, by shifting the cohort values in one direction and the period values in another, a new solution is produced that identically fits the data. The various shapes or rotations induced by the shifts will lead to different interpretations derived from the alternative solutions.

Osmond and Gardner (1982a) approached this problem by first finding solutions to each of the two-parameter sub-models (age-period, age-cohort, and period-cohort) and then obtaining a full solution by minimizing a function of the three weighted-squared differences between each two-factor sub-model and the full three-factor model. The result adds more weight to the two-parameter models that produce a better fit to the data. The method is unique in its approach to the lack of identifiability of the problem, and it is difficult to envisage an alternative approach that does not rely on arbitrary assumptions to overcome the association between the three variables. The method's results seem relevant, and the period and cohort values broadly resemble those obtained by calculating period- or cohort-based standardized mortality ratios.

Applying the method to England and Wales's lung cancer data, Osmond, Gardner (1982b) showed a sharply rising age effect, little period effect, and an inverted V cohort pattern peaking around 1900–1905 for men and 1925 for women. The cohort pattern was attributed to different smoking patterns in successive generations; however, Lee et al. (1990) noted that it was difficult to explain the recent cohort decline for women regarding changes in cigarette consumption.

7.1.1. Extrapolating death rates fitted by the Osmond and Gardner model to future years.

In addition to fitting the Osmond and Gardner model (O&G model) to observed rates, we were interested in predicting future rates. Previous unpublished work by P.N. Lee Statistics and Computing Ltd. examined lung cancer in England and Wales and suggested four prediction methods based on O&G analysis: 1) A-P-C model with linear extrapolation of P and C values; 2) A-P-C model with log-linear extrapolation of P and C values; 3) A-C model with log-linear extrapolation of C values; and 4) A-C model with log-linear extrapolation and residual correction.

A distinct peak in lung cancer rates occurred between 1941 and 1980. Extrapolating cohort values worked best with a 0 weighting for values before the peak and a 1 weighting at the peak and after. Extrapolating period values using Methods 1 and 2 and residuals using Method 4 applied weights that decreased exponentially into the past to give recent values more influence than values from the distant past.

From the then available 1941–1980 data, investigators used various (4, 5, or 6) initial periods to predict the remaining periods and compare age-specific numbers of deaths. They found that predictions improved when more points were used, except that pre-1950 data did not improve predictions. The A-P-C model produced better results for men, but the A-C model was better for women. Log-linear extrapolation gave poorer results than linear extrapolation, but linear extrapolation could produce negative results. They proposed that new cohort values be estimated by log-linear extrapolation using powers of two decreasing into the past as weights. The last cohort value from the fitted model should be excluded from this extrapolation procedure and replaced by an estimated value. They also proposed that new period values be estimated by applying the percentage change between the last two period values to the succeeding periods. In the work carried out here, the proposed method for extrapolation in addition to the more standard method using weighted averages for the estimated period effects.

7.2. Estimating transition probabilities from PATH Waves 2-5

7.2.1. Analysis sample

We used data on adults (ages 18+) in four waves of the PATH study: Wave 2 (Oct. 2014–Oct. 2015), Wave 3 (Oct. 2015–Oct. 2016), Wave 4 (Dec. 2016–Jan. 2018), and Wave 5 (Dec. 2018–Nov. 2019).

Our individual data have been restricted to only those waves in which participants were adults (some participants were youth in earlier waves), and we removed any participants from the sample who had only a single tobacco state observation. We further restricted our analysis to participants who completed an adult interview in wave 5. The time between follow-up for each participant was approximately 1year.

PATH offers a number of different participant weights appropriate to different types of analyses. Here, we used Wave 5 all-wave adults' weights (R05_A_A01WGT) to represent the data analysis results at the US population level. We incorporated these weights into analysis by normalizing them according to the final sample size.

In addition to the questions informing our tobacco use state definitions (see below), we used information on age. Participant age was derived from PATH variables R0xR_A_AGECAT7 (Waves 2–3) or R0xR_A_AGECAT6 (Wave 4-5), with categories collapsed to our six groups: "18–24," "25–34,", "35-44", "45-54", "55-64" and "65+." Age was allowed to change between waves.

We removed participants still missing information for any covariate in a given wave (14.5% of participants)

In total, we analyzed 19'450 participants with 71'873 total observations and 6'662 transitions. Participant weights were normalized to the number of participants. Descriptive characteristics of the sample are given in Table 1.

Table 1. Descriptive statistic of the analyzed sample from PATH Waves 2-5

Demographic	Wave 2	Wave 3	Wave 4	Wave 5
Age				
18-24	4464	5014	6003	4958
25-34	3282	3590	4003	4632
35-54	4782	4855	4983	5191
55 plus	3568	3791	4088	4669
Reduced Number Participants	16096	17250	19077	19450
Total Number Participants	28362	28148	33822	34309

7.2.2. Nicotine-use state definitions

To align with PHIM terminology, we considered five nicotine-use states: (1) never-user, (2) former-user, (3) exclusive cigarette user (CC), (4) exclusive electronic cigarette user (ECIG), and (5) Dual cigarette and electronic cigarette user (CC + ECIG). In PHIM, Never-users have never used cigarettes or either of the ECIG considered and Former users have previously used at least one product but currently do not use any (Former product users = Former CC or Former ECIG or Former Dual).

"Recent former" (or "non-current") user in PATH data refers to at least 30-day abstinence and to transitions to this state as 'stopping' use as a short-term cessation. For modeling purposes, we neglect this difference with the "former" user definition ('quit' generally refer to longer term cessation) and consider former user state.

In our model, the smoking status of individuals can only change at most once per year. The states are unknown between observation times (waves) in PATH data. Therefore, we changed two consecutive statuses Never–Former to Never–Never by assuming that participant didn't reach the status of product use in between the waves.

We assigned each PATH participant to a tobacco use state in each wave according to the PATH data variables (see list of variables in Table 2) which are derived from the answers to questions about the products use.

We defined established use for cigarettes as ever using 100+ cigarettes in one's lifetime and established ENDS use as ever using fairly regularly. ENDS were defined as e-cigarettes in Waves 2 and as e-cigarette, e-cigar, e-pipe, e-hookah, or other electronic nicotine product in Waves 3,4 and 5.. Participants who were not established for either product were considered never users. Former ENDS user has used an e-cigarette fairly regularly, and currently does not use at all, where as Former CC smoker has smoked more than 100 cigarettes in lifetime, and now does not smoke at all. Former users were considered the Former users of either cigarettes or ENDS. Dual users were established users of both cigarettes and ENDS, who had used both cigarettes and ENDS in the past 30 days.

Table 2. List of PATH Study variables used to define the statuses of participants according to PHIM requirement

R0xR_A_CUR_ESTD_CIGS	Wave x Adult Current Established Cigarette User Long Description: Has ever smoked a cigarette, has smoked more than 100 cigarettes in lifetime, and currently smokes every day or some days.
R0xR_A_CUR_ESTD_ECIG, R03R_A_CUR_ESTD_EPRODS	Wave x Adult Current Established E-Cigarette User with two levels 1= Yes and 2 = No Long Description: Has ever used an e-cigarette, has used fairly regularly, and uses every day or some days. Since wave 3 this variable is replaced by R03R_A_CUR_ESTD_EPRODS which reflects to all electric nicotine delivery devices.
R0xR_A_FMR_ESTD_CIGS	Wave x Adult Former Established Cigarette User which can have two levels 1= Yes and 2 = No Long Description: Has ever smoked a cigarette, has smoked more than 100 cigarettes in lifetime, and now does not smoke at all
R0xR_A_FMR_ESTD_ECIG	Wave x Adult Former Established E-Cigarette User Long Description: Has ever used an e-cigarette, has used fairly regularly, and currently does not use at all.

7.2.3. Estimated transition probabilities

The age-specific transition probabilities between the five nicotine-use states can be found in Table 3. Note that while the youngest age in the PATH Adult survey is 18 years, PHIM requires transition probabilities starting from age 10. We assumed that 15-19 year-olds have the same transition probabilities as 18-24 and 10-14 year-olds have 1/3 of the product-transitions of the 18-24 year-olds.

Table 3. Transition probabilities between tobacco use states estimated by multistate transition model methodology

Note that while this table does not contain the 10-14 and 15-19 year-old categories, we assumed that 15-19 year-olds have the same transition probabilities as 18-24 year-olds and 10-14 year-olds have 1/3 of the product-use transitions of 18-24 year-olds.

Age cat	to→ from↓	Never	Former	CC	ECIG	DUAL
18-24	Never	0.96	0	0.01	0.02	0.003
	Former	0	0.68	0.17	0.11	0.04
	CC	0	0.13	0.71	0.05	0.11
	ECIG	0	0.22	0.08	0.58	0.12
	DUAL	0	0.09	0.32	0.15	0.45
25-34	Never	0.99	0	0.01	0	0.001
	Former	0	0.82	0.14	0.03	0.01
	CC	0	0.12	0.78	0.03	0.07
	ECIG	0	0.20	0.06	0.61	0.13
	DUAL	0	0.06	0.37	0.10	0.46
35-54	Never	0.99	0	0.01	0	0
	Former	0	0.94	0.05	0.01	0
	CC	0	0.08	0.85	0.01	0.05
	ECIG	0	0.18	0.06	0.62	0.14
	DUAL	0	0.04	0.41	0.08	0.46

Age cat	to→ from↓	Never	Former	CC	ECIG	DUAL
55+	Never	1	0	0	0	0
	Former	0	0.98	0.02	0	0
	CC	0	0.11	0.87	0.01	0.02
	ECIG	0	0.13	0.05	0.78	0.04
	DUAL	0	0.03	0.43	0.07	0.47

7.3. Estimating the transition probabilities for IQOS

Based on marketing data, we assumed that the initiation and re-initiation of IQOS will be 0.5% of CC initiation in the first 8 years and then increases to 3 % of CC. The likelihood of quitting is assumed to be the same CC. As we don't have sufficient evidence, we assumed that consumers do not switch between IQOS and e-cigarette, however, switching between IQOS and CC is assumed to be equal to the switching between ECIGS and CC (see Appendix 7-a05-transition-table).

7.3.1. Sensitivity analysis

We conducted sensitivity analyses to investigate the population health effect if the likelihood of switching to IQOS from combusted cigarettes was higher than to e-cigarettes as assumed in the Conversion scenario. Increasing likelihood of switching to IQOS was implemented in terms of increasing (coef >1) switching from CC to IQOS and decreasing (1/coef) switching from IQOS to CC.

$$new\ P_{CC\ to\ IQOS} = P_{CC\ to\ IQOS} * coef,\ newP_{IQOS\ to\ CC} = P_{IQOS\ to\ CC}/coef, coef = \overline{1;n}$$

The sensitivity analyses were evaluated in 2034, 10 years after the introduction of IQOS. The evaluation consisted of examining its population prevalence and reduction in smoking-attributed deaths until 2080.