Assessing the Potential Population Health Impact of Market Authorization of E-cigarettes in the U.S.

Raheema Muhammad-Kah, Yezdi. B Pithawalla, Thaddeus Hannel, Lai Wei, Ryan Black, Thomas Bryan, and Maria Gogova

Altria Client Services LLC, 601 East Jackson Street, Richmond, VA 23219 USA

CORESTA Congress 2018, 22-26 October 2018, Kunming, China

Abstract

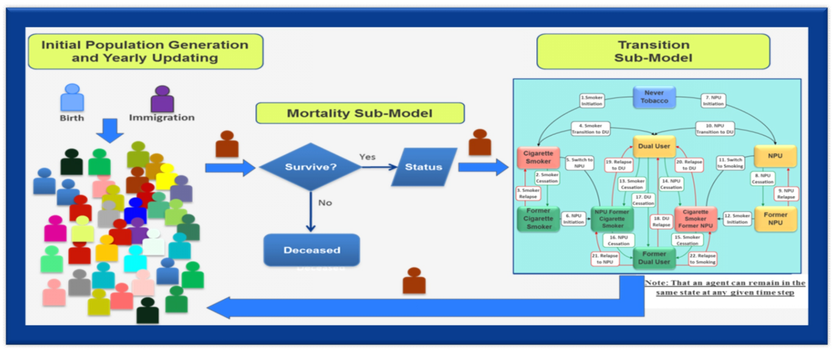
When evaluating a Premarket Tobacco Product Application (PMTA) or Modified Risk Tobacco Product Application (MRTPA), the Food and Drug Administration (FDA) employs a Population Health Standard, which requires evaluation of risk and benefit to the population as a whole; including tobacco users and non-users. In the absence of epidemiological data, computational models are valuable tools for predicting the likely impact of introducing a new tobacco product on the U.S. population. Using best modeling practices, we have developed and validated an Agent Based Model which assesses the impact of introducing a new product into a hypothetical population by estimating changes in tobacco use prevalence and premature death prevented for a Modified Case Scenario (where both cigarettes and e-cigarettes have authorization to be marketed in the U.S.) against a Base Case scenario (where cigarettes are the predominately used tobacco product and e-cigarettes do not have authorization to be marketed). The model allows us to integrate information about relative risks between existing and new products, with learnings from published literature, national dataset analyses and consumer perception studies that provide insights about potential behavioral changes, which may occur when a new product is introduced into the market. Survival probabilities of current and former e-cigarette users were determined by combining statistical models with excess relative risks (ERR). Base Case transition probabilities were obtained from nationally representative databases. The Modified Case transitions probabilities were estimated from an analysis of Wave 1 and Wave 2 data from the Population Assessment of Tobacco and Health (PATH) study. Employing these transition probabilities and a ERR value of 0.05 for e-cigarette use compared to smoking, we demonstrate a net benefit to the population of ~600,000 premature death prevented, along with a reduction in cigarette smoking prevalence, over the simulation follow-up period. Results from sensitivity analysis will also be discussed.

Introduction

- Computational models can be used to predict the likely impact of introducing a new tobacco product within a population.
- We have developed and validated a population model using best modeling practices to assess the potential population health impact of market authorization of E-cigarettes in the U.S.
- In our model, agents form a hypothetical population in which they transit between different tobacco use states using defined transition probabilities. The set of attributes associated with each agent (e.g., age, gender, current use status, and tobacco use history) determines the path an agent may consider. Statistical mortality models combined with excess relative risks are used to determine the survival probabilities of an agent at each time step.

Methods

Initial Population: 2.81MM (1/100th of U.S. Population in Yr. 2000)



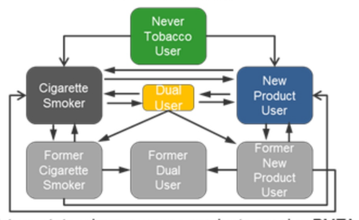
The model population is updated on a yearly basis over the 60 year time frame (Yr. 2000 to Yr. 2060)

Evaluating Impact of Introducing E-cigarettes into the U.S. Market

Base Case

Cigarettes continue to be the pre-dominant tobacco product in the U.S. market

Modified Case



A future state where e-vapor products receive PMTA approvals and both cigarettes and e-vapor products co-exist in the U.S. market

OUTPUTS

Difference in tobacco use prevalence & all-cause mortality:
Base Case (status quo; the current market, where cigarettes are the predominantly used tobacco product) & Modified Case (where cigarettes and E-cigarettes are both available on the market)

INPUTS and ASSUMPTIONS

Transition Sub-model

- **Base Case Transition Probabilities:**
  - Smoking Initiation & Cessation: Reflective of the year 2000 (NHIS & CISNET)
  - Relapse: Set to zero since cessation rates reflect successful smoking cessation for at least two years (CISNET)
- **Modified Case Transition Probabilities:**
  - Estimated from in-house analysis of transition behavior data on non-users and established users from Wave 1 to Wave 2 of the Population Assessment of Tobacco and Health (PATH) study
  - Never Users of tobacco do not initiate cigarettes or e-cigarettes after the age of 30
  - Cessation: Reflective of the year 2000 (NHIS & CISNET)

Mortality Sub-model

- **Never Tobacco Users, Smokers and Former Smokers Mortality:**
  - Tobacco-related mortality was estimated from a Kaiser Permanente Medical Care Program Cohort study and adjusted for U.S. mortality rates in the year 2000 using data from the Human Mortality Database (HMDB).
  - Employed Gompertz methodology to build survival curves based on *age, gender, years smoked, years quit and interaction terms*.
- **E-cigarette Users and Former E-cigarettes Users Mortality:**
  - Excess relative risk (ERR) of E-cigarettes use compared to smoking was 0.05 (i.e. a 95% reduction in risk compared to mortality risk from smoking cigarettes) proposed by Nutt et al.
- **Dual Use assigned same mortality risk as that of exclusive cigarette smoking**

ANALYSES

- **PATH Analysis:** determine transition behaviors of non-users and established users from Wave 1 to Wave 2 of the PATH study (Figure 1)
- **Modified Case Scenario:** the effect of all the most-likely changes in tobacco use patterns occur simultaneously (Figure 2)
- **Sensitivity Analyses:** evaluating the effects of varying input parameters on the net population

Figure 1: Transition probabilities value under the Modified Case Scenario

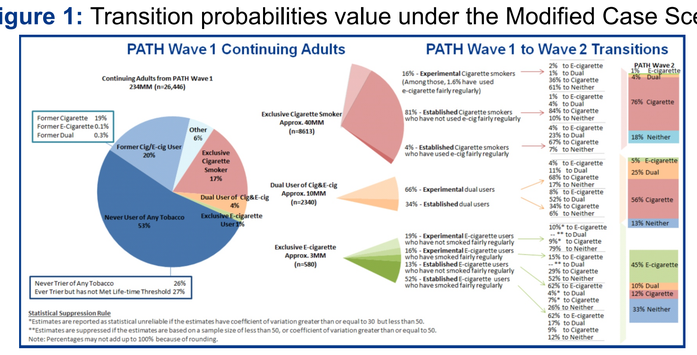
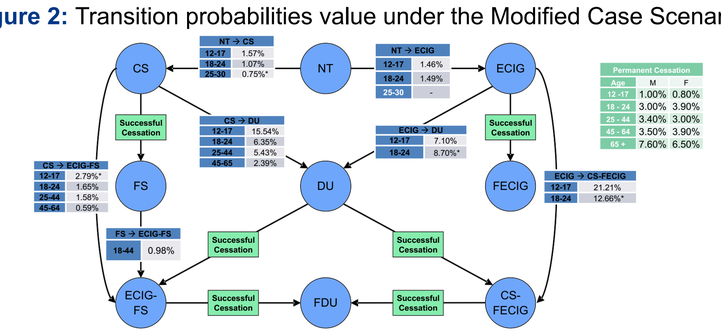


Figure 2: Transition probabilities value under the Modified Case Scenario



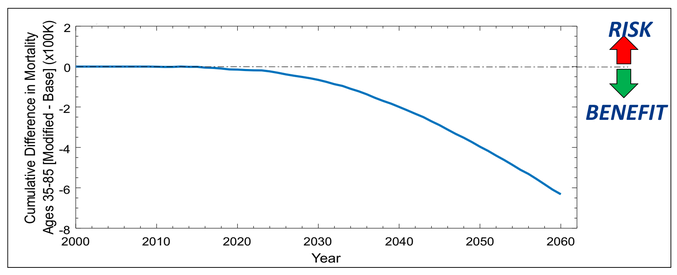
Statistical Suppression Rule
*Estimates are reported as statistical unreliable if the estimates have coefficient of variation greater than or equal to 30 but less than 50.
Estimates are suppressed if the estimates are based on a sample size of less than 50, or coefficient of variation >=50.
Successful Cessation= Long term cessation without relapse (i.e. reflects successful smoking cessation for at least two years)

NT = Never-Use of Tobacco *ECIG= E-cigarette User* *DU = Dual User*
CS = Current Cigarette Smoker *FECIG = Former E-cigarette User* *FDU = Former Dual User*
FS = Former Cigarette Smoker *CS-FECIG = Current Cigarette Smoker Former E-cigarette User* *ECIG-FS = E-cigarette User Former Smoker*

Results

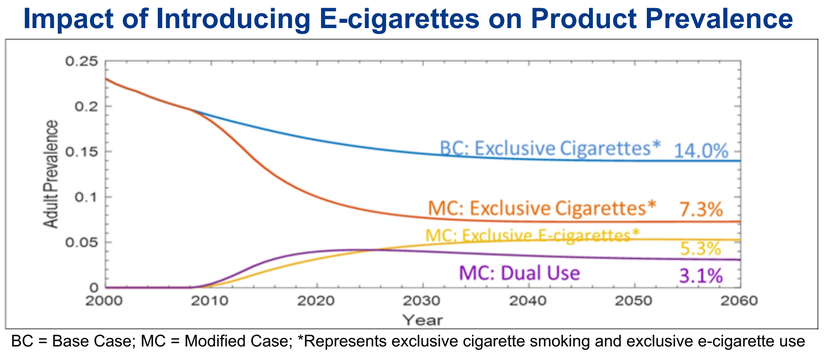
Impact of Introducing E-cigarettes on All-Cause Mortality

Base Case: Cigarette smoking continues to be the pre-dominant tobacco use behavior in the U.S. market
Modified Case: E-cigarettes co-exist in the U.S. market since 2009 and receive authorization to be marketed over the remaining simulation timeframe



Modeling results predict that ~629,000 premature deaths could be prevented, over a 50-year period, following introduction of e-cigarettes into the U.S. market

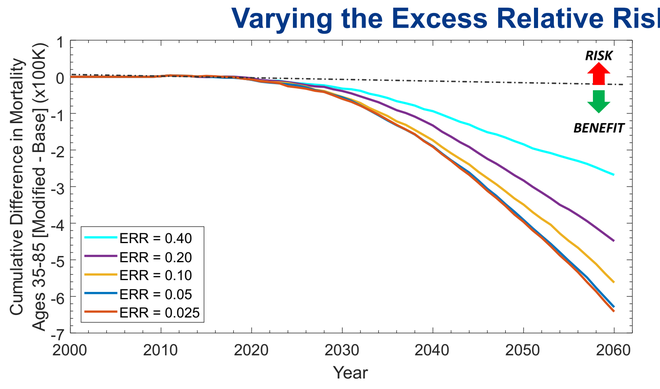
Impact of Introducing E-cigarettes on Product Prevalence



BC = Base Case; MC = Modified Case; *Represents exclusive cigarette smoking and exclusive e-cigarette use

Modeling results predict that introduction of e-cigarettes into the U.S. market would result in a decrease of exclusive cigarette smoking prevalence and increase in exclusive e-vapor use and dual use prevalence

Varying the Excess Relative Risk (ERR) Value



Line Color	ERR	Premature Death Prevented
	0.40	268,000
	0.20	449,000
	0.10	562,000
	0.05	629,000
	0.025	641,000

Varying Each Individual PATH Transition Rate by Its Upper and Lower 95% Confidence Interval

Transition	Premature Deaths Prevented in the Year 2060 (Modified - Base)	
	Lower Confidence Interval	Upper Confidence Interval
NT ⟶ CS	754,000	417,000
NT ⟶ ECIG	667,000	571,000
CS ⟶ ECIG-FS	441,000	850,000
ECIG ⟶ CS-FECIG	649,000	568,000
CS ⟶ DU	662,000	581,000
ECIG ⟶ DU	656,000	581,000
FS ⟶ ECIG-FS	642,000	611,000

CS = Current Cigarette Smoker;
CS-FECIG = current cigarette smoker who was a former e-cigarette user;
DU = dual user;
ECIG = current e-cigarette user;
ECIG-FS = current cigarette smoker who was a former e-cigarette user;
FS = former cigarette smoker; NT = never-user of tobacco

Sensitivity analysis results demonstrate that under defined conditions, the greatest impact on number of premature deaths prevented was observed for changes in transition probabilities from the NT to CS and from exclusive cigarette smoking to exclusive e-cigarettes use and would still result in a net benefit to the population

Conclusions

- Our model suggests overall net benefit of introducing E-cigarette into the US market, as indicated by likely reduction in smoking prevalence and a decreased mortality (629,000 premature deaths prevented) in the US population compared to the status quo.
- The sensitivity analysis indicates that relatively large changes to the ERR of an E-cigarette would still predict a net benefit to the population under our defined scenario.
- As more real world data on smoking/E-cigarette transition, initiation and cessation rates become available, we could further refine our assumptions and model inputs.

References

- PATH Study Public Use Files: User Guide. www.icpsr.umich.edu/icpsrweb/NAHDAP/studies/36498. Accessed September 5, 2017.
- Anderson, C. M., Burns, D. M., Dodd, K. W., & Feuer, E. J. (2012). Chapter 2: Birth-cohort-specific estimates of smoking behaviors for the U.S. population. Risk Anal, 32 Suppl 1, S14-24. doi:10.1111/j.1539-6924.2011.01703.x
- Friedman G, Tekawa IS, Sadler M and Sidney S (1997). Smoking and Mortality: the Kaiser Permanente Experience. In Changes in Cigarette-Related Disease Risks and Their Implication for Prevention and Control. Shopland DR, Burns DM, Garfinkel L and Samet J, eds. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute. p 477-499.
- Nutt, D. J., Phillips, L. D., Balfour, D., Curran, H. V., Dockrell, M., Foulds, J., . . . Sweanor, D. (2014). Estimating the harms of nicotine-containing products using the MCDA approach. Eur Addict Res, 20(5), 218-225. doi:10.1159/000360220

This poster may be accessed at www.altria.com/ALCS-Science