POPULATION MODELING IN TOBACCO REGULATION TO QUANTIFY THE RISKS AND BENEFITS TO THE POPULATION AS A WHOLE

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CENTER FOR TOBACCO PRODUCTS

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OUTLINE

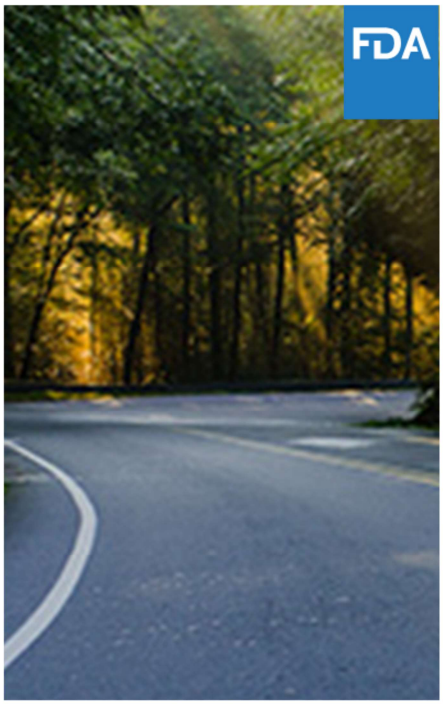
I. Overview

II. Examples of modeling strategies used by CTP

III. Dynamic population modeling approach

- Input/output data
- Example: Modeling a potential Nicotine Product Standard
- Limitations

IV. Challenges for population modeling



OVERVIEW

- Population models have been used in tobacco regulatory science:
  - ✓ to model the potential impact(s) of a regulatory policy on the population as a whole, including users and nonusers of tobacco products
  - ✓ to evaluate the potential population health impact associated with the introduction of new tobacco products through Premarket Tobacco Product Application (PMTA) and Substantial Equivalence (SE) pathways
- Because of the changes in the tobacco market (introduction of e-cigarettes, IQOS, flavored tobacco products, etc.), population modeling frameworks have been adapted to account for dual/poly use and switching between products
- This presentation will discuss:
  - ✓ a modeling approach used by CTP
  - ✓ limitations and challenges for population modeling

EXAMPLES OF MODELING STRATEGIES USED BY CTP

- In 2015, in collaboration with Sandia National Laboratories, CTP developed a Dynamic Population Model (DPM). **The model can be used to evaluate the potential population health impact associated with the introduction of new tobacco products or policies**

- In 2018, CTP used a DPM to quantify the potential public health effects of enacting a regulation that makes cigarettes minimally addictive (**nicotine product standard**)
- On March 16, 2018, FDA issued an advance notice of proposed rulemaking* to develop a "Tobacco Product Standard for Nicotine Level of Combusted Cigarettes"

PLOS ONE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Modeling the Potential Effects of New Tobacco Products and Policies: A Dynamic Population Model for Multiple Product Use and Harm

Eric D. Vugrin, Brian L. Rostron, Stephen J. Verzi, Nancy S. Brodsky, Theresa J. Brown, Conrad J. Choiniere, Blair N. Coleman, Antonio Paredes, Benjamin J. Apelberg

Published: March 27, 2015 • https://doi.org/10.1371/journal.pone.0121008

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States

Benjamin J. Apelberg, Ph.D., M.H.S., Shari P. Feirman, Ph.D., Esther Salazar, Ph.D., Catherine G. Corey, M.S.P.H., Bridget K. Ambrose, Ph.D., M.P.H., Antonio Paredes, M.S., Elise Richman, M.P.H., Stephen J. Verzi, Ph.D., Eric D. Vugrin, Ph.D., Nancy S. Brodsky, Ph.D., and Brian L. Rostron, Ph.D., M.P.H.

* https://www.federalregister.gov/documents/2018/03/16/2018-05345/tobacco-product-standard-for-nicotine-level-of-combusted-cigarettes

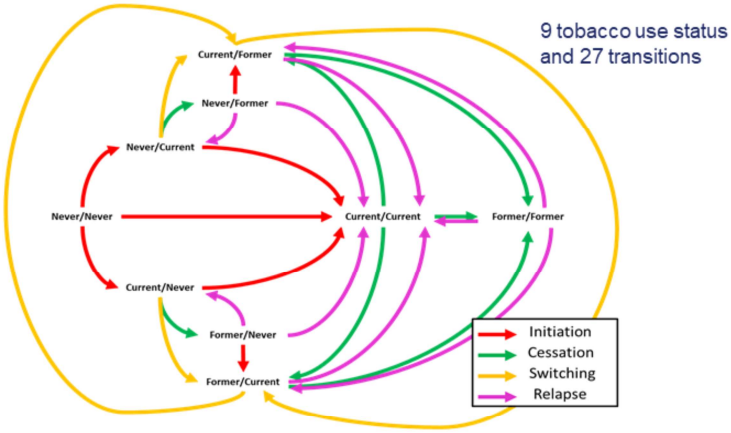
DYNAMIC POPULATION MODEL APPROACH

The DPM is a multi-state dynamic population model* used to assess the effects of product initiation, cessation, relapse and dual use on product use prevalence and mortality attributable to tobacco use

One-product scenario

Two-product scenario

9 tobacco use status and 27 transitions



* Vugrin et al. (2015) Modeling the Potential Effects of New Tobacco Products and Policies: A Dynamic Population Model for Multiple Product Use and Harm. PLOS ONE

DYNAMIC POPULATION MODEL APPROACH (CONT.)

At each discrete time step "t", the model updates each subpopulation "*i*", accounting for births, mortality and net migration

$$x_i(t+1) = x_i(t) - x_i^{out}(t+1) + x_i^{in}(t+1) + b_i(t+1) + m_i(t+1)$$

- $x_i(t)$: # individuals in subpopulation "i" at time "*t*"
- $x_i^{out}(t+1)$: # individuals that leave subpopulation "*i*" between t and t+1 due changes in tobacco use, death or aging
- $x_i^{in}(t+1)$: # individuals that join subpopulation "*i*" and do not die between t and t+1
- $b_i(t+1)$: # of births into subpopulation "*i*" between t and t+1
- $m_i(t+1)$: Net international migration into subpopulation "*i*" between t and t+1

DYNAMIC POPULATION MODEL APPROACH (CONT.)

- The DPM was used to project impacts of a hypothetical scenario on tobacco use, morbidity and mortality in the U.S. Examples of hypothetical scenarios include:
  - ✓ Introduction of a new tobacco product
  - ✓ Implementation of a new policy (i.e., nicotine product standard, menthol ban, etc.)
- For a specified simulation period, the model simulated product use prevalence and morbidity/mortality attributable to tobacco use and compared between

Baseline Scenario vs Hypothetical Scenario

- The DPM is a deterministic model, and because of this feature, the model does not incorporate uncertainty. To account for uncertainty, we used Monte Carlo simulation to compute range estimates (details not discussed in this talk).

INPUT DATA

Scenario	Input model parameter	Source
Baseline scenario	U.S. Population by sex and age	U.S. Census: National Population Projections
	Births and net international migration	U.S. Census National Population Estimates
	U.S. mortality rates and relative risk (all-cause) by smoking status, sex and age groups	National Health Interview Survey – Linked Mortality Files (NHIS-LMF)
	Tobacco-use status (never, current, dual, former) by sex, age groups and tobacco product use	National Health Interview Survey (NHIS), National Youth Tobacco Survey (NYTS), PATH
	Smoking transition behaviors by sex and age (initiation, cessation, relapse, switching)	Reconstructions of cohort smoking histories from NHIS data (CISNET estimates)
Hypothetical regulatory scenario	Regulatory-specific values to change transition behaviors. For example: • % reduction in smoking initiation • % increase in cessation • Changes in switching from one product to the other	Regulatory-specific expert elicitation, tobacco research papers

OUTPUT DATA

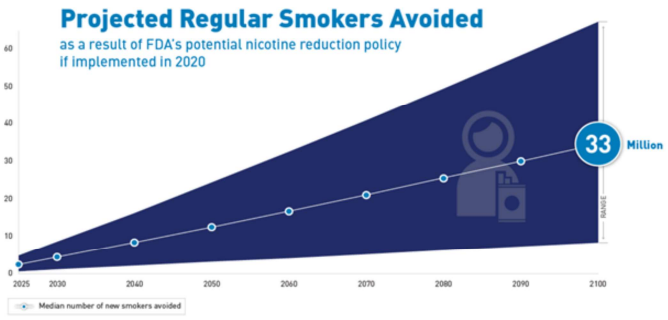
For each year in the simulation period (i.e., 2015-2100):

- ✓ U.S. population projections by sex, age, and tobacco use status
- ✓ Tobacco use prevalence (never, current, dual, former users)
- ✓ Projected regular smokers dissuaded
- ✓ Projected life years gained
- ✓ Projected tobacco-attributable deaths prevented

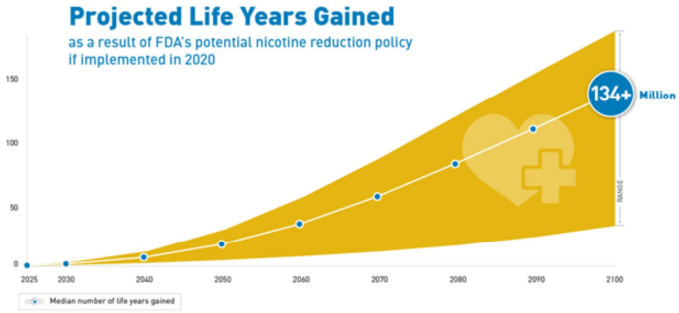
EXAMPLE: MODELING A POTENTIAL NICOTINE PRODUCT STANDARD*

Baseline scenario: cigarette smoking would continue to decline based on recent trends in smoking initiation and cessation

Policy scenario: a product standard is put in place in 2020 to lower levels of nicotine in cigarettes and other combustible tobacco products



By 2100, 33million people would avoid becoming regular smokers



By 2100, more than 134 million years of life gained among the U.S. population

* **Source**: How Could Lowering Nicotine Levels in Cigarettes Change the Future of Public Health? May 2020. https://www.fda.gov/tobacco-products/public-health-education/how-could-lowering-nicotine-levels-cigarettes-change-future-public-health

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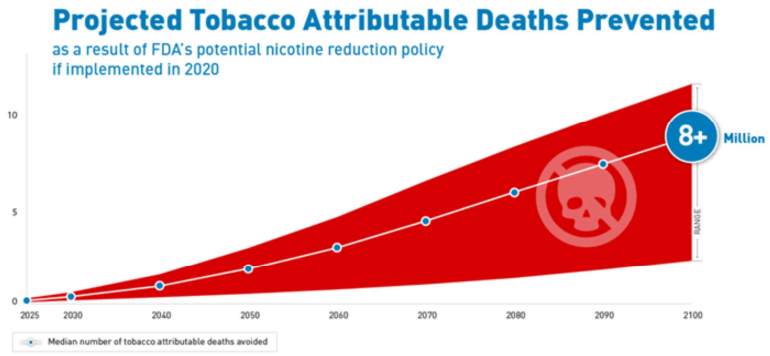

By 2100, more than 8 million premature deaths from tobacco could be avoided

* **Source**: How Could Lowering Nicotine Levels in Cigarettes Change the Future of Public Health? May 2020. https://www.fda.gov/tobacco-products/public-health-education/how-could-lowering-nicotine-levels-cigarettes-change-future-public-health

LIMITATIONS OF THE DYNAMIC POPULATION MODEL

Regarding input parameters:

- Although the model can be used to run stratified analyses (i.e., by race/ethnicity) and for different tobacco products, in some cases incorporating group-specific mortality estimates is not possible due to the lack of follow-up data and small sample size for some tobacco products
- To date, cause-specific (tobacco-related) mortality and morbidity data has not been incorporated
- Some CTP reported analyses using the DPM assume constant tobacco use transition rates (initiation, cessation, switching) over the simulation period

Regarding modeling framework:

- DPM is a deterministic model approach and does not incorporate uncertainty for model predictions
- To account for uncertainty, Monte Carlo simulations were used (details not discussed in this talk)

CHALLENGES FOR POPULATION MODELING

Construction of input parameters:

- Tobacco use prevalence can be derived from complex surveys (NYTS, NHIS, PATH, TUS-CPS); however, estimates can be different across surveys. Sensitivity analysis (or other analysis to account for input parameters uncertainty) is needed to assess the impact of various data sources on model outcomes
- There is not enough mortality follow-up data to estimate mortality risk associated with the use of new tobacco products marketed in the U.S.

CHALLENGES FOR POPULATION MODELING (CONT.)

Modeling framework:

- Ideally, model outcomes (prevalence, morbidity and mortality) should be reported with uncertainty metrics (such as confidence intervals, standard errors, range values). Other modeling frameworks, such as probabilistic models or Bayesian approaches, could be explored to incorporate uncertainty.

- Micro-simulation (including agent-based modeling) could be used to simulate changes in tobacco use transitions under hypothetical regulatory scenarios. Results from micro-simulation analysis could provide model-based assumptions and input data to model the impact of regulatory scenarios.

- It may be difficult to incorporate available biomarker data from tobacco users to the model. However, biomarker data could be used on mortality/disease risk analysis; results from that analysis could be informative as input model parameters.

THANK YOU

Questions?