MODELING APPROACH TO QUANTIFY THE POTENTIAL PUBLIC HEALTH EFFECTS OF REDUCING NICOTINE LEVELS IN CIGARETTES IN THE UNITED STATES

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OUTLINE

I. Overview

II. A modeling approach used by CTP

- ✓ Dynamic population model
- ✓ Construction of input parameters
- ✓ Model outputs

III. Example: Modeling a potential nicotine product standard in the U.S.

IV. Limitations and challenges for population modeling

OVERVIEW

- Population models have been used in tobacco regulatory science:
  - ✓ to model the potential impact 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
- This presentation will focus on:
  - ✓ describing a modeling strategy to quantify the potential public health effects of enacting a regulation in the United States that makes cigarettes minimally addictive by setting a maximum level of nicotine in cigarettes
  - ✓ pointing out some challenges regarding the construction of input model parameters and assumptions needed to populate these models

A MODELING APPROACH 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 standard**)
- A paper published in the *New England Journal of Medicine* in 2018 shows the potential health effects of the nicotine rule

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.

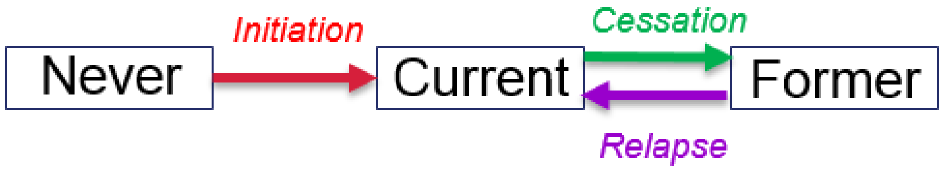
DYNAMIC POPULATION MODEL APPROACH

- 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, mortality, and morbidity attributable to tobacco use
- The model is initiated with a starting population, divided into subgroups defined by age, sex, and tobacco use status
- Population and subgroups are tracked over time and updated through birth, net international migration, and death
- The members of each subpopulation have a specified probability of dying and set of probabilities for transitioning from one tobacco use state to another.

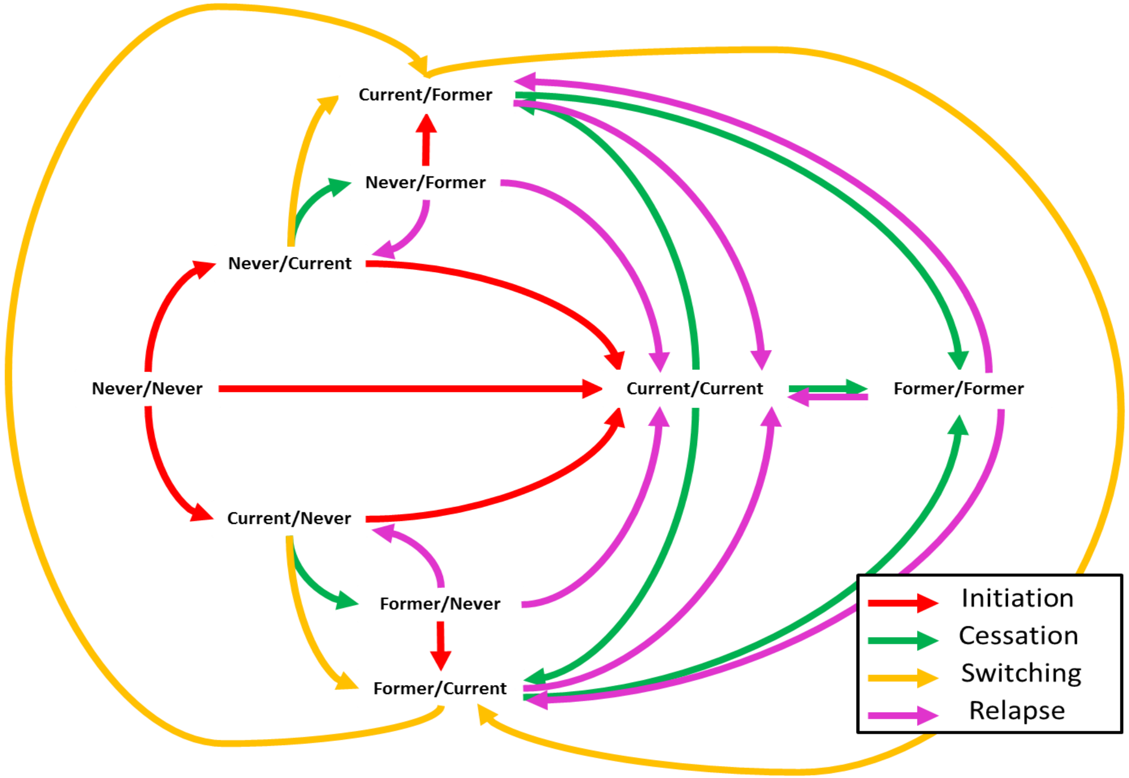
DYNAMIC POPULATION MODEL APPROACH (CONT.)

Tobacco use transitions for one- and two-product scenarios:

One-product scenario
(3 tobacco use statuses and 3 transitions)



Two-product scenario
(9 tobacco use statuses and 27 transitions)



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 prohibition, 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, Monte Carlo simulation was used to compute range estimates (details not discussed in this presentation)

CONSTRUCTION OF INPUT PARAMETERS

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, switching)	- Reconstructions of cohort smoking histories from NHIS data (CISNET estimates) - Results from PATH data analyses
Hypothetical regulatory scenario	Potential changes in transition behaviors as a result of the implementation of a regulatory scenario: • % reduction in smoking initiation • % increase in cessation • Changes in switching from one product to the other	Regulatory-specific expert elicitation, tobacco research papers

MODEL OUTPUTS

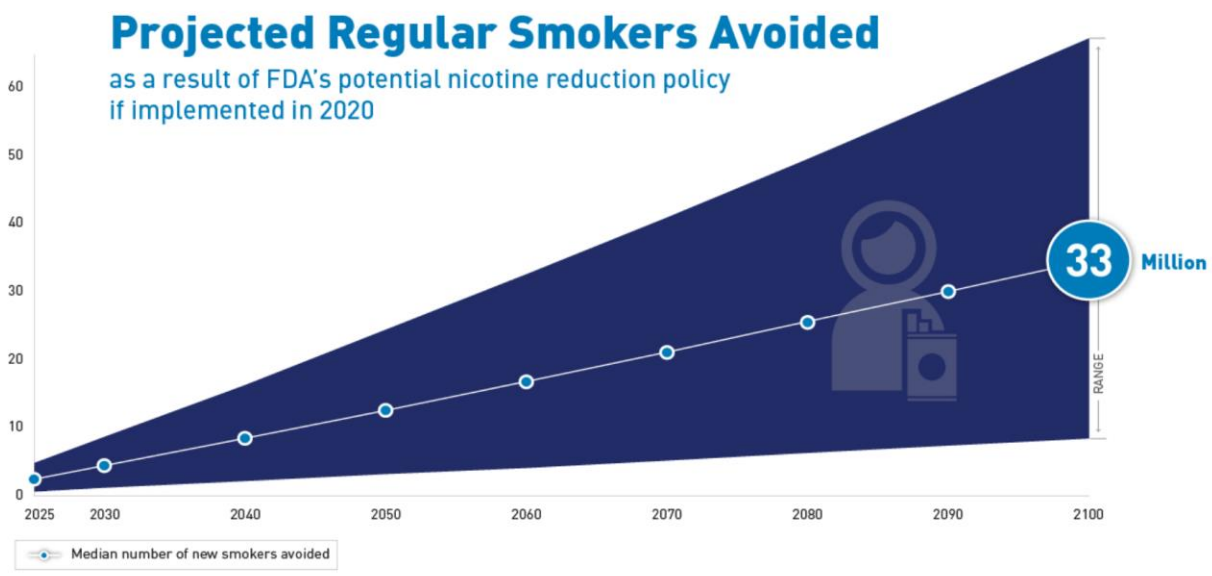
For each year in the simulation period, the model provides estimates for:

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

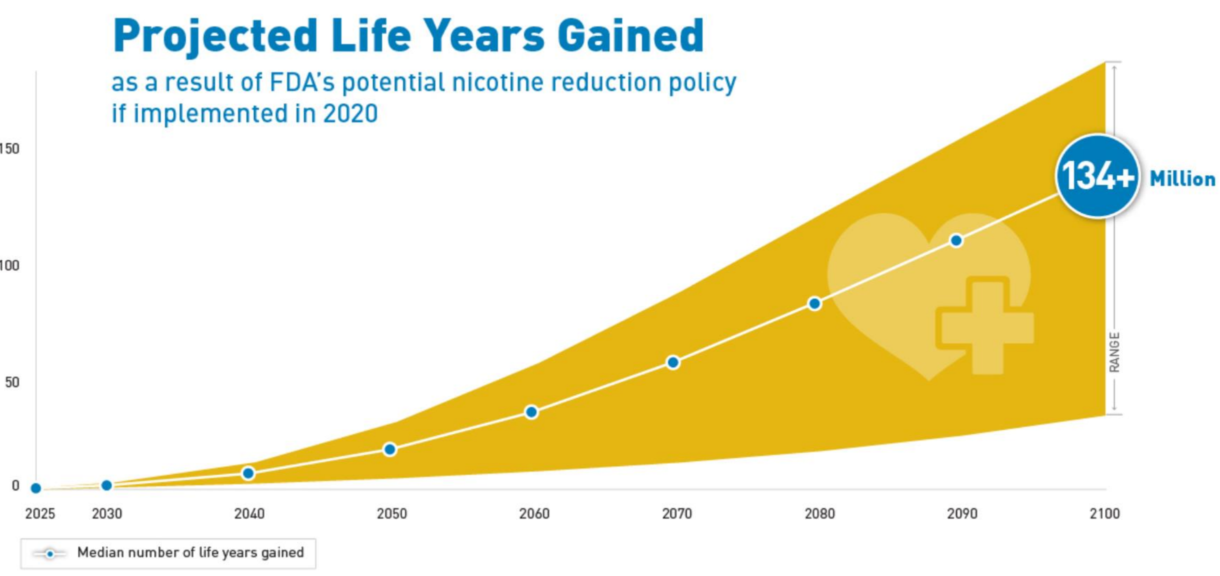
EXAMPLE: MODELING A POTENTIAL NICOTINE PRODUCT STANDARD

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, 33 million people would avoid becoming regular smokers



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

Figures' 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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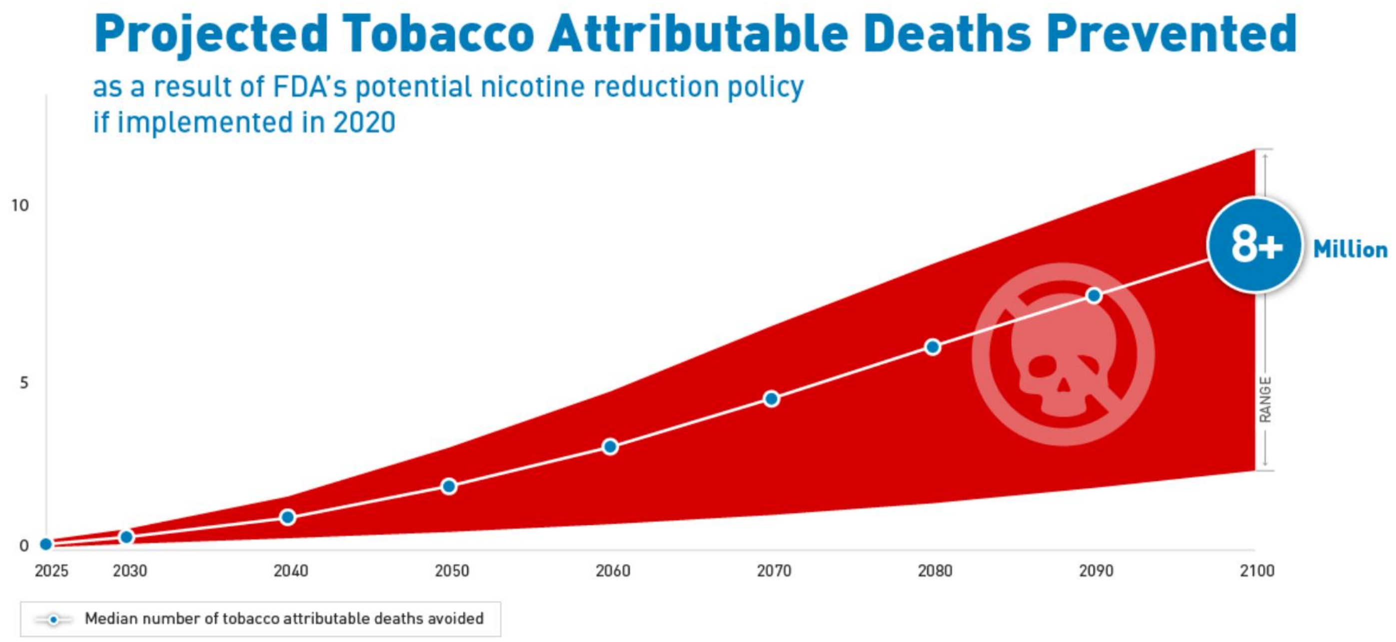

By 2100, more than 8 million premature deaths from tobacco could be avoided

Figure's 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 AND FUTURE DIRECTIONS FOR POPULATION MODELING

FDA

Limitations:

- Currently age and sex are the only population level variables. Potential update: consider disparity variables such as race, socio-economic status, geographic area, etc.
- The model is restricted to all cause mortality. Potential update: incorporate cause-specific mortality (tobacco related) and morbidities

Future Directions

- Ideally, model outcomes (prevalence, morbidity and mortality) should be reported with uncertainty metrics (such as confidence intervals, standard errors, range values). Other modeling frameworks could be explored to incorporate uncertainty
- Explore ways to incorporate assumptions regarding the impact of a policy that doesn’t have real-world data (i.e. a policy that has never been implemented)
- Could biomarker data be used on mortality/disease risk analysis? Results from those analyses could be informative as input model parameters

THANK YOU

Questions?