Modeling the impact of an existing Tobacco product with a Modified-Risk Claim on Population Health: The Role of Sensitivity Analyses

CORESTA, October 3, 2019

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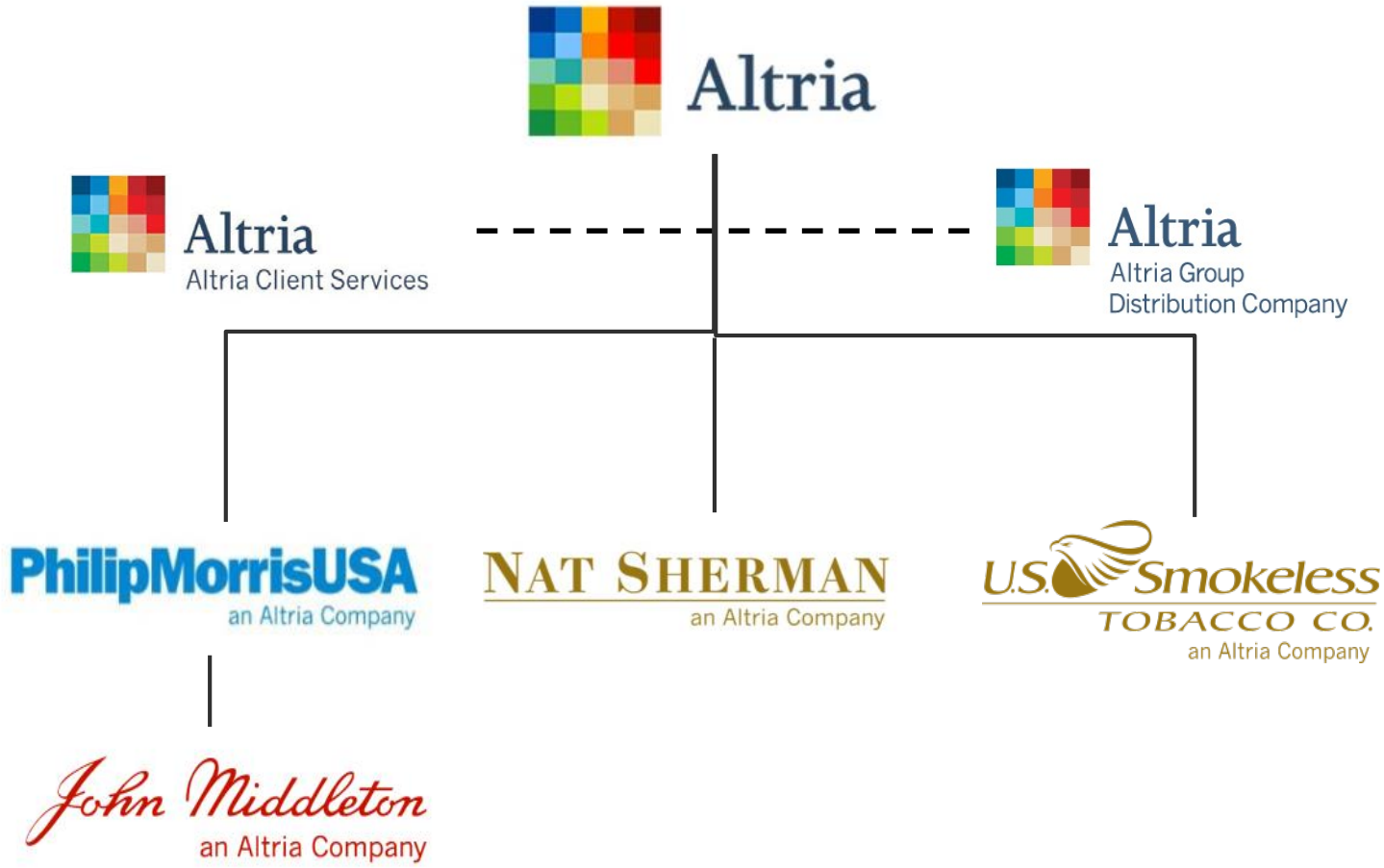
Altria Operating Structure



* For illustrative purposes only. Not actual corporate structure; does not reflect all Altria subsidiaries

Continuum of Risk

- Not all tobacco products present the same risk

(Directional only – not to scale; adapted from Hatsukami* *et al*.)

Range of Potentially Lower Risk Products

Heat-not-Burn

E-Vapor

Smokeless

Note: Third party trademarks are the property of their respective owners and are included for informational purposes only.

MRTPA Statutory Requirements (§ 911(g)(1))

- The candidate product, as it is actually used by consumers, will:

1. Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and

2. Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.

"**FDA encourages** the development and application of innovative analytical methods to make preliminary estimates of the potential effects of some change in the marketplace. Methods ….include secondary data analyses and **computational modeling**."

Source: Food and Drug Administration Center for Tobacco Products, 2012: Guidance for Industry - Modified Risk Tobacco Product Applications: Draft Guidance. Center for Tobacco Products.

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Copenhagen® Snuff Fine Cut – Proposed Claim

1. **Draws the attention of adult smokers**

2. **Single disease focus**
   Neither states nor implies that the product presents no risk of lung cancer or other disease

3. **Desired single use behavior**

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ALCS Cohort Model

- Developed and validated the cohort model
  - Used best practices as described by
    - Institute of Medicine (IOM)
    - Society for Medical Decision Making (SMDM)
    - International Society of Pharmacoeconomics and Outcomes Research (ISPOR)

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ISPOR TASK FORCE REPORTS

Modeling Good Research Practices—Overview: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1

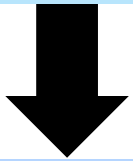
J. Jaime Caro, MDCM, FRCPC, FACP[1,2,], Andrew H. Briggs, Dphil[3], Uwe Siebert, MD, MPH, MSc, ScD[4,5], Karen M. Kuntz, ScD[6], on Behalf of the ISPOR-SMDM Modeling Good Research Practices Task Force*

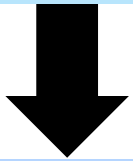
[1]Faculty of Medicine, McGill University, QC, Montreal, Canada; [2]United BioSource Corporation, Lexington, MA, USA; [3]Health Economics & Health Technology Assessment, Institute of Health & Wellbeing, University of Glasgow, Glasgow, UK; [4]UMIT – University for Health Sciences, Medical Informatics and Technology, Hall i.T., and Oncotyrol Center for Personalized Cancer Medicine, Innsbruck, Austria; [5]School of Public Health and Medical School, Harvard University, Boston, MA, USA; [6]School of Public Health, University of Minnesota, Minneapolis, MN, USA

Modeling the Impact of the Claim

Risk of using smokeless tobacco relative to cigarette smoking

Changes in product use patterns due to the modified risk claim





Benefit/Risk

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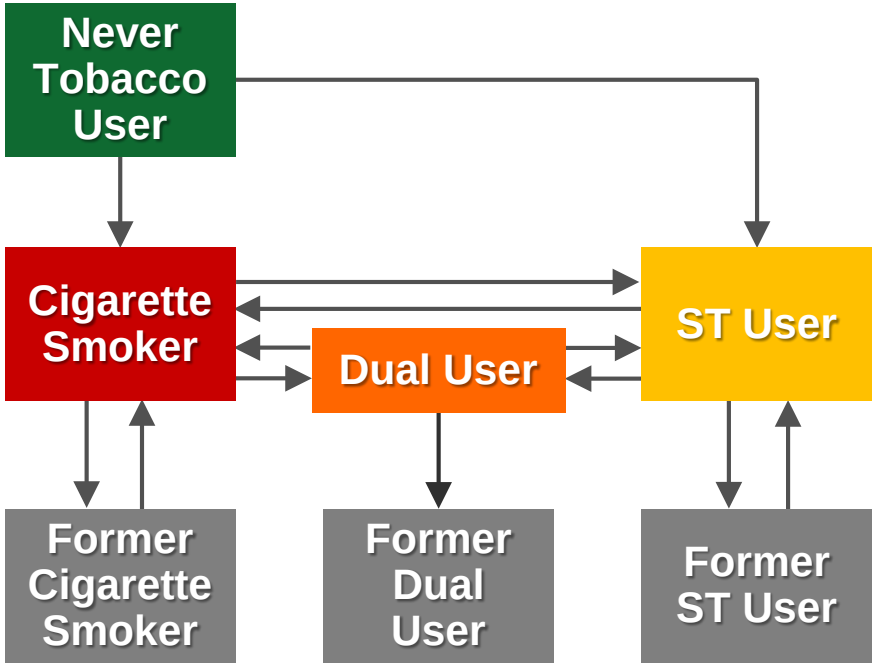
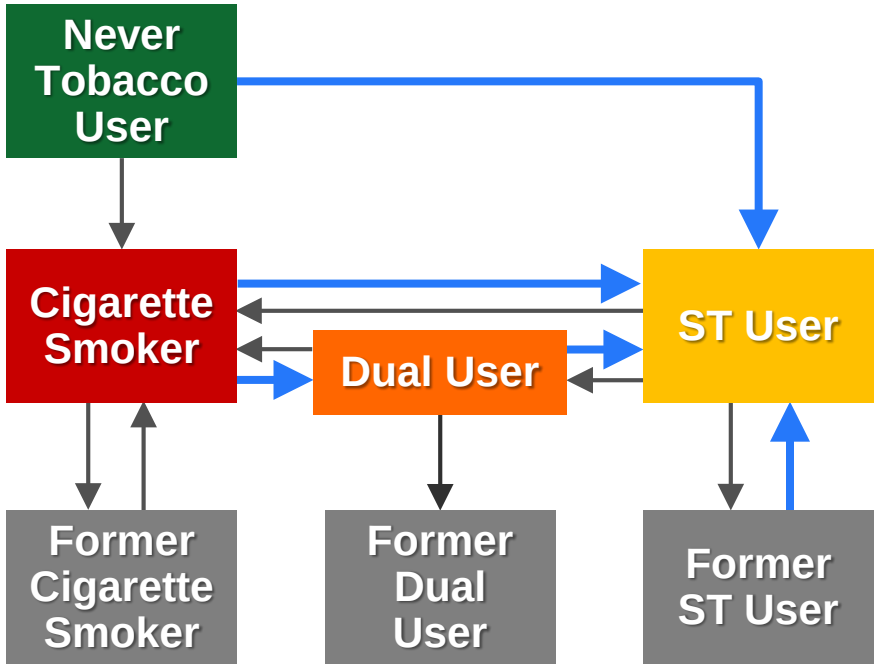
Modeling Framework

Base Case – World As Is Today



Modified Case – Future World



Estimate population benefit/risk by comparing the difference in All-cause Mortality between the Base Case and Modified Case

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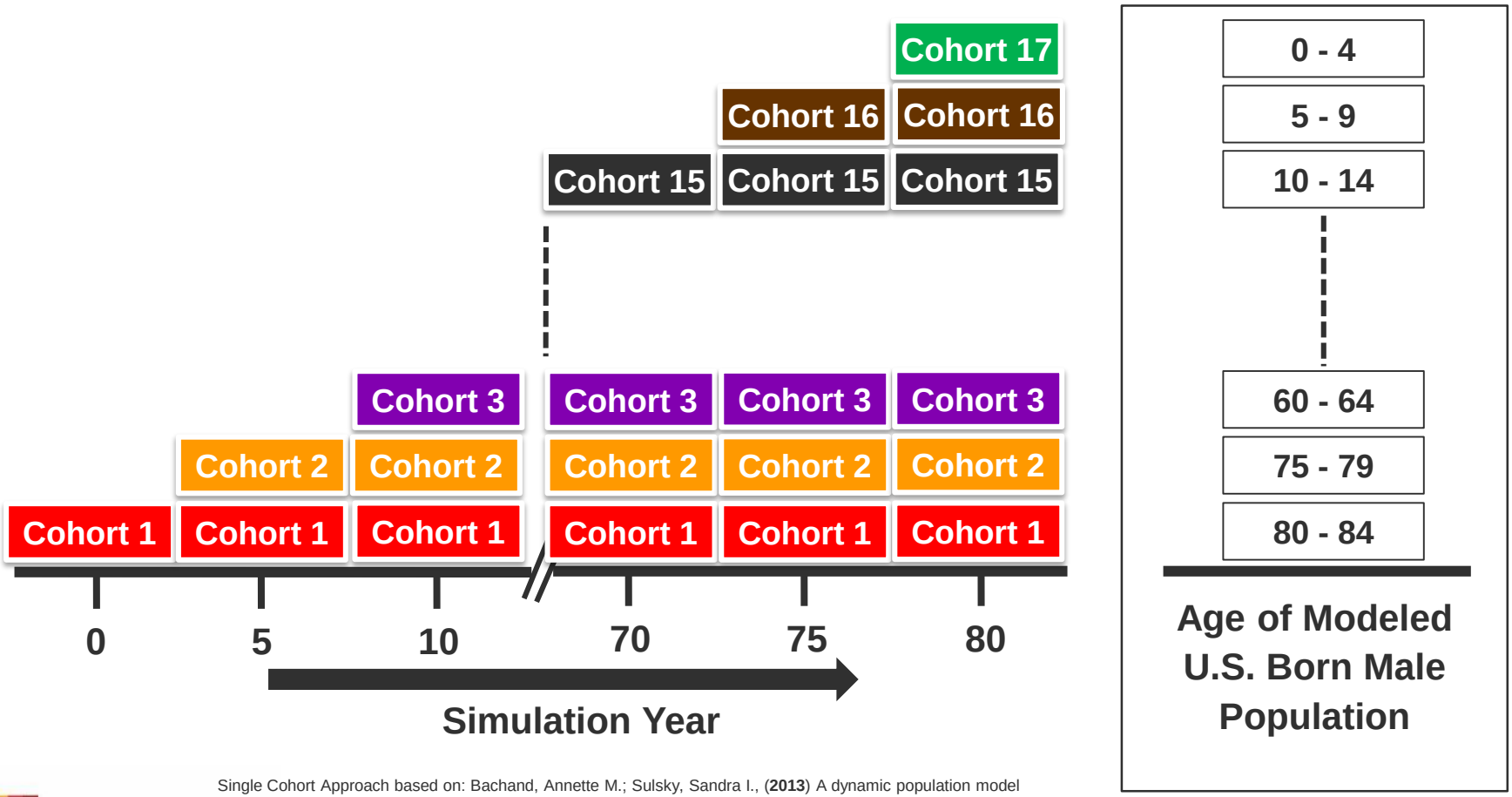
Time-Staggered Multiple Cohort Approach

- Models a complete population of Males Born in the U.S.



Single Cohort Approach based on: Bachand, Annette M.; Sulsky, Sandra I., (**2013**) A dynamic population model for estimating all-cause mortality due to lifetime exposure history. Regul. Toxicol. Pharmacol. 67;2

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Modeling the Impact of the Claim

Linked Mortality Analysis

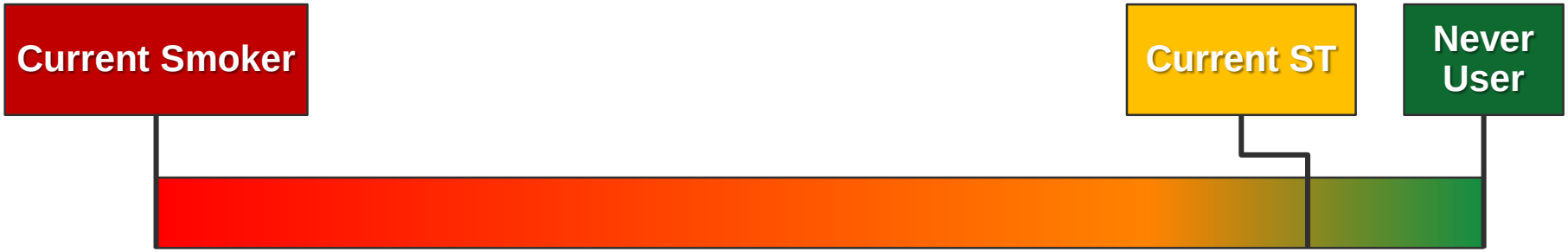
Risk of using smokeless tobacco relative to cigarette smoking

Changes in product use patterns due to the modified risk claim

Benefit/Risk

Risk of Smokeless Tobacco (ST) Use Relative to Cigarette Smoking

- The increased likelihood of all-cause mortality estimated from ALCS Linked Mortality Analysis*

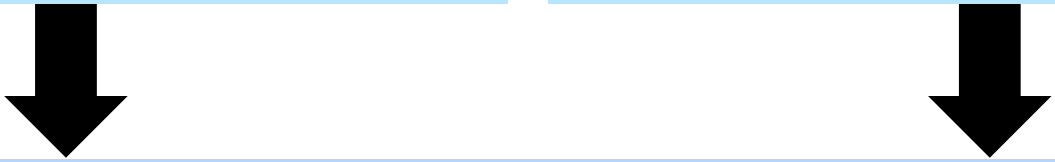


- We estimated the risk for Smokeless Tobacco Use to be 9% of Cigarette Smoking

*Fisher, M.T.; Tan-Torres, S.M.; Gaworski, C.L.; Black, R.A.; Sarkar, M., (**2019**) Smokeless tobacco mortality risks: An analysis of two contemporary nationally representative longitudinal mortality studies. Harm Reduct. J. 16;27

Modeling the Impact of the Claim

Linked Mortality Analysis	Altria Claim Comprehension & Intentions Study
Risk of using smokeless tobacco relative to cigarette smoking	Changes in product use patterns due to the modified risk claim



Benefit/Risk

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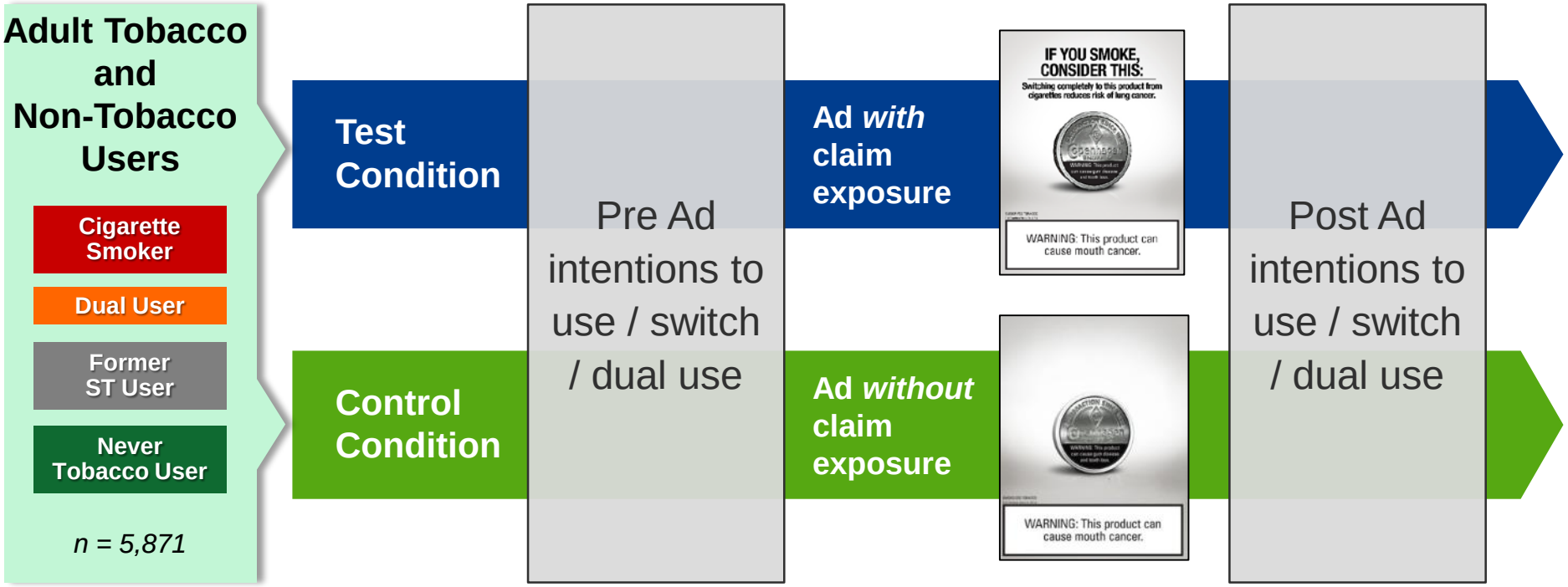
Altria Claim Comprehension & Intentions Study (CCIS)



- Estimate relative percent difference between response of Test and Control group
- Applied the estimated relative percent differences to Base Case transition rates to generate the Modified Case transition rates

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Relative Impact

	Adult Tobacco Use Behavior	Change in Likelihood of Behavior* (Relative Impact Factor)
1	Cigarette Smokers Switching to Copenhagen® Snuff	1.21
2	Cigarette Smokers Transitioning to Dual Use	1.25
3	Dual Users Switching to Copenhagen® Snuff	1.06
4	Former Smokeless Tobacco Users Relapsing to Copenhagen® Snuff	1.00
5	Never Users Initiating with Copenhagen® Snuff	0.94

*Results not statistically significant.

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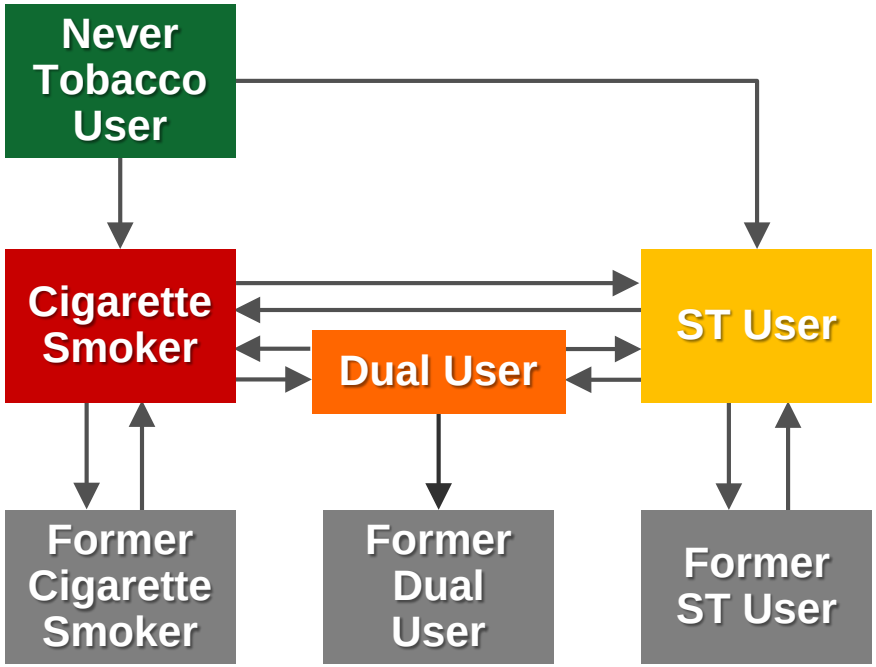
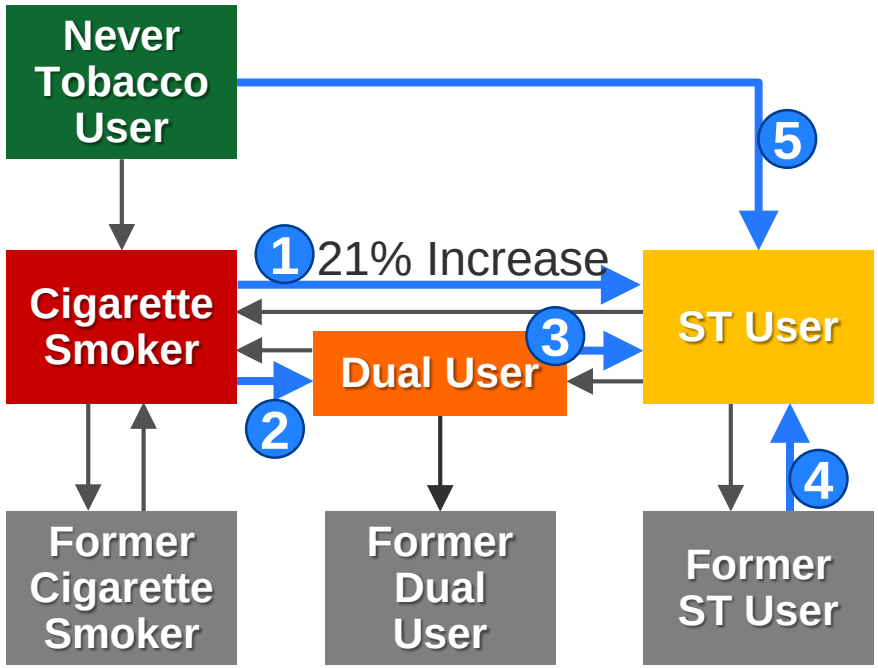
Modeling Framework

Base Case – World As Is Today



Modified Case – Future World



Adult Male Transition Rates

	Tobacco Use Transition	Base Case Transitions* (From the Literature)	Modified Case Transitions* (Adjusted from CCI Study)
1	Current smoker → ST	1.4%	1.7%
2	Current smoker → Dual user (ST + cigarettes)	3.2%	4.0%
3	Dual user → ST	17.4%	18.4%
4	Former ST → ST	1.8%	1.8%
5	Never user → ST	1.6%	1.5%

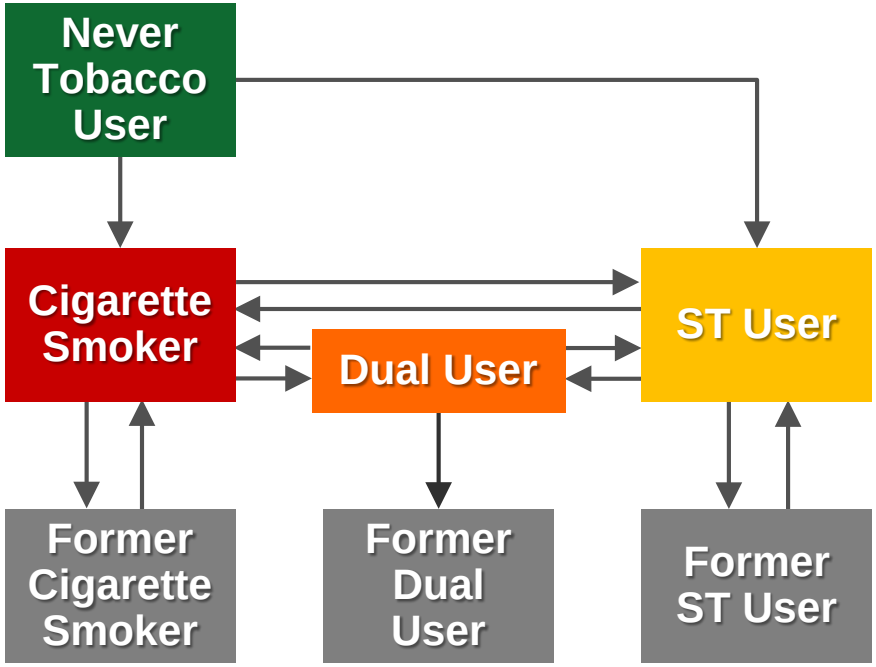
21% Increase

*Five year transition rates

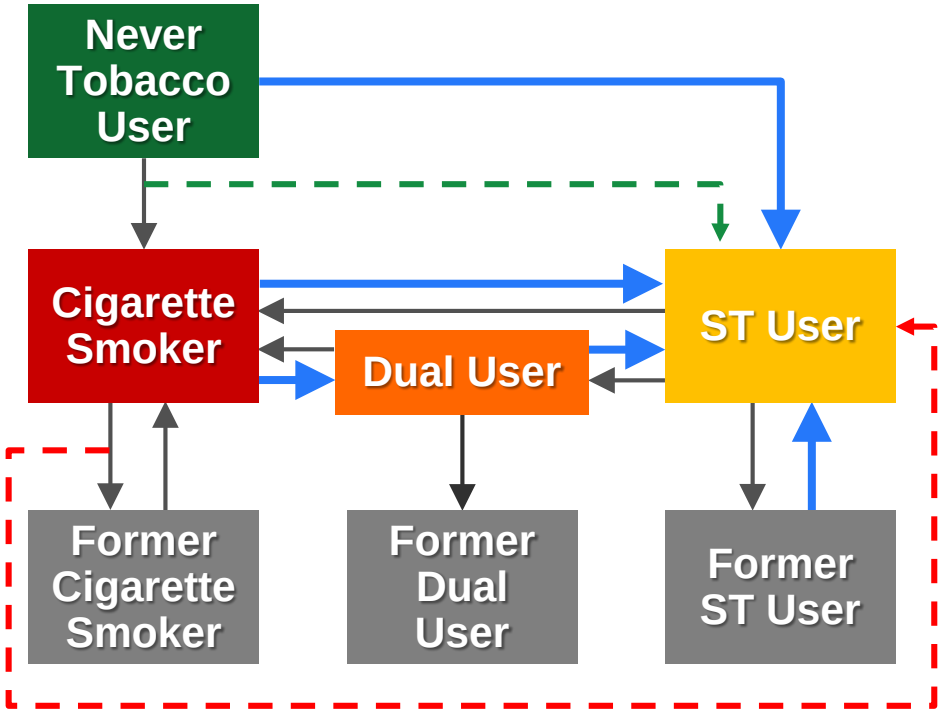
Base case transition rates largely informed by Tam J., Day H.R., Rostron B.L., Apelberg B.J. A systematic review of transitions between cigarette and smokeless tobacco product use in the United States. BMC Public Health. 2015;15:258

Modeling Framework

Base Case – World As Is Today



Modified Case – Future World



Approximately 93,000 premature deaths prevented over 60 years following claim authorization

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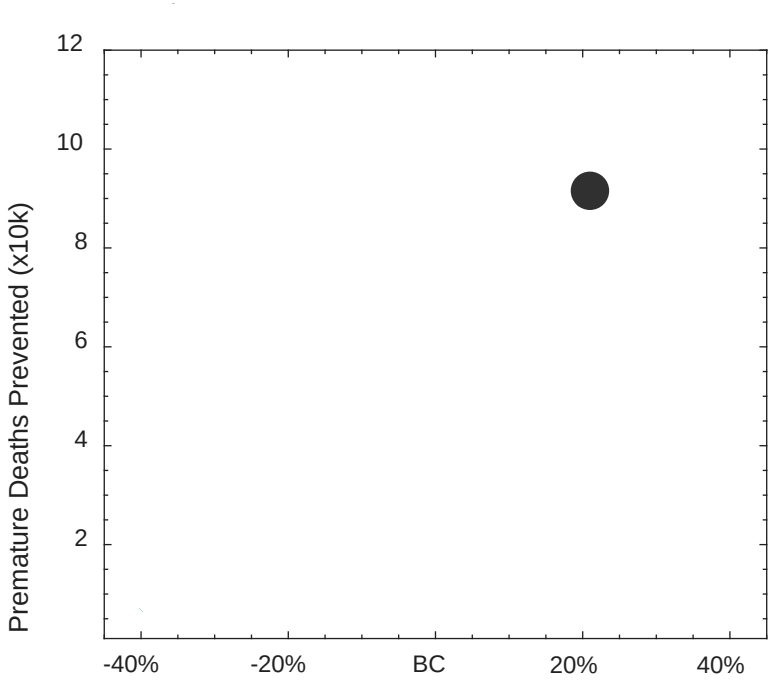
Sensitivity Analysis: What if?

Switching:

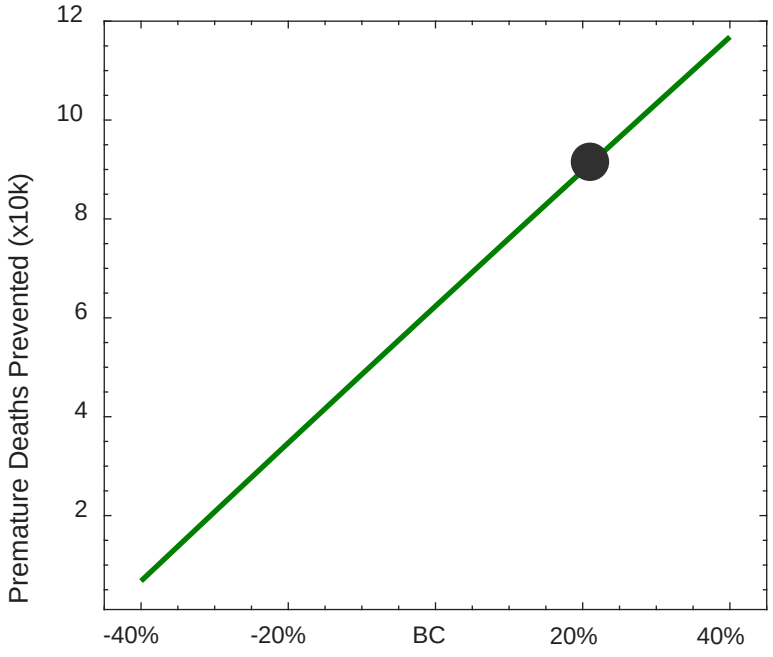
Change in rate of Cigarette Smokers switching to smokeless tobacco



- All other transition rates kept the same as those in the Modified Case scenario

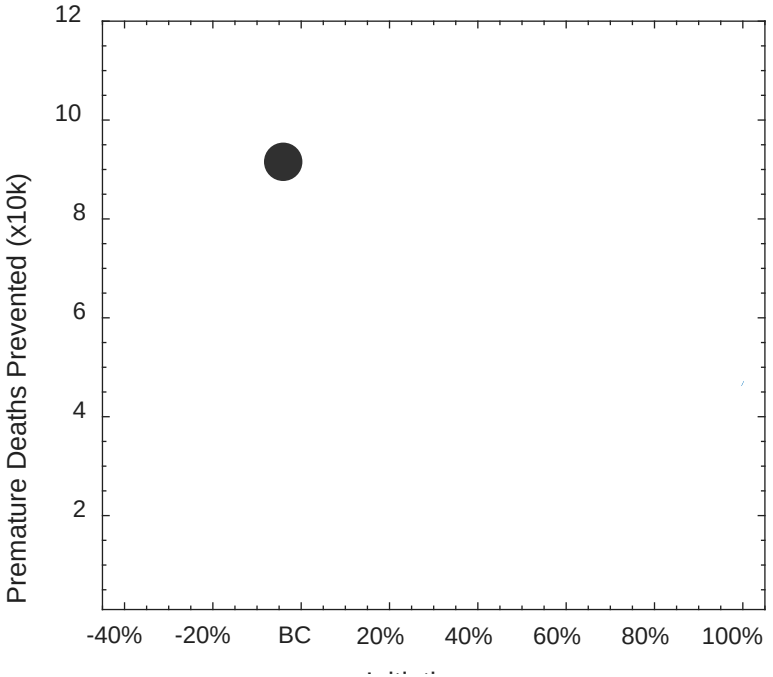
Sensitivity Analysis: What if?

Switching:
Change in rate of Cigarette Smokers switching to smokeless tobacco



Switching from Smoking to Using ST

Initiation:
Change in rate of Never Tobacco Users initiating on smokeless tobacco



Smokeless Tobacco Initiation

- All other transition rates kept the same as those in the Modified Case scenario

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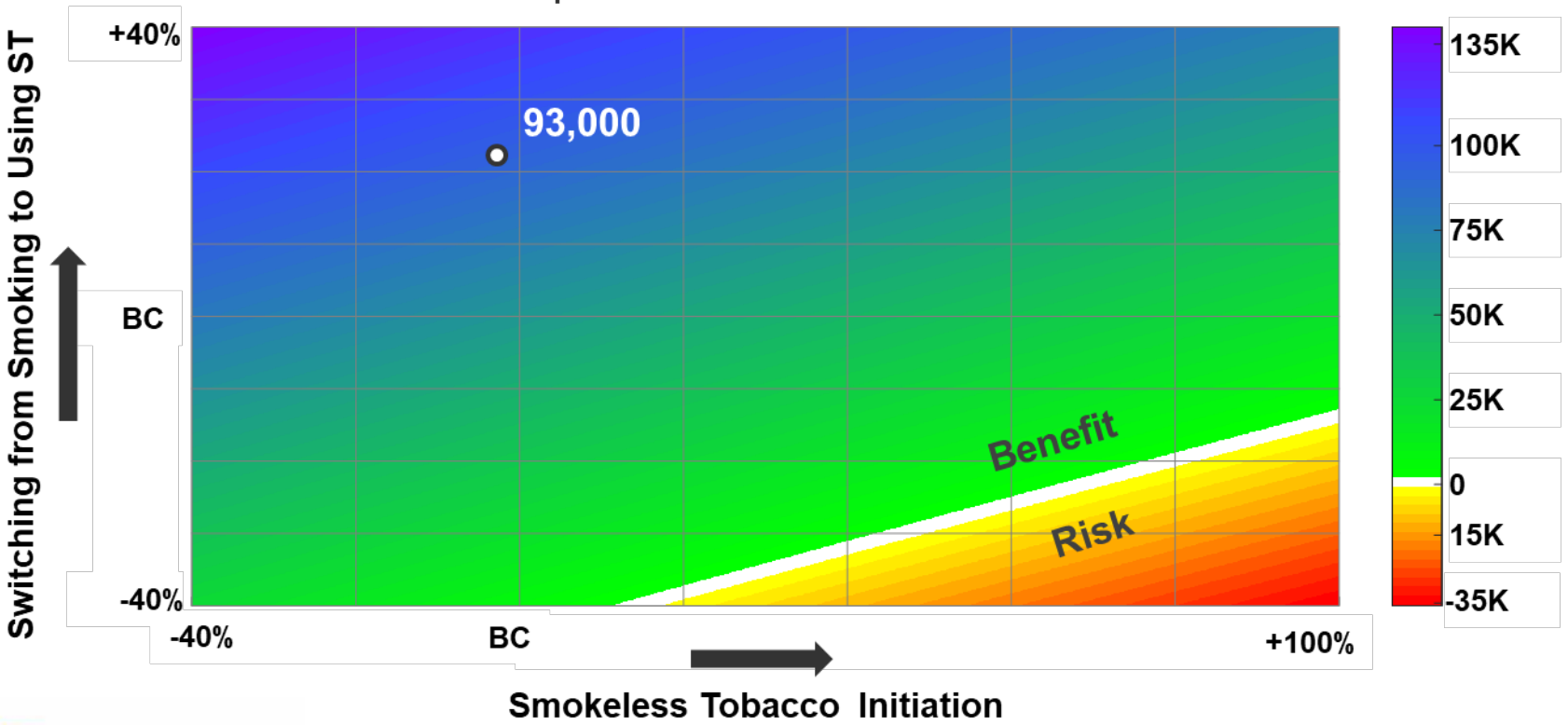
Sensitivity Analysis

- Concurrently vary:
  - Change in rate of Never Tobacco Users initiating on smokeless tobacco (*Initiation*)
  - Change in rate of Cigarette Smokers switching to smokeless tobacco (*Switching*)

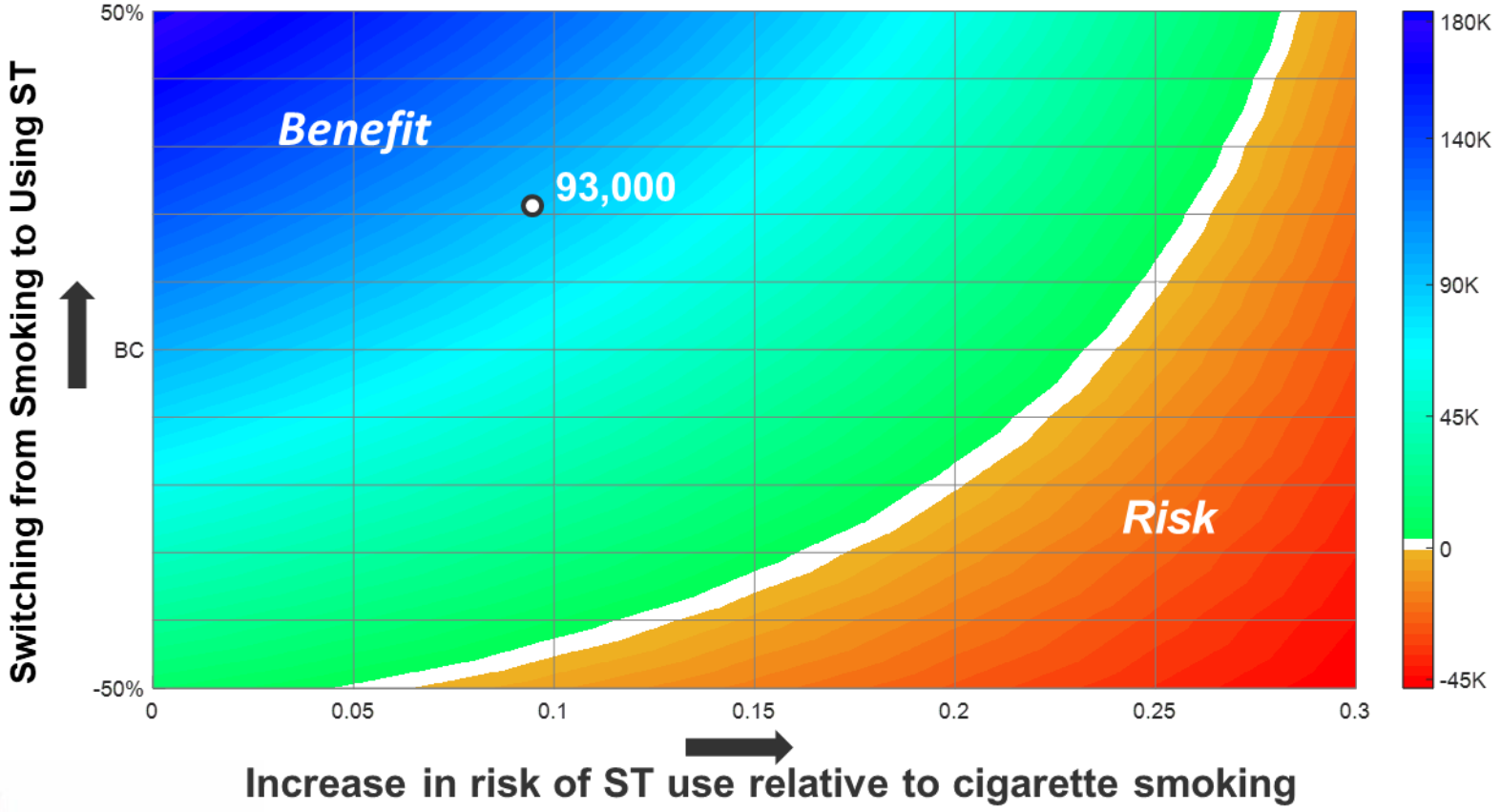
- All other transition rates kept the same as those in the Modified Case scenario



Sensitivity Analysis

- Concurrently vary:
  - Change in rate of Cigarette Smokers switching to smokeless tobacco (*Switching*)
  - Change in risk of ST use relative to cigarette smoking

- All other transition rates kept the same as those in the Modified Case scenario



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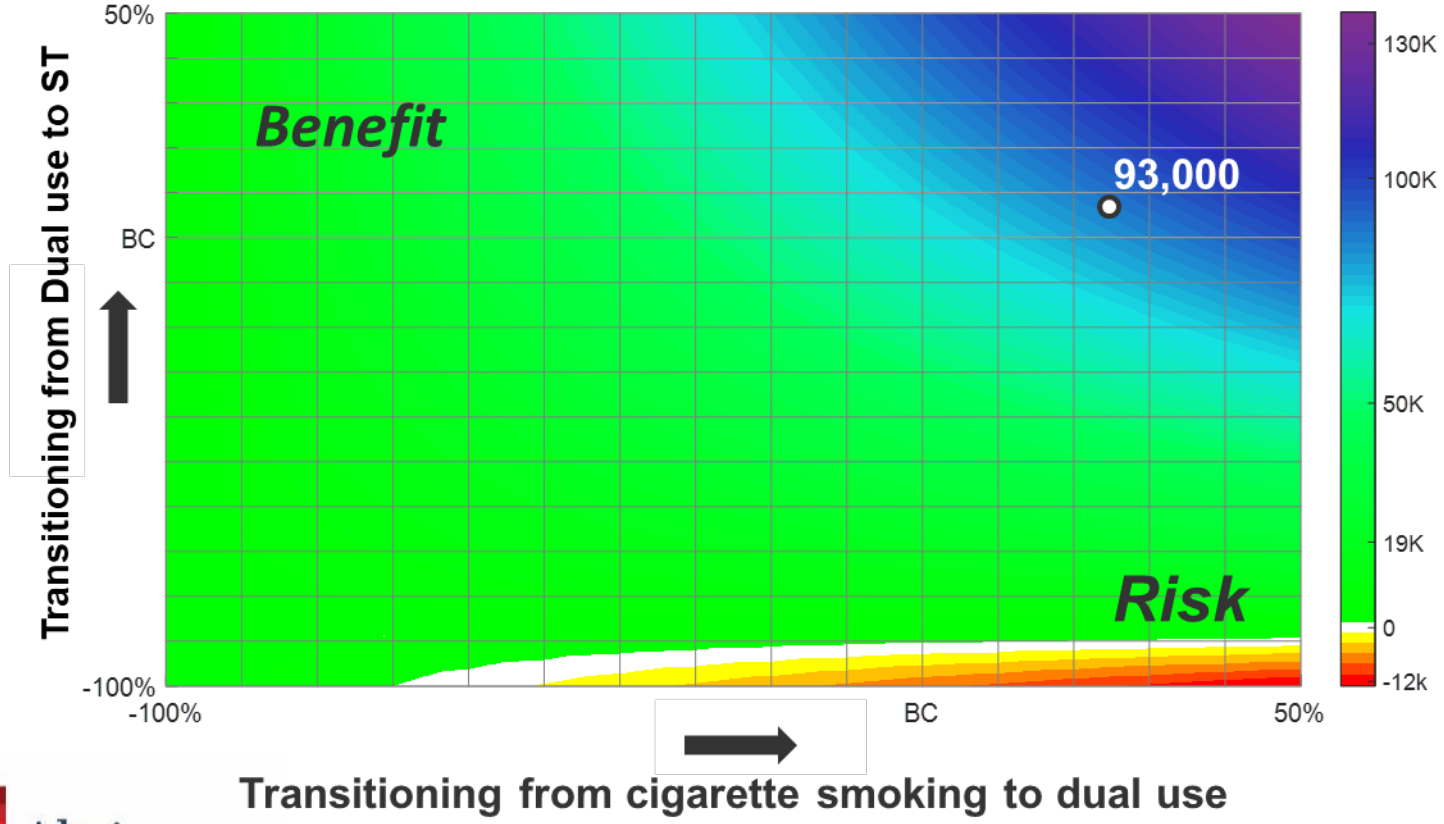
Sensitivity Analysis

- Concurrently vary:
  - Change in rate of Dual Users transitioning to smokeless tobacco
  - Change in rate of Cigarette Smokers transitioning to Dual Use

- All other transition rates kept the same as those in the Modified Case scenario



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Summary

- Models can serve as important tools for evaluating population health impact
- Sensitivity Analysis is important in examining the robustness of model projected outcomes

FDA Remarks on Population Health Benefit

FDA: “Computational modeling estimated a relatively small net population health benefit from market authorization of Copenhagen Snuff Fine Cut with the proposed modified risk claim.”

Source: FDA TPSAC presentation slide 49.

International Journal of
Environmental Research and Public Health

MDPI

Article

A Computational Model for Assessing the Population Health Impact of Introducing a Modified Risk Claim on an Existing Smokeless Tobacco Product

Raheema S. Muhammad-Kah [1,*], Yezdi B. Pithawalla [1], Edward L. Boone [2], Lai Wei [1], Michael A. Jones [1], Ryan A. Black [1], Thomas M. Bryan [1] and Mohamadi A. Sarkar [1]

1 Regulatory Affairs, Center for Research & Technology, Altria Client Services LLC, 601 East Jackson Street, Richmond, VA 23219, USA; Yezdi.B.Pithawalla@altria.com (Y.B.P.); Lai.Wei@altria.com (L.W.); Michael.A.Jones@altria.com (M.A.J.); Ryan.A.Black@altria.com (R.A.B.); Thomas.M.Bryan@altria.com (T.M.B.); Mohamadi.A.Sarkar@altria.com (M.A.S.)

2 Department of Statistical Sciences & Operations Research, Virginia Commonwealth University, Richmond, VA 23284, USA; elboone@vcu.edu

* Correspondence: raheema.s.muhammad-kah@altria.com; Tel.: +1-804-335-2493; Fax: +1-804-335-2095

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