Assessing the Likelihood and Magnitude of a Population Health Benefit Following Market Introduction of an MRTP

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Disclosures/Attributions

This research was supported by RAI Services Company (RAIS).

Dr. Curtin is employed by RAIS, a wholly owned subsidiary of Reynolds American Inc., whose operating companies market smokeless tobacco and vapor products.

The Dynamic Population Modeler (DPM(+1)) was developed by Ramboll Environ, with the support of RAIS, to address regulatory requirements for new tobacco products.

Ramboll Environ's contribution to any regulatory submission on behalf of RAIS is strictly limited to the technical implementation of the DPM(+1), and does not include advocating the use of any specific tobacco (or nicotine) product.

Modeling of Population Health Effects

Introduction of Modified Risk Tobacco Product

Introductory Remarks

Modeler Framework

Modeling Input and Counterfactuals

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Concluding Remarks

Introductory Remarks

Modeling Tobacco Harm Reduction

Those responsible for evaluating interventions intended to reduce population harm must assess potential for both intended and unintended consequences

- for tobacco harm reduction, would entail changes in use patterns

In absence of sufficient empirical data on use patterns, decisions to pursue harm reduction interventions can be informed by population modeling

- estimates effects on population health (*e.g.*, changes in mortality) that might result from specified changes in use patterns
- estimates magnitude of benefit (harm) due to changes in use patterns, and allows ranking of likelihood of intended and unintended consequences

Modeler Framework

Dynamic Population Modeler (DPM(+1)) Framework[1,2]

Hypothetical population of one-million 12 year-old male never tobacco users followed in 5-year intervals (single cohort), with survival used as surrogate for population health

Mortality calculated for each age interval - based on age, duration of smoking, and duration of quit; mortality rates for modified-risk tobacco product (MRTP) users based on excess relative risk (ERR) estimate (relative to smoking)

Individual use patterns tracked (base case and counterfactual), and number of survivors estimated at each age interval (including difference between scenarios)

[1] Bachand AM, Sulsky SI. A dynamic population model for estimating all-cause mortality due to lifetime exposure history. *Regul Toxicol Pharmacol.* 2013;67(2):246-51.

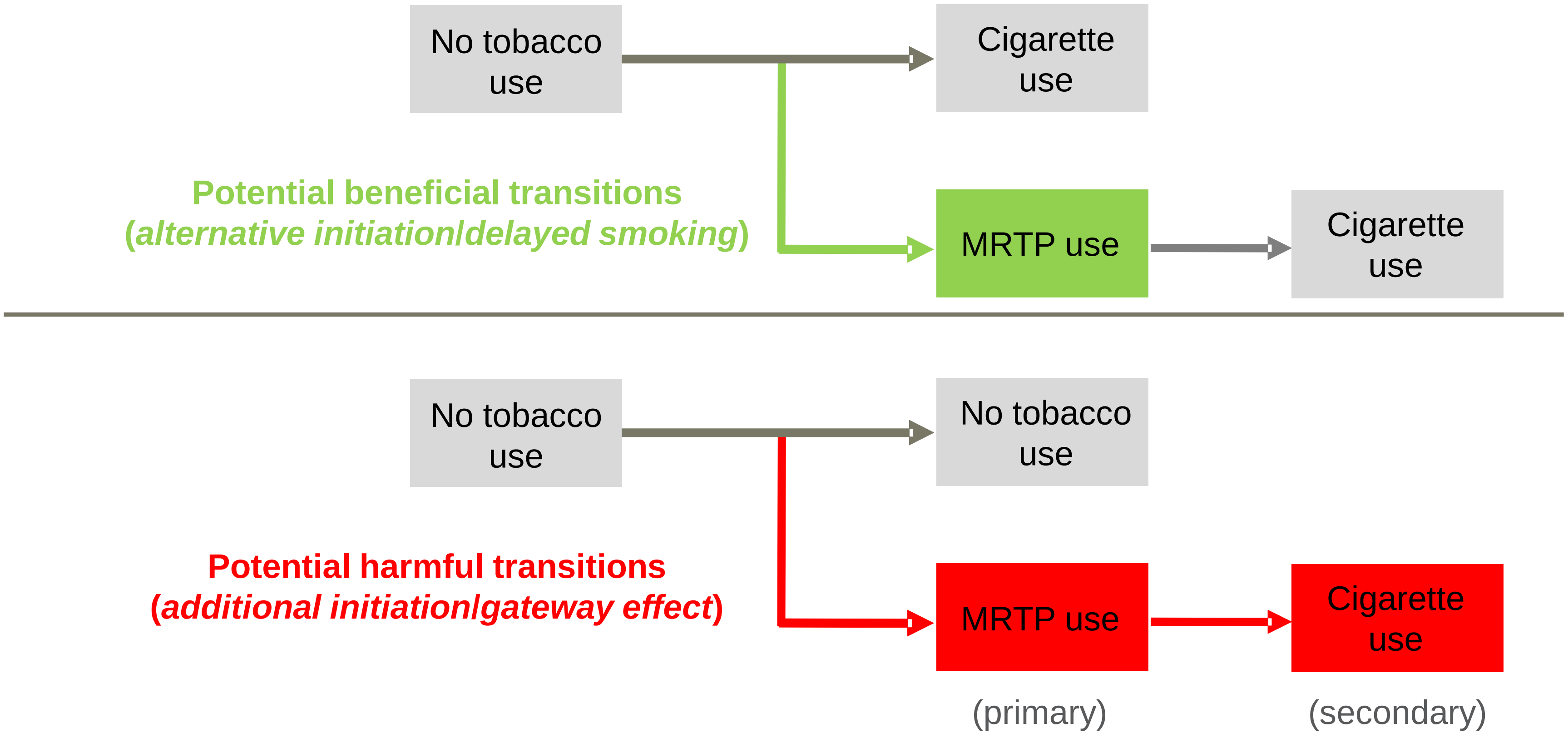
[2] Bachand AM, Sulsky SI, Curtin GM. Assessing the likelihood and magnitude of a population health benefit following the market introduction of a modified-risk tobacco product: Enhancements to the Dynamic Population Modeler, DPM(+1). *Risk Anal.* Apr 24 2017 [Epub ahead of print].

Research Objectives

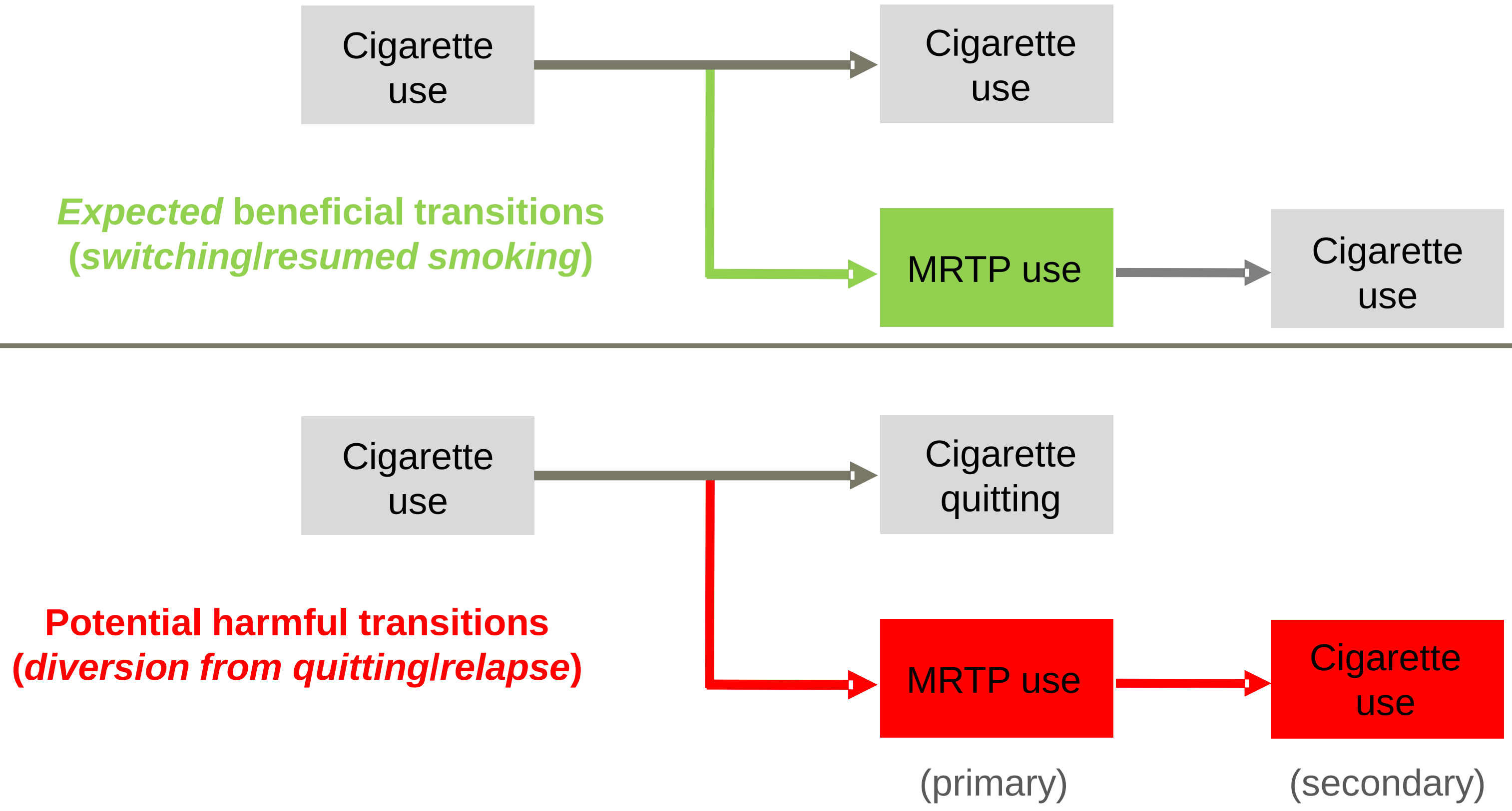
Assess population health impact of beneficial changes in tobacco use patterns likely to result from increased MRTP use

Assess likelihood and magnitude of beneficial changes in MRTP use needed to completely offset population harm resulting from extreme harmful use patterns

Increased MRTP Use among Never Tobacco Users



Increased MRTP Use among Current Cigarette Users



Modeling Input and Counterfactuals

Base Case (cigarette use only)

Age-specific mortality rates for never, current and former smokers calculated based on data from Kaiser-Permanente Cohort Study and 2000 U.S. Census

Transition probabilities calculated based on 2009 U.S. cigarette smoking initiation and 2005-2008 U.S. smoking cessation rates

Counterfactual Scenario (cigarette and/or MRTP use)

Beneficial and harmful use patterns (cigarettes and MRTP) based on hypothetical or empirically derived probabilities

Mortality rates for MRTP users based on ERR estimates of 0.08 and 0.11 (consensus estimates for all-cause mortality risk associated with use of low-nitrosamine smokeless tobacco)

Counterfactual Scenarios

Beneficial tobacco use patterns

- base case (continuing) cigarette users instead switch to MRTP use (*switching*)
- base case cigarette initiators instead initiate MRTP use (*alternative initiation*)

'Tipping point' analyses, versus beneficial patterns for *switching*

- base case never tobacco users instead initiate MRTP use (*additional initiation*)
- some portion of *additional initiators* transition to cigarette use (*gateway effect*)
- base case cigarette quitters instead initiate MRTP use (*diversion from quitting*)
- collective effect of *additional initiation* with some g*ateway effect* and *diversion from quitting*

Modeler Projections

Beneficial Tobacco Use Patterns

switching (%)	difference in survivors (age 68-72)	95% posterior interval	
2	3,127	2,751	3,508
4	5,989	5,270	6,720
6	8,610	7,574	9,660
8	11,011	9,685	12,354
10	13,213	11,619	14,827

alternative initiation (%)	difference in survivors (age 68-72)	95% posterior interval	
5	909	777	1,047
10	1,818	1,554	2,093
20	3,636	3,108	4,186
50	9,089	7,770	10,466

Within single cohort, continuing smokers switching from cigarettes to MRTP use (ages 18-72) more likely to lead to population health benefit than never users initiating tobacco use with MRTP instead of cigarettes (ages 13-27)

Tipping Point Analyses

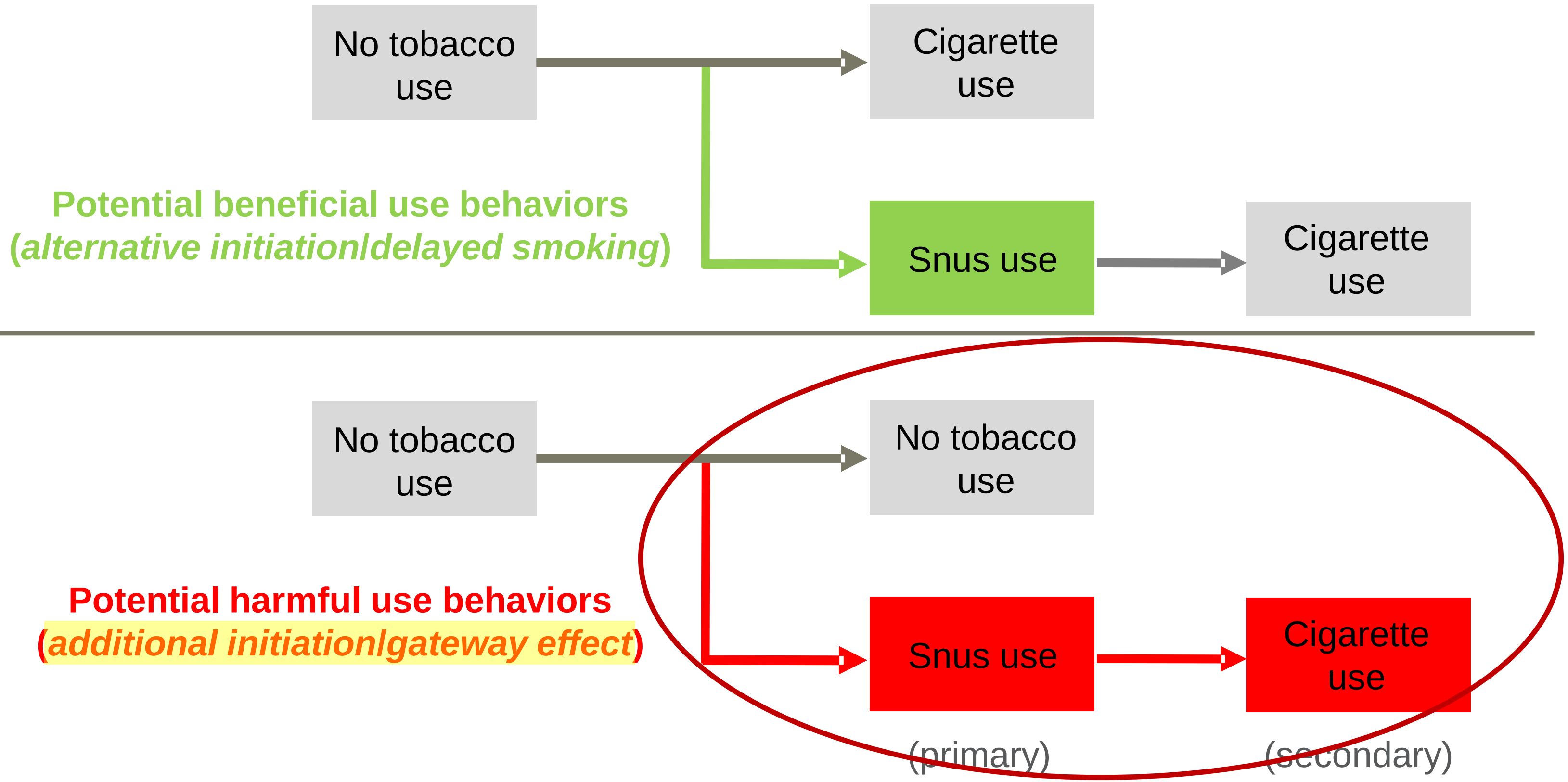
Additional initiation (50% of smoking initiation rates, ages 13-27) reduces population survival by 1,969 individuals (95% PI: -2,155 to -1,772)

- ~1.3% increase in *switching* (each age interval) offsets survival deficit

Additional initiation with *gateway effect* (20% of *additional initiators*, ages 18-32) reduces survival by 3,318 individuals (-3,530 to -3,100)

- ~2.2% increase in *switching* (each age interval) offsets survival deficit

Increased Use of Camel Snus among Never Tobacco Users



Tipping Point Analyses

Additional initiation (50% of smoking initiation rates, ages 13-27) reduces population survival by 1,969 individuals (95% PI: -2,155 to -1,772)

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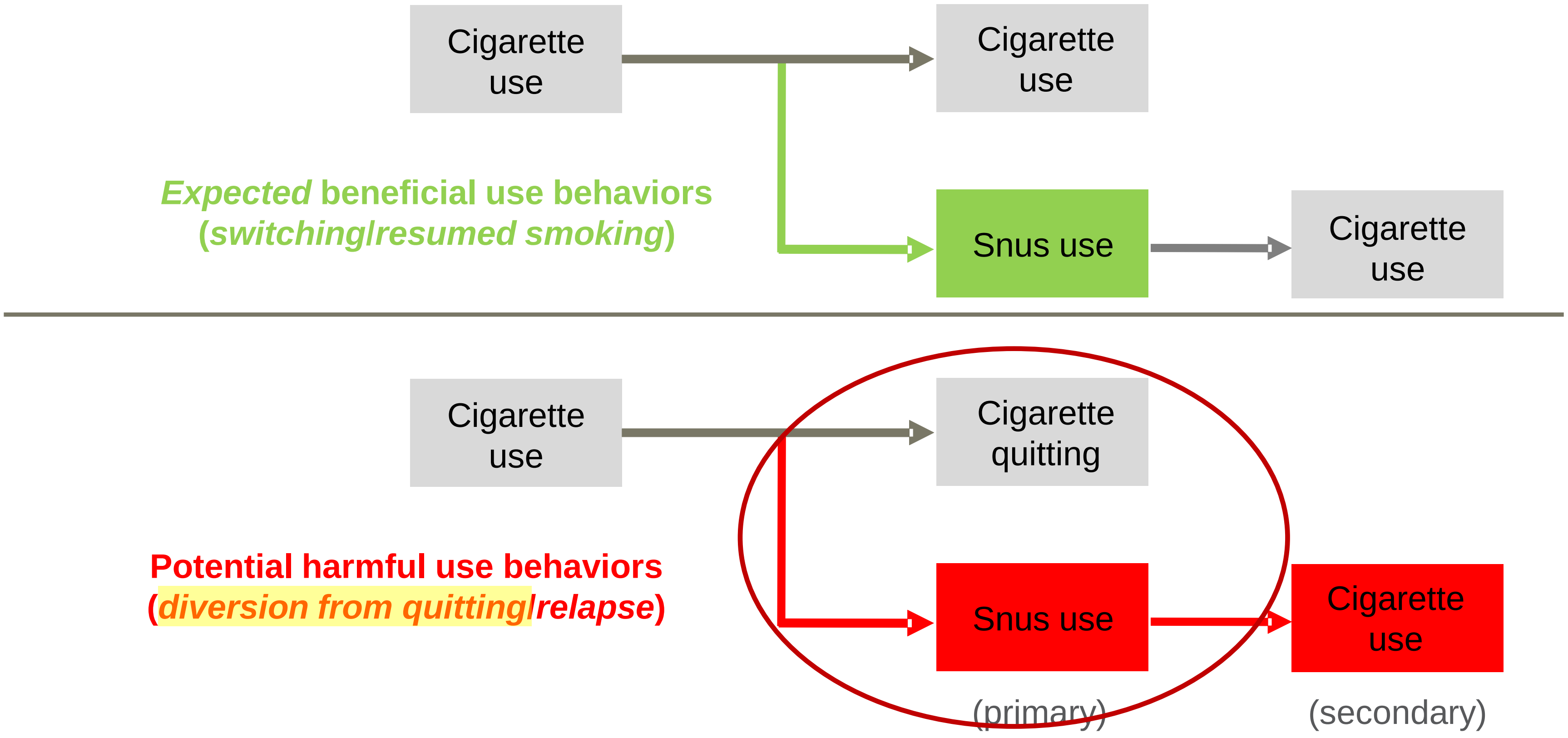
Additional initiation with *gateway effect* (20% of *additional initiators*, ages 18-32) reduces survival by 3,318 individuals (-3,530 to -3,100)

- ~2.2% increase in *switching* (each age interval) offsets survival deficit

Diversion from quitting (50% of smoking quitters, ages 18-72) reduces population survival by 1,477 individuals (-1,655 to -1,303)

- ~0.9% increase in *switching* (each age interval) offsets survival deficit

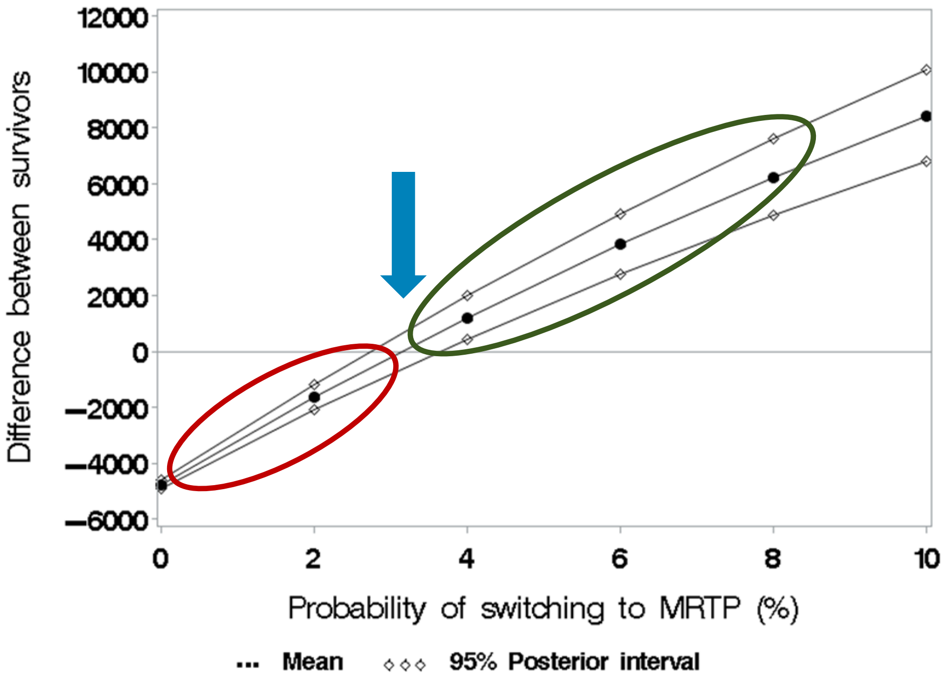
Increased Use of Camel Snus among Current Cigarette Users



Tipping Point Analyses

Additional initiation with *gateway effect* AND *diversion from quitting* reduces population survival by 4,756 individuals (-4,913 to -4,590)

- ~3.2% increase in *switching* (each age interval) offsets deficit



Concluding Remarks

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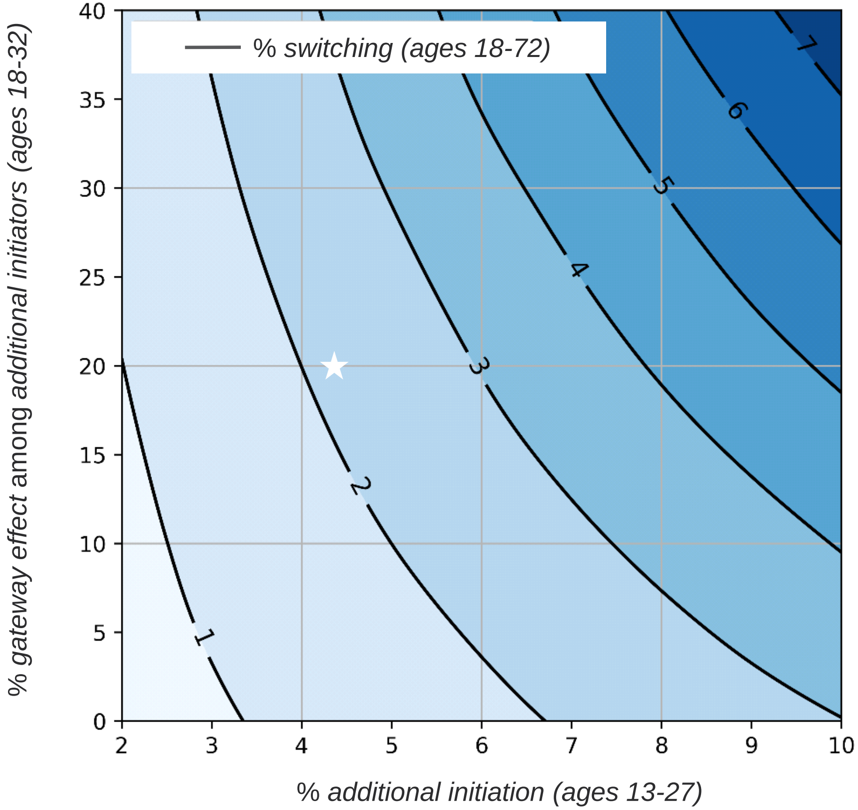
In absence of sufficient empirical data on likely changes in tobacco use patterns, decisions to pursue harm reduction interventions informed by population modeling

Within single cohort, switching completely from cigarettes to MRTP more likely to benefit population health than initiating tobacco use with MRTP instead of cigarettes

Complete switching among small proportion of continuing smokers in each age interval expected to offset survival deficit resulting from extreme changes in harmful use patterns

Population Modeling Innovations



50% additional initiation in age categories 13-17, 18-22 and 23-27 years is ~7%, 5% and 0.5%, for average of 4.2%