Evaluating the Population Impact from Introduction of a Novel Oral Tobacco-Derived Nicotine Product in the U.S.

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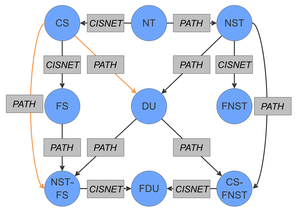
Abstract

Computational modeling can inform FDA in evaluating evidence of the population impact with the market authorization of new tobacco products in the US. We present an agent-based model (ABM) to inform the population impact of introducing novel oral tobacco derived nicotine products (NP). The ABM allows prediction of changes in tobacco use prevalence and all-cause mortality by assessing the difference between a Base Case (cigarettes and novel smokeless tobacco (NST) products) and a Modified Case (NP added to the Base Case). We define NST products as dissolvable and snus tobacco products. Base Case transition probabilities for NST products were estimated from an analysis of Wave 1 and Wave 2 data from the Population Assessment of Tobacco and Health (PATH) study. The NP transition probabilities (cessation, switching and future intentions to use NP) were estimated from an Actual Use Study (AUS) at the end of 6 weeks of product use, and were adjusted to reflect the US population. The AUS included 783 adult smokers who expressed intent to use the NP. The excess relative risk (ERR) compared to cigarettes was estimated at 5% based on a multi-criteria decision analysis model developed by an international expert panel (Nutt et al 2014). Dual use of NP and cigarettes was assigned the same ERR as cigarette smoking. Extremely stringent criteria were applied to estimate product adoption by only considering those adult smokers in the AUS with the highest intentions to use (i.e., respondents who only selected "Strongly Agree" on a six-point scale, ranging from "Strongly Disagree" (1) to "Strongly Agree" (6)) and selected "Yes" to future purchase intentions. With market authorization of the NP, we demonstrate a net benefit to the population of ~ 19,000 premature deaths prevented with a reduction in cigarette smoking prevalence by 2060. Sensitivity analysis, utilizing moderate to high intentions to use the NP (i.e., respondents "Somewhat Disagree" to "Strongly Agree") resulted in an estimate of ~146,000 premature deaths prevented. Limitations of model predictions should be taken into consideration when drawing inferences from these results.

Agent Based Model (ABM) Transition Diagram



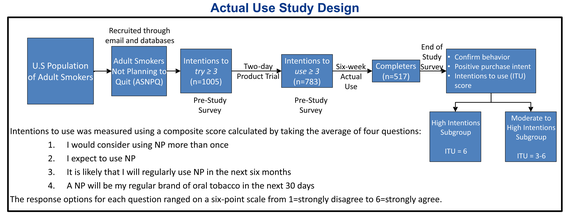
NT = Never-Use of Tobacco
CS = Current Cigarette Smoker
FS = Former Cigarette Smoker
DU = Dual User
FDU = Former Dual User

NST= Novel Smokeless Tobacco User
FNST = Former NST / NP User
CS-FNST = Current Cigarette Smoker Former NST User
NST-FS = NST / NP User Former Smoker

- Initial population: 2.81MM agents, (1/10000th of U.S. population in 2000 by age, gender, & smoking status)
- At each 1 yr. time step
  - Survivability of agents evaluated based on mortality risk factors dependent on tobacco use history
  - Agents who survive transition between use states
  - New agents are introduced due to birth & immigration
- Mortality Risk Factors
  - NT, CS, and FS - derived from Kaiser Permanente data adjusted for U.S. mortality rates in the year 2000
  - NST - Excess Relative Risk (ERR) of NST use compared to smoking set to 0.05; conservative compared to 0.02 value determined by Nutt et al. for oral nicotine-containing products
  - Dual Use - same risk as exclusive smoking
- ***Transition Probabilities***
  - **Base Case:** source for each transition probability is indicated in the grey boxes
  - **Modified Case:** all rates same as in the Base case, except the two identified by orange arrows. (1) CS switching to exclusive NST/NP use & (2) CS switching to DU

- ***Modified Case Transition probabilities*** for switching from cigarette smoking to exclusive NP use and from cigarette smoking to dual use estimated from an Actual Use Study (AUS)

Actual Use Study Design



Intentions to use was measured using a composite score calculated by taking the average of four questions:

1. I would consider using NP more than once
2. I expect to use NP
3. It is likely that I will regularly use NP in the next six months
4. A NP will be my regular brand of oral tobacco in the next 30 days

The response options for each question ranged on a six-point scale from 1=strongly disagree to 6=strongly agree.

Introduction

- Computational models can estimate the likely impact of introducing a new tobacco product on the U.S. population.
- Models require transitions and associated transition probabilities for how tobacco users and non users are likely to transition between tobacco product use states, once a new product is introduced into the market.
- New tobacco products cannot be introduced into the U.S. market without FDA authorization which limits the ability to estimate how tobacco users and non users may transition between use states.
- Combining data from an actual use study (AUS) on the new product with behavioral use data on similar products currently on the market can allow for estimating transition between current and the new tobacco product use states.

Methods

Modeling Framework for Estimating the Changes in the Novel Smokeless Tobacco (NST) Category Related to the Introduction of Novel Oral Tobacco Derived Nicotine Products (NP)

Net Benefit/Risk:
Difference in tobacco use prevalence and all-cause mortality between Base and Modified Case

Base Case Transition Probabilities

Adult Transition rates from Analysis of Wave 1 to Wave 2 PATH Snus and Dissolvable Data

*Never User of Tobacco (NT) Who has never used any tobacco	0.1% to NST
*Exclusive Cigarette Smokers (CS) Who have not used NST "everyday or somedays"	0.11% to NST 0.76% to Dual
*Exclusive NST Users (NST) Who have not smoked cigarettes "everyday or somedays"	11.9% to CS 8.6% to Dual
*Former Cigarette Smokers (FS) Who smoke cigarettes "not at all"	0.3% to NST
*Dual Users (DU) Who currently smoke cigarettes and use NST "fairly regularly"	61.8% to CS 3.4% to NST

Adult Cigarette Initiation and Cessation Rates from CISNET & NHIS Year 2000 Data

*Never User of Tobacco (NT) Who has never used any tobacco	2.0% to CS
*Exclusive Cigarette Smokers (CS) Who have smoked 100 or more cigarettes in life	3.5% to FS

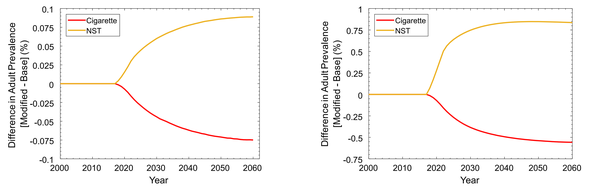
*Ages 18-24, *Ages 18-64, &Ages 18+

Assumption: Cessation transition rates from CISNET reflect successful cessation for at least two years, therefore relapse from CS - FNST and NST - FS states are set to zero.

- The proportion of participants in the AUS that switched to NP use was adjusted to be representative of the U.S. population of adult cigarette smokers
- Transition rates were applied to the NST category based on the new NP product's projected market share

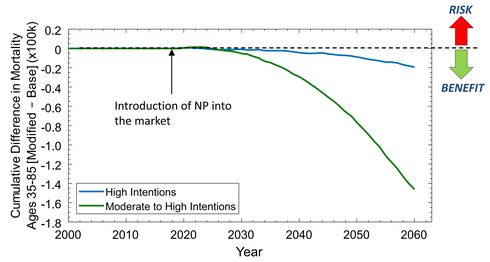
Results

Change in Adult Tobacco Product Use Prevalence Between the Base and Modified Case



Year 2060: Difference in Adult Prevalence between Modified & Base Case		
AUS Subgroup	**Cigarette**	**NST**
High Intentions	-0.07%	+0.09%
Moderate to High Intentions	-0.56%	+0.84%

Impact of a Market Authorization of NP on All-Cause Mortality



Year 2060: Difference in All-cause Mortality between Modified & Base Case	
AUS Subgroup	**Premature Deaths Prevented**
High Intentions	19,000
Moderate to High Intentions	146,000

Impact of Changes in Never Tobacco User Initiation of NP

- Table below shows the impact of never tobacco users initiating with the NP. Analyses included increasing initiation rates from 30% to 300%. All other rates remain the same as in the High Intentions Subgroup scenario.

	Percent Increases to Initiation Rate	Cumulative Difference in Mortality [Modified Case – Base Case]
High Intentions Subgroup	300%	-300
	250%	3,400
	100%	11,700
	50%	16,200
	30%	17,500

Conclusion

- Our model suggests an overall net benefit from introducing a novel smokeless tobacco product into the U.S. market, as indicated by likely reduction in smoking prevalence and a decreased mortality (19,000 deaths prevented over a 60 year follow-up period) in the U.S. population compared to the Base Case.
- Utilizing transition rates associated with moderate to high intentions to use the NP exclusively (i.e., respondents "Somewhat Disagree" to "Strongly Agree") resulted in an estimate of ~146,000 premature deaths prevented.
- Sensitivity analysis on initiation of NP indicates that this transition is unlikely to negate the benefit observed in the Modified case based on the AUS high intentions subgroup.
- Models shed light on trends and are not intended to predict future outcomes with numerical precision.

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