Estimating the Population Health Impact of Authorizing the Marketing of a Smokeless Tobacco Product with a Proposed Modified Risk Claim

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Abstract

Computational models are valuable tools for predicting the population effects following market authorization of a tobacco product with a modified risk claim. We have developed and validated a population model for Moist Smokeless Tobacco (MST) products using best modeling practices. Since MST is primarily utilized by males, the Markov compartmental model is based on a theoretical cohort of one million males starting at age 13 and followed to age 73, accounting for up to thirty transition states with defined transition probabilities. The model was coupled with statistical mortality models and excess relative risk to determine the survival probabilities from use of a MST product (candidate product). Our model results are presented as the difference in number of survivors and years of additional life expected by comparing a Base Case (where cigarettes and MST products are available under the existing scenario) and Master Case (where the candidate product is available with a modified risk claim authorized by FDA). Nationally representative transition probabilities were used for the Base Case. A Master Case scenario was estimated from a study involving 3,290 male participants, where we measured the percent difference between the relevant responses of a test group of users and nonusers of tobacco products (exposed to the modified risk claim associated with the candidate product) and control group (exposed to the candidate product without the modified risk claim), and then applied the percent difference to the Base Case transition probabilities. The estimated likely outcome of authorization of a modified risk claim for MST is 1120 additional survivors with 32,856 additional years of expected life, for the one million male cohort followed to age 73. Extending inferences from a single-cohort to a time-staggered multi-cohort approach, leads to ~ 93,000 additional survivors over a 60 year period. Our results suggest that a net benefit to the population can be expected upon market authorization of the proposed modified risk claim for the candidate product. Limitations of model predictions should be taken into consideration when drawing inferences from these results.

Introduction

- Computational models are valuable tools for assessing the likely impact on the U.S. population from authorization by FDA of a proposed modified risk claim for a tobacco product.
- We have developed and validated a population model using best modeling practices to assess the population effects following authorization to market a Moist Smokeless Tobacco (MST) product with a proposed modified risk claim.
- MST in the US is primarily utilized by males, therefore our model is based on a hypothetical cohort of one million males starting at age 13 and followed to age 73.
- Our model accounts for up to thirty transition states with defined transition probabilities and is coupled with statistical mortality models and excess relative risk (ERR) to determine the survival probabilities from use of a MST candidate product with a modified risk claim.

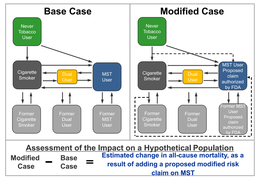
Table 1.

Tobacco Use Transition	Relative Percentage Change*
Never-user of tobacco° initiating MST candidate product	- 5%
Former MST users initiating MST candidate product	0%
Current cigarette smokers^ switching to MST candidate product	21%
Current cigarette smokers switching to Dual use (MST candidate Product & cigarettes)	24%
Dual users (MST and cigarette) switching to MST candidate product	6%
Hypothetical Subpopulations*	
Would-be smoker° initiating MST candidate product	1%
Would-be smoking quitter' switching to MST candidate product	5%

°Never-user of tobacco are ever-past trier of tobacco that did not reach the smokers lifetime criteria (smoked 100+ cigarettes) or never- trier of tobacco.
^Current cigarette smokers consist of those both planning to quit and not planning to quit.
* These two subpopulations do not exist in the base case so the percentages increases from zeros and is not a percentage change.
°Would-be smoker: adult never-tobacco users who would otherwise initiate cigarette smoking but, in the Master Case, initiate use of the MST candidate product instead.
'Would-be smoking quitter: adult cigarette smokers who would otherwise quit cigarette smoking but, in the Master Case, initiate use of the candidate product instead.

* Calculation of Relative Percentage Change = $\frac{\frac{\text{Test Group with Claim exposure}}{\text{Test Group without Claim exposure}} - \frac{\text{Control Group with Claim exposure}}{\text{Control Group without Claim exposure}}}{\frac{\text{Control Group with Claim exposure}}{\text{Control Group without Claim exposure}}} \times 100$

Methods



Outputs

Difference in all-cause mortality & years of lives added between:

- **Base Case** (status quo, where both tobacco product use behaviors for cigarettes and MST products exist) &
- **Modified Case** (future state, where transition between use states changes upon authorization of the proposed modified risk claim by FDA)

Inputs

- **Mortality:**
  - Tobacco-related mortality was estimated from a Kaiser Permanente Medical Care Program Cohort study and adjusted to the US population using Vital Statistic data
  - Excess relative risk (ERR) of MST candidate product use compared to smoking was estimated at 0.09 from analysis of the National Health Interview Survey mortality linkage public use data (i.e. a 91% reduction in risk compared to smoking)
- **Base Case Transitions:** Nationally representative transition probabilities were estimated from Tam et al. (2015); a systematic review of published literature on transitions between smokeless tobacco use and cigarette smoking in the U.S.
- **Modified Case Transitions:**
  - Transitions are estimated from an ALCS study involving 5871 participants of which 3,290 were male, we measured the percent difference between the relevant responses of a test group of users and nonusers of tobacco products (exposed to the modified risk claim associated with the MST candidate product) and control group (exposed to the MST candidate product without the modified risk claim) [See Table 1 for Definitions & estimated impact on tobacco use transitions]
  - Determination of the percent by which the Base Case transition rates will change upon authorization of the MST candidate product (Master Case) is estimated by applying the percent differences (Table1) to Base Case transition rates

Assumptions

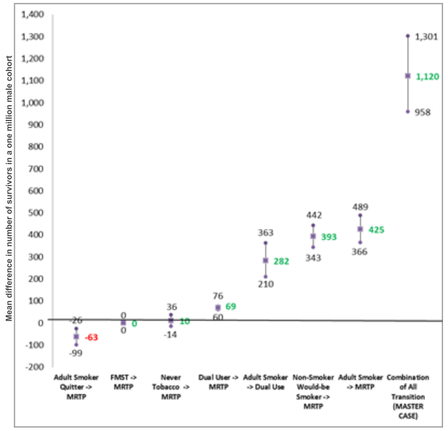
- Dual use (smoking and MST) were assigned the same mortality risk as that of exclusive cigarette smoking
- Switching rates to cigarettes from exclusive MST and Dual use will remain the same as established in the literature

Analyses

- **Master Case Scenario:** The impact of all the most-likely changes in tobacco use patterns occurring simultaneously
- **Component Analyses:** Understanding the contribution of each individual transition on the net population effect (Figure 1)
- **Sensitivity Analyses:** Evaluating the effects of varying input parameters on the net population
- **Multiple-Cohort Analyses:** Extends our results from the single-cohort model to the U.S. native-born male population, by employing a single-cohort model in a time-staggered multiple-cohort setting (Table 2)

Results

Figure 1: Mean Difference in number of Survivors in a one million male cohort between the Modified and Master Case Scenario: Point Estimates and Credible Intervals for 7 transitions of interest (Component Analysis) are shown below



Dual User = current cigarette smoker and MST user; MRTP = MST with a modified risk claim

Table 2. The expected difference in the total people alive in the Year 2075 between the Modified and Base Case Scenario by Age Groups

Age Group (years)	Difference in people alive between Modified and Base
10-14	0
15-19	0
20-24	0
25-29	153
30-34	473
35-39	973
40-44	1,920
45-49	3,731
50-54	6,788
55-59	9,771
60-64	12,307
65-69	14,813
70-74	15,614
75-79	14,470
80-84	12,310
Total Additional People Alive in the Modified vs. Base Case	**93,323**

This scenario assumes market authorization of the proposed modified claim 2015, and multiple cohorts were followed until the year 2075, under both Base Case and Master Case scenarios.
The difference in the number of people alive in all age categories from ages 10 to 84 years between the Base Case and Master Case scenarios in the year 2075 is compared.
Initial cohort populations were acquired from US Census Bureau.

Conclusions

- The estimated likely outcome of authorization of a modified risk claim for MST is:
  - 1120 additional survivors with 32,856 additional years of expected life, for a one million male cohort followed from age 13 to age 73.
  - Extending inferences to the U.S. native-born male population leads to approximately 93,000 additional survivors over a 60 year period.
- Cigarette smokers switching to exclusive MST use has the largest influence on the impact to the population with the market authorization of a modified risk claim.
- Our results suggest that a net benefit to the population can be expected upon market authorization of a proposed modified risk claim.

References

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No conflict of interest