Multidimensional Tipping Point Analyses: Assessing Simultaneous Shifts in Tobacco Use Patterns from a Higher to a Lower Risk Product

AUTHORS

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DESIGN OF DPM(+1)

The Dynamic Population Modeler (DPM(+1)) estimates effects on all-cause mortality if tobacco use patterns in a population shift from a higher- to lower-risk product, in specified ways.[1,2]

- Follows hypothetical birth cohort over time; keeps track of exposure histories
- Estimates mortality expected under modeled changes in use patterns
  - Smokers: embedded Poisson model age, age^2, years of smoking, years since quitting, age x years of smoking, age x years since quitting. Coefficients of Poisson model estimated using multidimensional Bayesian approach; uncertainty incorporated using Markov Chain Monte Carlo techniques
  - Modified risk tobacco product (MRTP) users: Rates for current (former) smokers reduced by excess relative risk (ERR) for MRTP users vs. smokers
- Compares age-specific survivors between base case (cigarette use only) and counterfactual scenario (MRTP and/or cigarette use)
- Allows for uncertainty in model input; estimates uncertainty in model output through 95% posterior intervals; implemented in R[3], JAGS[4]

TIPPING POINT ANALYSES

Analyses estimate magnitude of beneficial use pattern needed to offset population health effect of one or more harmful use patterns, or vice versa.

Primary beneficial use patterns:

- **Switching:** Switching to MRTP use by some current cigarette smokers who otherwise would have continued to smoke
- **Alternative initiation:** Initiation with MRTP instead of smoking by some never tobacco users who would have initiated cigarette smoking

Primary harmful use patterns:

- **Additional initiation:** Initiation of MRTP use by some never tobacco users who otherwise would have remained never users
- **Diversion from quitting:** Switching to MRTP use by some current smokers who would have quit smoking

Secondary harmful use patterns include (among others):

- **Gateway effect:** Transitioning to cigarette use among those never tobacco users who initiated MRTP use instead of remaining never users

Tipping points determined:

- Based on point estimate of 0 (no difference in survivors between counterfactual scenario and base case)
- Based on statistically significant survival benefit in counterfactual scenario (lower bound of 95% posterior interval > 0)

MODEL INPUT FOR CURRENT ANALYSES

- Hypothetical population of 1 million 12 year-old male never tobacco users[a]
- Followed from age 13, in 5-year intervals, through age 102[b]
- Age-specific mortality rates for never, current and former smokers based on data from Kaiser-Permanente Cohort Study (KP)[5] and 2000 US Census[6]
- Base case defined and calibrated using 2009 US cigarette smoking initiation rates[7] and 2005–2008 smoking cessation rates[8],c,d
- ERR = 0.08 (based on consensus estimate for all-cause mortality risk associated with long-term use of low-nitrosamine smokeless tobacco product, relative to smoking)[10]
- To account for uncertainty, base case transition probabilities and ERR modeled as left-truncated normal random variables with mean equal to respective estimates and standard deviations of 0.01

SIMPLIFYING ASSUMPTIONS

- Effects of only 2 types of tobacco products compared
- Mortality rates dependent on overall duration of product use or quitting, but not on amount of each product used
- Analyses consider only direct effects of tobacco product use and do not account for changes to second-hand smoke exposure

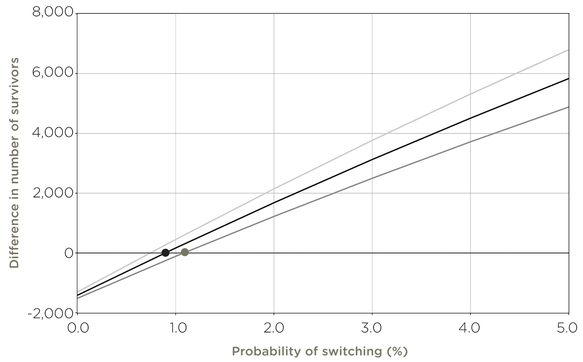
STRENGTHS

- DPM(+1) can simultaneously evaluate up to 3 harmful and/or beneficial transitions in flexible tipping point analyses, with all other transition probabilities held fixed
- Allows analysts to enter a range of transition probabilities or a single, pre-specified value for each transition
- Wide ranges of use behaviors can be assessed simultaneously
- If input data are available, any higher-risk product can be compared to any lower-risk product

RESULTS

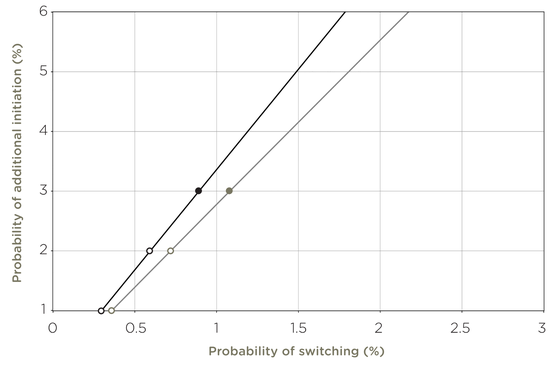
Counterfactual scenario 1: 3% additional initiation

Tipping points based on difference in survivors (counterfactual scenario vs base case at age 68–72 years) for analyses with 3% additional initiation, by probability of switching



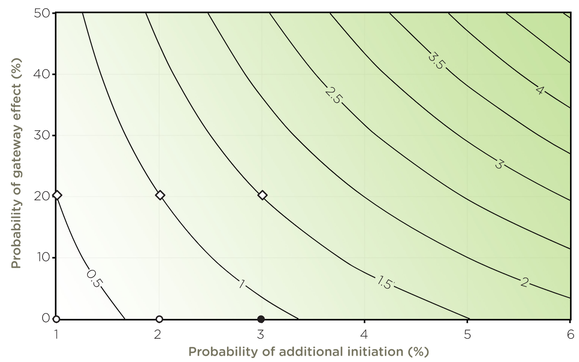
Counterfactual scenario 2: 1–6% additional initiation

Combinations of transition probabilities for additional initiation and switching resulting in a zero difference between counterfactual scenario and base case (black line) and statistically significant survival benefit in counterfactual scenario (gray line) at age 68–72 years

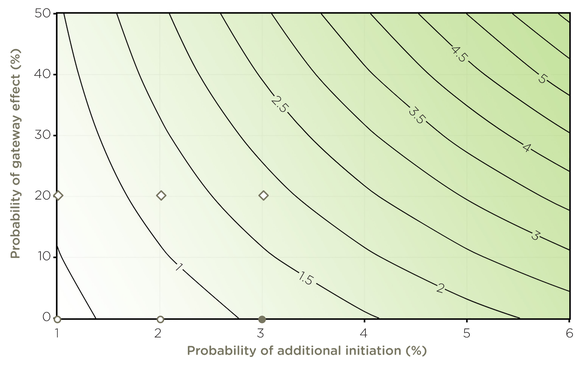


Counterfactual scenario 3: 1–6% additional initiation and 0–50% gateway effect

Combinations of transition probabilities for additional initiation, gateway effect and switching resulting in zero difference between counterfactual scenario and base case at age 68–72 years

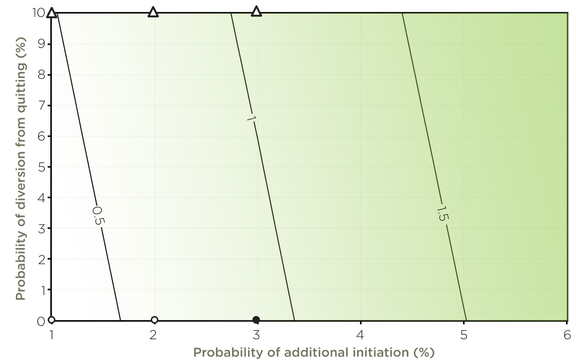


Combinations of transition probabilities for additional initiation, gateway effect and switching resulting in statistically significant survival benefit in counterfactual scenario at age 68–72 years

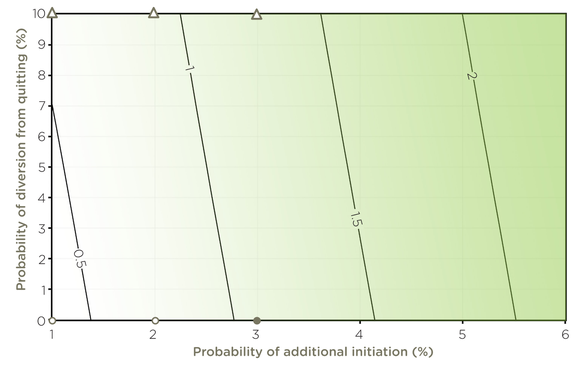


Counterfactual scenario 4: 1–6% additional initiation, 0% gateway effect and 1–10% diversion from quitting

Combinations of transition probabilities for additional initiation, diversion from quitting and switching resulting in a zero difference between counterfactual scenario and base case, at age 68-72 years



Combinations of transition probabilities for additional initiation, diversion from quitting and switching resulting in statistically significant survival benefit in counterfactual scenario, at age 68-72 years



CONCLUSIONS

- Tipping point analyses allow regulators to assess magnitude of simultaneous changes in tobacco use patterns likely to result in overall population health benefit or harm
- Based on magnitude, likelihood of such changes can be assessed
- Analyses may reduce immediate need for empirically based projections of beneficial or harmful changes in use patterns during regulatory decision making
- Change in tobacco use with greatest impact on population health is complete switching to lower risk tobacco product among smokers who otherwise would continue to use cigarettes

[a] Current examples restricted to men because use of low-nitrosamine smokeless tobacco products extremely rare among women[5]

[b] Results presented at age 72 (results after age 72 increasingly uninformative, as number of survivors in both counterfactual scenario and base case approach zero)

[c] Smoking cessation definitions in more current estimates different from definitions in KP study (cessation > 2 years)

[d] Also, alternative products, such as vapor products, have increased in popularity since 2009; more recent smoking initiation and cessation rates are likely affected by this shift in use patterns and do not provide a valid basis for base case with no MRTP use

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4. Licensed under the GNU General Public License version 2; http://mcmc-jags.sourceforge.net/.

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