POPULATION HEALTH IMPACT MODEL TO ESTIMATE THE EFFECT OF INTRODUCING MODIFIED RISK TOBACCO PRODUCTS ON MORTALITY

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Introduction and Objective

Philip Morris International (PMI) is currently developing potentially reduced risk products (RRPs) with the intention to reduce the risk of tobacco-related morbidity and mortality. Prior to marketing a new RRP, there is a lack of epidemiological data available on health risks associated with the product. Therefore, in addition to a comprehensive pre-market global clinical assessment program, PMI is developing a Population Health Impact Model (PHIM) as a tool to quantify the effect that marketing an RRP may have on the health of the population as a whole.

Approach

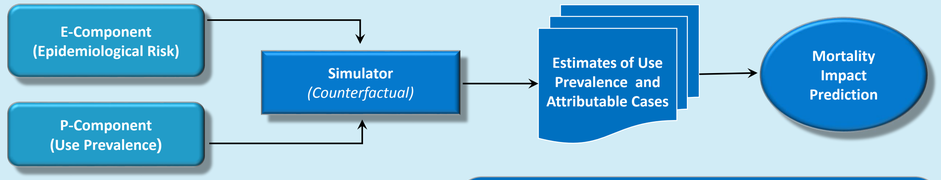
The general approach taken has been to develop a modeling framework that minimizes the number of required assumptions, while relying on scientifically accepted epidemiological methods and data.

The model uses excess relative risk (RR) estimates of lung cancer (LC), chronic obstructive pulmonary disease (COPD), stroke and ischemic heart (IHD) for continued smoking compared to smoking cessation to estimate the reduction in the number of deaths as an indicator of the population harm.

The PHIM is comprised of two complementary components:

1. The Product Use Prevalence component (**P-Component**): uses a Markov chain state transition model to estimate changes in the distribution of smoking habits (combustible cigarette (CC), RRP, dual use, no use).
2. The Epidemiological Risk component (**E-Component**): uses RRs for smokers compared to both never smokers and former smokers (by time quit) to estimate the number of smoking-attributable deaths.

Methods



Negative Exponential Model

Is used to calculate the reduction in excess relative risk over time, using the known relationships between smoking cessation and reduced disease-specific excess relative risks.

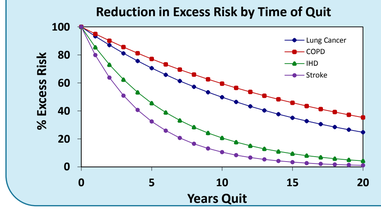
$$RR_{RRP}(t) = 1 + (RR_{CC} - 1) \cdot [F + (1 - F) \cdot \exp(-t \cdot \ln(2)/H)]$$

Reduction of Risk Over Time since Cessation

Disease-specific Half Lives (H) of Excess Relative Risk

H_{LC} = 9.9 years H_{COPD} = 13.3 years

H_{IHD} = 4.4 years H_{stroke} = 4.8 years



Product-Specific "F" Factor

- The "F" Factor is the quantification of the effective dose achieved by the RRP relative to continuing smoking.
- The "F" Factor will be supported by a weight of evidence risk assessment methodology that integrates the information related to the product characteristics, marketing of the product, its potential effects on health, and tobacco use behavior (including initiation and cessation).

Modeling Assumptions

P-Component: a set of assumptions related to the distribution of the use of CCs and RRPs and change over time following the introduction of the RRP.

E-component: a set of assumptions related to how the health risks associated with the RRP will compare to CC and cessation (the "F" Factor).

Model Output

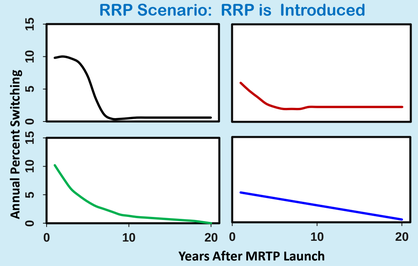
Estimated reduction in smoking-attributable mortality associated with the introduction of an RRP; simulations and sensitivity analyses to explore the impact of the assumptions on the rate of uptake of an RRP and relative exposure from an RRP.

Null Scenario: RRP is not Introduced

End of interval \ Start of interval	N	C	F
N	P_{NN}	Ø	Ø
C	P_{NC} (=1-P_{NN})	P_{CC} (= 1-P_{CF})	P_{FC} (= 1-P_{FF})
F	Ø	P_{CF}	P_{FF}

N = Never smoker **C** = Current smoker
F = Former smoker **P** = Transition probability

RRP Scenario: RRP is Introduced



Patterns of tobacco transitions; The patterns correspond to a cumulative switching rate of 50% over the period

Conclusions

- The PHIM estimates the population harm by calculating the reduction in the number of smoking-attributable deaths related to the introduction of an RRP.
- The model will need to be substantiated and tested using an elaborate set of simulation and sensitivity analyses to understand counterfactual scenarios following a hypothetical population through time after the introduction of an RRP.

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COMPETING FINANCIAL INTERESTS

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