MODELING THE POPULATION YEARS OF LIFE SAVED BY INTRODUCING A REDUCED-RISK PRODUCT IN THE U.S. AND IN JAPAN

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Introduction

Philip Morris International has developed a population health impact model (PHIM) allowing estimation of the reduction in smoking-attributable mortality and years of life saved due to the introduction into a market of a Reduced-Risk Product (RRP*). The assessment of harm reduction due to the introduction of an RRP is a function of the risk associated with the product for the individual and its prevalence of use in a population.

The overall reduction in tobacco-attributable deaths and years of life saved (YLS) from lung cancer (LC), ischemic heart disease (IHD), stroke, and chronic obstructive pulmonary disease (COPD) was estimated by using the PHIM for men and women in the U.S. and Japan under assumptions of RRP uptake in these markets.

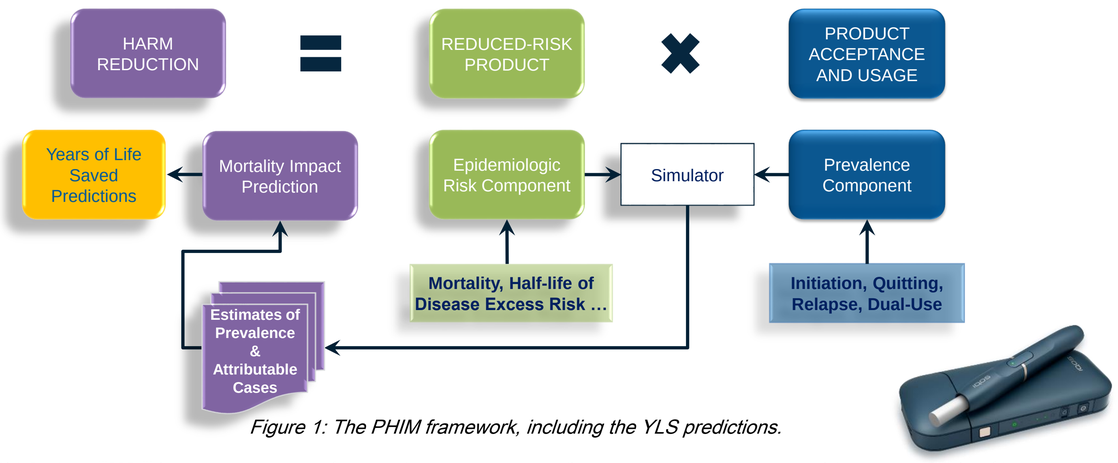

Figure 1: The PHIM framework, including the YLS predictions.

* Reduced-Risk Products ("RRPs") is the term we use to refer to products that present, are likely to present, or have the potential to present less risk of harm to smokers who switch to these products versus continued smoking. We have a range of RRPs in various stages of development, scientific assessment and commercialization. Because our RRPs do not burn tobacco, they produce far lower quantities of harmful compounds than found in cigarette smoke.

Methods

The methodology used to assess the population health impact of introducing an RRP in a country has been previously described [1] and involves two components:

❑ Prevalence Component

The prevalence (P) component is a Markov chain state-transition model that starts in a specified year with a group of individuals of a given sex and age range who have a distribution of cigarette smoking habits representative of the national population at that time. This hypothetical population is followed over discrete time intervals for a defined length of time, under both a "Null scenario" and an "RRP scenario," using different sets of tobacco use transition probabilities (TTP).

Figure 2: Schematic representation of a hypothetical population of 100,000 males and 100,000 females with smoking states under Null and RRP scenarios over a 20-year simulation period (1990-2010).

❑ Epidemiological Component

The epidemiologic (E) component uses the tobacco use histories to estimate, for each individual, the relative risks (RR) of LC, IHD, stroke, and COPD compared with those of never tobacco users at each year of follow-up and for each scenario. The estimation involves an extension of the negative exponential model (NEM), described in detail elsewhere [2], which allows for multiple changes in tobacco use habits.

Apart from the tobacco use histories, the NEM also requires estimates of the effective dose for current RRP use and for dual use, compared to that for current cigarette smoking, as well as estimates of the RR for continued smoking and of the quitting half-life (H) for each disease, with H being the time after quitting when the excess RR ($RR_{CC}-1$) reaches half of that for continued cigarette smoking.

In the RRP scenario, at each simulated year, an individual can be a never tobacco user, current cigarette smoker, current RRP user, current dual user (RRP and cigarettes), or former tobacco user. These five groups have an associated effective dose (f) of, respectively, 0, 1, f (<1), (1+f)/2, and 0 [3].

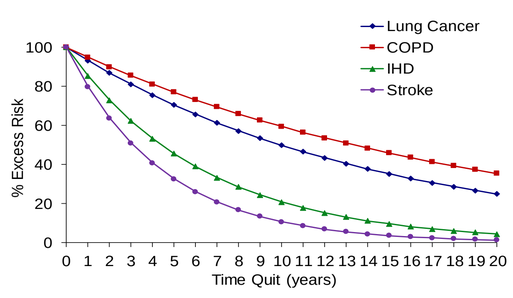

Figure 3: Reduction in excess RR for four diseases as a function of time after quitting, as described by the NEM.

The NEM is used to calculate the excess relative risk over time t (RR_t-1) given the effective dose, the excess relative risk for a continuing cigarette ($RR_{cc}-1$) smoker [2,4,5], and the disease-specific half-life of excess risk (H):

$$RR_t = 1 + (RR_{cc} - 1)\left(f + (1-f)exp\left(\frac{-tln(2)}{H}\right)\right)$$

Separately for each scenario, the average RRs for each disease for individuals of a given sex and age group are calculated for each follow-up year, from which proportions of tobacco-attributed deaths can be derived. These are converted to numbers using national mortality estimates by sex, age group, and year.

❑ Estimated Years of Life Lost / Saved

In addition to estimating effects on numbers of deaths and death rates, one can also compare years of life lost (YLL) between both scenarios and calculate YLS as described in [6]. Assuming that the expected time of death in a certain age range i lies in the middle of that range and a life expectancy of 75 years, the years lost by a death in age range i, L_i, can be calculated. With N_i being the number of deaths attributable to tobacco product use in age range i, YLL is calculated by summing the product of L_i and N_i.

$$\boldsymbol{YLL} = \sum_i L_i \times N_i$$

The final result is expressed in YLS for all diseases for the entire simulation period as the difference between YLL calculated for the RRP and Null scenarios.

Results

❑ Null Scenario

Null scenario TTPs have been developed and verified for the U.S. and Japan. U.S. TTPs are the same for males and females; Japan TTPs differ per gender due to smoking prevalence differences.

Various RRP scenarios have been evaluated by varying TTPs according to the expected RRP uptake. The results presented here consider an uptake of 17% in the U.S. and 55% in Japan 10 years after introduction of RRP in the market. Both scenarios assume around 85% exclusive RRP use and 15% dual use, and an effective dose f=0.1 and 0.3.

❑ RRP Scenario for the U.S.

This simulation assumes that 17% of the smoking population would be using RRP within 10 years following its commercial launch (15% RRP users and 2% dual users).

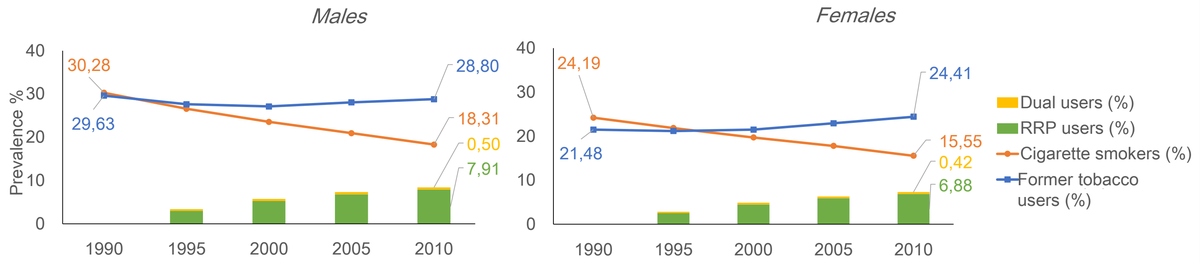

Figure 4: Prevalence of smoking states for males and females over all age groups, under the RRP scenario for the U.S.

Table 1: Reduction in cumulative attributable deaths and YLS for LC, IHD, stroke, COPD, and all four diseases over all age groups, for males and females, following the introduction of an RRP in the U.S.

Effective Dose RRP	Reduction in LC Deaths	Reduction in IHD Deaths	Reduction in Stroke	Reduction in COPD	Reduction in Cumulative Attributable Deaths (all four diseases)	Years of Life Saved (all four diseases)
f=0.1	20,519	46,103	8,888	13,519	89,028	1.15 million
f=0.3	15,434	34,897	6,768	10,224	67,324	0.97 million

❑ RRP Scenario for Japan

This simulation assumes that 55% of the smoking population would be using RRP within 10 years following its commercial launch (48% RRP users and 7% dual users).

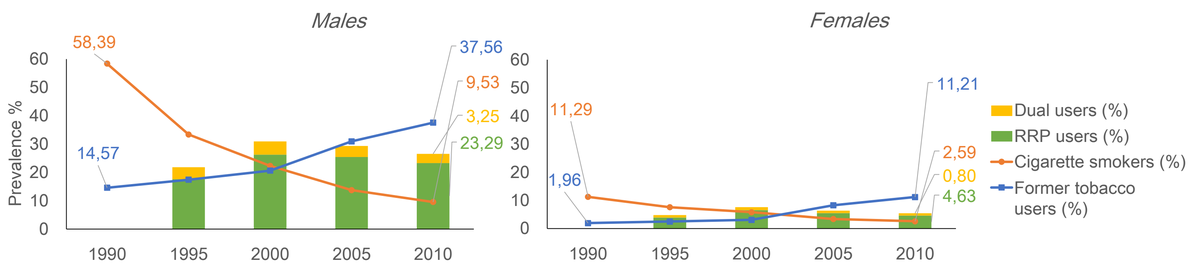

Figure 5: Prevalence of smoking states for males and females over all age groups, under the RRP scenario for Japan.

Table 2: Reduction in cumulative attributable deaths and YLS for LC, IHD, stroke, COPD, and all four diseases over all age groups, for males and females, following the introduction of an RRP in Japan.

Effective Dose RRP	Reduction in Lung Cancer Deaths	Reduction in IHD Deaths	Reduction in Stroke Deaths	Reduction in COPD Deaths	Reduction in Cumulative Attributable Deaths (all four diseases)	Years of Life Saved (all four diseases)
f=0.1	27,462	27,849	28,842	2,730	86,884	1.10 million
f=0.3	20,644	20,643	21,770	2,070	65,126	0.82 million

Introducing an RRP in the U.S. and Japan markets shows a net public health benefit with reduced tobacco-related mortality and increased YLS.

The model is limited by considering only four smoking-related diseases and does not account for smokeless tobacco, nicotine replacement therapy, or e-cigarettes.

Conclusions

- The introduction of an RRP can lead to substantial impact on population harm reduction in the U.S. and Japan over a 20-year period by reducing smoking-attributable deaths and, consequently, increasing YLS.
- It has been calculated that 0.97 to 1.15 million years of lives in the U.S. and 0.82 to 1.10 million lives in Japan could have been saved between 1990 and 2010.

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Competing Financial Interest

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