MODELING THE IMPACT OF CHANGES IN TOBACCO USE ON INDIVIDUAL DISEASE RISKS

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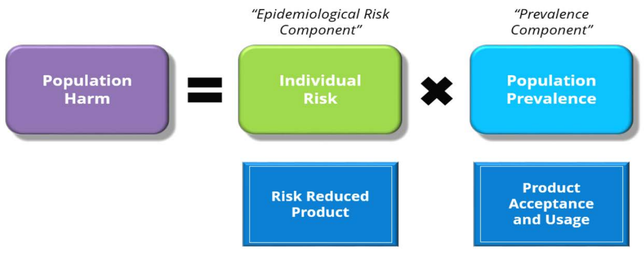
Introduction

Philip Morris International has developed a Population Health Impact Model (PHIM) to estimate the effects that marketing of Reduced Risk Products (RRPs)* has on population health. It was designed to assess the impact of an RRP on population harm as a function of the risk or toxicity of the product to the individual user, and the prevalence of use in the population.

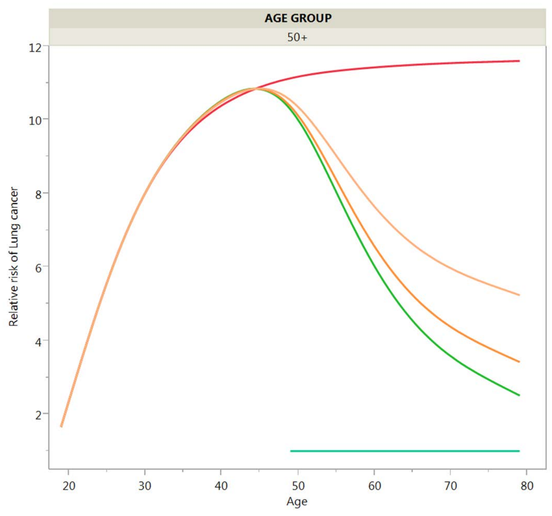


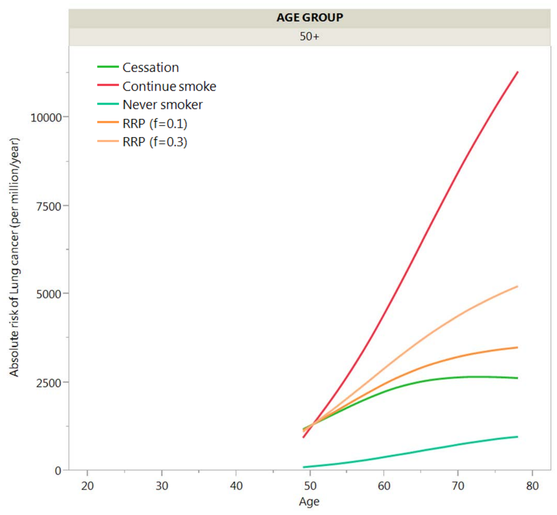
This modeling exercise aims at understanding the impact of harm reduction to smokers who quit or switch to RRP products versus continued smoking or never smoking across different age groups (20+, 30+, 40+ and 50+ years old) evaluated as changes in relative and absolute risk over time for the four main smoking-related diseases: lung cancer (LC), ischemic heart disease (IHD), stroke and chronic obstructive pulmonary disease (COPD).

*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.

Results

- Work described in here covers the series of modeling simulations (1-4) on different age groups (20+, 30+, 40+ and 50+ years old) to understand the:
  1) Impact of quitting tobacco smoking – **CESSATION**
  2) Impact of switching to an RRP with low and high effective dose – **RRP (*f*=0.3) and RRP (*f*=0.1)**
  3) Impact of continuing to smoke cigarettes – **CONTINUE SMOKING**
  4) Impact of never smoking – **NEVER SMOKING**
- All individuals initiated smoking at 20 years old. Cessation and switching to RRP take place 1 year after entering the simulation. The effective dose for RRP are estimates derived from non-clinical and clinical data in PMI.
- Simulated profiles for LC in a 50+ year old male shows the reduction in relative and absolute risk over time follow a negative exponential decay. Switching to an RRP brings a noticeable reduction in relative and absolute risk of LC versus continued smoking and therefore can be considered as an alternative to smoking.





Methods

The method of estimating the excess relative risk (ER) of product use for each disease depends on:

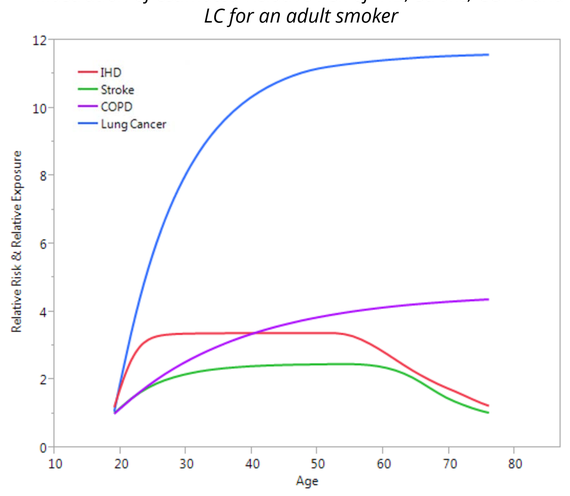
- First calculating what the "equivalent dose" (ED) is at each age, and then
- Multiplying the ED by the disease-specific ER for a smoker continuing to use cigarettes at that age.

The ED for an individual is derived from relative exposures (RE) relating to tobacco use patterns at different ages as illustrated in the Table below.

Tobacco Product Use Pattern	Relative Exposure (RE)
Non Smoker (Never or Former tobacco product user)	0
Conventional Cigarette Smoker (Current smoker)	1
RRP User (*f* <1, tested *f*=0.1 and *f*=0.3)	*f*
Dual user (assumed to be half-way between RRP and smoking)	(1+*f*)/2

The ED at birth and for non-smoker is 0, once an individual starts to use a tobacco product, their RE will increase, and their equivalent dose will gradually move towards the RE related to their specific tobacco product use pattern or switches in tobacco products.

Illustration of estimated Relative risk of IHD, Stroke, COPD and LC for an adult smoker



The method of estimating ER is :

- Assume that, at each year of age (*a*), an individual's RE is $f(a)$ and the half-life of excess risk is H(*a*).
- The negative exponential factor for a single year is calculated as:

$$N(a) = \exp(-\log_e(2) / H(a))$$

- The ED(*a*) at birth is 0, and subsequent values of are then calculated as:

$$ED(a) = N(a)\, ED(a\text{-}1) + (1\text{-}N(a))\, f(a)$$

- In addition to the changes in RE over time (the individual's smoking history), the model requires estimates of age- and disease-specific relative risks of smoking [1] and H(*a*) following cessation.

The disease-specific H(*a*) presented in the Table below, were derived from meta-analyses of published data [2].

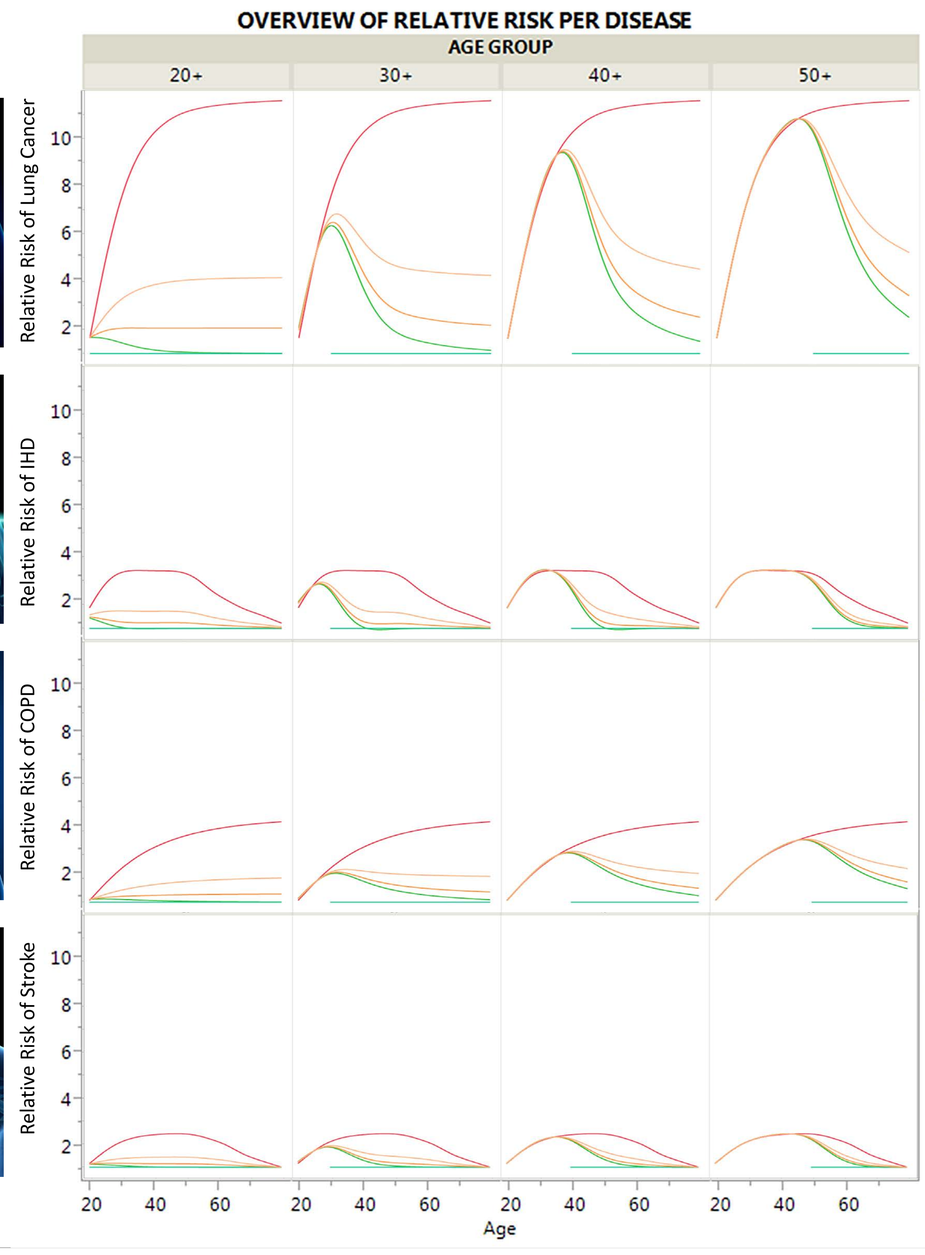
	Age (*a*)	LC	IHD	Stroke	COPD
Half-life (H)	Any			4.78	13.32
	to 49	6.98	1.47		
	50 to 59	10.39	5.22		
	60 to 69	10.60	7.48		
	70 to 79	12.99	13.77		

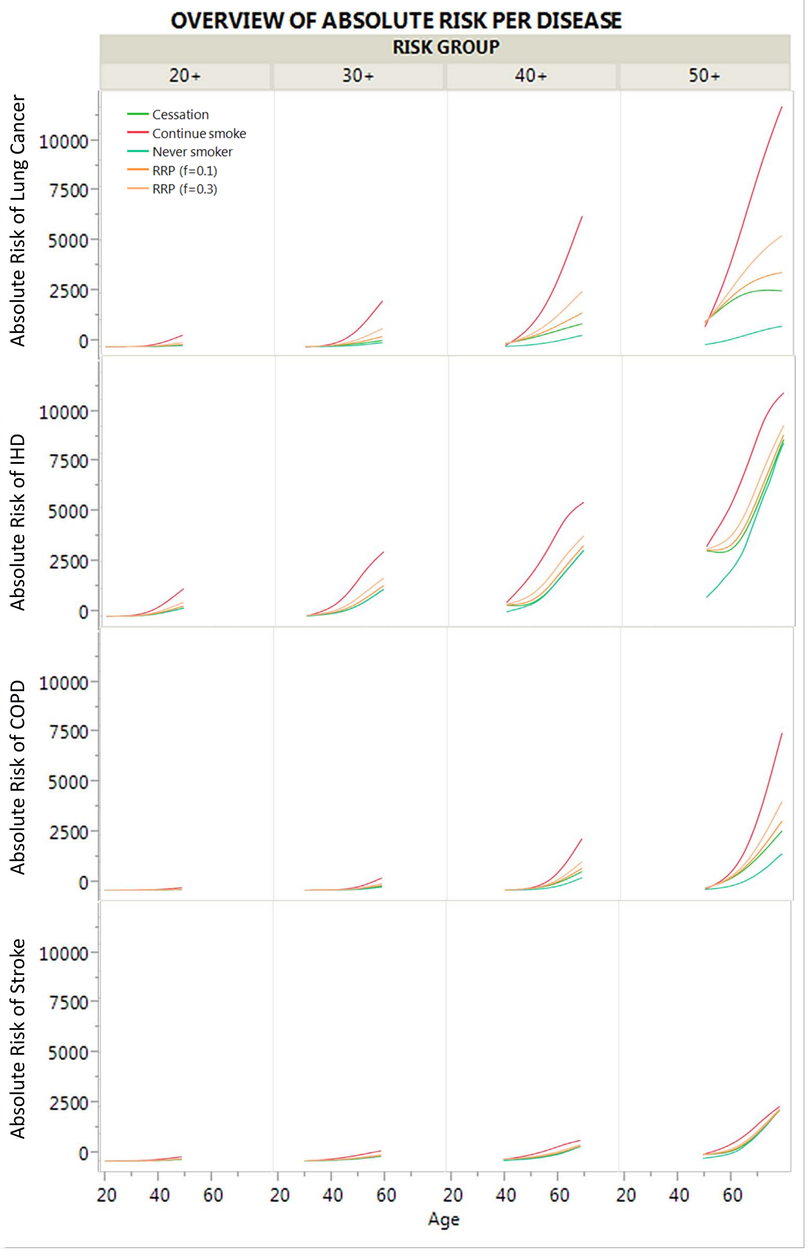
The negative exponential model [3] is used to estimate the decline in disease-specific relative risk following smoking cessation, but can also estimate the change in relative risk (RR) following a change in product use – e.g., switching from cigarettes to RRP as:

$$RR_{RRP}(a,t) = 1 + (RR_C(a) - 1)\,(f + (1- f)\exp(-t \ln(2)/H))$$

where *t* is the time since switching to the product, H is the disease-specific half-life of the excess relative risk, and *a* is age. The PHIM [4] derives estimates of absolute risks for each individual in hypothetical population given an overall estimate of absolute population risk for a given country, year, sex and age-group.

Overview of Results





Conclusions

Overview of all simulation results for four smoking diseases and age groups show a differentiation in relative and absolute risk in line with what is expected from the changes in effective dose (0 for never smoker; 1 for smoker; *f*=0.1 and *f*=0.3 for RRPs).

Cessation is overall the most effective in population harm reduction.

These simulations demonstrate the extent to which an RRP could contribute to population harm reduction across the different smoking-related diseases given a reasonable assumption that the reduced exposure from the RRP resulted in an effective dose of between 0.1 and 0.3.

Switching to RRPs for smokers in their 20s and 30s can be considered as mostly risk prevention; while for smokers in their 40s and 50s this can be more risk reduction.

Population Health modeling is an established and recognized field of science. The PHIM described here can be a valuable tool to quantify both individual and population changes that can be expected from marketing RRPs, with the ability to test a variety of different scenarios in both pre- and post- market settings.

REFERENCES:
[1] Sources for relative risks: Lung cancer: (Lee 2012a); COPD: (Forey 2011); IHD and Stroke (Lee 2016 – not yet published).
[2] Sources for half-lives: Lung cancer: (Fry 2013); COPD: (Lee 2014a); IHD: (Lee 2012b); Stroke: (Lee 2014b)
[3] Lee PN, Hamling J, Fry J, Forey B. 2015.. Advances in Epidemiology Article ID 487876, 13.
[4] Weitkunat, R., Lee, P.N., Baker, G., Sponsiello-Wang, Z., González-Zuloeta Ladd, A.M., Lüdicke, F., 2015. Regul. Toxicol. Pharmacol. 72, 87-93.

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