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MODELING THE POPULATION HEALTH IMPACT OF INTRODUCING A REDUCED-RISK PRODUCT INTO THE JAPAN MARKET

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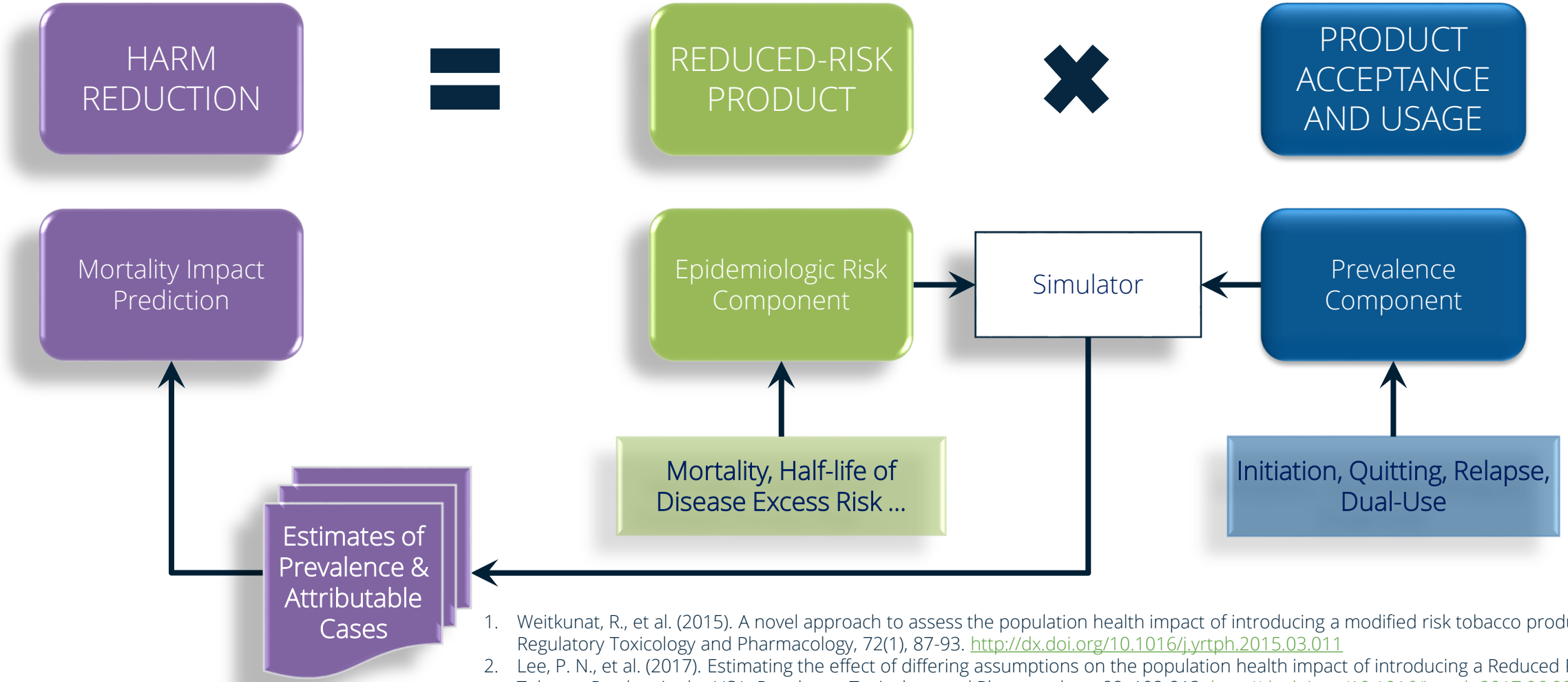
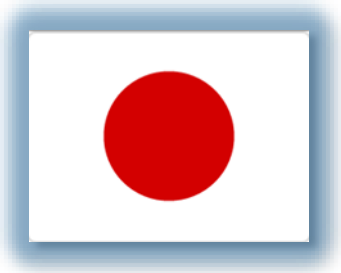
Population Health Impact Model



1. Weitkunat, R., et al. (2015). A novel approach to assess the population health impact of introducing a modified risk tobacco product. Regulatory Toxicology and Pharmacology, 72(1), 87-93. http://dx.doi.org/10.1016/j.yrtph.2015.03.011
2. Lee, P. N., et al. (2017). Estimating the effect of differing assumptions on the population health impact of introducing a Reduced Risk Tobacco Product in the USA. Regulatory Toxicology and Pharmacology, 88, 192-213. http://dx.doi.org/10.1016/j.yrtph.2017.06.009
3. Djurdjevic, S., et al. (2018). Modeling the impact of changes in tobacco use on individual disease risks. Regulatory Toxicology and Pharmacology, 97, 88-97. https://doi.org/10.1016/j.yrtph.2018.06.001
4. Djurdjevic, S., at al. (2018). Modeling the Population Health Impact of Introducing a Modified Risk Tobacco Product into the US Market. Healthcare 6 (2), 47. https://doi.org/10.3390/healthcare6020047

Methodology – P-Component



Hypothetical population
(10–79 years old)*
100,000 Males and 100,000 Females

- Initiation
- Quitting
- Re-Initiation

- Switching products

Year 0
(1990)

Year 20
(2010)

<u>Null scenario:</u>
No RRP on the market

<u>Smoking status:</u>

- Never smokers
- Cigarette smokers
- Former smokers

<u>RRP scenario:</u>
RRP (*IQOS*® and other heated tobacco products) on the market

<u>Smoking status:</u>

- Never smokers
- Cigarette smokers
- RRP users
- Dual users (RRP and cigarettes)
- Former smokers

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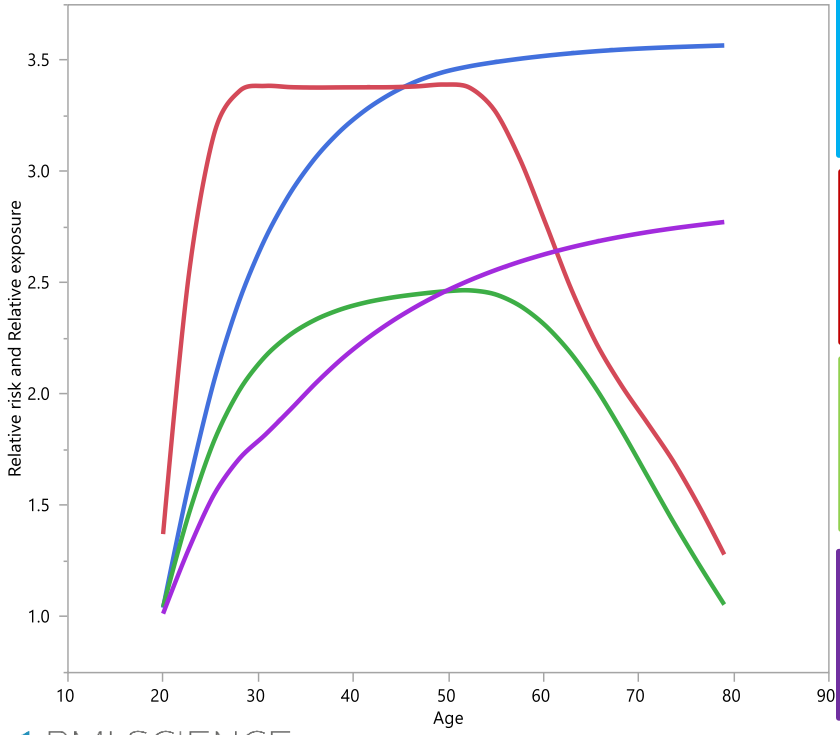
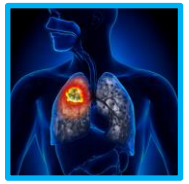
* The simulation is based on an age range extending beyond the legal age for smoking in order to capture real life initiation patterns.

Relative Risk and Disease Risk Half-Lives (Adult Smoker)

The PHIM requires disease-specific relative risk (RR) and disease risk half-lives (H) for epidemiological component predictions.

Relative risk of lung cancer, IHD, stroke, and COPD for an adult male cigarette smoker in Japan.





Lung cancer

IHD

Stroke

COPD

Disease risk half-life [1],[2] (by age)

The time at which half of the excess risk associated with cigarette smoking has disappeared

Age (years)	Lung cancer	IHD	Stroke	COPD
Any	-	-	4.78	13.32
To 49	6.98	1.47	-	-
50 to 59	10.39	5.32	-	-
60 to 69	10.60	7.48	-	-
70 to 79	12.99	13.77	-	-

[1] Sources for relative risk:
Lung cancer (Lee 2018), COPD (Forey 2011), IHD and Stroke (Lee 2016)
[2] Sources for half-life of risk:
Lung cancer (Fry 2013), COPD (Lee 2014), IHD (Lee 2012), Stroke (Lee 2014)

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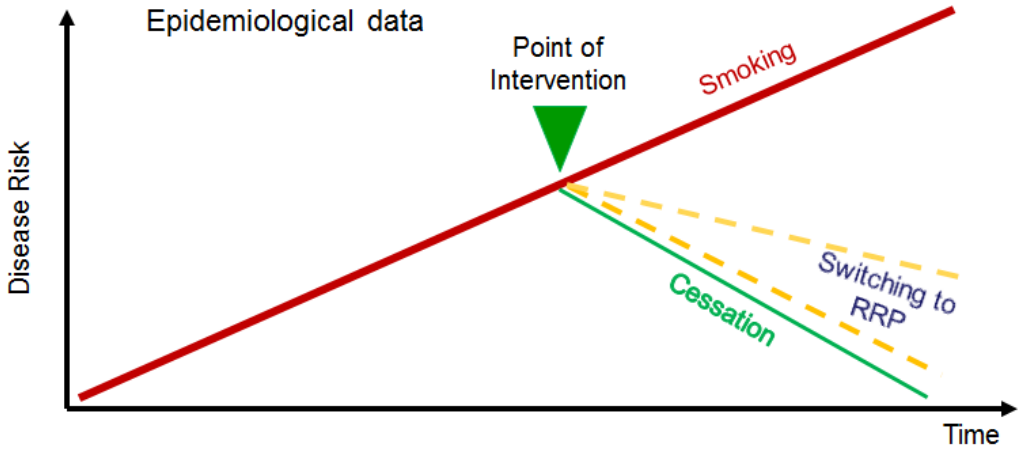
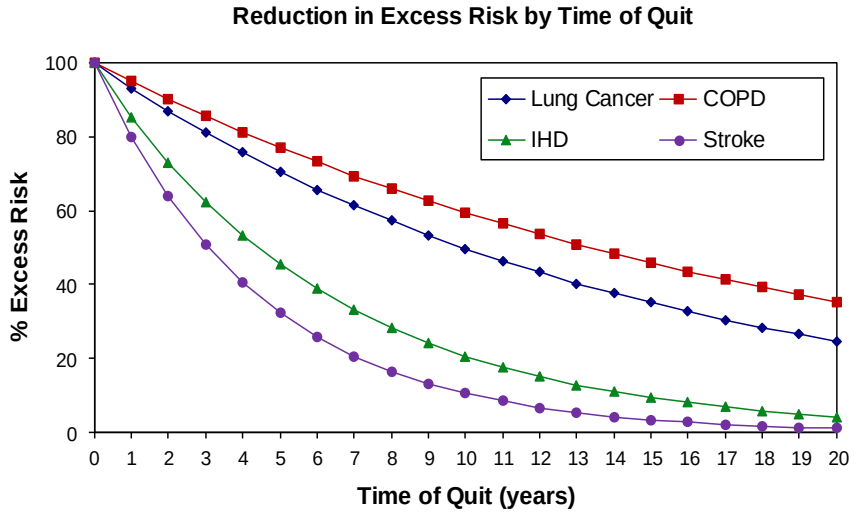
Methodology – E-Component

- Convert smoking histories to RR to estimate smoking attributable death
  - RR for smoking cigarettes
  - H for RR by time quit for smoking cessation
  - "f -factor" - effective dose for RRP users (tested at f =0.1 to 0.3 [3])





- Negative exponential model is used to calculate the reduction in excess RR over time using the relationships between smoking cessation and reduced excess RR

$$RR(t) = 1 + (C-1)\left(f + (1 - f)\exp(-t \ln(2)/H)\right)$$

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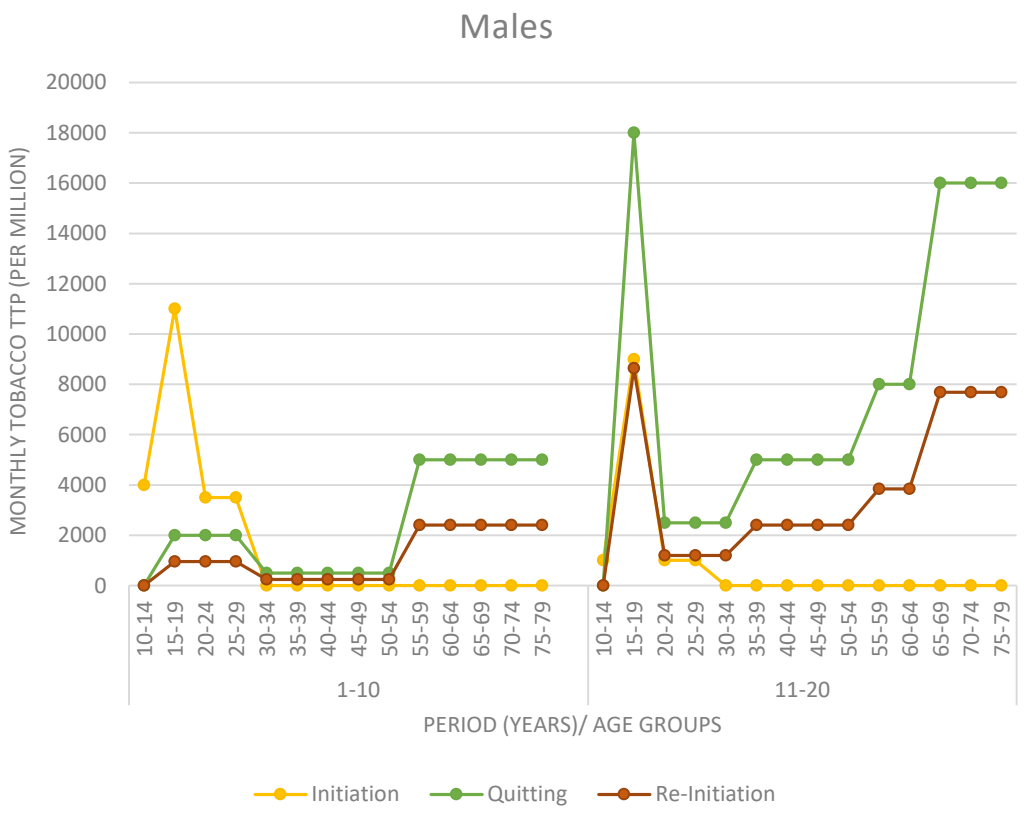
[3] Effective dose of IQOS is tested as 10–30% of that of cigarette smoking. Martin, F., et al. (2018). Quantifying the risk-reduction potential of new Modified Risk Tobacco Products. Regulatory Toxicology and Pharmacology 92, 358–369. https://doi.org/10.1016/j.yrtph.2017.12.011

Null Scenario

TTPs developed for null scenario differ by sex and by period (1990–1999, 2000–2009)



Null scenario assumptions:

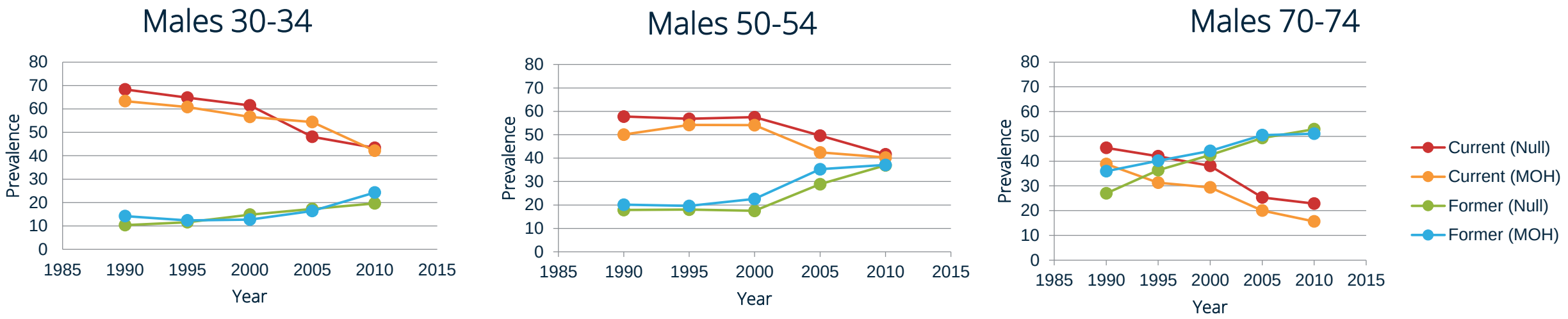
1. Initiation rates from age 35 years are 0 (no initiation after 35 years) [4]
2. The re-initiation rates are higher in middle age than in the younger and older segment of the population and are 48% of cessation rates [5]
3. Cessation rates are 2x higher in those who have recently attempted to quit
4. The re-initiation rates are 2x higher in quitters who have quit within the last two years

[4] Weinberger, A., et al. (2014). Stability of smoking status in the US population: a longitudinal investigation. Addiction, 109(9), 1541-1553. https://doi.org/10.1111/add.12647
[5] Marcon, A., et al. (2018). Trends in smoking initiation in Europe over 40 years: A retrospective cohort study. PloS one, 13(8), e0201881. https://doi.org/10.1371/journal.pone.0201881 .

Verification of Null Scenario

The model was tested under the Null Scenario for Japan

Distribution of smoking habits for males as given by MOH compared with estimates from PHIM using the set of TTPs developed for the Null Scenario.



Overall, the assumptions for the PHIM were a reasonable fit with actual smoking prevalence from MOH for 30–34, 50–54, and 70–74 age groups in the Japanese market over the time of the tested simulations [5].

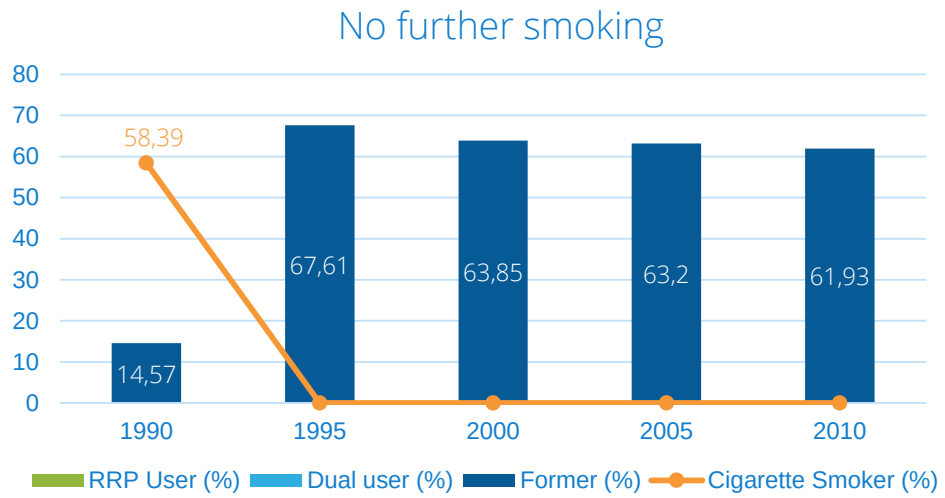
[5] Djurdjevic, S., at al. (2018). Estimating the population health impact of introducing a reduced-risk tobacco product into Japan. The effect of differing assumptions, and some comparisons with the U.S.. Regulatory Toxicology and Pharmacology – submitted

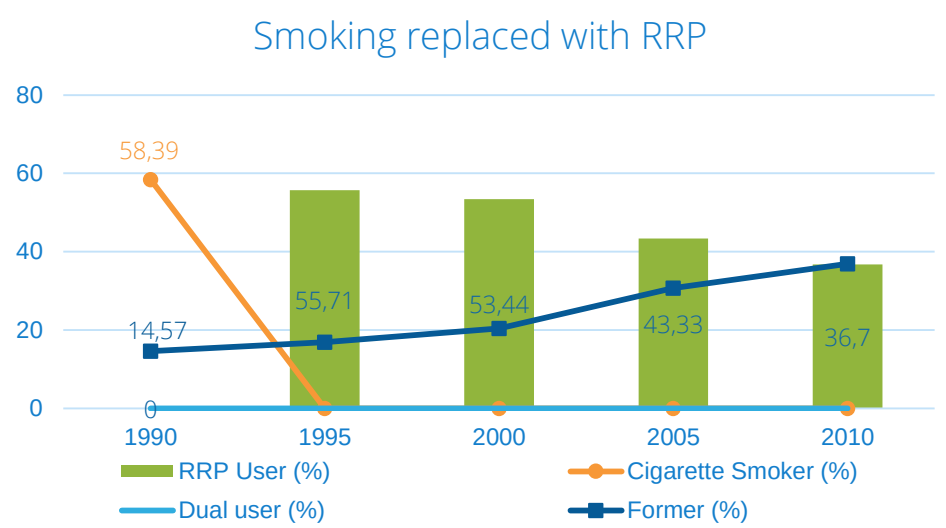
RRP Scenarios Prevalence

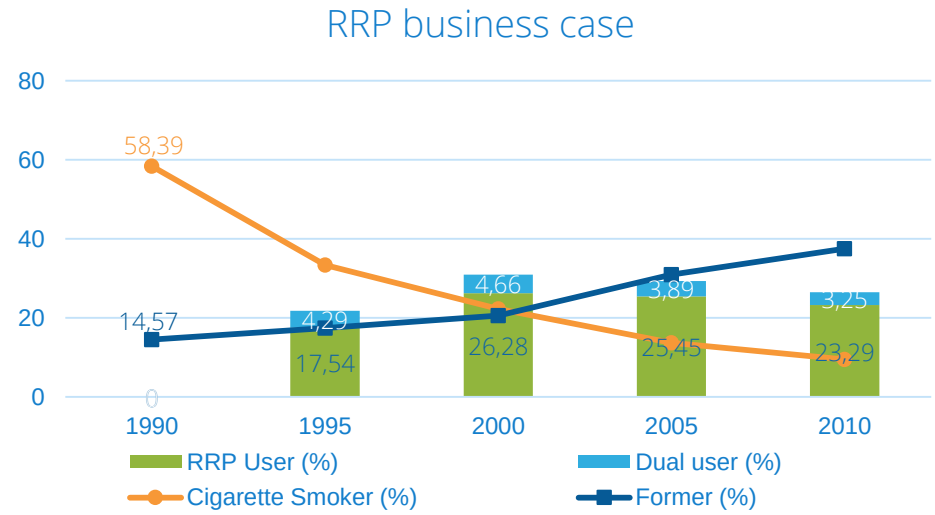
The model was tested under many RRP Scenarios for Japan; three selected examples shared:

Scenarios*
1. No further smoking (all stop smoking after one year)
2. Smoking replaced by RRP (exclusive RRP use after one year)
3. RRP business case (RRP uptake of 55% with 85% being exclusive RRP use and 15% dual use after 10 years)

*Presented only data for males







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RRP Scenario Predictions

Scenario (males and females)		Reduction in lung cancer deaths 	Reduction in IHD deaths 	Reduction in stroke 	Reduction in COPD 	Reduction in cumulative attributable deaths (all 4 diseases)	Years of life saved 75 years (life expectancy) (all 4 diseases)
No further smoking (all stop smoking after one year)		88,510	87,885	84,819	8,699	269,916	3.4 Million
Smoking replaced by RRP (exclusive RRP use after one year)	f=0.1 f=0.3	76,473 55,051	74,449 52,179	73,964 54,179	7,630 5,630	232,518 167,041	2.9 Million 2.1 Million
RRP business case (RRP uptake of 55% with 85% being exclusive RRP use and 15% dual use after 10 years)	f=0.1 f=0.3	27,462 20,644	27,849 20,642	28,842 21,770	2,730 2,069	86,884 65,126	1.1 Million 0.8 Million

Takeaways

Smoking cessation is the best option for smokers to reduce their risk of smoking-related disease, however, switching to PMI's Tobacco Heating System (*IQOS*) is a better option than continuing to smoke

Introducing an RRP into the Japan market may lead to a net public health benefit in terms of reduced tobacco-related mortality

This predicted benefit will be larger if the rate of uptake for *IQOS* and other heated tobacco products in Japan is faster or if the proportion of the smoking population that switches is larger

PHIM is an appropriate tool to monitor and assess RRP post-market development in Japan and other countries of interest

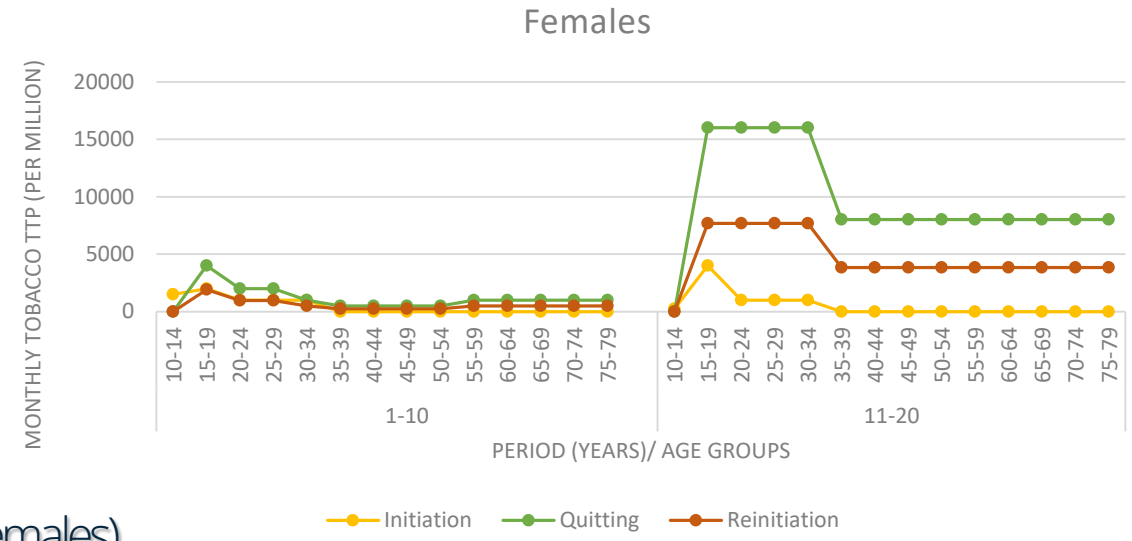
Acknowledgements

- Peter N. Lee (PNL Statistics and Computing LTD)

- Tomoko Lida (Phillip Morris Japan LTD)
- Emi Konishi (Phillip Morris Japan LTD)

Backup slides

Null Scenario (Females)



Verification of null scenario (Females)