

Population Modelling Assessing the Health Effects of Launching Tobacco Heated Products in Japan

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Introduction

In less than 2 decades, the nicotine use landscape has changed substantially. In 2001, the Institute of Medicine (IOM) introduced the concept of Tobacco Harm Reduction. They suggested a strategy for harm reduction based on the replacement of risky tobacco products like cigarettes with lower risk products, stating that products with potential for harm reduction should reduce users' exposure to one or more toxicants in smoke; and reductions in exposure to toxicants should have a disease relevant impact [IOM, 2001][1]. Soon after, technological advances would enable the development of devices providing an acceptable alternative to smokers while reducing the exposure to harmful constituents found in cigarette smoke. Within the Tobacco Harm Reduction paradigm, these new products could have a lower risk profile than conventional cigarettes and be identified as Potentially Reduced Risk Products (PRRP). In the aerosol delivery space, products belonging to two main categories, e-cigarettes and Tobacco Heated Products (THP) are being investigated as PRRPs. Following FDA lead with their Modified Tobacco Product Application (MRTPA), several governments around the world are considering scientific evidence which could help substantiate the potential of PRRPs. Products' risk could be considered a composite of the intrinsic risk of the product (individual risk) and by who/how products are used i.e., the behavioural aspect (population risk). In 2012, the FDA's MRTPA guidance suggested using mathematical models as tools for assessing the impact of PRRPs in terms of population health outcomes. These models provide simplified representations of the behaviours and mechanisms associated with nicotine use which combined with risk estimates can provide informative projections for different health outcomes overtime. British American Tobacco (BAT) in collaboration with Ventana Systems UK has developed a System Dynamics compartmental model for two nicotine product categories [2]. This initial model built and calibrated using data from the United Kingdom has now being adapted to provide projections for mortality and morbidity endpoints as result of launching Tobacco Heated Products in Japan.

Aim

This work has two aims: 1. To assess the appropriateness of real life data collected through surveys as model inputs. 2. To provide projections of the impact on population health outcomes (mortality and morbidity) as result of launching tobacco heated products in the Japanese market.

Methods

The model is comprised of two distinct parts: A structural part representing the basic mechanisms or relationships between the all possible nicotine use statuses for a two product model as well as the inflows (birth rates, migration) and outflows (mortality, morbidity). The second element are the data inputs which allows to provide projections, a model implementation, by using estimates observed for that population and the product being investigated.

Model Structure

The model structure has been previously defined. Briefly, in the model, different smoking statuses are represented by stocks (compartments) and arrows represent the flows (Figure 1). It allows representation of complex non-linear mechanisms, including feedback effects, by simply calculating inbounds and outbounds based on Systems Dynamics methodology.

The model is initiated in the past, with data from a specific year. It is not a cohort model. The idea is to represent the whole of the population, including births, deaths and migration rates. All possible transitions for a two-nicotine product model are also considered differentiating between current/former and dual PRRP users and, with and without smoking history. The reason for separating stocks with different smoking history is not only because these categories are likely to have different relative risks but it is also necessary to investigate initiation from never and former smokers. Full description of the model and structural/conceptual assumptions can be found in Hill & Camacho, 2017 [2].

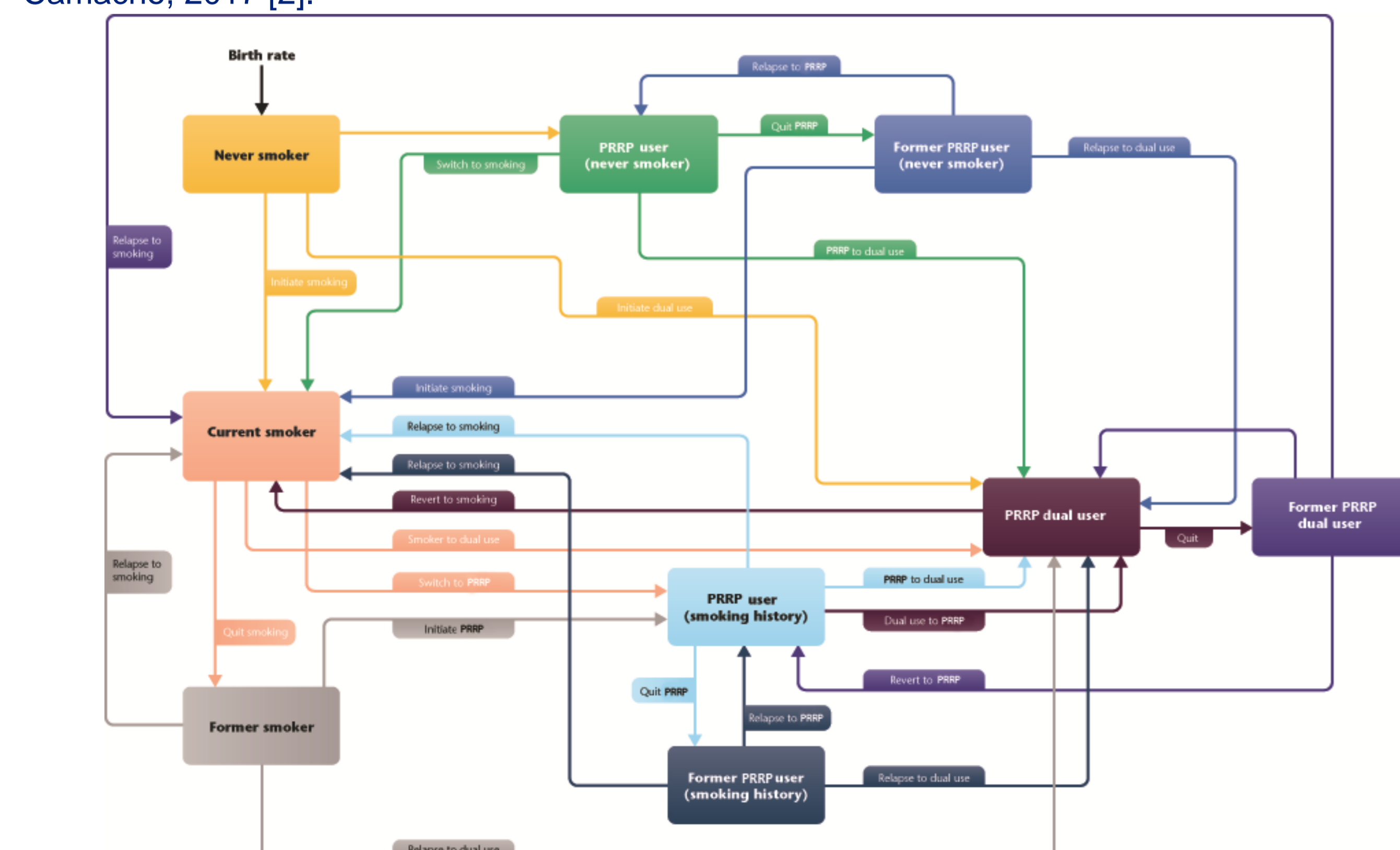


Figure 2. Representation of the full model. This includes all possible outcomes that can occur at a time step.

Data inputs

Public use data was identified to initialise the model at year 2004. This included Japanese specific demographic data and smoking prevalence by age and gender, with birth and death rates for these same categories. Additionally, demographic data was used to calibrate the model for a period of 13 years up to 2016, with a time step of a year. Mortality relative risks between smokers and never smokers were extracted from a report by the Epoch-Japan Research Group. Data sources are listed in Table 2.

Transition estimates between THP use and other stocks were not publicly available. A population study to estimate transition rates between different products, among other endpoints, was carried out in Japan. The study is ongoing and will provide data about different products prevalences, risk perception, quality of life (QoL) measurements and model transitions' estimates between combustible products and THP for a period of 3 years (Q2 2018 to 2020). The study is planned to collect data in 6 waves, two cross-sectional waves per year, with the initial wave considered to be a pilot wave used to test the methodology. Learnings from the pilot have been used to refine the self-reported instrument. The results presented here are based on questions about current and past use from 4,154 participants during the pilot study. This first wave only surveyed three areas in Japan: Sendai city, Tokyo metropolitan area and Osaka-fu. Next waves will be implemented nationwide.

Table 1. Data sources for smoking related data inputs in Japanese population.

Input Data	Study/Report/Survey
Initialisation data – Demographic data	Population Census by Statistics Bureau. Ministry of Internal Affairs and Communications (MIAC, Japan)
Population and Birth Rate Projections	National Institute of Population and Social Security Research (NPSSR, Japan)
Smoking Prevalence	National Health and Nutrition Survey (annual). Ministry of Health, Labour and Welfare (MHLW, Japan)
Smoking Initiation	National Health and Nutrition Survey (MHLW, Japan)
Calibration data	National Health and Nutrition Survey (annual). Ministry of Health, Labour and Welfare (MHLW, Japan)
Mortality Rates	Life Table by Ministry of Health, Labour and Welfare (MHLW, Japan)
Relative Risks	Murakami et al. EPOCH-JAPAN Research Group. Population attributable numbers and fractions of deaths due to smoking: A pooled analysis of 180,000 Japanese. Prev Med, 2011, 52(1):60-5.

Results

During our survey in Japan, 34,197 households were visited with 4,154 participants self-completing their paper questionnaires adding to an overall response of 12%. The sample was able to successfully capture the age and gender distribution. The biggest discrepancy was for the 30-39 years old where weighted sample points to 15.9% of the population within this age category while the sample was 12.1% of respondents.

The weighted and unweighted number of participants by age and gender are displayed in Figure 2.

Our survey estimated an overall smoking prevalence of 15.5% for these 3 regions in Japan, underestimating overall Japanese prevalence which is estimated to be around 18%. THP use, including dual use, was estimated to be at 5.3% with male prevalence significantly higher across all categories but not proportionally (Table 2).

Table 2. Number of respondents weighted and unweighted by age and gender.

Parameter	CC n(%)	THP n(%)	Other products n(%)
Male	478.4 (23.4%)	156.0 (7.6%)	26.0 (1.3%)
Female	167.0 (7.9%)	64.5 (3.1%)	2.9 (0.1%)
Total	645.4 (15.5%)	220.5 (5.3%)	28.9 (0.7%)

Due to these limitations, smoking prevalence from publicly available data was used to inform the model. Smoking initiation rates were calculated from the National Health and Nutrition Survey 2010 by MHLW (Figure 3 left). Smoking cessation rates were estimated through calibration (3 Right).

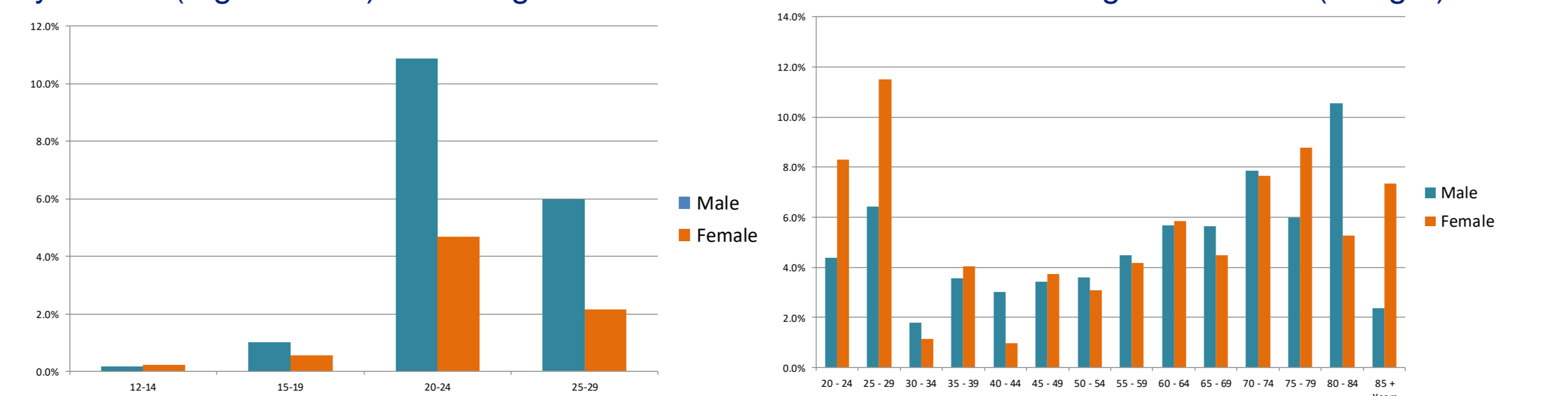


Figure 3. Estimated smoking initiation rates (left) and quitting rates calculated through calibration (right).

Scenarios

With the data presented to this point we generated a Status Quo scenario, i.e., without considering THP use. Projections from this Status Quo scenario were assessed against Japan projected data to confirm it was able to draw sensible projections (Figure 4).

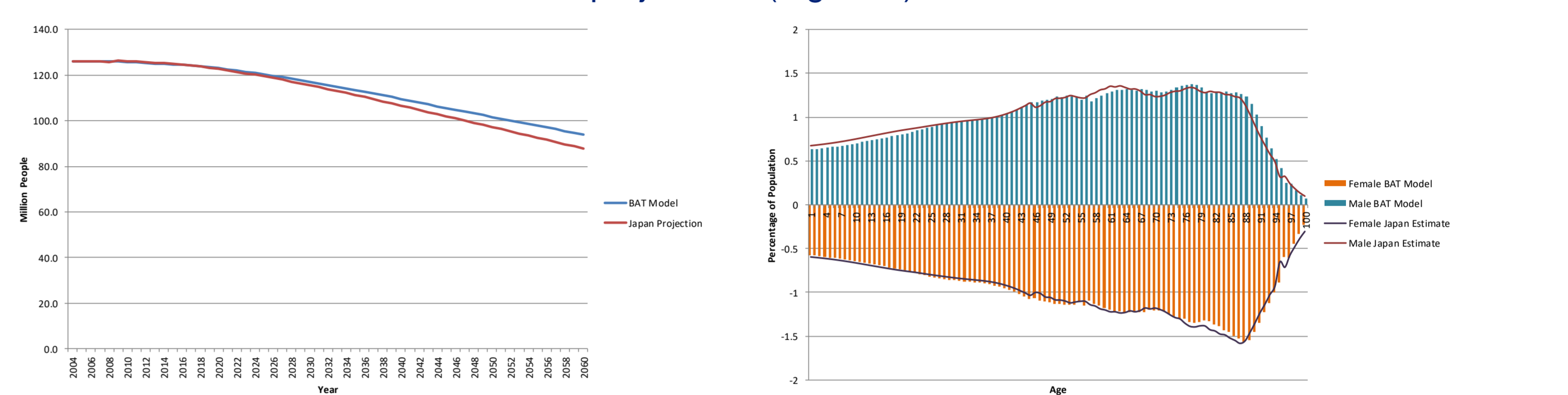


Figure 4. Japanese population projection Status Quo scenario up to 2060 vs. Census office projection (Left) and Population distribution by age and gender from Status Quo scenario vs. Japanese Census estimates (Right).

The alternative scenario, including the introduction of THPs was difficult to populate using estimates from our survey. We found that even though the survey was large enough to produce satisfactory estimates for smoking, the lower prevalence for THP made the sample size insufficient for calculating reliable prevalence rates by age and gender. There was an scattered absence of observations for some age/gender transitions which we believe to be a result of insufficient sampling within those age/gender groups. To mitigate this effect results were collapsed by gender i.e., same rates across all age categories or overall if frequency was also low by gender (Table 3). THP relative risk was assumed to be 0.1 as per UK House of Commons Report.

Table 3. Estimates of transition rates from and to THP calculated from pilot study outputs.

Initiation of THP from never used was estimated 0.23%
Initiation of THP from smoking to dual use was estimated 11.7% of males and 13% of females
Initiation of THP from smoking, complete switching was estimated 0.4% of males and 0.6% of females
Dual users were estimated to have 2.9% rate quitting both products
Dual users relapsing rate to smoking was estimated to be 3.6%
Dual users rate completely quitting smoking but remaining as THP users was 37.1% for males and 44% for females
The relapse rate to THP use for both genders was at 18.5%
Quitting rate of exclusive THP use was estimated to be at 1.8%

Based on these assumptions and estimates, overall smoking prevalence could go as low as 5% as prevalence of THP use reaches 11.9% in 2060. In terms of population health outcomes, we investigated incidence of lung cancer and mortality, expressed as premature deaths under 85 and life-years lost (Figure 5). In numbers, by introducing THP products in the Japanese market there could be up to 400 thousand fewer cases of lung cancer by 2060 and 4.3 million life-years saved when compared to the scenario where THP were not available in Japan.

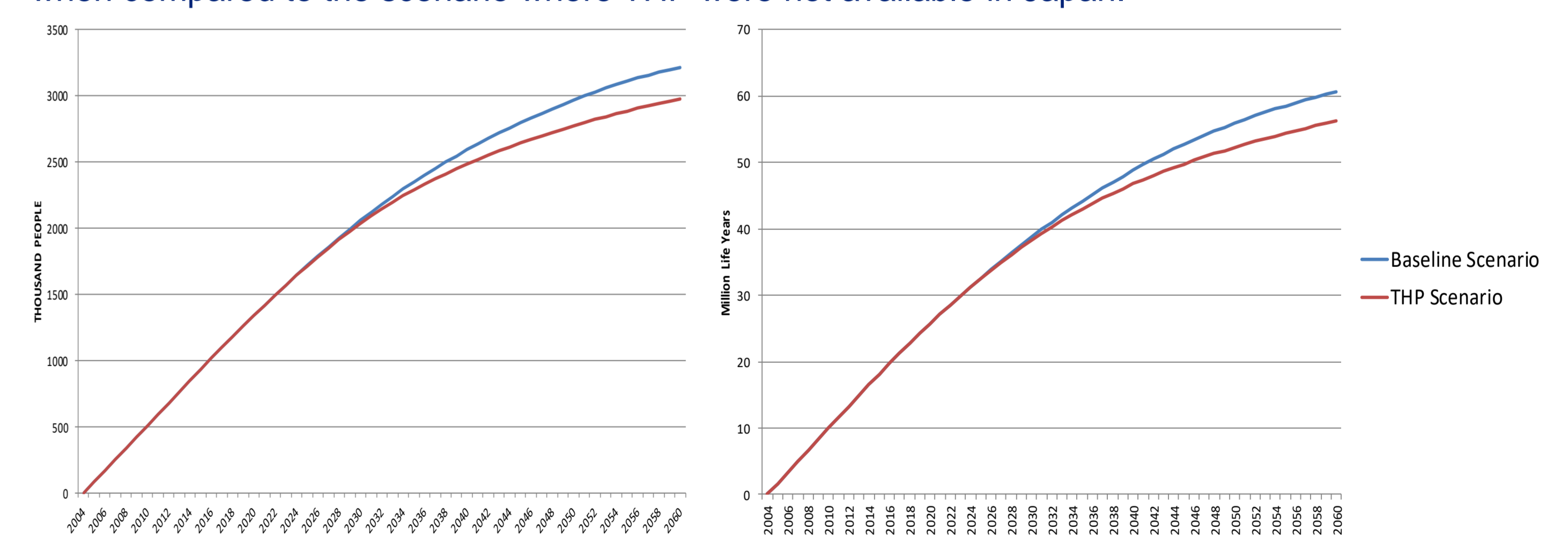


Figure 5. Premature deaths of under 85 (Left, in thousands) and life-years lost (Right, in millions).

Limitations

There are some clear limitations to the work presented here as it is largely based on a pilot survey which suggested to be of insufficient size to produce all estimates required in the model. Next waves will be collecting responses from over 10,000 respondents per year which is expected to enable calculation of those estimates by gender and age.

Conclusions

The data collected from the instrument has been shown to be appropriate to inform our population model although larger samples will be required to capture all THP transitions. Assessment of the data available using our population model, based on current trends of nicotine use in Japan and assumptions about THPs risk with respect to smoking, suggests that launching THPs will lead to a clear benefit in terms of population health by 2060.

- References
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 - Hill A, Camacho OM. A system dynamics modelling approach to assess the impact of launching a new nicotine product on population health outcomes. Regulatory Toxicology and Pharmacology 2017 Jun;86:265-278.

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