Supplement 1: More details on the methods

Data sources

Singapore: We obtained the age structure and mortality rates of the population aged 12 to 80 years from 1992 to 2017 from the website of the Department of Statistics Singapore.[1] The smoking prevalence was extracted from the results of National Health Surveys in 1992, 1998, 2004, 2010, and 2017, and the National Health Surveillance Surveys in 2001, 2007, and 2013[2].

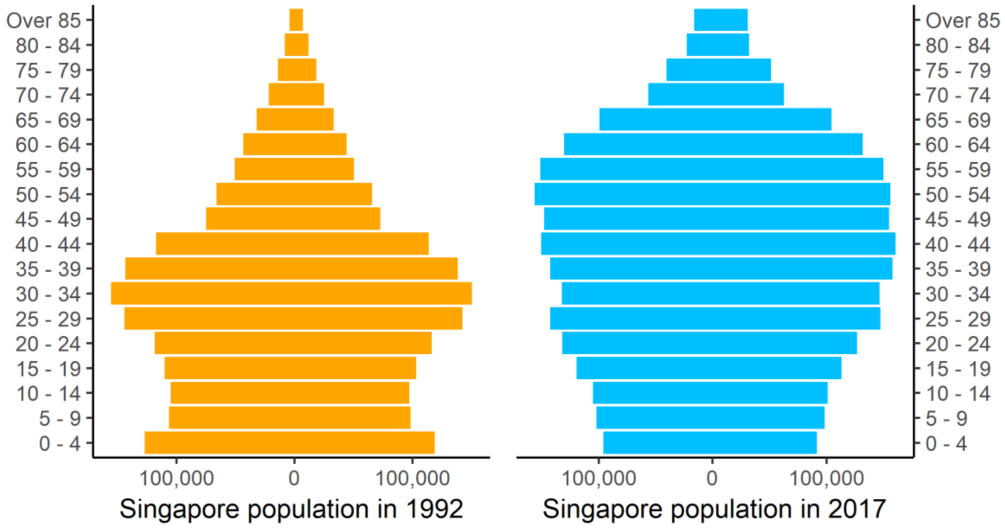

Figure S1 - 1: Singapore population in 1992 and 2017

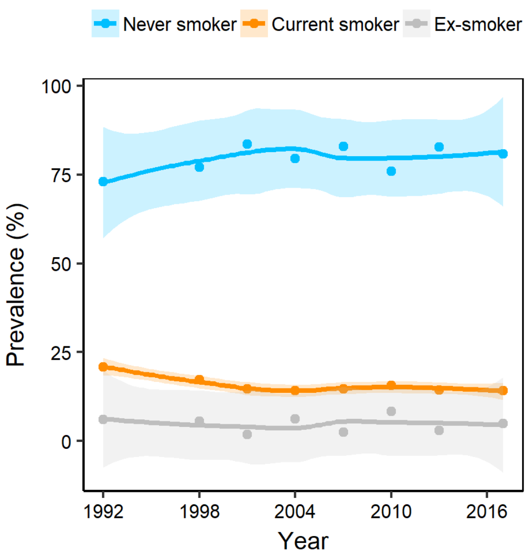

Figure S1 - 2: Prevalence of smoking in Singapore

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United States (US): We used data from the Population Assessment of Tobacco and Health (PATH) longitudinal study. Wave 1 includes 32,320 adults and 13,651 youths from September 2013 to December 2014; Wave 2 includes 28,362 adults and 12,172 youths from October 2014 to October 2015; and Wave 3 includes 28,148 adults and 11,814 youths from October 2015 to October 2016. Adults include people aged 18 and above, and youths include people aged 12 to 17. Data were available from the website of the United States National Institute on Drug Abuse.[3]

United Kingdom (UK): We accessed the age structure, mortality rates, prevalence of cigarette and e-cigarette use among people aged 15 to 90 years in 2014 to 2017 from the Office for National Statistics website.[4]

Japan: Prevalence of e-cigarette use was estimated from the aggregate results of a longitudinal internet survey from 2015 to 2017.[5] The study included 8240, 5403 and 4304 respondents aged 15 to 69 years in the baseline, first and second follow-up surveys respectively. The authors of the study used inverse probability weighting to account for online-response as well as non-response.[6]

We used the data from the US, the UK, and Japan primarily because of the availability of data on e-cigarettes for these countries. Moreover, these countries are large markets for e-cigarettes. These three countries all have a cultural connection to Singapore: like Singapore, the US and UK are similarly anglophonic, while Japan is the country in Asia closest in development level to Singapore.

Regarding the differences between these three model countries, only the data from the US is longitudinal. The data from the UK and from Japan are cross-sectional and involve smaller samples than that in the US. Regulation wise, for the UK, the European Union has revised the Tobacco Products Directive to restrict youth exposure to e-cigarette advertising in 2016[7]. At that time, in the US, Food and Drug Administration (FDA) imposed no other limitations on e-cigarette advertising than avoiding misleading claims[8]. In September 2018, the FDA has added to its Youth Tobacco Prevention Plan fines for retailers and manufactures that sell e-cigarettes illegally to youth[9]. However, as this regulation is only issued recently, its effects are not yet reflected in the data that we used in this research. In Japan, e-cigarettes with nicotine are illegal, however e-cigarettes without nicotine is sold without restriction to adults and minors.

Definition of cigarette users and e-cigarette users

For the US transition probabilities, we define cigarette users as users who declared that they used cigarettes sometimes or every day and had used at least 50 cigarettes in their lifetime for age 12–17 years and at least 100 cigarettes in their life time for age 18 years and above. The same definition was used applies for e-cigarette users. For the UK and Japan transition probabilities, the numbers of cigarettes that users smoked in their lifetime were not available in the datasets. Hence, for these datasets, cigarette (or e-cigarette) users are those who had used cigarettes (or e-cigarettes) in the last 30 days. For Singapore, we defined smokers (of cigarettes only) to be those reporting being regular or occasional smokers.

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Estimation of transition probabilities

Annual transition probabilities for the US

As the US data is longitudinal at individual level and comprises large sample size (more than 25,000), we estimated the transition probabilities between any two states by the proportion of people convert from one state to another. These estimates correspond to the Maximum Likelihood Estimates for the transition probabilities. Then, we estimated the variance with Fay's method as instructed in the user guide provided with the dataset[3].

Also, we pooled the transition probabilities from Wave 1 to Wave 2 with those from Wave 2 to Wave 3. As well, for age groups from 25 to 80 years, because there are only a few e-cigarette users who satisfy the definition as specified above, we estimated common values of the transition probabilities from e-cigarette users or dual users to another state for people 25 years old and above. The estimates of transition probabilities for the US are available in Supplement 2.

For Singapore, the UK, and Japan, because we only have access to cross-sectional data, we use the Monte Carlo Markov Chain (MCMC) method to estimate the transition between the states. The posterior distributions of the transition probabilities are available in Supplement 2, and more information on the MCMC for each dataset is described below.

Annual transition probabilities for Singapore

First, we estimated the average transition probabilities among the 3 states: never user, cigarette user, and ex-smoker with the local cross-sectional data in Singapore by initializing the open-cohort model with the population, mortality rates, and the prevalence of smoking with data from the National Health Survey 1992. The posterior distribution for all parameters was then calculated with the expected and actual cigarette smoking prevalence in 1998, 2001, 2004, 2007, 2010, 2013, and 2017.

The MCMC comprises 10,000 iterations, with a burn-in length of 1000 iteration. The prior distribution for the probability of smoking initiation (NC), quitting (CQ), and relapse (QC) are as follows:

$$\begin{cases} NC_{age} \sim N(0.05, 0.05^2), \text{ for 12 years} \leq age \leq 80 \text{ years} \\ CQ_{age} \sim N(0.1, 0.14^2), \text{ for 12 years} \leq age \leq 80 \text{ years} \\ QC_{age} \sim N(0.04, 0.04^2), \text{ for 12 years} \leq age \leq 80 \text{ years} \\ NC_{age-1} \leq NC_{age} \leq 0.10, \text{ for 12 years} \leq age \leq 18 \text{ years} \\ NC_{age} \leq NC_{age-1}, \text{ for 19 years} \leq age \leq 25 \text{ years} \\ CQ_{age-1} \leq CQ_{age} \leq 0.10, \text{ for 12 years} \leq age \leq 80 \text{ years} \\ QC_{age} \leq QC_{age-1} \leq 0.05, \text{ for 12 years} \leq age \leq 80 \text{ years} \end{cases}$$

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The prior distribution for the relapse rate of smoking as shown above is based on the study by Hawkins *et al.*[10] which followed 1,578 individual in the UK for mean 5.2 years after 1 year of quitting and reported a relapse rate of 37.1% (95% CI: 34.0–40.5%) in 10 years. Moreover, the rate of quitting smoking in England was about 6% in 2007–2018[11].

In the two tax scenarios, the tax on tobacco consumption is raised 10 times by 10% each time relative to the previous price. The tax is raised once every 2 years in the TAX2 scenario, and once every 5 years in the TAX5 scenario. Based on previous estimates, the price elasticity of smoking prevalence is about -0.2 for developed countries[12]. To determine the approximate change in the initiation rate, quit rate, and relapse rate of cigarettes, we used MCMC to estimate the rates that would lead to such a change in prevalence. Below are the estimates of multipliers that we obtained where kNC, kCQ, and kQC are multipliers for initiation, quitting, and relapse rates respectively.

Table S1 - 1: Multipliers for transition probabilities under TAX scenarios

Multiplier	Under TAX2 scenario	Under TAX5 scenario
	Posterior mean (95% CI)	**Posterior mean (95% CI)**
kNC	96% (86%, 100%)	98% (96%, 100%)
kCQ for age 12 to 25 years	108% (100%, 126%)	106% (100%, 119%)
kCQ for age 26 to 80 years	102% (100%, 107%)	102% (100%, 106%)
kQC for age 12 to 25 years	50% (2%, 98%)	50% (2%, 98%)
kQC for age 26 to 80 years	96% (81%, 100%)	98% (91%, 100%)

That kNC is 96% means that the smoking initiation rate after the tax raise is 96% that was before the tax raise. The interpretation is similar for other transition rates. These values of multipliers are consistent with the finding that young people are more sensitive to the price than old people[12].

Annual transition probabilities for the UK

Using the cross-sectional UK data, we estimated the average transition probabilities among the five states by initialising the open-cohort model with the population, mortality rate, and prevalence of cigarette and e-cigarette use in 2014. The posterior was calculated from the expected and the actual prevalence in 2015 and 2016.

The MCMC comprises 300,000 iterations, with a burn-in length of 1000 iterations. The prior distributions are as follows:

$$\begin{cases} (NN_{age}, NC_{age}, NQ_{age}, ND_{age}, NE_{age}) \sim Dirichlet(100, 5, 0, 0.1, 1), \text{ for 15 years} \le age \le 80 \text{ years} \\ (CN_{age}, CC_{age}, CQ_{age}, CD_{age}, CE_{age}) \sim Dirichlet(0, 15, 1, 1, 1), \quad \text{for 15 years} \le age \le 80 \text{ years} \\ (QN_{age}, QC_{age}, QQ_{age}, QD_{age}, QE_{age}) \sim Dirichlet(0, 1, 14, 0.05, 1), \quad \text{for 15 years} \le age \le 80 \text{ years} \\ (DN_{age}, DC_{age}, DQ_{age}, DD_{age}, DE_{age}) \sim Dirichlet(0, 1, 1, 3, 1), \quad \text{for 15 years} \le age \le 80 \text{ years} \\ (EN_{age}, EC_{age}, EQ_{age}, ED_{age}, EE_{age}) \sim Dirichlet(0, 1, 1, 1, 3), \quad \text{for 15 years} \le age \le 80 \text{ years} \\ NC_{age\ group[i]} < NC_{age\ group[i-1]}, \text{ for } 9 \le i \le 10 \\ NE_{age\ group[i]} < NE_{age\ group[i-1]}, \text{ for } 4 \le i \le 10 \end{cases}$$

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In the equations above, N, C, Q, D, E are Never smoker, Cigarette smoker, Ex-smoker, Dual user, and E-cigarette user states respectively. The 10 age groups are 15-16 years, 17-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40-49 years, 50-59 years, 60-69 years, and 70-80 years.

Annual transition probabilities for Japan

For the Japan dataset, a closed-cohort model was used to estimate the transition probabilities because the survey was longitudinal without addition of new subjects over the years. The closed-cohort model was initialised with the prevalence of cigarette and e-cigarette use in 2015, and the posterior was calculated from the expected and the actual prevalence in 2016 and 2017. We only managed to fit an overall transition matrix because the age-specific prevalence of e-cigarette was absent. To make the effect of different e-cigarette policies more realistic for the SGJP variant, we scaled the estimated initiation rates of e-cigarettes so that the initiation of e-cigarettes is only attributed to people below 30 years old.

The MCMC comprises 800,000 iterations, with a burn-in length of 1000 iterations. The prior distributions are as follows:

$$\begin{cases} (NN_{age}, NC_{age}, NQ_{age}, ND_{age}, NE_{age}) \sim Dirichlet(10, 5{,}0{,}0.05{,}1), & \text{for 15 years} \le age \le \text{69 years} \\ (CN_{age}, CC_{age}, CQ_{age}, CD_{age}, CE_{age}) \sim Dirichlet(0, 8{,}1{,}1{,}1), & \text{for 15 years} \le age \le \text{69 years} \\ (QN_{age}, QC_{age}, QQ_{age}, QD_{age}, QE_{age}) \sim Dirichlet(0, 1{,}8{,}0.05{,}1), & \text{for 15 years} \le age \le \text{69 years} \\ (DN_{age}, DC_{age}, DQ_{age}, DD_{age}, DE_{age}) \sim Dirichlet(0, 1{,}1{,}3{,}1), & \text{for 15 years} \le age \le \text{69 years} \\ (EN_{age}, EC_{age}, EQ_{age}, ED_{age}, EE_{age}) \sim Dirichlet(0, 1{,}1{,}1{,}3), & \text{for 15 years} \le age \le \text{69 years} \end{cases}$$

To account for the fact that most people initiate e-cigarette use before 30 years old, we estimated the rate of e-cigarette initiation (NE) for people below 30 years old from the overall rate of e-cigarette initiation obtained from MCMC by the formula below. Then we set the rate of e-cigarette initiation for people 30 years old and above to 0.

$$NE_{15\ to\ 29\ years\ old} = NE_{15\ to\ 69\ years\ old} \times \frac{\text{number of people aged 15 to 29 years}}{\text{number of people aged 15 to 69 years}}$$

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Scaling method

To obtain the final transition probability matrix for all five states—never user, cigarette user, ex-smoker, e-cigarette user and dual user—we scaled down the transition probabilities of the first three states using Singapore data to fit with the remaining transition probabilities from either of the three other markets (the US, the UK and Japan).

For the result in the main text, we assumed that the introduction of e-cigarettes affects both the probability of transferring from current smokers to ex-smokers and the probability of remaining in the ex-smokers status; hence we scaled the local transition probabilities in Singapore down by equations Equation S1 - 1 to Equation S1 - 6:

$$NN_{scaled} = NN_{local} \times (1 - ND_{other} - NE_{other})$$ **Equation S1 - 1**

$$NC_{scaled} = NC_{local} \times (1 - ND_{other} - NE_{other})$$ **Equation S1 - 2**

$$CC_{scaled} = CC_{local} \times (1 - CD_{other} - CE_{other})$$ **Equation S1 - 3**

$$CQ_{scaled} = CQ_{local} \times (1 - CD_{other} - CE_{other})$$ **Equation S1 - 4**

$$QC_{scaled} = QC_{local} \times (1 - QD_{other} - QE_{other})$$ **Equation S1 - 5**

$$QQ_{scaled} = QQ_{local} \times (1 - QD_{other} - QE_{other})$$ **Equation S1 - 6**

We also examined another scaling method which favours the e-cigarette policies by assuming that these two probabilities—the probability of transferring from current smokers to ex-smokers and the probability of remaining in the ex-smokers status—do not change after the introduction of e-cigarettes. In this case, we used the equations Equation S1 - 7 to Equation S1 - 12 to scale down the original transition probabilities in Singapore:

$$NN_{scaled} = NN_{local} \times (1 - ND_{other} - NE_{other})$$ **Equation S1 - 7**

$$NC_{scaled} = NC_{local} \times (1 - ND_{other} - NE_{other})$$ **Equation S1 - 8**

$$CC_{scaled} = 1 - CD_{other} - CE_{other} - CQ_{local}$$ **Equation S1 - 9**

$$CQ_{scaled} = CQ_{local}$$ **Equation S1 - 10**

$$QC_{scaled} = 1 - QD_{other} - QE_{other} - QQ_{local}$$ **Equation S1 - 11**

$$QQ_{scaled} = QQ_{local}$$ **Equation S1 - 12**

In the equations above, N, C, Q, D, E represent the five states never smoker, cigarette smoker, ex-smoker, dual user, and e-cigarette user respectively. And AB represents the transition from state A to state B, for example NC represents the transition from never users (N) to cigarette smokers (C).

Relative mortality

We used a value of 2.8 as the all-cause relative risk of mortality for cigarette users below 60 years

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old[13]. The excess risk for ex-smokers was assumed to be 5% that for cigarette users. It has been suggested that a plausible range for the excess relative risk for e-cigarette use is 5–40% of the excess risk experienced by cigarette users[14–18]. Therefore, for the result in the main text, we used an excess risk value of 10% for SGUS and SGUK variants (on the optimistic end of the range), and of 5% for SGJP variant as e-cigarettes in Japan do not contain nicotine. The relative risk for dual users was calculated as the geometric mean of the relative risk for cigarette users and e-cigarette users. In addition, we stratified the relative mortality values according to age groups to account for the decrease of the relative mortality with age[19]. The values that we used are as follows:

Table S1 - 2: Relative mortality of five groups of users for SGUK and SGUS variants

Age (years)	Relative mortality for				
	Never smoker	Cigarette smoker	Ex- smoker	E-cigarette user	Dual user
12-59	1	2.8	1.09	1.18	1.82
60-69	1	2.5	1.08	1.15	1.70
70-80	1	2.0	1.05	1.10	1.48

Table S1 - 3: Relative mortality of five groups of users for SGJP variant

Age (years)	Relative mortality for				
	Never smoker	Cigarette smoker	Ex- smoker	E-cigarette user	Dual user
12-59	1	2.8	1.09	1.09	1.75
60-69	1	2.5	1.08	1.08	1.64
70-80	1	2.0	1.05	1.05	1.45

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Formula for mortality rate of never smokers

The mortality rate of a never smoker is calculated from the overall mortality rate of the population without e-cigarettes with the formula below:

$$m_N = \frac{m_{overall} \times 100}{prev_N + RR_C \times prev_C + RR_Q \times prev_Q} \quad \textbf{Equation S1 - 13}$$

The mortality rate of a never smoker is calculated from the overall mortality rate of the population without e-cigarettes with the formula below:

$$m_N = \frac{m_{overall} \times 100}{prev_N + RR_C \times prev_C + RR_Q \times prev_Q + RR_D \times prev_D + RR_E \times prev_E} \quad \textbf{Equation S1 - 14}$$

where:

m_N : mortality rate of a Never smoker

$m_{overall}$: mortality rate of the overall population

RR_C : the relative risk of mortality of a Cigarette smoker to that of a Never Smoker

RR_Q : the relative risk of mortality of a Quitter to that of a Never Smoker

RR_D : the relative risk of mortality of a Dual User to that of a Never Smoker

RR_E : the relative risk of mortality of a E-cigarette user to that of a Never Smoker

$prev_N$: the prevalence of Never smokers in the population (%)

$prev_C$: the prevalence of Cigarette smokers in the population (%)

$prev_Q$: the prevalence of Quitters in the population (%)

$prev_D$: the prevalence of Dual users in the population (%)

$prev_E$: the prevalence of E– cigarette user in the population (%)

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Transitions of Relative mortality risk (RR) and Quality-adjusted life years (QALY)

We incorporate the transition over time of RR and QALY into the micro-simulation. When a person transfers to a state of lower risk (e.g. from Current smoker state to Ex-smoker state), the RR for the person gradually decreases while his QALY increases as illustrated in Figure S1 - 3.

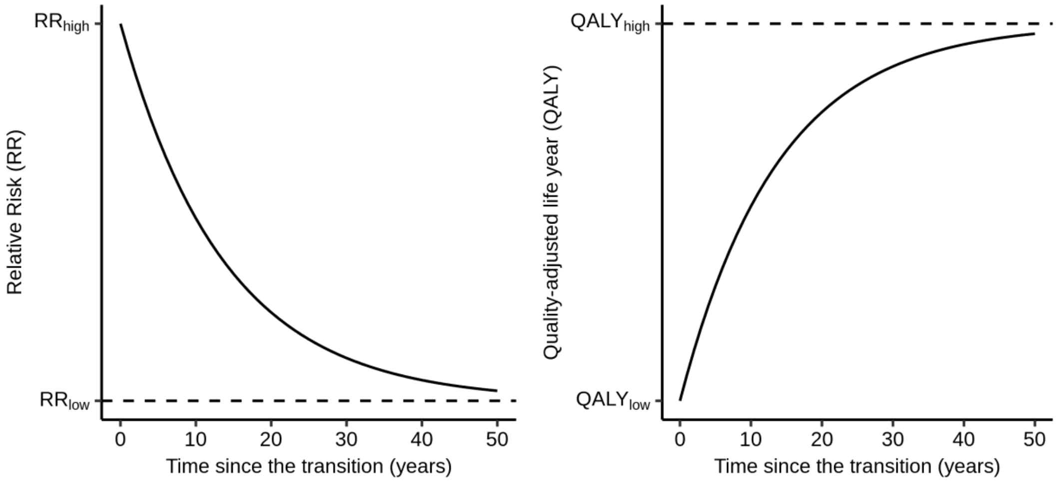

Figure S1 - 3: Transition of relative risk (RR) and quality-adjusted life year (QALY) over time when a person transfers to a state of lower risk

We have adapted equation (2) from Hoogenveen et al. (2008)[20] to get the following equation for the transition of relative risk of mortality from a higher risk state to a ***new*** state with lower risk:

$$R_{new}(a,\tau,s_0,s_1) = R(a,s_1) + [R(a,s_0) - R(a,s_1)]\exp(-\gamma(a)\tau) \qquad \textbf{Equation S1 - 15}$$

$$= R(a,s_1) + [R(a,s_0) - R(a,s_1)]b(a)^{\tau}$$

where a is the current age, τ the time (in years) since moving from the old state, s_0, to the new state, s_1, $b(a)$ controls the speed at which risk declines, $R(a,s)$ is the long-term relative risk of mortality for a person aged a who is in state s. We approximated $\boldsymbol{b(a)}$ from the average $\gamma(a)$ terms in Hoogenveen et al (2008), who consider multiple outcomes. The values of $b(a)$ are as in Table S1–3:

Table S1 - 4: *b(a)* for Relative Risk (RR)

age, *a*	$\boldsymbol{b(a)}$
12 to 15	0.92
16 to 20	0.93
21 to 34	0.94
35 to 55	0.95
56 to 80	0.96

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The all-cause relative risk of mortality for smoker is as follows (also provided in Table S1–2):

Table S1 - 5: All-cause relative risk for smokers ($R(a,C)$)

age, a	$R(a,C)$
12 to 59	2.8
60 to 69	2.5
70 to 80	2.0

Other values we used include the relative risk for a non-smoker or former smoker (in the long-run), namely:

$$R(a,N) = 1 \quad \textbf{Equation S1 - 16}$$
$$R(a,Q) = 1 \quad \textbf{Equation S1 - 17}$$

The relative risk for e-cigarette smokers is taken to be:

$$R(a,E) = 0.1[R(a,C) - 1] \text{ for SGUS and SGUK} \quad \textbf{Equation S1 - 18}$$
$$R(a,E) = 0.05[R(a,C) - 1] \text{ for SGJP} \quad \textbf{Equation S1 - 19}$$

to account for the different make-up of e-cigarettes in Japan and the US and UK. Meanwhile, the risk to dual-users was taken to be:

$$R(a,D) = \sqrt{R(a,C) \times R(a,E)}\,. \quad \textbf{Equation S1 - 20}$$

Similarly, we use the following equation to calculate quality-adjusted life years (QALY) when an individual transfers from state of lower QALY to a ***new*** state with higher QALY.

$$Q_{new}(a,\tau,s_0,s_1) = Q(a,s_1) - [Q(a,s_1) - Q(a,s_0)]\exp(-\gamma_Q(a)\tau)$$
$$= Q(a,s_1) - [Q(a,s_1) - Q(a,s_0)]b_Q(a)^\tau \quad \textbf{Equation S1 - 21}$$

where $Q(a,s)$ is the long-term quality adjusted life years per year for a person aged a who is in state s and $b_Q(a)$ controls the speed at which the QALY improves, and is derived from the QALY value for smokers and that for smokers who have quit for at least 15 years from Fiscella and Franks (1996)[21]

Table S1 - 6: $b_Q(a)$ for Quality-adjusted Life Years (QALYs)

age, a	$b_Q(a)$
12 to 29	0.98
30 to 49	0.96
50 to 64	0.97
65 to 80	0.98

The QALYs of smokers are from Table 2 of Fiscella and Franks (1996)[21] and extrapolated for age 12–24, and age 70–80 to the QALY of the nearest age available in the table.

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Table S1 - 7: Quality-adjusted Life Years for smokers $Q(a, C)$)

age, a	$Q(a, C)$
12 to 29	0.91
30 to 34	0.88
35 to 39	0.86
40 to 44	0.83
45 to 49	0.81
50 to 54	0.78
55 to 59	0.76
60 to 64	0.74
65 to 69	0.71

As e-cigarettes are a relatively new product, there is not yet enough data to estimate its long term health impacts on vapers. Hence, we approximate the eventual QALY for vapers (E) and dual users (D) by the following formulae:

$$Q(a, N) = 1$$ **Equation S1 - 22**

$$Q(a, Q) = 1$$ **Equation S1 - 23**

$$Q(a, D) = \sqrt{Q(a, C) \times Q(a, E)}$$ **Equation S1 - 24**

$$Q(a, E) = 0.1[1 - Q(a, C)] \text{ for SGUS and SGUK}$$ **Equation S1 - 25**

$$Q(a, E) = 0.05[1 - Q(a, C)] \text{ for SGJP}$$ **Equation S1 - 26**

where again differential values are used for the Japanese scenarios.

We assume that when an individual transitions to a state of higher risk, the higher relative risk (RR) and the corresponding lower QALY apply immediately.

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