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Potential country-level health and cost impacts of legalizing domestic sale of vaporized nicotine products

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Data availability: Supporting information regarding the multi-state life-table model approach and data inputs can be found online in Blakely *et al* and Pearson *et al*. Data sharing with other researchers or official agencies of the precise data used in the modeling is potentially possible subject to agreement with the government agencies making it available to the researchers (the Ministry of Health).

Key words: vaporized nicotine products, e-cigarettes, vaping, quality-adjusted life-years, health system costs

Background

The net impact on population health and health system costs of vaporized nicotine products is uncertain. We modeled, with uncertainty, the health and cost impacts of liberalizing the vaporized nicotine market for a high-income country, New Zealand (NZ).

Methods

We used a multi-state life-table model of 16 tobacco-related diseases to simulate lifetime quality-adjusted life-years (QALYs) and health system costs at a 0% discount rate. We incorporated transitions from never, former, and current smoker states to, and from, regularly using vaporized nicotine and literature estimates for relative risk of disease incidence for vaping compared to smoking.

Results

Compared to continuation of baseline trends in smoking uptake and cessation rates and negligible vaporized nicotine use, we projected liberalizing the market for these products to gain 236,000 QALYs (95% uncertainty interval (UI): 27,000 to 457,000) and save NZ$3.4 billion (2011 $) (95%UI: NZ$370m to NZ$7.1b) or US$2.5 billion (2017 $). However, estimates of net health gains for 0-14 year olds and 65+-year olds had 95%UIs including the null. Uncertainty around QALYs gained was mainly driven by uncertainty around the impact of vaporized nicotine products on population-wide cessation rates and the relative health risk of vaping compared to smoking.

Conclusions

This modeling suggested that a fairly permissive regulatory environment around vaporized nicotine products achieves net health gain and cost-savings, albeit with wide uncertainty. Our results suggest that optimal strategies will also be influenced by targeted smoking cessation advice, regulations around chemical constituents of these products, and marketing and age limits to prevent youth uptake of vaping.

INTRODUCTION

The most appropriate regulatory approach for vaporized nicotine products, such as e-cigarettes and other vaping devices, is widely debated. Regulations on these products range from fairly liberal (e.g., United Kingdom (UK), United States (US)) to bans on sale, possession, and use (e.g., Australia, Thailand, Singapore).[1] Vaping prevalence has increased rapidly among smokers in settings with liberal access to vaporized nicotine products,[2] while regular use among never smokers remains low. For example, in the US, 12% of current smokers, and 13% of recent former smokers vape regularly, whereas only 0.3% of never smokers vape.[3] Vaping prevalence has also increased,[4] but remains much lower in countries with more restrictive policies (e.g. only 4.4% of current smokers in Australia vape).[5]

The population health and health system cost impacts of vaporized nicotine products will depend on multiple factors, including their impact on smoking uptake and cessation. A recent extensive review suggests a positive impact on quit rates,[2] particularly in settings with less restrictive regulation.[4] However, concerns remain about potential adverse impacts on youth smoking,[6] and the health impact of long-term vaping. Vaping is likely to be less harmful than smoking, but more health-damaging than complete abstinence.[2,7]

While experimental trials and cohort studies have researched these components individually, computer simulation models can bring all factors together,[8] and incorporate uncertainty. Thus far, one tobacco-industry study[9] and seven independent studies[2,10-15] have used simulation models. Future net health benefits from the introduction of vaporized nicotine products were found in most or all scenarios of six studies,[2,9,10,12,13,15] in only a few scenarios in one study,[11] and in none of the scenarios of the most recent study.[14] This latter study failed to account for potential health benefits of youth taking up vaping instead of tobacco smoking, and the potential small reductions in health harm among those who simultaneously vape and smoke tobacco (dual use).

In our study, we model the impacts of liberalization of the vaporized nicotine product market in New Zealand (NZ). As a result of a NZ court ruling, the products became legal to sell in 2018. The Ministry of Health has interpreted the laws covering smoked tobacco as also applying to vaporized nicotine products (e.g., age limits on sales) but specific new regulations are being drafted. Overall, NZ vaporized nicotine product regulation is moving towards that of the UK and the US, and away from the more restrictive setting in Australia.

Our study aimed to advance previous studies modeling vaporized nicotine products in two key ways. First, we performed probabilistic uncertainty analyses and scenario analyses around input parameters related to these products, to determine which parameters (and their attendant uncertainty) are most influential on the estimated health gains. This type of analysis can help prioritize areas for further research. Secondly, none of the previous models have reported changes in health system cost outcomes from vaping, despite costing issues being important to policy-makers.

METHODS

Overview of the model

We adapted an established[16-18] tobacco multi-state life-table model (see the online supplementary information in Pearson *et al*[17] for a detailed description) to estimate the impacts of legalizing the domestic sale of vaporized nicotine products on population health outcomes and health system costs over the lifetime of the NZ population alive in 2011 (4.4 million). Briefly, the core multi-state life-table model is populated with epidemiologic parameters for disease-specific incidence, prevalence, and case-fatality rates for each of the 16 tobacco-related diseases (see eTable 1, http://links.lww.com/EDE/B465), calculated from rich NZ data and then processed for epidemiologic coherence using DISMOD II.[19] Tobacco-related disease costs were those excess to non-diseased citizen costs, estimated for the first year of diagnosis, last year of life if dying of that disease, and otherwise prevalent disease.

These costs were estimated using national linked hospitalization, pharmaceutical, laboratory, primary care, outpatient, and other data, linked to cost weight data. All costs were estimated by sex and age, and all epidemiologic estimates additionally by ethnicity (Māori and non-Māori). For the remainder of this Methods section, we focus on the modeling aspects specific to vaporized nicotine products.

The multi-state life-table model was adapted by incorporating transitions from the existing never smoker, former smoker, and current smoker states to, and from, regularly vaping (either sole or dual use) with specification of disease incidence relative risks of vaping compared to tobacco smoking and patterns of use, drawing on expert judgments in recent major reports.[2,7] Table 1 details the six smoking and vaping states distinguished in the model. In the business as usual scenario (by 5-year age group and by sex and ethnicity) the NZ population alive in 2011 was simulated in a life-table until death or age 110 years, under projected all-cause mortality and morbidity rates.[18] The impact of the legalization of VNP sales on future quality-adjusted life-years (QALY) and costs was captured via changes in the distribution of population members in the six states compared to business as usual, mathematically combined with the relative risks of vaping and smoking for the 16 diseases to generate population impact fractions. For example, assume a simple scenario of 30% smoking prevalence in business as usual, reducing to 25% after an intervention, with the incidence rate ratio (RR) of coronary heart disease (CHD) for smokers compared to non-smokers being 1.66. (Actual CS versus NS disease incidence RRs used in the model are in eTable 1, http://links.lww.com/EDE/B465). Then after the intervention, the CHD incidence rate will reduce by 2.75%, through the population impact fraction (*PIF*):

$$PIF = \frac{\sum_i p_i \times RR_i \; - \sum_i p_i' \times RR_i}{\sum_i p_i \times RR_i} = \frac{(0.3 \; \times 1.66 + 0.7 \times 1) - (0.25 \; \times 1.66 + 0.75 \times 1)}{(0.3 \; \times 1.66 + 0.7 \times 1)}$$

$$= 2.75\%$$

where p_i is the prevalence of smoking and non-smoking pre-intervention, and p_i' is the post-intervention prevalence of smoking. The model is actually far more sophisticated than this, with time lags such that quitters are directed through a 20-year long tunnel state with annual reductions in disease incidence rates according to formulae in Hoogenveen et al (2008),[22] and multiple smoking-vaping combination states. The population impact fraction is used to set intervention disease incidence rates in the 16 parallel disease life-tables, which flow onto disease-specific changes in morbidity and mortality rates, and health system costs. The total QALYs (life years lived, adjusted for morbidity) and health system cost are then tallied up for each annual cycle of the model, for all sex by age cohorts propagated through the model, for both business as usual and intervention arms, with the difference between these arms being the "intervention effect".

Approach to parametric specification of input parameter uncertainty

We used the following principles to specify uncertainty in the parameters. First, we used beta or logistic distributions for proportions, log–normal distributions for ratios, and normal distributions for other measures. Second, where robust confidence intervals from external studies were available, we used those. Third, where expert opinion was relied upon (as is inevitably the case for harms from vaporized nicotine products), we aimed to include all plausible estimates within the 95 uncertainty interval for a parametric distribution with a mean and median approximating the 'expected' values. Fourth, for other variables with unknown but likely wide uncertainty (e.g., prevalence of vaping, and other examples in eTable 2, http://links.lww.com/EDE/B465), we used 20% of the mean as the standard deviation (SD). Fifth, most random draws from input parameter uncertainty distributions were 100% correlated across sex, age, and ethnic cohorts in each iteration (see eTable 2, http://links.lww.com/EDE/B465 for details).

The business as usual scenario

The business as usual scenario assumed no domestic vaporized nicotine product sales. In line with our previous modeling work,[16-18] this scenario assumed a continuation of current annual net cessation rates (i.e. the annual permanent quit rate, or the net of cessation attempts and relapse) and smoking uptake rates specified by sex, ethnicity, and age group, resulting in ongoing reduction in smoking prevalence into the future.[23]

The intervention base-case: The domestic sale of vaporized nicotine products is legalized

For consistency with our previous modeling work[16-18] and to allow for comparisons in a tobacco control intervention league table,[24] we modeled the intervention base-case as if legalization occurred at the start of base year 2011. The intervention cost was that of a new law to legalize the domestic sale of vaporized nicotine products (see eTable 2, http://links.lww.com/EDE/B465).

The US data on vaporized nicotine products in a liberalized market setting is probably the highest quality data internationally, which we used to parameterize the intervention base-case. Rapid growth in vaporized nicotine product sales was observed from 2011 to 2014 in the US, but sales stayed relatively steady from mid-2014 till the end of 2016,[25] suggesting an achieved steady state. A recent US study estimated current use of vaporized nicotine products to be 2.4% using a definition of vaping every day or some days, with use highest in 18-24 year olds (3.4%) and lowest in 65+ year olds (0.9%).[3] In addition, current vaping is reported by 11.5% of current smokers (i.e. dual users), 13.2% of former smokers who quit between one and two years ago (i.e. former smoker current vaper), and 0.3% of never smokers (i.e. never smoker current vaper).[3] We applied an age gradient to prevalence of vaping for the latter three categories of vapers (see eTable 2, http://links.lww.com/EDE/B465).

Given uncertainty around the applicability of US vaping patterns to other high-income countries, we applied wide uncertainty intervals to prevalence estimates (eTable 2, http://links.lww.com/EDE/B465).

State transitions in the model in the intervention base-case

At the end of each annual model cycle, population members could either remain in the same state or transition to other states. eFigure 1, http://links.lww.com/EDE/B465 shows the possible transitions between the six smoking and vaping states. Transitions between the states in the intervention base-case were calculated by combining NZ data on the prevalence of never smokers, former smokers, and current smokers and annual baseline smoking uptake and cessation rates specified by age group[23] with the above US data on vaping prevalence[3] (see eTable 2, http://links.lww.com/EDE/B465).

Transitions from non-smoking to other states

As per our previous modeling work we assumed that future never smokers transitions directly to never smoker current vaper, current smoker or dual user states only occurred at the age of 20 years reflecting the transition from youth experimentation to adult smoker status (90% of NZ adult smokers start smoking by this age;[26] transitions from current smoker to dual user at all ages described below). We used probabilities for these transitions at age 20 from the US[13] (Figure 1). The framework distinguished such transition rates for never smokers who would have become smokers in the absence of vaporized nicotine products (i.e., baseline annual smoking uptake rate in the multi-state life-table model), and those who would have remained non-smokers (i.e., 1 – baseline annual smoking uptake rate). This distinction is necessary as vaping uptake among the first group could result in harm reduction, whereas in the latter group uptake could result in increased harm. Given that evidence on these transition probabilities is incomplete[13] and future uptake patterns are uncertain, we applied wide uncertainty.

To illustrate how these transitions work, Figure 1 enumerates a fictitious 20-year old cohort where the baseline smoking uptake was 15%. As such 15% of never smokers would have become current smokers under business as usual, while 85% would have remained never smoker in the absence of vaporized nicotine products. When applying evidence-based transition rates around the use of vaporized nicotine products, it is estimated that approximately 14.5% of the cohort becomes a current smoker when including dual use (3% + 5.7% + 3% + 0.7% + 2.1%), 5.1% never smoker current vaper (3% + 2.1%), and 80.4% remain never smoker (0.3% + 12.1% + 68%). Depending on the proportion that would have taken up smoking by age 20 in the absence of vaporized nicotine products, this framework mostly resulted in a slightly lower youth smoking uptake rate compared to business as usual. Yet, the specified uncertainty around these transition rates (see eTable 2, http://links.lww.com/EDE/B465) also captured worsening of these trends, e.g. for the 14.5% value above (current smokers + dual users) had uncertainty ranging from 12.3% to 15.7% (compared to 15% under business as usual).

Transitions from smoking and dual use states

Studies suggest smokers frequently transition back and forth between current smoker and dual user states, at all ages.[27,28] At each point in time, we forced 11.5% of all smokers to 'reside' in the dual user state and the remainder (88.5%) in the current smoker state, consistent with US data. Population members in the current smoker and dual user states could transition to former smoker or former smoker current vaper states under annual net cessation rates specified by sex, age and ethnicity.[23]

There is evidence that liberalization of vaporized nicotine products increases tobacco smoking cessation rates in the total population. Using estimates from the largest and most recent cohort study,[3] we specified an increase in annual net (tobacco smoking) cessation rates of 14% (95%UI: 1.4% to 28%) in the intervention base-case. As our model was a closed

cohort, the vaping prevalence diminished over cycles by 1.3%. Accordingly, we decayed the initial 14% increase in net cessation by 1.3% per annum (95%UI: 0.6% to 1.9%) (eTable 2, http://links.lww.com/EDE/B465).

Of all the current smokers and dual users who quit smoking at the end of each annual cycle, 13.2% transitioned to the former smoker current vaper state (i.e., the prevalence of vaping among former smokers[3]), and the remaining 86.8% transitioned to the former smoker state. However, studies suggest that dual users are more likely than current smokers to transition to being a former smoker current vaper, with an odds ratio of 2.53 (95%CI: 1.29-4.97)[27,28] that we specified within the model to ensure dual users were more likely to transition to former smoker current vaper than current smokers.

Transitions from current vaper to other states

Never smokers current vapers could quit vaping at any age after 20 (i.e., transition back to never smoker) and former smokers current vapers could quit vaping at any age after 21. Due to scarce data on vaping cessation patterns, vaping quit rates were assumed to be the same as baseline annual net smoking cessation rates consistent with other models (with scenario analysis described in eTable 2, http://links.lww.com/EDE/B465).[9,10,13]

Relative harm of vaping compared to tobacco smoking

The multi-state life table model used relative risks of tobacco smoking for current smokers compared to never smokers for the incidence of 16 tobacco-related diseases as detailed in Blakely *et al*[16] and eTable 1, http://links.lww.com/EDE/B465. The model was extended for this study by including different relative risks of vaping compared to smoking, thereby differentiating disease incidence risks for those who were vaping only (former smokers current vapers and never smokers current vapers) and those who were both vaping and smoking (dual users). We followed the National Academies of Sciences Engineering and Medicine[2] and Public Health England[7] Report estimates that vaping confers approximately

5% of the risk of increased disease incidence due to tobacco smoking, and in parallel that dual use decreases the risk by 5% (see eTable 2, http://links.lww.com/EDE/B465). Accordingly, we specified the relative harm for those who were vaping only (former smokers current vapers and never smokers current vapers) compared to current smokers as a logistic distribution with a median of 5% (95%UI: 0.5% to 38%; a logistic distribution better approximated the uncertainty range given in the National Academies of Sciences Engineering and Medicine Report than a beta distribution; see eTable 2, http://links.lww.com/EDE/B465). Similarly, for dual users, the relative health harm was specified as a logistic distribution with a median of 95% (95%UI: 62% to 99.5%).

Simulation

The intervention base-case was simulated 2000 times in Monte Carlo simulations, drawing from the probability density function about all input parameters. The default was 0% discounting, with 3% and 6% discount rates used in scenario analyses. We also ran other scenario analyses as detailed in eTable 2, http://links.lww.com/EDE/B465. While the underlying model structure, demography, and epidemiology were stratified by ethnicity, limited or no data on vaporized nicotine product parameters by ethnicity meant it was inappropriate to present results by ethnic group.

RESULTS

Liberalization of the vaporized nicotine product market, compared to the business as usual scenario, was estimated to gain 236,000 QALYs (95%UI: 27,000 to 457,000) for the NZ population alive in 2011 over the remainder of their lives and save $NZ3.4 billion [b] (95%UI: 370 million to 7.1 billion; or $2.5 billion in 2017 $US). This translates to 0.054 QALYs gained per capita (i.e., 19 additional days lived in full health for each person alive in 2011), and $NZ 780 health system costs saved per capita or avoidance of 0.43% of all future health care expenditure in this cohort (bottom row of Table 2). By time horizon, 5.9% of all

QALY gains were estimated to occur within the first 20 years (1.3% in the first 10 years, and 4.6% in the second 10 years).

About 85% of health gains and cost-savings accrued among those aged 44 years or less in 2011. However, the 95%UI for lifetime QALYs gained and cost-savings for 0-14 year olds included the null (Table 2), suggesting possible net health harm. QALY gains (35,000; 95%UI: -1,200 to 61,200) for 45-64 year olds were still substantive, although the 95%UI just included the null.

The tornado plot in Figure 2 shows the impact of vaporized nicotine product-related input parameters on overall uncertainty in QALYs when running the model separately for the 2.5th and 97.5th percentile for each of the input parameters. Uncertainty in QALY gains was mainly driven by the uncertainty about the impact of vaporized nicotine products on population-wide smoking cessation rates, the health harm from vaping among former smokers current vapers and never smokers current vapers relative to harm among smokers, and the annual transitions among never smokers to current smoker, dual user or never smoker current vaper (i.e., the impact on youth smoking uptake rates).

Table 3 reports scenario results. Discounting by 3% or 6% per annum dramatically reduced the estimates. The second panel of Table 3 shows the cumulative impact of the three most uncertain variables revealed in Figure 2. A negligible 1.4% increase in population-wide cessation rates (the 2.5% percentile of this variable) lowered lifetime QALY gains to 116,000 (consistent with lefthand end of its bar in Figure 2). Under the most pessimistic scenario where vaping has near zero impact on cessation rates, 38% the risk of smoking, and results in an increase in smoking uptake among young people, vaporized nicotine product liberalization results in a loss of 52,200 QALYs. However, the probability of these three assumptions all being true is low (i.e., roughly $2.5\%^3 = 0.002\%$) and well outside the 95% uncertainty intervals presented above.

Assuming the positive impact of vaporized nicotine products on population-wide smoking cessation rates would decay faster than assumed in the base-case (10% and 50% per year instead of 1.3%, see eTable 2, http://links.lww.com/EDE/B465, and explanatory footnotes to Table 3), QALYs, and cost-savings reduced by 30%-50%. Using 1-year vaping quit rates from a recent small prospective cohort study,[29] instead of assuming they were equal to tobacco cessation rates, increased health gains and cost-savings by 17%. Finally, using a different definition for current vaping by only including daily vapers (final row of Table 3; estimates from Zhu et al[3]), reduced QALYs by 22% and cost-savings by 28%.

DISCUSSION

We used Monte Carlo simulation modelling, drawing from probability distributions about each input parameter, to estimate net health gains and health system cost impact of liberalizing access to vaporized nicotine products. Our results suggest that, widening access to vaporized nicotine products in NZ and other countries with (to date) restrictive policies around these products could achieve substantive overall health gains and cost-savings to the health system. Even given generous specification of uncertainty about the input parameters to this modeling, our 95%UI about the total health gains did not include zero. However, our modeling could not confidently rule out potential net health harm for the youngest age cohort (0-14 year olds) or for the 65+ year olds, under base-case assumptions. For the young this is due to uncertainty about the percentage of non-smoking youth becoming long-term vapers (i.e., beyond short-term experimentation) and the impact on tobacco smoking uptake rates. Policies to prevent youth uptake of either smoking or vaping should be an important adjunct to vaporized nicotine product liberalization. For 65+ year olds (and to some extent 45-64 year olds), there is potential net health harm as a proportion of smokers who quit smoking will move into long-term vaping. In sum, while overall health gain appears likely, this gain will be decades into the future given health gains and cost-savings were predominantly for the

younger age groups who are decades away from their peak non-communicable disease rates.[16,18]

The uncertainty and scenario analyses identify vaporized nicotine product parameters that drive uncertainty around QALYs and costs the most, and in turn what type of future research should be prioritized, most notably: the impact of vaping liberalization on population-level smoking cessation rates; the relative health harm of vaping; and the impact of vaporized nicotine products on tobacco smoking uptake rates among youth (Figure 2).

A strength of our study is the use of probabilistic uncertainty analyses to generate a total 95%UI about health gains and cost-savings (as opposed to deterministic uncertainty analyses in previous modeling studies[2,9,10,12,13]). We used tornado plots (Figure 2) to identify which parameter's uncertainty contributes the most uncertainty. We also used recent evidence on the impact of the availability of vaporized nicotine products on the population-level smoking cessation rate, and estimates for the relative health harm from vaping compared to smoking based on two substantive reports recently published (National Academies of Sciences Engineering and Medicine[2] and Public Health England[7]). By using an evidence-based transition framework for the impact of vaporized nicotine products on youth smoking uptake,[13] we were able to account for both potential beneficial and negative health impacts of these products for youth. This is a strength compared to a recent modeling study[14] that did not take into account the potential benefits of youth taking up vaping instead of smoking. Our study is also the first study to report results for both younger and older age groups.

While previous modeling studies have hinted at potential health care expenditure savings from the availability of vaporized nicotine products,[12] ours is the first study to quantify it. We estimated that health system cost-savings in $NZ 2011, over the remainder of the population's lifespan, were $3,420 million (95%UI $379 to $7050), or $780 per capita. Only 12.7% of these undiscounted cost-savings accrued in the first 20 years post-intervention.

Financial projections are often considered with discounting; 3% per annum discounting reduced cost savings by two thirds to 2011 $NZ1260 million, or to $US908 million in 2017 real dollars (Table 3).

Limitations include prevalence estimates of current vaping corresponding to vaping every day and only some days.[3] The latter group could in theory also include vapers who vape once a week or once a month or less, with likely lower health risk than daily vaping. There is insufficient information to accurately parameterize a model for vaping frequency; improving such data is a research priority (as also recommended previously[21]). Nevertheless, we ran a scenario analysis with lower vaping prevalence (bottom row Table 3), resulting in a 22% reduction in health gains due to the lower prevalence of daily vaping.

Many parameters were assumed to have a constant mean and uncertainty range into the future – an implicit stationarity assumption. Prevalence of vaporized nicotine product use may change in the future due to changes in price, promotion, and regulation. Acceptability of these products to users and health risks of vaping may also change due to quality control of ingredients and improvements in product design. These are inherent future uncertainties beyond what we could confidently include in the modeling. We used estimates from the US where the vaping market has developed with little regulation. Future regulation of vaporized nicotine products may affect these estimates. For example, restrictions on flavours and settings where vaping is permitted may further reduce health risk and use by non-smoking youth, but may also lower their uptake by current smokers.

Third, we assumed that the reduced harm from vaping (and dual use) applied to all tobacco-related diseases with the same percentage reduction in excess risks from smoking (an assumption also used in current peak body reports[2,7]).

Fourth, we assumed dual users had the same cessation rate as that from current smokers based on a longitudinal study[27,28]; if dual users are less likely to quit smoking than if they remained current smokers, then we will have overestimated the health gain and cost-savings. Conversely, if dual users quit at a higher rate than current smokers, we will have underestimated these outcomes. Further quality longitudinal data is needed for this parameter. Finally, we did not model the potential impact of combining vaporized nicotine product availability with other tobacco control policies which could further encourage smokers to switch to vaping. For example, the US Food and Drug Administration announced it is considering implementing mandated nicotine reduction for smoked tobacco products while allowing innovation in vaporized nicotine products and other lower risk nicotine products.[30] Similarly, the ASPIRE2025 network has recommended legalization for these products in NZ in combination with other policies, including an annual 20% tax increase on smoked tobacco, reducing the number of tobacco retailers, and mandated nicotine-reduction in smoked tobacco.[31] Evidence from experimental studies suggests that vaporized nicotine products are economic substitutes for smoked tobacco and that the availability of the products is likely to increase the impact of tobacco tax increases on smoking.[32,33]

Whilst our study, and those of others, have inherent uncertainty, there are findings that point to where precautionary regulation should focus. First, our findings support a fairly permissive regulatory environment where vaporized nicotine products are readily available to adult smokers along with regulations that limit the risks of youth uptake. The former may be facilitated by relatively light regulation of permitted retail settings and having no excise taxes on vaporized nicotine products (to ensure that vaping is less expensive than smoking). Product sales could be combined with targeted cessation advice (what type of device to use, nicotine strength, etc). Second, standards for chemical constituents of the products to minimize health risk would be desirable. Third, regulations to reduce youth uptake might

include age limits on sales, bans on any marketing aimed at youth, and possibly restrictions on flavors that might be particularly attractive to youth.[3]

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Figure legends and footnotes

Figure 1: Transitions among 20-year old never smokers to never smoker, current smoker, dual user or never smoker current vaper[a]

[a] NS = never smoker, NSCV = never smoker current vaper, CS = current smoker, DU = dual user, and VNPs = vaporized nicotine products. Bold black rates represent evidence-based estimates of transitions sourced from Levy et al.[13] The blue percentages represent an example cohort of 20 year olds in the multi-state life-table model (as per explained in more detail in the Methods). Red shaded boxes indicate net health harm relative to business as usual and the green shaded boxes indicate net health benefits compared to business as usual.

Figure 2: Tornado plot for QALYs gained for the base-case vaporized nicotine product scenario for the total NZ population alive in 2011, for the 2.5th and 97.5th percentiles (in parentheses) of the eight most influential input parameters[a]

[a] VNPs = vaporized nicotine products, NS = never smoker, FS = former smoker, CS = current smoker, NSCV = never smoker current vaper, FSCV = former smoker current vaper, DU = dual user, SD = standard deviation, and QALY = quality-adjusted life-year. Analyses used in the tornado plot were run for the expected value from the base-case only (i.e., uncertainty switched off). The expected value for the intervention base-case was 236,000 QALYs. As such the tornado plot presents incremental QALY loss or gain compared to the central estimate of 236,000 QALYs. For more information on how the 2.5th and 97.5th percentiles of these input parameters were specified, see Methods and eTable 2.

Table 1: The six smoking and vaping states used in the multi-state life-table model

Smoking and/or vaping state	Definition
Never smoker (NS)	A person who has never smoked at all or has never regularly smoked one or more manufactured or roll-your-own (RYO) tobacco cigarettes per day.[20]
Never smoker and current vaper[a] (NSCV)	As above for NS and currently vapes daily or non-daily (i.e., "Do you now use an e-cigarette every day, some days, or not at all?").[3,20]
Current smoker (CS)	A person who currently smokes one or more manufactured or RYO tobacco cigarettes per day.[20]
Dual user (DU)	As above for CS and who currently vapes daily or non-daily (i.e., "Do you now use an e-cigarette every day, some days, or not at all?").[3,20]
Former smoker (FS)	A person who does not smoke currently, but previously smoked one or more manufactured or RYO tobacco cigarettes per day.[20]
Former smoker and current vaper (FSCV)	As above for FS and currently vapes daily or non-daily (i.e., "Do you now use an e-cigarette every day, some days, or not at all?").[3,20]

VNP indicates vaporized nicotine product

[a] The definition of current vaping included both daily and non-daily vaping as all VNP-related input parameters used in this modeling (parameters 4 to 11 in eTable 2) are based on this definition. While it is likely that VNP parameter effects and thus related health outcomes differ by frequency and duration of VNP use, at present there is insufficient evidence to parameterize this accurately. As such, prioritizing this type of VNP research was a key recommendation by the National Academies of Sciences Engineering and Medicine following their substantive investigation into the public health consequences of VNPs.[21]

Table 2: Lifetime health gains (in QALYs) and health system cost-savings for the NZ population alive in 2011 under the intervention base-case compared to BAU (0% discounting[a])

	Remaining lifetime (with 95% uncertainty intervals)		First ten years: 2011 to 2022 (% of lifetime for age group)[b]		Second ten years: 2021 to 2030 (% of lifetime for age group)[b]	
Age-group (at baseline)	**QALYs gained**	**Net cost-savings ($NZ million for year 2011)**	**QALYs gained**	**Cost-savings ($NZ million)**	**QALYs gained**	**Cost-savings ($NZ million)**
0-14 year olds	68,100 (-23,900 to 188,000)	$1,010 (-$530 to $2,930)	5 (0.01%)	$0 (0.00%)	57 (0.08%)	$2 (0.16%)
15-24 year olds	59,100 (13,000 to 117,00)	$930 ($218 to $1,910)	52 (0.09%)	$1 (0.08%)	662 (1.12%)	$23 (2.49%)
25-44 year olds	72,000 (13,200 to 126,000)	$1,070 ($257 to $1,910)	924 (1.3%)	$25 (2.3%)	3,400 (4.7%)	$161 (14.8%)
45-64 year olds	35,000 (-1200 to 61,200)	$400 ($11 to $712)	1,820 (5.2%)	$53 (13.1%)	5,960 (17.0%)	$164 (40.6%)
65+ year olds	1,690 (-4,020 to 3,950)	$11 (-$24 to $26)	240 (14.3%)	$4 (35.1%)	689 (41.2%)	$6 (55.3%)
All age-groups combined	236,000 (27,000 to 457,000)	$3,420 ($370 to $7,050) [d]	3,040 (1.3%)	$83 (2.4%)	10,775 (4.6%)	$356 (10.3%)
Per capita[c]	0.054	$780				
% change[d]	0.14%	0.43%				

Note: All results >1000 rounded to three meaningful digits.
[a] 3% discounted results are shown in Table 3. Of note, for all age-groups combined (at 3% discounting), the net cost-savings were NZ$1,260 ($280 to $2,170), or in 2017 $US (allowing for CPI inflation from 2011 to 2017 in NZ, then OECD purchasing power parity from NZ$ to US$) US$908 ($201 to $1,564).
[b] Expected value (i.e., without probabilistic uncertainty).
[c] Per capita results used the total NZ population in 2011 as the denominator.
[d] Percentage QALYs gained of all QALYs lived (173,000,000 for the 2011 population under no intervention) and percentage costs saved of all future health care expenditures ($NZ 796 billion) over the remaining lifetime of the NZ population alive in 2011.

Table 3 Scenario analyses around lifetime health gains (in QALYs) and health system cost-savings for the NZ population alive in 2011 under the intervention base-case compared to business as usual (0% discounting unless stated otherwise)[a]

Alternate scenarios (only differences in parameters from base-case listed)	QALYs gained	Net cost savings (NZ$ million)	% change from base-case QALYs gained	% Change from base-case cost-savings
Base-case (expected value)	236,000	$3,450		
Discounting				
3% discounting	60,900	$1,240	-74%	-64%
6% discounting	21,800	$566	-91%	-84%
Pessimistic scenarios of parameters that drive uncertainty most in tornado plot in Figure 2				
Top parameter: Close to zero cessation impact[b]	116,000	$1,900	-51%	-45%
Top two parameters: Close to zero cessation impact and 38% of smoking health risk for vaping[b]	-27,400	-$196	-112%	-106%
Top three parameters: Close to zero cessation impact, 38% of smoking health risk of vaping, and an increase in youth smoking uptake rates [b]	-52,200	-$497	-122%	-114%
Annual decay in impact of liberalization of vaporized nicotine products on population-wide tobacco smoking cessation rates[c]				
10%	152,000	$2,375	-36%	-31%
50%	110,000	$1,828	-53%	-47%
Vaping quit rates				
52% of current vapers quit one year later	276,000	$4,020	+17%	+17%
Using a different definition of current vaping[d]				
Current vaping only includes daily vaping	185,000	$2,470	-22%	-28%

[a] Changes in base-case assumptions for vaporized nicotine product-related parameters are described in detail in the last column of eTable 2

[b] For the cessation impact, the 2.5th percentile value was selected (1.4% increase in net cessation rates), the 97.5th percentile value of the smoking health risk for vaping was selected (38%), and the 97.5th percentile values

for the transition rates from 20-year old never smoker to current smoker, dual user, or never smoker current vaper were selected (i.e., resulting in an increase in youth smoking uptake rates).

[c] As described in the Methods, we increased net cessation rates (for tobacco) by 14% (95%UI: 1.4% to 28%) in the intervention base-case, due to evidence from Zhu et al[3] and as described in eTable 2. Because our cohort was a closed cohort, vaping prevalence fell over time meaning we decayed net cessation rates by 1.3% per annum. As the novelty of vaporized nicotine products may be responsible for initial spill-over effect onto increasing population-wide net cessation rates, we undertook scenario analyses here about a 10% and 5% annual decay (rather than 1.3% per annum) in the 14% elevated net cessation rates back to business as usual net cessation rates.

[d] For this scenario, we reduced the prevalences of never smokers current vapers, former smokers current vapers and dual users to only include daily vaping (this scenario analysis is described in eTable 2).

Figure 1

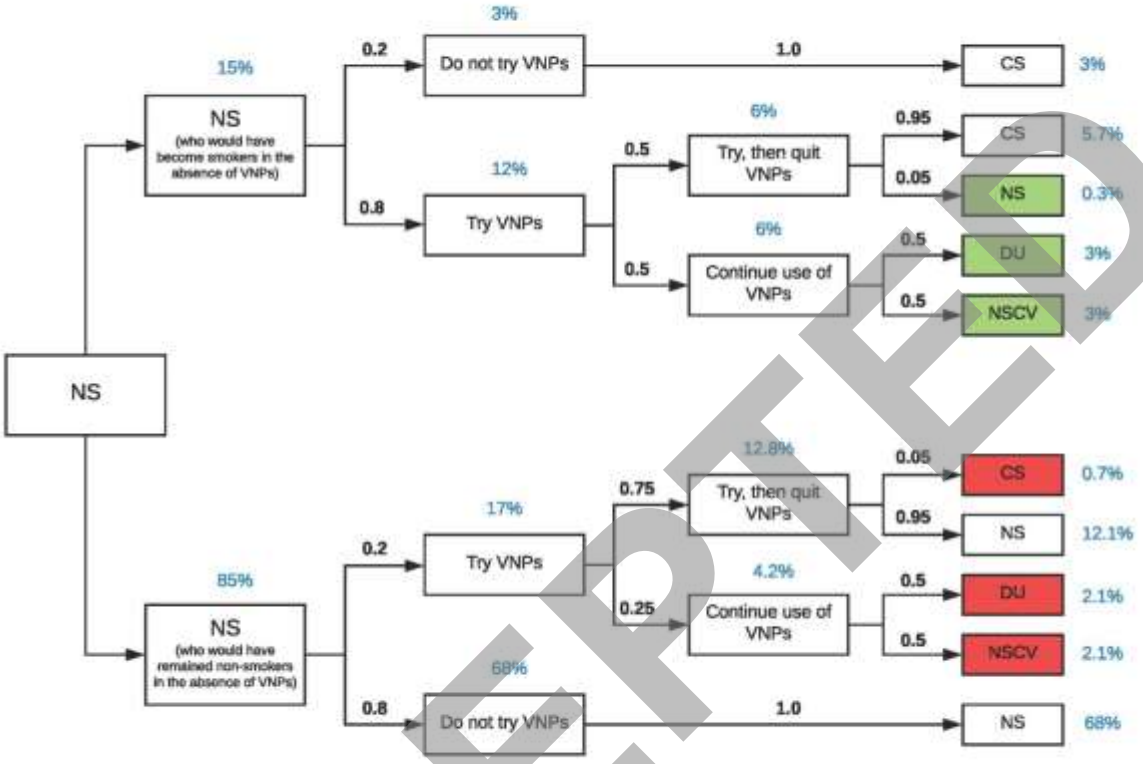

Figure 2