

Predicting the long-term effects of electronic cigarette use on population health: a systematic review of modelling studies

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ABSTRACT

Objective To systematically review and synthesise the findings of modelling studies on the population impacts of e-cigarette use and to identify potential gaps requiring future investigation.

Data source and study selection Four databases were searched for modelling studies of e-cigarette use on population health published between 2010 and 2023. A total of 32 studies were included.

Data extraction Data on study characteristics, model attributes and estimates of population impacts including health outcomes and smoking prevalence were extracted from each article. The findings were synthesised narratively.

Data synthesis The introduction of e-cigarettes was predicted to lead to decreased smoking-related mortality, increased quality-adjusted life-years and reduced health system costs in 29 studies. Seventeen studies predicted a lower prevalence of cigarette smoking. Models that predicted negative population impacts assumed very high e-cigarette initiation rates among non-smokers and that e-cigarette use would discourage smoking cessation by a large margin. The majority of the studies were based on US population data and few studies included factors other than smoking status, such as jurisdictional tobacco control policies or social influence.

Conclusions A population increase in e-cigarette use may result in lower smoking prevalence and reduced burden of disease in the long run, especially if their use can be restricted to assisting smoking cessation. Given the assumption-dependent nature of modelling outcomes, future modelling studies should consider incorporating different policy options in their projection exercises, using shorter time horizons and expanding their modelling to low-income and middle-income countries where smoking rates remain relatively high.

INTRODUCTION

Despite decades of tobacco control efforts, smoking remains the leading cause of preventable premature death and disease globally¹ and is responsible for 7.7 million deaths worldwide annually. Encouraging people who smoke to switch to less harmful nicotine products has been advocated for people who would otherwise continue smoking.² The use of e-cigarettes, also known as vaping, has increased substantially since their introduction to the market just over a decade ago.³ While their popularity among people who smoke has been evident,

WHAT THIS PAPER ADDS

- ⇒ Modelling studies generally predicted favourable long-term population impacts of e-cigarette use, as lower smoking prevalence and reduced burden of disease are commonly projected.
- ⇒ Outcomes are dependent on assumptions regarding patterns of use and disease risk. Therefore, the best and most current real-world data available and realistic estimates should be employed when conducting modelling exercises.
- ⇒ The lack of studies on low- and middle-income countries, where smoking rates remain relatively high, indicates an urgent need for research funding and data related to modelling in these nations.

uncertainty remains about whether e-cigarettes will result in overall net benefit or harm to population health, especially from a longer term perspective of several decades.

E-cigarettes have provoked debates between health authorities, policy makers and the general public. Advocates claim that e-cigarettes are an effective smoking cessation tool^{4–6} and are less harmful than cigarette smoking because they expose people who use them to fewer toxins. Critics argue that e-cigarettes still expose people to harmful chemicals that can damage health and lead to addiction among people who do not smoke. There are also concerns that their use by young people who are tobacco-naïve may lead to tobacco smoking via a ‘gateway effect’.^{7–8} Contributing to uncertainty about their public health impact is the high variability in estimates of the relative health risks of e-cigarettes compared with cigarette smoking that range from 5% to 50%.^{8–9} There is a lack of epidemiological evidence on the long-term effects of e-cigarette use on individuals and the population given their short history of use and rapidly changing design characteristics.⁵

While waiting for better epidemiological data to accumulate, some researchers have used simulation-based modelling to project the possible population impact of e-cigarette use. Multiple modelling studies have been published that employ different mathematical techniques and report results on a range of outcomes.¹⁰ These modelling studies can

provide useful insights that inform the formulation of appropriate and effective e-cigarette regulations.¹¹ However, these models can employ considerably different assumptions, structure and parameters, many of which can influence the outcomes and hinder the ability to compare outputs across studies, as in the case of tobacco control interventions simulation.¹² We conducted this review to summarise the findings from modelling studies that examine the public health impact of e-cigarette and critically examine the models used in these studies to identify potential gaps that require further investigation.

METHODS

Design and protocol

This systematic review was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)¹³ and prospectively registered on PROSPERO (registration number CRD42020193808).

Eligibility criteria

Studies were eligible when satisfying the pre-determined Population, Exposure, Comparison, and Outcome (PECO) selection criteria. Specifically,

- ▶ Population: General population, typically based on census or other national data sources.
- ▶ Exposure: e-Cigarette use.
- ▶ Comparison: Extrapolation of the status quo (eg, a scenario where e-cigarettes are unavailable and combustible cigarettes are the only tobacco product) and comparison to alternative scenarios (scenario where product availability is different from the status quo scenario, eg, e-cigarettes are available).
- ▶ Outcomes: Health outcomes (primary outcomes) defined as mortality-related outcomes (eg, premature deaths, years of life lost), morbidity-related outcomes (eg, quality-adjusted life-year (QALY), quality-adjusted life expectancy (QALE)), other health outcomes including public health costs/gain and health costs in monetary terms. Smoking prevalence outcomes (secondary outcomes) including the prevalence of smoking and smoking initiation rates were also included.

The exclusion criteria included (1) studies without simulation modelling in the methods; (2) editorials, commentaries, opinion pieces, review papers and book chapters; and (3) studies without full-text available (eg, published abstract only) or quantifiable data (eg, no quantitative estimate provided or no clear source data reported).

Search strategy

We used a two-step approach to identify studies for inclusion. First, the search strategy was developed based on previous literature on e-cigarettes and/or modelling and then consulted with a librarian for further refinement. The search terms employed covered e-cigarette-related terms and modelling study-related terms. PubMed, Web of Science (WoS), Scopus and PsycINFO were systematically searched on 9 March 2022 for peer-reviewed studies.

In the second step, we employed a 'snowball' technique to identify additional potential work that did not appear from the database searches. Potential studies were identified using (1) references from existing reviews, editorials and commentaries; and (2) by examining the studies that cited the included works using Google Scholar and Web of Science. This step was conducted on 16 March 2022.

An updated search was conducted on 13 May 2023.

Data extraction process

The results of initial searches were screened for duplicates using Covidence, an online reference management programme. Following duplicate removal, two researchers (DS and JC) screened the titles and abstracts of remaining studies for inclusion and exclusion. This screening process was repeated for full-text screening. Disagreements between the reviewers regarding which studies to include were resolved through discussions in reference to the study's eligibility criteria.

One reviewer (GTV) extracted the data of included studies into Airtable, a cloud-based spreadsheet-database hybrid. A second reviewer (DS) then independently checked the extracted data, and issues relating to discrepancies in data extraction were resolved through discussion. Extracted information included study details (eg, authors, publication year, study setting, data source, tobacco industry affiliation), model characteristics and variables included (eg, model type, baseline population, age at start, smoking states in alternative scenarios, whether model calibration and sensitivity analysis were conducted), outcomes measured and quantitative results.

Risk of bias assessment

No formal risk of bias tool exists to assess risk of bias in simulation studies; therefore, no risk of bias assessment could be conducted. We investigated if studies had any tobacco industry (TI) affiliations, which may potentially bias the findings. We assessed the characteristics of the models and summarise the strength and limitation qualitatively.

Synthesis of results

The findings were synthesised narratively. Meta-analyses of results were not conducted due to heterogeneity in designs and outcomes between the included studies.

RESULTS

Study selection

A total of 3846 publications were identified from the systematic database and supplementary search conducted in 2022 (original search). Duplicates were removed to obtain 1110 unique titles and abstracts for screening. Among the 55 studies assessed for full-text eligibility, 27 were excluded because they did not meet PECO criteria or inclusion criteria for publication type (for instance, being a review paper, editorial or letter) and study design (not a modelling study). Snowballing identified an additional three papers. A total number of 31 studies were included for data extraction.

The updated search conducted in 2023 found an additional of 208 publications, of which 129 were retained after duplicate removal for title and abstract screening. One article was obtained for full-text assessment and data attraction. A final number of 32 studies was included in this review (figure 1).

Study characteristics

Among the 32 included studies, 23 were modelled using the US population,^{11 14–35} 3 from the UK,^{35–37} 2 studies from Canada,^{38 39} 2 studies from New Zealand^{40 41} and 1 study each from Italy,⁴² Japan,³⁰ Singapore⁴³ and Australia⁴⁴ (see online supplemental table S1). Seven studies were TI-affiliated,^{14 15 28 30 32 33 42} with four sponsored by Philips Morris International.^{14 28 30 33}

Five studies employed an agent-based model,^{15 22 24 34 38} which accounted for the characteristics of and interactions between each simulated individual to estimate an emergent effect at population level,⁴⁵ or in other words, considered each individual

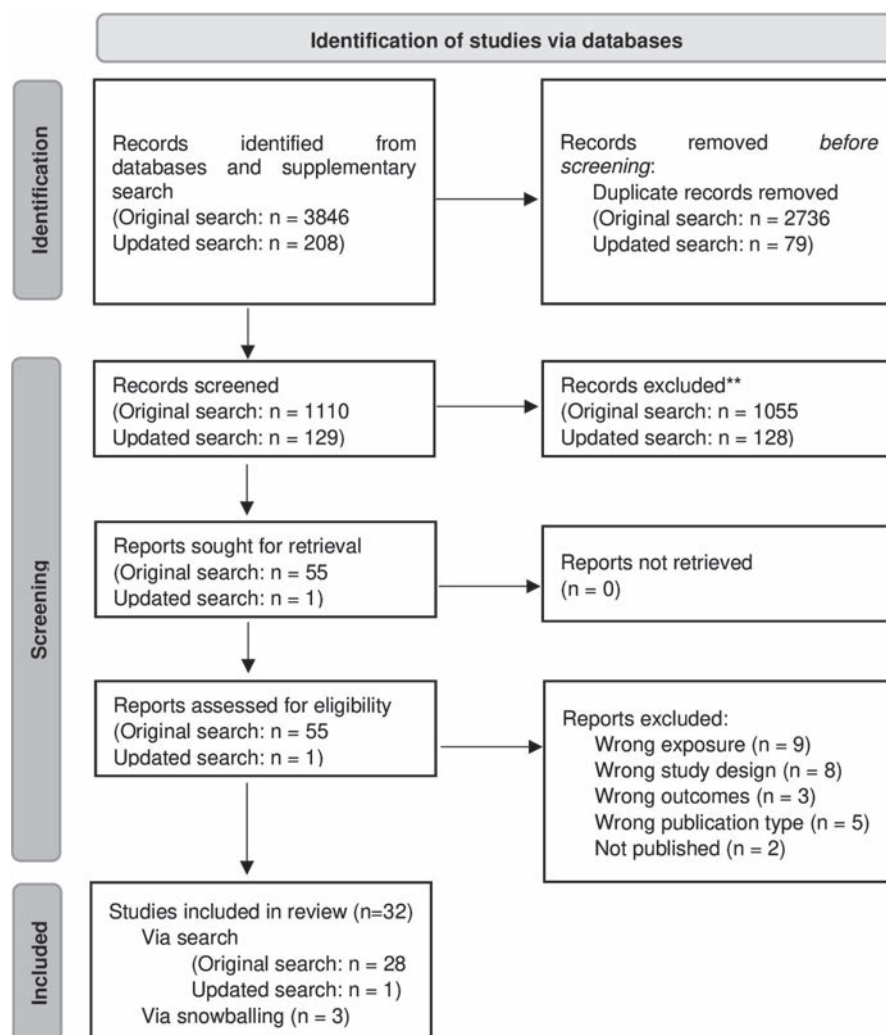


Figure 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of search results and inclusion of studies.

(agent) separately. Twenty-six studies used cohort-based modelling,^{11 14 16–21 23 26–33 35–37 39–44 46} where a group of individuals (cohort) sharing one or more characteristics or experience was modelled.⁴⁷ The remaining study employed open-cohort micro-simulation, which can be considered a ‘hybrid’ between agent-based and cohort-based models where new individuals were allowed to enter the model in each follow-up interval rather than having a closed, static cohort.⁴³

All modelling approaches started with an initial hypothetical population which was generally simulated from census or similar national data (see online supplemental table S1). Each individual within the population (agent-based modelling) or the whole cohort (cohort-based modelling) would then be followed over time (3–110 years forward, with a median of 50 years) at pre-determined intervals (eg, 3 months, 1 year) under different scenarios. Among the 32 studies included in this review, 4 employed a time horizon of 100 years or more,^{15 17 40 41} 4 projected less than 20 years into the future,^{16 18 24 27} while the rest were in between 20 and 100 years. The models varied in their incorporation of different states of tobacco use (eg, never use, exclusive smoking, dual use of cigarettes and e-cigarettes) and the probabilities of transitioning between these states, under the influence of factors such as social influence and tobacco control policies. The distribution of tobacco

use states and transition probabilities were usually derived from observed national smoking prevalence and estimates reported by relevant literature such as published cohort studies, or, in the absence of data, they were assumed by the authors. Among the 32 studies, 22 incorporated future trends in their baseline smoking prevalence.^{11 14–18 22 24–26 28 30 32–34 37 38 40–44 48}

The risk of exclusive e-cigarette use and dual use, expressed as relative to risk of disease arising from exclusive smoking, was also incorporated. The assumed relative health risk of exclusive e-cigarette use compared with cigarette smoking varied from 0% to 50%. The most commonly used figure was 5%: 7 of 32 included studies used a point estimate of 5%, while 8 others incorporated a range of estimates that included 5%. This assumed that e-cigarette use was approximately 95% less harmful than cigarette smoking. The models then combined risk and tobacco use estimates to project population outcomes under different scenarios.

Sensitivity analysis was not conducted in eight studies.^{24–26 28 30 32 37 40} Seventeen studies reported some form of model validation and calibration.^{11 15–20 24 25 28 29 34 36–39 43 44}

Health outcomes

Twenty-four studies simulated the impact of e-cigarette availability on population health outcomes. The most common

health outcomes examined were mortality-related (ie, premature deaths, years of life lost or saved, survivors) (n=20 studies).^{14 15 18–21 23 25 26 29 31–33 36 37 39 42 44} Then followed morbidity-related outcomes (ie, QALY and QALE) (n=5),^{25 39–41 43} health costs in monetary terms (n=3)^{39–41} and general (unitless) public health costs or gain (n=2)^{20 35} (see online supplemental table S2).

Mortality-related outcomes

Eighteen studies, of which seven were TI-affiliated,^{14 15 28 30 32 33 42} projected improvements in mortality-related health outcomes at the population level when e-cigarettes were available, compared with a hypothetical scenario in which combustible cigarettes were the only product in the market. Improvements were assessed in the form of the number of deaths averted^{14 15 18 23 26 31–33 37 44} or survivors,²⁵ fewer number of deaths,^{19 36} increased number of years of life saved^{14 20 21} or a reduction in the years of life lost^{18 23 26 31 42 44} at the population level.

Three studies, of which one was TI-affiliated,³³ estimated detrimental outcomes in some or all scenarios modelled. Pound and Coyle³⁹ conducted a Monte Carlo simulation and reported higher life expectancy (expressed as life-years) in scenarios where e-cigarettes were unavailable or available through prescription only, compared with when e-cigarettes were readily available.³⁹ Soneji *et al*²⁹ assessed the impact of e-cigarette use on current adult smokers and adolescent never-smokers, and projected that e-cigarettes would produce, on aggregate level, additional years of life lost. The authors assumed that, among current adult smokers, only smokers who attempted to quit in the previous year would switch to e-cigarette use (as a cessation tool) and that the OR of quitting among those who use e-cigarettes was 0.86. Meanwhile, the odds of initiating cigarette use among youths who ever used e-cigarette was assumed to be 3.5 times higher than those who had never used them.²⁹

Lee *et al*³³ identified a zero-benefit scenario, that is, where e-cigarettes or reduced risk products (RRPs) did not produce any improvement in the number of deaths averted compared with status quo. This would occur if allowing RRP produced a combination of a 30% increase in re-initiation of cigarette smoking (ie, people who quit smoking started using cigarettes again), a 10.8% decrease in the quit rate of people who currently smoked, and if people who smoked 20-cigarettes-a-day converted to dual use of 21 cigarettes and 21 RRP a day.³³

Morbidity-related outcomes

Four studies reported improved QALY or QALE outcomes associated with policies that allowed the use of e-cigarettes, subjected to the specific conditions modelled. Petrović-van der Deen *et al* estimated that a liberalisation of the market for vaporised nicotine products would add an additional 236 000 QALYs to the remaining lifespan of the New Zealand population, compared with a projection of the baseline trend where e-cigarette use was insignificant.⁴¹ The authors, however, highlighted the uncertainty interval around the QALY estimates, which included a null value for the age groups of 0 to 14 and over 65.⁴¹ Summers *et al*⁴⁰ updated the Petrović-van der Deen *et al* model by replacing the 5% estimate of the relative harms of e-cigarette use and smoking, with an estimate based on a biomarker analysis conducted by Wilson *et al*.⁴⁹ The 'updated' model estimated a smaller number of QALYs gained (compared with Petrović-van der Deen estimates) with a wide uncertainty interval resulting in a 3.2% probability of net health loss.⁴⁰ Nonetheless, the biomarker-dependent method of estimating the relative health

harm of vaping by Wilson *et al*⁴⁹ was later advised against by the same authors (Wilson *et al*) due to its limitations.⁵⁰

Doan *et al* modelled the impact of e-cigarettes on population health in Singapore using e-cigarette use data from the USA, the UK and Japan. Compared with the status quo of an e-cigarette ban, the model estimated annual QALYs gained in scenarios where e-cigarettes were available combined with other tobacco control policies of (1) no smoking allowed, (2) raising tobacco-tax, (3) e-cigarette availability through prescription only and (4) minimum age for e-cigarette purchase set at 25.⁴³ A QALY loss was reported for the scenario of the minimum purchase age for e-cigarettes set at 18 years.⁴³ By contrast, Pound and Coyle³⁹ projected that the policy scenarios of e-cigarettes being unavailable or available only through prescription would produce greater QALYs than making e-cigarettes readily available for the Canadian population.³⁹

Bachand *et al*²⁵ compared the estimated QALE gained for US population from (1) 'product switching' in which people completely switched from smoking cigarettes to using e-cigarettes and (2) 'alternative initiation' which referred to e-cigarette use initiation among those who would otherwise have initiated cigarette smoking. They estimated that 'product switching' would be more likely to lead to a population health benefit (lower QALE loss) than 'alternative initiation'.²⁵ The QALE gained from having a small proportion of smokers in each age category completely switching from cigarettes to e-cigarettes would offset the loss from having otherwise non-smokers become cigarette users via e-cigarette initiation and otherwise smoking quitters become exclusive e-cigarette users.²⁵ The authors noted that the magnitude of differences in outcomes (eg, number of survivors or QALE) between the base case (no e-cigarette use) and the two counterfactual scenarios would change subject to different input data (eg, initiation and cessation rates), for instance, the number of survivors gained when 'alternative initiation' and 'product switching' happened may be reduced if lower cigarettes use initiation and higher cessation rates were used.²⁵

Other health outcomes

Three studies estimated the economic impact on the health system after the introduction of e-cigarettes. Applying a 0% discount rate for health system costs for 16 smoking-related diseases, Petrović-van der Deen *et al*⁴¹ and Summers *et al*⁴⁰ estimated cost savings for the New Zealand health system if e-cigarettes were introduced to the market. In contrast, Pound and Coyle³⁹ estimated that health system costs would be lower if e-cigarettes were not available or were restricted to prescription only in Canada. The analysis adopted a publicly funded health system perspective and considered four smoking-attributable diseases of chronic obstructive pulmonary disease, coronary heart disease, stroke and lung cancers and used a 1.5% health cost discount rate.³⁹

Two studies examined the impacts of introducing e-cigarettes into a new market on general (unitless) public health costs or benefits. Wagner and Clifton²⁰ used a social group competition model developed by Lang *et al*⁵¹ to accommodate the transitions between groups of people who (1) abstain from tobacco use, (2) smoke cigarettes and (3) use e-cigarettes. They did not report definitive estimates of public health costs or benefits but suggested that a net public health benefit would be achieved in the year 2030 if the health risk of smoking compared with vaping was at minimum 1.2 times for adults and 4.8 times for adolescents, respectively.²⁰ Kalkhoran and Glantz³⁵ estimated that net health harms would occur for

scenarios in which e-cigarette promotion increased e-cigarette use among non-users by 10% to 50% and decreased intention to quit among people who currently smoked by 25% or increased cigarette smoking among both groups by renormalising smoking.³⁵

Smoking prevalence or transition outcomes

Secondary outcomes including current smoking prevalence and e-cigarette initiation rate were modelled in 20 studies (n=20)^{15 16 19–23 27 29–31 33–38 42 43} (see online supplemental table S3).

Nineteen studies, of which three were TI-affiliated,^{15 30 42} projected a lower smoking prevalence after the introduction of e-cigarettes.^{15 16 19–23 27 29–31 33–38 42 43} These studies varied widely in the assumptions they made about the impact of e-cigarette introduction on transition probabilities between smoking and e-cigarette use states. Nevertheless, it was commonly assumed that the introduction of e-cigarettes would allow for (1) the initiation of an alternative product for young people who would otherwise take up smoking (thus reducing smoking initiation rate by 10% to 25%^{15 35}); (2) product switching from cigarettes to e-cigarettes (from a gradual yearly switching rate of 5% to complete switching of 100%, reflecting a best case scenario^{30 31 37}); (3) access to an additional smoking cessation tool (consequently increasing the smoking cessation rate by 10% to 100%^{21 34} and allowing 5% to 10% of people who previously smoked to relapse to a product other than cigarettes³⁷). In some scenarios, the availability of e-cigarettes was assumed to be followed by a 10% increase in smoking initiation,²¹ a rise of 50% in both smoking initiation and cessation^{21 34} or a 10% decrease in smoking cessation.³¹ A number of studies allowed the transition probabilities to vary in response to policy changes (eg, raising the minimum legal age of purchase, smoke-free generation)^{15 43} or to achieve a target prevalence (eg, 47% of tobacco smokers in Japan in 2000 would be e-cigarette users with cigarette use prevalence reduced by 14% by 2005).^{22 30}

The four studies that reported higher rates of tobacco smoking used scenarios in which the introduction of e-cigarettes was assumed to: increase smoking initiation by between 20% and 200%,³⁴ decrease smoking cessation by 20% to 25%,³⁵ increase e-cigarette initiation by 50% to 10 times among people who do not smoke,^{22 35} or increase dual use that offset the reduction in the number of people who exclusively smoked.²⁴ Two of these studies considered the effects of social influence on tobacco use behaviour. In the study conducted by Chao *et al*²⁴ the increase in dual use was motivated by social influence, proxied by individuals' 'openness' to smoking.²⁴ Chu *et al*²² reported that when social contagion, that is, the odds of initiating e-cigarette use among students influenced by e-cigarette use prevalence at their school, was included, the model estimated an increase in smoking rates compared with baseline.²²

Selya attempted to estimate the e-cigarette initiation rate that would achieve a smoking rate reduction goal, assuming that increasing e-cigarette access would reduce harm.¹⁷ The author simulated different scenarios involving a set of policies that promoted e-cigarette use. They found that the desired e-cigarette initiation rate would be achieved in 2050 if policies promoting e-cigarettes were approved and implemented without obstacles (ideal-case), and in 2070 after periods of fluctuation compared with the ideal-case in which policies promoting e-cigarettes faced: (1) implementation obstacles or (2) delays in their approval.¹⁷

DISCUSSION

This paper systematically reviewed studies that employed modelling techniques to project the long-term population impacts of e-cigarette use. In 29 of the 32 included studies, the modelling predicted that the introduction of e-cigarettes would be associated with decreased mortality, increased QALY and a reduction in costs for the health system, compared with a smoking only baseline. The majority of studies (18/32) projected lower rates of cigarette smoking if e-cigarettes were made available. Studies predicting detrimental health outcomes generally assumed that non-smokers would have a high uptake of e-cigarettes and that e-cigarettes would strongly discourage smoking cessation in smokers. Social influence, proxied by the number of people in individuals' peer network or society who smoked or used e-cigarettes, amplified the effect of e-cigarettes on smoking initiation and cessation. In the limited number of studies where the introduction of different tobacco control policies was also modelled, mixed results were reported.

The strength of these modelling studies is that they employed sophisticated techniques based on existing baseline data to project potential future public health outcomes. Their limitations, however, lie in the dependence of the findings on theory-driven scenarios and assumptions. 'Worst-case' scenarios, where the introduction of e-cigarettes was assumed to be associated with an extreme increase in smoking initiation and/or significant reduction in smoking cessation, produced estimates of deteriorated population health outcomes and higher tobacco smoking rates (compared with baseline scenarios). While the concerns that e-cigarette use may lead to later tobacco smoking in tobacco-naïve and a renormalisation of cigarette smoking are reasonable, the extreme assumptions made in these studies are not supported by recent epidemiological evidence. Instead, the association between availability of e-cigarettes and increased smoking initiation/decreased smoking cessation at population level has been found to be modest.^{52–54}

Majority of studies included in our review assumed a decreasing trend in smoking prevalence, in their projection of future cigarette use. As pointed out by Singh *et al*¹² in their review of tobacco control intervention simulation studies, an absence of such consideration would lead to overestimation of health gains for alternative scenarios compared with a baseline, business-as-usual scenario (as the smoking prevalence would be reduced in the future anyway).¹² Including future trends in cigarette use when projecting scenarios should therefore be considered compulsory by future modelling studies. The choice of time horizon for a model can also influence the plausibility and accuracy of future health impact estimates. Although the population health effects of introducing e-cigarettes into the market would take some time to materialise, using a time horizon of decades into the future may render the projected health gains or losses less meaningful, especially with the declining trend of smoking prevalence (if incorporated). Models employing shorter time window of, for instance, 5–10 years, may be able to provide policy makers with more useful estimates of health impacts.

Meanwhile, nearly half of the studies reviewed in this paper (15/32) adopted the assumption that e-cigarette use produced only 5% of the adverse health effects of cigarette smoking. The source of this widely cited figure can be traced to assessments by Nutt *et al*⁵⁵ using a Multi-Criterion Decision Analysis approach,⁵⁵ and qualitative assessments by the Royal College of Physicians England and for Public Health England.^{56 57} These assessments estimated the relative risk based on the differences in the concentration of toxicants in e-cigarette vapour and

tobacco smoke. This was done in the absence of epidemiological evidence on the long-term risks of the two products.^{55–57} Nonetheless, an updated version of the Public Health England Report 2018⁹ which assessed more recent evidence on biomarkers of exposure from vaping in comparison with smoking reconfirmed their previous estimate of e-cigarettes being at least 95% less harmful than smoking.⁵⁸ Meanwhile, some critics of the 5% figure have pointed to mounting evidence on the potential harmfulness of e-cigarettes, but without offering an alternative estimate of relative harm.⁵⁹ An attempt to quantify health risk of e-cigarettes relative to smoking using biomarker studies and estimates of smoking-attributable health loss by Wilson *et al*,⁴⁹ was later declared by the authors to be ‘too problematic for a valid quantitative assessment’ due to the limitations of studies included and assumptions used.⁵⁰ While further research is needed to derive more accurate estimates of e-cigarettes health risk, modelling studies can provide more useful information on the possible impact of e-cigarette use at the population level by incorporating scenarios that model a range of relative risks of e-cigarette use to smoking, for example, 10%, 20% or 50%, as presented in 6 of 32 included studies.^{14 18 25 26 35 43}

Another concern regarding these modelling studies is how helpful they are for informing tobacco control policies involving e-cigarettes. Only 6 of 32 studies reviewed included policies promoting/restricting e-cigarette use or other tobacco control policies as risk factors for their models.^{15 17 19 22 36 43} In most other cases, the prevalence of tobacco use states and the transition probabilities between these states were estimated based on historical data or expert opinions: they were not driven by possible policy choice relating to e-cigarette. Allowing e-cigarette use with a restriction on packaging and flavours that may be appealing to young people, for instance, would lead to different use rate than in a scenario where e-cigarettes can be advertised freely. Policy makers may also be interested in knowing the potential impacts on e-cigarette use and smoking if e-cigarettes are subjected to the same MPOWER (a set of cost-effective and high impact tobacco control measures recommended by the WHO)⁶⁰ policies with strict regulation and enforcement similar to combustible cigarettes. Additionally, some have linked stricter policies on combustible cigarettes (eg, mandating a very low nicotine content that makes cigarettes non-addictive), while making e-cigarettes available as an alternative to cigarettes.⁶¹ For some countries, such as the New Zealand, e-cigarette availability may indirectly make more restrictive policies on combustible cigarettes more politically and publicly acceptable. Future modelling studies thus may better assist policy makers by allowing cigarette and e-cigarette use states and transition probabilities between these to be influenced by different policy options.

Similar arguments can be made for risk factors relating to the social determinants of smoking and vaping behaviours such as socioeconomic characteristics and the influence of social networks. Incorporating these factors in modelling exercises may be helpful especially in informing policies at regional or local levels, or in designing community-based programmes that target priority populations who experience a greater number of risk factors for smoking.

Although approximately 80% of people who smoke reside in low-income and middle-income countries (LMICs),¹ we identified no modelling studies in these populations. The future burden of disease attributable to smoking rests disproportionately on LMICs where effective smoking harm reduction strategies are urgently needed. Information on the potential impact of e-cigarette use on these countries’ population level health outcomes would assist their governments in policy making

related to both cigarettes and e-cigarettes. This indicates a need for future modelling studies that are based on LMICs. The feasibility of these studies, however, rests heavily on the availability of funding for modelling-related research and sufficient data to construct the models, both of which have currently been lacking in LMICs.

We systematically searched four different databases with the largest available collection of publications; however, our search may not include all publications relevant to the topic due to restrictions on language. We were also unable to conduct a risk of bias assessment or meta-analysis due to the unavailability of standardised tool for bias assessment for this type of review and the considerable differences in the study inputs (eg, different scenarios modelled) and outputs. However, we reviewed the studies by examining the assumptions they used and potential conflicts of interests from affiliation with tobacco industries. We found no significant difference between findings of studies sponsored by the tobacco industry and those that were not. We attempted model appraisal, focusing on several characteristics of the models used that we believed would influence the results; such assessment has not been comprehensive. It is thus recommended that future studies consider examining other model features that may also be important in driving the projections (eg, time lag between smoking cessation and reduction in mortality risk, relative risk), using and building on existing frameworks for general and tobacco control policy simulation modelling good practices.^{12 62 63}

CONCLUSION

This systematic review of modelling studies that projected the long-term effects of e-cigarettes found that the simulations generally predicted favourable population impacts of e-cigarette availability compared with a cigarette-only baseline scenario. Most studies estimated smoking prevalence reduction and reduced population health harms in the long run as e-cigarettes became available, especially when their use was restricted to adults who used them for smoking cessation. Modelling studies that predicted net harms from e-cigarette availability assumed that they produced high rates of smoking initiation in youth and would strongly discourage smokers from quitting; these assumptions have not been supported by recent epidemiological evidence. Because the outcomes of modelling studies are dependent on the assumptions used, future modelling research should use the best and most current real-world data available and realistic estimates where data are unavailable. Future modelling studies should also explore the situation in LMICs to guide policy making in those countries.

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Contributors GTV: Investigation; data extraction; writing initial draft; review and editing. DS: Conceptualisation; study registration and data quality assessment. TS and JL: Review and editing. J Chung: Investigation. J Connor, PKT, CEG and BT: Review and editing; data quality assessment. WDH: Conceptualisation; review and editing. GC: Conceptualisation; review and editing, guarantor. All authors contributed to the data interpretation, writing and revisions of the report and have full access to all data in the study.

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