SUPPLEMENTARY MATERIAL

Supplementary Table 1: PRISMA-ScR Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	6
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	6
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	9
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	9 and Supplementary Table 2

Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	11
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	N/A
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	11 and Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	11
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Supplementary Tables 6-18
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	11-25
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	25-26
Limitations	20	Discuss the limitations of the scoping review process.	30-31

Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	31
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	25, Supplementary Table 4

Supplementary Table 2: PubMed Search Terms*

1. Mandate very low nicotine levels in smoked tobacco products to make them non-addictive or minimally addictive
(smoking[Title] OR smoke*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("nicotine content"[TW] OR "very low nicotine"[TW] OR "VLNC"[TW] OR "nicotine reduc*"[TW] OR "reduced nicotine" OR "nicotine level"[TW] OR "maximum nicotine"[TW])
2. Set product standards for nicotine products that make combustible tobacco products unappealing or removed from the market on toxic emissions
(smoking[Title] OR smoke*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("product standard*"[TW] OR content[TW] OR ingredient*[TW] OR constituent*[TW] OR flavour*[TW] OR flavor*[TW] OR additive*[TW] OR menthol[TW] OR toxicant*[TW] OR emission*[TW] OR "pH"[TW] OR filter[TW]) AND (endgame[TW] OR eliminat*[TW] OR "phasing out" [TW] OR "phase out" [TW] OR abolish[TW] OR abolition[TW] OR prohibit*[TW] OR ban[TW])
3. Replace combustible tobacco products with non-smoked lower risk nicotine products (e.g. nicotine vaping products, snus)
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("alternative nicotine product*"[TW] OR "less harmful nicotine product*"[TW] OR "e-cigarette"[TW] OR "electronic cigarette"[TW] OR vaping[TW] OR vape[TW] OR "electronic nicotine delivery system*"[TW] OR "vaporiser*"[TW] OR "vaporizer"[TW] OR snus[TW] OR "vaping device"[TW] OR "oral snuff"[TW] OR "non-smoked"[TW] OR "non-smoked tobacco" [TW] OR "low nitrosamine smokeless"[TW] OR "reduced exposure product"[TW] OR "nicotine substitute"[TW] OR "tobacco substitute"[TW]) AND (endgame[TW] OR eliminat*[TW] OR "phasing out" [TW] OR "phase out" [TW] OR abolish[TW] OR abolition[TW] OR prohibit*[TW] OR ban[TW])

4. Require a licence or medical prescription to purchase tobacco
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("smoker's license"[TW] OR licens*[TW] NOT retail)
5. Restrict tobacco sales by year born (tobacco free generation)
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("tobacco free generation*"[TW] OR "tobacco-free generation*"[TW] OR "age-of-sale"[TW] OR "age of sale"[TW] OR "smoke-free generation*"[TW] OR "smoke free generation*"[TW])
6. End commercial retail sale of combustible tobacco
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND Sale*[TW] AND ("endgame*"[TW] OR end[TW] OR ban[TW] OR prohibit*[TW] OR "phasing out"[TW] OR "phase out"[TW] OR abolish[TW] OR abolition[TW])
7. Set a regularly reducing quota on the amount of tobacco products manufactured or imported into a country ('sinking lid')
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("Sinking lid"[TW] OR "sinking-lid"[TW] OR quota*[TW])
8. Measures to reduce industry viability, such as litigation (e.g. 'corporate manslaughter'), or require compensation for full impacts of tobacco use, or limiting profitability

(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("corporate manslaughter"[TW] OR compensation[TW] OR litigation[TW] OR profitability[TW])
9. Transfer management of tobacco supply to an agency with a mandate to phase out tobacco sales, e.g. regulated market model, non-profit agency
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW] or "special communication"[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("regulated market model"[TW] OR monopson*[TW] OR "non-profit agency"[TW] OR "tobacco control agency"[TW] OR "tobacco use management system"[TW])
10. Performance-based regulation where tobacco companies are required to meet smoking prevalence targets or be fined; or manufacturers pay a levy based on sales volume similar to 'polluter pays' schemes
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND ("polluter pays"[TW] OR "performance-based regulation" [TW] OR "performance based regulation" [TW] OR "performance-based agency" [TW] OR "performance based agency" [TW])
11. Tobacco tax increases
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND Tax*[TW] AND ("endgame*"[TW] OR end[TW] OR ban[TW] OR prohibit*[TW] OR "phasing out"[TW] OR "phase out"[TW] OR abolish[TW] OR abolition[TW])

12. Restrictions on tobacco retailer density/location/type/licensing that substantially reduces tobacco availability
(smoking[Title] OR smoker*[Title] OR tobacco[Title] OR cigarette*[Title] OR nicotine[Title]) AND ((review*[TW] OR consensus[TW] OR commentary[TW] OR meta-analysis[TW] OR synthesis[TW] OR "expert opinion"[TW] OR modelling[TW] OR modeling[TW]) OR (dynamic*[TW] OR "life table" [TW] OR forecast*[TW] OR simulation[TW] AND model[TW])) AND Retail*[TW] AND ("endgame*"[TW] OR end[TW] OR ban[TW] OR prohibit*[TW] OR "phasing out"[TW] OR "phase out"[TW] OR abolish[TW] OR abolition[TW])

*Note: The PubMed Search terms are provided as an example. Copies of search strategies used for other databases are available on request.

Supplementary Table 3. Summary of Research Questions Addressed and Evidence Gaps Identified in Tobacco Endgame Evidence Syntheses

Endgame policy	Research questions addressed	Remaining evidence gaps
Mandate very low nicotine content (VLNC) for smoked tobacco products to make them non or minimally addictive	• Modelling of long-term population health consequences[46-49] • Broad summary of existing evidence and evidence gaps[5, 28-30, 34, 38, 39, 45, 50, 53] • Assumptions implicit in a nicotine reduction strategy[32] • Feasibility[32, 36] • Safety[32] • Public education, surveillance and support services necessary for implementation[32] • Use and effects of VLNC cigarettes with other forms of nicotine or other drugs[28] or alcohol use[33] • Challenges in establishing the empirical basis for regulatory decisions[34] • Potential impacts on people experiencing mental illness,[28, 35, 40, 41] socio-economic disadvantage,[41] pregnancy,[28] or who are Indigenous[51] • Impacts of product design and non-nicotine constituents on addictiveness or abuse liability[53] • Impacts on behavioural and cognitive performance[52] • Utility of addictive threshold for nicotine for informing policy[38] • Risk perceptions among youth and adults[42] • Impacts on smoking cessation[43] • Optimal nicotine level for public health benefits[44] • Products a nicotine standard should apply to[44] • Necessity of other constituent standards to minimise addictiveness[44] • Impacts on tobacco use in women of childbearing age[37] • Public support for VLNC standard[5]	• Empirical evidence on potential impacts of the policy[5, 29, 30, 47, 53] • Impacts on mental and physical health outcomes[40, 46, 52, 53] • Impacts on use of or access to alternative nicotine products[28, 35, 50] • Tobacco industry responses[28, 50] • Potential scope of the illicit market[28, 50] • Impacts on other substance use[28, 33] • Impacts on priority populations[28, 29, 33-35, 40, 51, 53] • Impact of public communication and education strategies to maximise policy benefits[28, 53] • Nicotine threshold for addiction[36, 38, 53] • Impacts of product content and design on addictiveness[53] • Innovative approaches to address nicotine dependence and psychological dependence on cigarettes as the source of nicotine[43]
Set product standards for nicotine products that make	• Broad summary of existing evidence and public support for the policy[5, 30]	• Evidence on the practicality or legality of implementing endgame strategies[5]

combustible tobacco products unappealing or removed from the market for exceeding toxicity thresholds		
Move consumers from combustible tobacco products to non-smoked reduced risk nicotine products (e.g. nicotine vaping products, snus)	**E-cigarettes** • Broad evidence summary on health impacts and adverse smoking transitions[4, 90] • Evidence for use of lower risk products as tobacco harm reduction tools[54, 55, 91-94] • Modelling population health impacts of switching from combustible cigarettes to e-cigarettes[57-59] • Effectiveness for smoking cessation[39, 55, 95, 96] • Safety profile of e-cigarettes[55] • Biological properties of nicotine and its effects during development[56] • Protective measures to vulnerable populations[56] **Heated tobacco products** • Impacts on health[39] **Smokeless tobacco products** • Impacts on health and smoking cessation[4]	**E-cigarettes** • Long-term data on health impacts[39, 55, 57, 59, 90, 91, 96] • Effects of second-hand e-cigarette vapour[55, 59, 96] • Precise estimates of effectiveness for smoking cessation[55, 58, 90, 95, 96] • Precise estimates of impacts on subsequent tobacco use[4, 55, 56, 90, 96, 97] • Role of 'choice' versus 'compulsion' in nicotine addiction[4] • Data on safety and efficacy for patients with chronic diseases including cancer[55] • Precise fraction of adverse foetal effects attributable specifically to nicotine (rather than other tobacco product components)[56] • Definitive human studies that fully quantify the effects of nicotine on the developing brain[56] **Heated tobacco products** • Long-term health impacts of heated tobacco products[39]
Restrict tobacco sales by year born (tobacco-free generation)	• Modelling population health impacts of tobacco-free generation proposal[59-61] • Key legal and ethical issues of the tobacco free generation proposal[62]	• Evidence for the policy's effectiveness [61, 62] • Database of disease-specific healthcare expenditure for each country (to model economic impacts)[60] • The exact meaning of human rights articles within the sphere of public health[62]
End commercial retail sale of combustible tobacco (Abolition)	• Simulated population health impacts of the hypothetical eradication of cigarettes[60] • Summary of available literature[5]	• Lack of disease cost database providing disease-specific healthcare expenditures for each country[60]
Set a regularly reducing quota on the volume of	• Simulated impact of tobacco companies bidding for quotas to supply tobacco to the New Zealand market[31] • Simulated impacts on population's smoking prevalence,	• Evidence for the policy's effectiveness, practicality or legality[5, 61] • Substitution relationships between different tobacco products[31]

tobacco products manufactured or imported into a country ('Sinking lid')	health gains and cost savings[61]	
Increases in tobacco tax that make tobacco products generally unaffordable	• Modelling impacts on population health outcomes[59-61, 63] • Modelling impacts on health inequalities[63] • Modelling impacts on health system costs[61, 63] • Modelling impacts on smoking prevalence[59, 61, 64, 66] • Modelling impacts on tax revenue[64, 66] • Modelling impacts of a lower tax category for very-low-nicotine content cigarettes[65]	• Country-specific research on price elasticity variation by age and social groups[63] • Impact of tax increases in conjunction with other policies (e.g. mass media campaigns)[63] • Cost-effectiveness[60] • Lack of disease cost database providing disease-specific healthcare expenditures for each country[60]
Restrictions on tobacco retailer density/location/type/licensing that substantially reduces tobacco availability	• Overview of policies or evidence to restrict quantity/ type/ location of retailers to hasten endgame[5, 71, 72] • Association between smoking and density/proximity of retailers from schools and homes[73, 74] • Modelling impacts on smoking prevalence,[61, 66, 68-70] health gains,[61, 67, 69] health system costs,[61, 67, 69] and tobacco prices[68] • Potential implementation strategies[74, 98]	• Effectiveness in reducing tobacco use [68, 70, 74, 98] • Cost-effectiveness[74] • Burden on individuals[74] • Evaluation of existing restrictions' intended and unintended impacts[71] • Modelling studies to predict impact on tobacco use[71] • Impact of retailer density in rural areas[73] • Mediators of retail density and adolescent smoking, e.g., exposure to marketing, price, anti-smoking norms, risk perceptions[73] • Price elasticity methods associated with increased travel to purchase[67] • Effectiveness of restricting sales to supply via pharmacies[69]

Supplementary Table 4: Characteristics and Findings of Individual Evidence Syntheses: Mandate Very Low Nicotine Content (VLNC) for Smoked Tobacco Products to Make Them Non or Minimally Addictive

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Ahmad & Billimek (2005)[46]	Simulation modelling study	Population data on demographics and mortality rates.	Yes	The United States population in the year 2003	None	What are the estimated long-term population health consequences of a range of tobacco regulation policies that manipulate the contents of cigarettes to impact their harmfulness and addictiveness?	Reducing the addictiveness of cigarettes such that smoking behaviour improved by 60% would produce a net population health gain at every plausible estimated level of increased smoking-related harm. Reducing the harmfulness of cigarettes by 40% reduction in smoking-related harm would produce a net QALY gain at every level of behaviour change modelled.	The relationship between reductions in specific toxins and impact on health outcomes. Synergistic effects of the tobacco smoke constituents.	Funded by the US National Institute of Drug Abuse (NIDA)
Apelberg, Feirman, Salazar, Corey, Ambrose, Paredes, Richman, Verzi, Vugrin, Brodsky & Rostron (2018)[47]	Simulation modelling study	Population data on demographics and mortality rates; cross-sectional survey data; Formal expert elicitation.	Yes	The United States population in the year 2015	None	What are the potential public health effects of regulating cigarettes to make them minimally addictive by setting a maximum level of nicotine in cigarettes?	A mandated very low nicotine content (VLNC) standard for cigarettes would substantially reduce tobacco- related mortality in the United States, despite uncertainty about the precise magnitude of the effects on smoking behaviours.	There is an absence of empirical evidence on the impact of the policy. A formal expert-elicitation process was used to inform estimates of likely behavioural responses.	Several authors affiliated with Food and Drug Administration (FDA)'s Center for Tobacco Products (CTP), and study funded by FDA
Benowitz & Henningfield (2013)[32]	Traditional (narrative) review	Not stated	No	General population	None	What are the assumptions implicit in a nicotine reduction strategy, the available data on the feasibility and safety of nicotine reduction, and the public education, surveillance and support services that would be needed for implementing such a policy?	A mandated nicotine reduction policy for cigarettes has become increasingly feasible (technical, social, medical and regulatory) due to scientific advances, the FCTC and regulatory authority by agencies such as the US FDA.	None stated	Funded by the US National Cancer Institute
Berman & Glasser (2019)[50]	Systematic review	RCTs, Cross-sectional, animal studies, chemical analyses of emissions, human exposure (biomarker) studies, experimental behavioural economic studies, consumer views on regulation and anticipated behavioural responses.	Yes	General population	None	What is the existing evidence and what are the information gaps to guide future research and allow the FDA to characterize the potential effects of nicotine reduction according to the public health standard?	VLNC research is weighted towards RCTs. Regulators (e.g., FDA) must consider a wide range of factors that may influence the public health impact of a VLNC standard, including factors difficult to assess in RCTs, such as impact on smoking uptake and relapse. Studies of the health impact of VLNCs (animal and human studies) generally indicate that the health risks will be of similar magnitude to regular nicotine content cigarettes or slightly lower when smoked in a similar way. However, fewer VLNC cigarettes are likely to be smoked in practice. Reducing nicotine levels abruptly, rather than gradually will reduce toxicant exposure faster. Potential adverse impacts of rapid nicotine reduction include cognitive function and memory. There may be a role for less	Research on how consumers might use VLNCs in the context of other tobacco/ nicotine products. A limited number of trials have examined the impact of access to alternative nicotine products. No studies directly assessed how VLNCs could influence relapse among ex-smokers. External factors have not been fully integrated into research designs. Research has not addressed possible tobacco industry responses to a VLNC standard (e.g., synthetic nicotine products to evade regulation or promotion of alternative combustible products) or the potential scope of the illicit market.	Funded by the US National Cancer Institute

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
							harmful alternative nicotine products. The evidence base is sufficient for FDA to progress to rule-making on a VLNC standard.		
Dermody & Donny (2014)[33]	Traditional (narrative) review	Not stated	No	General population	Several populations were highlighted (adult women, daily smokers, and individuals who have co-occurring psychiatric conditions or alcohol dependence) who are at risk of increased withdrawal symptoms and alcohol consumption. Gradually reducing nicotine content among these populations to prevent withdrawal symptoms, and to supply NRT to support cessation may be indicated.	What literature exists examining the effects of very low nicotine content (VLNC) cigarettes on smoking-related outcomes (nicotine exposure, nicotine withdrawal, and smoking as a cue to drink) and, in turn, the effects of those outcomes on alcohol use?	Reducing the nicotine content of cigarettes may reduce alcohol consumption and problematic drinking by reducing exposure to nicotine and the smoking-related drinking cues. A temporary increase in alcohol consumption could result from nicotine withdrawal and could be reduced by use of other nicotine products.	Only one study directly examined effects of VLNC cigarettes on drinking. Future research should examine the impact of VLNC on alcohol consumption among populations at risk of withdrawal symptoms and subsequent self-medication The risk of compensation by co-use or product switching should be investigated particularly among populations with high prevalence of poly-tobacco use (e.g., young, white men).	Funded by NIDA, FDA CTP and US National Institute on Alcohol Abuse and Alcoholism
Donny, Hatsukami, Benowitz, Sved, Tidey & Cassidy (2014)[34]	Traditional (narrative) review	Not stated	No	General population	None	What is the current science on nicotine reduction and what are some of the challenges in establishing the empirical basis for regulatory decisions about reduction of nicotine in smoked tobacco?	Research suggests that mandating VLNC cigarettes would reduce nicotine exposure, smoking, and dependence, without significant safety concerns.	The public health impact of a nicotine standard, the impact of gradual versus abrupt reduction in nicotine content, and impacts on "vulnerable populations (e.g. psychiatric co-morbidity)" and youth.	Funded by NIDA and the FDA CTP
Ferris Wayne, Donny & Ribisl (2019)[28]	Traditional (narrative) review	RCTs	No	Adolescents and adults; people with moderate or severe mental illness; pregnant women	VLNC cigarettes have similarly lower reinforcing effects compared to regular cigarettes among various potentially vulnerable populations, including people with affective disorders, those with harmful alcohol or other substance use and women of	What are the use and effects of VLNC cigarettes in non-smoking adolescents and adults and non-dependent smokers? What is the use and effects of VLNC cigarettes in vulnerable populations such as those with moderate or severe mental illness and pregnant women? What is the use and effects of VLNC cigarettes with other forms of nicotine or other drugs?	*Individual level outcomes*: Switching to VLNCs reduces CPD and does not increase toxicant exposure in clinical trials. Compensatory smoking occurs with modest nicotine reduction but not VLNCs. Smoking reduces at a ≤ 2.4 mg/g. Reduced nicotine dependence and more quit attempts are most reliably observed at 0.4 mg/g, but long-term studies are needed. Reducing nicotine to ≤0.4 mg/g may benefit the broadest population. Most evidence suggests that VLNCs increase abstinence, including among those with no quit intention. A VLNC standard would likely reduce adolescent smoking. VLNCs may increase use of e-cigarettes, cigars,	Potential impacts of VLNC in other smoked products (e.g., roll-your-own tobacco, little cigars, cigarillos, waterpipe tobacco). Impacts on priority populations (including women of reproductive age), adolescents and tobacco-naive users. Concomitant use of VLNCs, and alternative nicotine products, by both dependent and non-dependent smokers and tobacco naive users. Interaction between VLNC use and alcohol or dependence on other substances (such as cannabis). Impact of public communication strategies to maximize policy benefits. Tobacco industry misuse of VLNC. The extent of illicit sales or of product tampering and related factors that could mitigate the effects of nicotine reduction.	Authored by the WHO Study Group on Tobacco Product Regulation. Study funded by the WHO

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
					childbearing age of low socioeconomic status.		cigarillos and NRT; reducing nicotine content of these other products should be considered. Non-compliance in clinical trials indicates some people will seek alternative nicotine products. No significant adverse health effects of VLNCs compared with regular cigarettes were identified. Reducing nicotine similarly decreases the reinforcing effects of smoking among various priority populations, including people with affective disorders, substance use disorders, women of childbearing age of low socioeconomic status. *Population level outcomes*: VLNC cigarettes partially but incompletely substitute for regular cigarettes. A subset of people would likely quit smoking rather than switch to VLNCs if regular cigarettes were not legally available. Most who continue to smoke would be unlikely to use VLNCs exclusively. Enforcement to limit illicit trade and internet sales of regular cigarettes will be needed when implementing a VLNC standard. Demand reduction policies (e.g., treatment services, substitute nicotine products) may also reduce illicit trade, but evidence is limited. VLNCs are seen as less harmful than regular cigarettes, which might encourage more use than expected from subjective ratings. Health communication can address misperceptions of risk. Physical or chemical parameters of cigarette construction could be manipulated to alter the reinforcing effects of VLNCs, and the effects might not be readily anticipated. Public support for nicotine reduction is reported from both population-based and trial surveys. Overall, the research suggests that a nicotine reduction policy, as part of a comprehensive approach and implemented with appropriate safeguards, could be an effective method for reducing the smoking prevalence.		
Gaalema, Miller & Tidey (2015)[35]	Traditional (narrative) review	Not stated	No	Adult smokers with affective disorders	People with affective disorders who smoked	What is the potential severity and persistence of possible unintended negative impacts of a nicotine reduction policy in smokers with affective disorders, and how could these be mitigated?	Smokers with anxiety or depression experience adverse mood impacts of greater severity on quitting smoking, than those without these conditions. Smoking VLNC cigarettes may mitigate these adverse mood effects. Longer-term abstinence is associated with mental	There is insufficient evidence (animal and human studies) on the impact of switching to VLNC on affective symptoms among people with anxiety or depression, whether smoking VLNC cigarettes, or use of other nicotine products or pharmacotherapy ameliorates withdrawal-related increases in affective	Funded by NIDA, FDA, and US National Institute of General Medical Sciences

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
							health improvement. Smokers with affective disorders will need additional support If a mandated VLNC standard were implemented to overcome initial withdrawal symptoms but long-term outcomes are likely to be positive.	symptoms, and whether nicotine reduction should be implemented abruptly or gradually.	
Hatsukami, Perkins, LeSage, Ashley, Henningfield, Benowitz, Backinger & Zeller (2010)[53]	Consensus/ expert opinion study	Animal studies, human laboratory and clinical studies	No	General population	The authors review the evidence on the moderating effects of sex, comorbid disorders (mental illness and comorbid drug dependence), individual differences in nicotine pharmacokinetics, ethnicity/race, genetic and lifestyle factors.	What are the effects of a reduced nicotine policy? What factors modulate nicotine reinforcement? What are the contributions of product design and non-nicotine constituents that may moderate the influence of low nicotine content on the addictiveness or abuse liability of a cigarette product?	Laboratory and residential human studies suggest abrupt switching to VLNC does not appear to produce significant withdrawal symptoms and may maintain similar levels of smoking reward and reinforcement in the short term. Over more extended exposure, the positive reinforcing properties of VLNC appear to decrease. Longer-term clinical studies suggest substantial nicotine reduction may not lead to compensatory smoking. Long-term clinical trials suggest reduced smoking behaviour and increased cessation could occur with VLNC of no more than 0.1 mg in nicotine yield. Addition of nicotine patch may promote smoking cessation, although the evidence is limited. Animal studies show dose dependent development of nicotine dependence.	More research is needed on individual and population-specific effects of VLNCs, including: nicotine threshold dose(s) for addiction and the population distribution of thresholds and moderating influences, effects of VLNC on the brain (receptor numbers, sensitisation, binding potential, and temporal changes) in adult smokers and adolescent experimenters, extent of compensatory smoking with abrupt reduction vs gradual, interventions that could minimise compensatory smoking (e.g., lower risk nicotine products or non-nicotine pharmacotherapies), impacts on subpopulations (e.g., mental health comorbidity or severe tobacco addiction), how product content and design features affect addictiveness (e.g., balance of acids and bases, the relationship between smoke chemistry and aerosol physics and respiratory tract deposition), exploring other non-nicotine targets that should be reduced, the effect of banning ventilated filters or specific additives in cigarettes. In longer term: public reaction to and perception of a marketplace containing only VLNC, effective message framing and public education about VLNC, and potential unwanted consequences and how to monitor and mitigate them.	Funded by NIDA and the American Legacy Foundation
Henningfield, Benowitz, Slade, Houston, Davis, & Deitchman, for the Council on Scientific Affairs, American Medical Association (1998)[36]	Traditional (narrative) review	RCTs, Experimental (not RCT), Qualitative, Cross-sectional, Longitudinal/ cohort, Regulatory studies	No	General population, including focus on preventing adolescent nicotine addiction.	None	What is the feasibility of reducing tobacco-caused disease by gradually removing nicotine from cigarettes until they would be non-addictive?	Gradually eliminating nicotine from cigarettes is technically feasible. A nicotine reduction strategy holds great promise in preventing adolescent tobacco addiction and assisting smoking cessation. Compensatory over-smoking of VLNCs and illicit sales could be minimised by providing alternate nicotine delivery products with less health risk, as part of expanded access to treatment; and mandatory nicotine reduction would need to be accompanied by research and education for consumers and health professionals.	Rapid and comprehensive monitoring of all nicotine products to allow midcourse policy corrections, guide regulation, and enable rapid dissemination of new treatments. Basic research on the pathophysiology and development of nicotine dependence to provide a rationale for prevention and treatment efforts. Prevention and treatment research to develop and evaluate new prevention and treatment approaches. Regulatory research by the FDA to keep regulations consistent with the science underlying existing and new tobacco products and nicotine delivery systems, e.g., on how product modification affects nicotine dosing.	Authors affiliated with the American Medical Association
Institute of Medicine (2007)[30]	Traditional (narrative) review	Not stated	No	General population and multiple priority populations	Populations examined include people with mental health disorders,	What is the evidence on approaches that could irreversibly end the tobacco problem by reducing smoking to levels that would not be a	Regulatory agencies could mandate a VLNC standard for cigarettes independently or with mandated changes to other cigarette constituents to reduce or eliminate specific exposures,	The level of nicotine reduction for a VLNC standard needs to be determined by scientific research and monitoring people who smoke reduced nicotine products (cigarette consumption, exposure to nicotine and	Funded by the US National Academies of Sciences

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
					prisoners, military recruits, homeless persons, LGBT populations, people with a disability, low SES populations. High prioritisation of tobacco control measures were recommended for these groups, mostly related to smoke-free inpatient facilities and prisons, and smoking cessation programs.	significant public health problem in the US?	depending on perceived health risks and technical feasibility. The size of the reductions and the implementation timeline would depend on scientific considerations and practicality of modifying cigarette manufacturing. A VLNC standard would need to be applied to all manufactured cigarettes uniformly to avoid consumers moving to higher-nicotine–content cigarettes. A nicotine-reduction strategy is likely to need a gradual implementation over 10 to 15 years, with reductions of 10 to 15 percent per step. Research suggests a gradual reduction of nicotine content will be acceptable to consumers if other product characteristics remain unchanged. Research suggests that toxic exposures does not increase during gradual tapering down of nicotine content in cigarettes. However, withdrawal symptoms will be experienced by smokers who do not get enough nicotine from VLNC cigarettes to sustain their addiction, which will require access to inexpensive nicotine-replacement medicines. Both short-to-medium term use and long-term nicotine maintenance would be associated with lower harms than continuing to smoke. VLNC cigarettes are expected to be acceptable to only a very small proportion of consumers and mostly smoked in social situations because they would not be addictive, resulting in large population health benefits.	tobacco toxins through biomarker measurement and youth smoking uptake and consumption), which should be a key element in any VLNC regulatory proposal. Biomarker assessment could include cross-sectional or longitudinal studies of cohorts of smokers, with regulatory authorities determining the sample size and characteristics, and which biomarkers to monitor.	
Johnston, Westphal, Glover, Thomas, Segan & Walker (2013)[51]	Systematic review	RCTs	Yes	Indigenous populations who use tobacco	The articles focuses on Indigenous populations	Should tobacco control interventions be targeted for Indigenous groups and necessarily adapted for this audience?	The small number of studies reviewed here indicate that there is likely no significant difference between Indigenous and non-Indigenous populations regarding the effect of smoking cessation pharmacotherapies and provide some promising (albeit limited) evidence on the efficacy of behavioural interventions delivered via mobile phone technology, as well as using VLNC (in addition to Quitline support) to assist smokers to quit.	For Indigenous people, there is a shortage of robust evidence for either generic or culturally adapted tobacco control interventions.	Funded by the National Health and Medical Research Council of Australia, the Health Research Council of New Zealand, Cure Kids New Zealand, and the James Russell Lewis Trust, New Zealand
Keith, Kurti, David, Zvorsky & Higgins (2017)[52]	Systematic review	Experimental (not RCT)	Yes	General population	None	Do VLNC cigarettes ameliorate withdrawal induced impairments in behavioural/cognitive performance?	VLNCs may not fully ameliorate withdrawal-induced performance impairment. The strongest evidence is for reaction time. Combining VLNCs with NRT appears to ameliorate withdrawal impairments that are not reduced by VLNC cigarettes alone.	Effects of extended VLNC use to define the time-course of differences in behavioural and cognitive performance when using VLNC and regular cigarettes and when switching to VLNCs. Use of ecologically valid measures (e.g., driving simulator, virtual reality) to test the impact of VLNCs to determine the clinical	Funded by the US National Institute of General Medical Sciences

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
								relevance.	
Kurti (2020)[37]	Traditional (narrative) review	Not stated	No	Women of childbearing age	Robust findings were observed across three diverse populations: socioeconomically disadvantaged women of reproductive age, people with affective disorders; and people with opioid use disorder.	What is the potential impact of a nicotine reduction policy, if implemented by the FDA in the near future, on tobacco use in women of childbearing age?	VLNCs reduce the reinforcing effects of smoking among this population without causing excessive withdrawal, craving, or compensatory smoking consistent with effects of reduced nicotine content cigarettes observed among the general population of adult smokers. A national nicotine reduction policy may decrease the addiction potential of cigarettes. Manipulating response cost impacted preference for regular cigarettes. Hence, regulations that give an advantage to VLNCs over regular cigarettes may also shift consumer preference to these products.	None stated	None
Levy, Cummings, Heckman, Li, Yuan, Smith & Meza (2020)[48]	Simulation modelling study	Demographic data and expert elicitation, unspecified study designs.	Yes	People who smoked and lived in the USA between 1965–2018	None	When did cigarette manufacturers first have the technical capability to reduce the nicotine of cigarettes they produced? What are the estimated lost public health benefits of implementing a standard in 1965, 1975, or 1985?	A VLNC standard would have likely delivered large public health benefits, reducing smoking attributable mortality burden by 54% and life-years lost by 64%, if adopted in 1965. Similar, but smaller, gains would have resulted from a VLNC standard adopted in 1975 or 1985.	None stated	Funded by the US National Cancer Institute, National Institutes of Health (NIH) and NIDA
McDaniel, Smith & Malone (2016)[5]	Traditional (narrative) review	Not stated	Yes	General population	None	What different approaches have been suggested or could be considered as advancing the tobacco endgame?	There is limited research on VLNC cigarettes, however experimental studies indicate they do not lead to compensatory smoking (e.g., smoking more cigarettes or smoking more intensively). Exposure to harmful combustion products remained stable, or, in some cases, reduced. Heavy nicotine dependence may lead to greater compensation than light dependence. Greater reductions in nicotine content are associated with higher abstinence rates. Public support in the USA for a VLNC standard has ranged from 37% to 74% among people who smoke and between 46% and 81% among people who don't smoke. Support in NZ ranged from 56% for people who smoke who haven't recently tried to quit to 78% among those who made a recent quit attempt.	Research on VLNCs is limited. This proposal has not been implemented, making it difficult to evaluate the practicality or legality of the concept.	Funded by Cancer Research UK
Smith, Hatsukami, Benowitz, Colby, McClernon, Strasser, Tidey, White & Donny (2018)[39]	Traditional (narrative) review	Not stated	No	General population	None	What is the evidence for VLNC cigarettes and emerging alternative nicotine delivery systems, and what can contemporary reinforcement and addiction theories tell us about their likely success?	Producing VLNCs is technologically feasible. Critics have primarily expressed concern about the potential for VLNCs to lead to compensatory smoking, which could increase exposure to toxins. Data from clinical trials do not support this. The majority of the public (smoking and non-smoking) support mandatory VLNC standard to reducing cigarette addictiveness. Evidence shows that	None stated	Funded by NIDA and FDA CTP

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
							people find VLNCs unappealing to smoke. Implementing a VLNC standard will require evidence-based messaging to correct misperceptions about the harmfulness of VLNCs relative to regular cigarettes. Combining mandatory VLNCs with availability of alternative nicotine products will be the most effective endgame approach.		
Sofuoglu & LeSage (2012)[38]	Traditional (narrative) review	Not stated	No	General population	None	What are the current concepts and research regarding nicotine reduction and what is the utility of the addictive threshold for nicotine in this approach?	The nicotine reinforcement threshold is more clearly defined (than nicotine addiction) and easier to measure in short-term studies than the addiction threshold and may be a more sensitive index for predicting tobacco use. However, the usefulness of the nicotine reinforcement threshold in predicting tobacco use must be determined in real life settings.	Reliable and valid measures of nicotine addiction are needed for an addiction threshold to be used as a regulatory target. Complete dose-response curves need to be characterised to determine a nicotine reinforcement threshold.	Funded by the Veterans Administration Mental Illness Research, Education and Clinical Center (MIRECC) and NIDA
Tengs, Ahmad, Savage, Moore & Gage (2005)[49]	Simulation modelling study	Demographic data and unspecified study designs.	Yes	The United States adult population	None	What are the estimated long-term health gains or losses that are likely to accrue to the US population if the nicotine content of cigarettes is gradually reduced to trace levels over a 6-year period?	A mandated VLNC standard is likely to reduce smoking prevalence from 23% to 5% producing 157 million QALYs gained over 50 years. Illicit sales of high nicotine cigarettes and compensatory smoking is likely to increase risks for people already smoking. The policy will discourage youth from taking up smoking, saving lives.	There is uncertainty about the quit rate, compensatory smoking, and the magnitude of health risk of compensatory smoking.	Funded by the California Tobacco Related Disease Research Program and NIDA
Tidey, Davis, Miller, Pericot-Valverde, Denlinger-Apte & Gaalema (2018)[40]	Traditional (narrative) review	Not stated	No	Adult smokers with mental health conditions	Smokers with mental health conditions	What are the potential effects of nicotine reduction in smokers with mental health conditions?	VLNCs have significantly lower abuse liability than normal cigarettes among people with emotional disorders, schizophrenia, and the general population who smoke, as indicated by well-validated subjective and behavioural laboratory measures. VLNCs acutely reduce craving and withdrawal symptoms compared to cigarette abstinence. The impact of extended VLNC use on psychiatric symptoms has not yet been reported. A mandatory VLNC standard may increase quit attempts among people with mental health conditions, and may increase the effectiveness of other tobacco control approaches and smoking cessation treatments. The current evidence is promising, and research underway will further evaluate the safety and feasibility of a VLNC standard to reduce health inequalities.	Information on the effects of extended VLNC use on psychiatric symptoms is yet to be reported from current studies. Evidence on whether the adverse impacts of nicotine reduction on cognitive performance persist pas acute nicotine withdrawal phase.	Funded by NIDA and the FDA CTP
Tidey, Muscat, Foulds, Evins, Gaalema, Denlinger-Apte (2019)[41]	Traditional (narrative) review	RCTs, laboratory studies	No	People with mental health conditions and who experience	The article focuses on people with mental health conditions and who experience	What are the effects of using VLNCs on people with mental health conditions and socioeconomic disadvantage?	A VLNC standard is likely to reduce smoking in these populations, without increasing psychiatric symptoms or compensatory smoking.	None stated.	Funded by NIDA and the FDA CTP

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
				socioeconomic disadvantage.	socioeconomic disadvantage.				
Villanti, Byron, Mercincavage & Pacek (2019)[42]	Traditional (narrative) review	Not stated	No	General population	None	Would adults and youth perceive mandated VLNC cigarettes as 'safe'—and how might risk perceptions impact initiation, use, and cessation of cigarettes?	The evidence that VLNCs are viewed by some as lower risk could lead to perceptions that quitting is less important. Public education on nicotine and VLNCs is needed to correct misperceptions to maximise the positive impact of VLNCs.	More data is needed on the impact of risk perceptions on initiation and ongoing use of VLNCs.	Funded by NIH
Walker, Bullen & McRobbie (2009)[43]	Traditional (narrative) review	Not stated	Yes	General population	None	What is the effect of reduced-nicotine content cigarettes on quit rates?	The evidence suggests VLNCs are beneficial but the small sample size of studies and short follow-ups limits the data available from existing studies. Progressively reducing the nicotine content of cigarettes can reduce nicotine dependence with minimal compensatory smoking. The addition of NRT to VLNCs increases quit rates compared with VLNC alone.	"More definitive evidence from larger trials with longer follow-up is needed to clarify the role of reduced nicotine cigarettes as an aid to smoking cessation. New approaches are needed that address both nicotine dependence and psychological dependence on cigarettes as the source of nicotine."	None
White, Pickworth, Sved & Donny (2019)[44]	Traditional (narrative) review	Not stated	No	General population	None	What nicotine level for cigarettes would most benefit public health? To which tobacco products should a maximum nicotine standard apply? Are other constituent standards also needed to minimise addictiveness?	Evidence suggests the maximum nicotine level (nicotine content per weight of tobacco) should be set to ≤0.4 mg/g to minimize addictiveness. This standard should apply to cigarettes and other combusted tobacco products that could act as substitutes. Non-nicotine constituents are unlikely to maintain addiction, but additional standards for other constituents should be considered if data emerge indicating that such standards would further improve public health.	None stated	Funded by NIDA and the FDA CTP
White, Hatsukami & Donny (2020)[45]	Traditional (narrative) review	Not stated	No	General population	None	What evidence is available for estimating the public health impact of reducing nicotine in combusted tobacco?	A VLNC standard of 0.4 mg/g could minimize the reinforcing value of smoking, thus reducing tobacco-related disease burden by decreasing smoking, toxicant exposure and dependence. Nicotine reduction may not completely eliminate the reinforcing value of smoking. Extended use of VLNCs appears to reduce CPD, but did not lead to complete abstinence for most trial participants. The relative value of alternatives will affect the use of low nicotine cigarettes. The availability of alternative nicotine products that exceed the relative value of VLNCs in terms of both nicotine delivery and other reinforcing characteristics is likely to be harm reducing.	None stated	Funded by NIDA and the FDA CTP
WHO Study Group on Tobacco	Traditional (narrative) review	Not stated	No	General population	None	What are the population effects of VLNCs?	Reducing the nicotine content to a very low level can reduce cigarette addictiveness. The threshold nicotine	• Probable use and effects of VLNCs in non-smoking youth, non-smoking adults and non-dependent smokers or occasional smokers;	Funded by the WHO

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Product Regulation (TobReg; 2015)[29]							level for dependence formation likely varies by individuals and is possibly lower for young people. Thus, a VLNC standard should be as low as is technically feasible, currently 0.4 mg/g. Compensatory smoking has not been observed with VLNCs of 0.4 mg/g. Evidence indicates a VLNC standard would: • reduce smoking uptake and progression to addiction; • reduce smoking prevalence as a result of behavioural extinction; • increase the quit rate and reduce the relapse rate; and • increase the development, availability and use of alternative nicotine products (smokeless tobacco, nicotine aerosol products and medicinal nicotine), which may have some adverse impacts, including maintenance of addiction, but less than those of smoked tobacco.	• potential use of VLNCs as "gateway" products by youth, leading to other nicotine use or other substances; • the effects of VLNCs in people with depression or other conditions; • the comparative health risks of VLNCs and regular cigarettes, including in special populations (e.g. women of reproductive age); • long-term use of VLNCs and the long-term impact on smoking and health outcomes, including cancer; • comparison of the long-term public health effects of VLNCs and of other nicotine products; • surveillance and epidemiology to assess any adverse impacts (e.g. health outcomes), and to guide policy making.	

CPD: cigarettes per day; FCTC: Framework Convention on Tobacco Control; FDA CTP: Food and Drug Administration Center for Tobacco Products; NIDA: National Institute on Drug Abuse; NIH: National Institutes of Health; NRT: Nicotine Replacement Therapy; QALYs: Quality-Adjusted-Life-Years; RCT: Randomised Controlled Trial; VLNC: very low nicotine content; WHO: World Health Organization

Supplementary Table 5: Characteristics and Findings of Individual Evidence Syntheses: Set Product Standards to Make Tobacco Products Unappealing or Removed from the Market for Exceeding Toxicity Thresholds

Authors (Year)	Product standard(s) examined	Type of evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
McDaniel, Smith & Malone (2016)[5]	Menthol, Filters, Other additives, pH	Traditional (narrative) review	Yes	General population	None	What different approaches have been suggested or could be considered as advancing the tobacco endgame?	Raising the pH of cigarettes to 8 or more would make smoke harder to inhale. Banning all non-tobacco cigarette ingredients would make cigarettes distasteful, discourage uptake and encourage cessation. Banning menthol would increase the harshness of cigarettes and likely reduce smoking uptake and maintenance. Two surveys in the USA have reported conflicting results with one reporting majority support for a menthol ban, while the other reported the majority neither supported nor opposed a ban. Banning filters would increase the harshness of cigarettes and likely reduce smoking uptake and maintenance.	Evidence on the practicality or legality of implementing endgame strategies.	Funded by Cancer Research UK

FDA: Food and Drug Administration; LGBT: Lesbian, Gay, Bisexual and Transgender; SES: socioeconomic status

Supplementary Table 6: Characteristics and Findings of Individual Evidence Syntheses: Move Consumers from Combustible Tobacco Products to Non-Smoked Reduced Risk Nicotine Products (When Implemented as a Tobacco Endgame Policy)

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Type of lower risk product/Research focus/Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Abrams, Glasser, Villanti, Pearson, Rose & Niaura (2018)[54]	Traditional (narrative) review	Not stated	No	General population	None	Product: E-cigarettes Focus: Quit efficacy, Adverse health impacts, Adverse smoking transitions for youth and adults, Developing a framework for tobacco harm minimisation Question(s): What is the evidence for a tobacco harm minimisation framework?	Authors propose a three-dimensional framework in which non-smoked nicotine products have: low toxicity, consumer appeal and sufficient satisfaction to displace cigarettes. Policy and regulation can minimise youth uptake while facilitating product switching. Some residual risks Remain, but the potential harms of non-smoked nicotine products have exaggerated over potential benefits. Communication to correct misperception of relative harms will be needed to encourage switching.	None stated	Author affiliated with Truth Initiative Schroeder Institute
Brandon, Goniewicz, Hanna, Hatsukami, Herbst, Hobin, Ostroff, Shields, Toll, Tyne, Viswanath, & Warren (2015)[55]	Traditional (narrative) review	Cross-sectional surveys, longitudinal studies, clinical trials	No	General population, people with cancer, youth	None	Product: E-cigarettes Focus: Quit efficacy, Adverse health impacts, Adverse smoking transitions for youth and adults, Policy statement of American Association for Cancer Research Science Policy and Government Affairs Committee and American Society of Clinical Oncology. Question(s): What are the major public health and policy issues relevant to ENDS; clinical concerns health care providers face concerning ENDS; key research needed to understand the safety profile; and public health impact of ENDS to inform regulation and patient care?	The toxic exposures from ENDS are lower than cigarette smoke but there is wide variation in products, and it is unclear what the long-term health impacts are. The abuse liability of new generations of ENDS are likely to higher due to better nicotine delivery. ENDS use among youth (including non-smokers) is increasing, Adults who use ENDS are primarily smokers. The trajectory of dual users is unclear. Flavoured ENDS may increase youth appeal but may also assist more smokers to switch. The lack of data on public health and individual impacts of ENDS makes developing a comprehensive regulatory framework difficult. ENDS should not be recommended as first-line therapy	More data are needed on ENDS safety and efficacy for the general population and patients with chronic diseases including cancer. The composition, uptake, biologic effects, behavioural patterns, and health effects of active and passive ENDS exposure, including abuse liability; impacts on tobacco product use; and research on how ENDS use affects treatment and outcomes for patients with cancer.	Authors are members of the Tobacco and Cancer Subcommittee of the American Association for Cancer Research Science Policy and Government Affairs Committee and American Society of Clinical Oncology Tobacco Cessation and Control Subcommittee of the Cancer Prevention Committee.
Doan , Tan, Dickens, Lean, Yang & Cook (2019)[59]	Simulation modelling study	Demographic data, longitudinal survey data, other unspecified study designs	Yes	Synthetic population using data from Singapore	None	Product: E-cigarettes Focus: Modelling impact of tobacco control policies (including legalisation of e-cigarettes) on tobacco use prevalence and QALYs Question(s): What is the potential prevalence of nicotine use and of quality-adjusted life years (QALYs) gained under various alternative scenarios, including the legalisation of e-cigarettes, either on prescription or on general sale?	As people switch from cigarettes to e-cigarettes, smoking prevalence declines followed by a plateau as young adults transition from vaping to smoking. The relative health impact depends on the ratio of youth initiation rates to the e-cigarette adoption rates for smoking cessation.	Long-term trend data on e-cigarette transitions and health risk of e-cigarettes is needed to these improve estimates. Insufficient data is available to model the impacts of second-hand smoking or vaping.	Funded by Singapore's Ministry of Health, National Medical Research Council, and National Research Foundation
England, Bunnell, Pechacek, Tong and McAfee (2015)[56]	Traditional (narrative) review	Human, epidemiological and animal studies	No	Youth (children and adolescents), pregnant women (foetus)	None	Product: E-cigarettes Focus: Adverse impacts on developing foetus, children and adolescents. Question(s): What are the biological properties of nicotine and its effects during development, and what potential measures could protect	Nicotine exposure during developmental periods (in-utero to adolescence) impairs foetal brain and lung development and lowers birthweight, and alters brain development (cerebral cortex and hippocampus) in adolescents. It is most likely that e-cigarettes will beneficially impact population health if accessibility,	The precise fraction of adverse foetal effects attributable specifically to nicotine (rather than other tobacco product components) has not been precisely quantified. Definitive proof of the relationship between e-cigarette	One author declared funding from Pfizer.

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Type of lower risk product/Research focus/Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
						these vulnerable populations?	promotion, and use of combusted products are rapidly reduced. However, regulation to protect vulnerable populations are needed. Measures that would protect pregnant women and children include (1) prohibit youth-oriented marketing; (2) youth access laws; (3) appropriate health warnings for vulnerable populations; (4) packaging to prevent accidental poisonings; (5) protection against passive exposure; (6) pricing that minimizes youth uptake; (7) regulations to reduce product addiction potential and youth appeal; and (8) the age of legal sale.	experimentation and progression to smoking. Definitive human studies that fully quantify the effects of nicotine on the developing brain (unlikely to be conducted for ethical reasons).	
Levy, Borland, Lindblom, Goniewicz, Meza, Holford, Yuan, Luo, O'Conner, Niaura & Abrams (2018)[57]	Simulation modelling study	Demographic data, expert elicitation, and unspecified study designs.	Yes	The US population aged 15 to 99 in 2016	The health impacts of switching from smoking to e-cigarettes are expected to reduce health disparities, since smoking prevalence is highest among groups with lower income and education levels.	Product: E-cigarettes Focus: Modelling numbers of deaths avoided in various scenarios where smokers switch to e-cigarettes Question(s): What are the potential health impacts of an Optimistic and Pessimistic Scenario directed at replacing all or most cigarette smoking with e-cigarette use over a 10-year period in the USA?	Switching from smoking to e-cigarettes over a 10-year period would prevent 6.6 million premature deaths and 86.7 million life years gained in the Optimistic Scenario. Under a Pessimistic Scenario, only 1.6 million premature deaths and 20.8 million fewer life years lost are avoided. Younger cohorts (aged 15 in 2016) gain 0.5 years in average life expectancy. New technologies such as e-cigarettes could help achieve a tobacco endgame if there is sufficient political will to aggressively phase out tobacco cigarettes.	Evidence on the long-term health effects of e-cigarettes	Author affiliated with Cancer Council Victoria; author affiliated with Schroeder Institute for Tobacco Research and Policy Studies, Truth Initiative. Funded by NIDA and the US National Cancer Institute
Mendez & Warner (2021)[58]	Simulation modelling study	Demographic data and unspecified study designs.	Yes	The US population aged 0 to 110 years	None	Product: E-cigarettes Focus: Quit efficacy Question(s): What is the proportion of US smoking-produced mortality that e-cigarettes might eliminate under assumptions regarding vaping's ability to increase smoking cessation, vaping's health risks, and the possibility that vaping will increase youth smoking?	The model estimated millions of additional ex-smokers due to vaping in most of the tested scenarios, each gaining an extra 1.2–2.0 years of life compared to smokers who quit without vaping. E-cigarettes may provide an additional tool to other tobacco control strategies as part of a comprehensive approach.	None stated	Funded by the US National Cancer Institute and the FDA CTP
Smith, Hatsukami, Benowitz, Colby, McClernon, Strasser, Tidey, White & Donny (2018)[39]	Traditional (narrative) review	Not stated	No	General population	None	Product: E-cigarettes, Snus, Heated Tobacco Products Focus: Quit efficacy, acceptability, adverse health impacts Question(s): What is the evidence for alternative nicotine devices (ANDS) as part of an effective endgame approach? What do contemporary reinforcement and addiction theories tell us about their likely success?	ANDS are an important technological advance that could contributed to reducing smoking prevalence and associated harms. However, reasons exist to be sceptical about the role of ANDS as a tobacco endgame intervention on their own. A VLNC standard could reduce cigarette reinforcement and dependence. The most effective endgame approach is likely to be one that pursues both nicotine reduction in smoked tobacco and other nicotine products as complementary approaches.	More data on health risks of novel ANDS like e-cigarettes, which may confer health risks that are yet to be fully understood.	Funded by NIDA and FDA CTP
van der Eijk (2015)[4]	Traditional (narrative) review	Not stated	No	General population	None	Product: E-cigarettes, Smokeless tobacco Focus: Adverse health impacts, regulation, Adverse smoking transitions for youth and adults Question(s): What is the evidence for replacing cigarettes with alternative products (harm reduction), denying	All tobacco endgame policies have uncertainties, which require careful consideration and development into an international framework. Possible 'gateway' effects of e-cigarettes/smokeless tobacco could be avoided if their introduction is combined with a cigarette phase out. The WHO FCTC, the TFG proposal and harm	Evidence on the degree to which addictive behaviours are driven by 'choice' rather than 'compulsion'." More conclusive evidence on whether alternative nicotine products are a gateway into smoking.	None

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Type of lower risk product/Research focus/Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
						tobacco sales to people born after a certain year (the tobacco-free generation proposal), and further implementing measures based on the WHO Framework Convention for Tobacco Control (FCTC) treaty as strategies for phasing out tobacco consumption?	reduction options may provide an integrated endgame strategy that strengthens existing tobacco control approaches to facilitative an endgame that phases out cigarette sales and allows the sale of alternative products.		

FCTC: Framework Convention on Tobacco Control; FDA CTP: Food and Drug Administrations' Center for Tobacco Products; NIDA: National Institute on Drug Abuse; NRT: nicotine replacement therapy; QALYs: Quality-adjusted-life-years; RCT: randomised controlled trial; TFG: tobacco-free generation; WHO: World Health Organization.

Supplementary Table 7: Characteristics and Findings of Individual Evidence Syntheses: Restrict Tobacco Sales by Year Born (Tobacco-Free Generation)

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Doan, Tan, Dickens, Lean, Yang & Cook (2019)[59]	Simulation modelling study	Demographic data, longitudinal survey data, other unspecified study designs	Yes	Synthetic population using data from Singapore	None	What is the potential prevalence of nicotine use and of quality- adjusted life years (QALYs) gained under various alternative scenarios, including a tobacco-free generation (TFG) for birth-cohorts 2000 onwards, compared with a status quo scenario?	A biennial tax increase and the tobacco free generation proposal produced the best outcomes in the model. Raising of the minimum legal age was identified as an effective initial step, but that longer term impacts would require extending the policy to the TFG proposal.	None stated relevant to TFG policy.	Funded by Singapore's Ministry of Health, National Medical Research Council, and National Research Foundation
Singh, Petrović-van der Deen, Carvalho, Lopez & Blakely (2020)[60]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	Solomon Islands/ All current smokers for interventions 1 and 2; all smokers over 20 years of age for intervention 3 (TFG)	None	What are the estimated health-adjusted life years (HALY) gained in the Solomon Islands for the 2016 population over the remainder of their lives, for three interventions: eradication of cigarettes; 25% annual tax increases to 2025 such that tax represents 70% of sales price of tobacco; and a TFG?	A TFG policy would deliver 798 health-adjusted life years (HALYs) per 1000 people (52.5%).	Disease-specific healthcare expenditures for each country with similar data as used in the GBD study.	Funded by the Health Research Council of New Zealand
van der Deen, Wilson, Cleghorn, Kvizhinadze, Cobiac, Nghiem & Blakely (2018)[61]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	All New Zealanders born from the year 1993 onwards	Compared outcomes for Māori and non-Māori people	To estimate the smoking prevalence by 2025, health and cost impacts of a tobacco free generation	The TFG proposal would not deliver a 5% smoking prevalence by 2025 for either the Māori and non-Māori populations of NZ (5.6%/11.2%), but it would still deliver large health gains and health system cost savings to the health system, especially for Māori (5.6x greater health gain per capita compared to non-Māori, although the benefits are only realised decades into the future).	Evidence on the effectiveness of the TFG policy.	Funded by the Health Research Council of New Zealand
van der Eijk & Porter (2015)[62]	Traditional (narrative) review	Not stated	No	Global/ People born on or after 1 January 2000	None	What are some of the key legal and ethical issues of the tobacco free generation proposal?	Human rights framing can be used to both support or oppose the TFG policy., However, analysis of previous legal cases and human rights ethics debates indicate that the TFG proposal is consistent with human rights principles, and could contribute to a successful human rights-based tobacco control strategy.	Greater certainty in the interpretation of human rights articles, particularly when applied to public health.	Funded by the National Cancer Centre, Singapore

GBD: Global Burden of Disease; HALYs: Health-adjusted life years; NZ: New Zealand; QALYs: Quality-adjusted life years; TFG: Tobacco-free generation

Supplementary Table 8: Characteristics and Findings of Individual Evidence Syntheses: End Commercial Retail Sale of Combustible Tobacco (Abolition)

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
McDaniel, Smith & Malone (2016)[5]	Traditional (narrative) review	Not stated	Yes	Global/ General population	None	What different approaches have been suggested or could be considered as advancing the tobacco endgame?	The commercial sales of tobacco could be banned, with a long lead-in time ahead of implementation to give smokers time to quit. Bans on reduced risk nicotine products could be lifted. This policy would be different to alcohol prohibition as nicotine is not a recreational drug, and there is precedent for governments to ban a product that is exceptionally harmful. The measure may create hardship for people with low education or income, but these communities may implement targeted cessation aid to mitigate impacts. Surveys report some public support for ending tobacco sales, with different levels by smoking status. Support ranged from 12% (Ontario, Canada and NZ adolescents) to 88% (Bhutan) among people who smoke and from 24% (Ontario, Canada) to 68% (Hong Kong) among people who don't smoke.	None stated.	Funded by Cancer Research UK
Singh, Petrović-van der Deen, Carvalho, Lopez & Blakely (2020) [60]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	Solomon Islands/ All current smokers for eliminating tobacco	None	What are the estimated health-adjusted life years (HALY) gained in the Solomon Islands for the 2016 population over the remainder of their lives, for three interventions: eradication of cigarettes	Ending sales of tobacco in 2016 would deliver 1510 HALYs per 1000 people alive in 2016 over their lifetimes. (96 and 162 HALYs per 1000 people between 2016–2025 and 2026–2035, respectively).	Disease-specific healthcare expenditures for each country with similar data as used in the GBD study	Funded by the Health Research Council of New Zealand

GBD: Global Burden of Disease; HALYs: Health-adjusted life years; NZ: New Zealand

Supplementary Table 9: Characteristics and Findings of Individual Evidence Syntheses: Set a Regularly Reducing Quota on the Volume of Tobacco Products Manufactured or Imported into a Country ('Sinking Lid')

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Tait, Saunders & Rutherford (2013)[31]	Simulation modelling study	Publicly available data on tobacco imports	Yes	New Zealand population	None	What is the role of policy that sees tobacco companies bid for quotas to supply tobacco to the New Zealand market?	A tradeable quota scheme for tobacco supply would be equivalent to imposing an import quota restriction in NZ. A quota system could be applied to nicotine or another chemical in tobacco in a similar way to salt in food products.	The substitution effects between tobacco products need to be empirically established.	Funded by Health Research Council of New Zealand and the Ministry of Health of New Zealand.
van der Deen, Wilson, Cleghorn, Kvizhinadze, Cobiac, Nghiem & Blakely (2018)[61]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	All smokers in New Zealand	The authors examined the impact of five tobacco endgame strategies, including a sinking lid on tobacco supply for Maori vs non-Maori smokers.	What are the potential impacts on smoking prevalence, health gains (quality-adjusted life-years) and cost savings of five endgame strategies, including a sinking lid on tobacco supply?	The sinking lid would achieve close to 0% smoking prevalence by 2025 if legal commercial supply ended that year, which would produce large health gains and cost savings to the health system, especially so for Māori people.	More evidence on the effectiveness of the policy is needed.	Funded by the Health Research Council of New Zealand.

NZ: New Zealand

Supplementary Table 10: Characteristics and Findings of Individual Evidence Syntheses: Increases in Tobacco Tax that make Tobacco Products Generally Unaffordable

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Blakely, Cobiac, Cleghorn, Pearson, van der Deen, Kvizhinadze, Nghiem, McLeoud & Wilson (2015)[63]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	The New Zealand population alive in 2011	An equity analysis was conducted for Māori. A 10% annual tobacco tax increase from 2011 to 2031would increase health gains for Māori (105,000 to 156,000) by 50% and produce 5.5 times greater health gains per capita for Māori than non-Māori.	What are the potential impacts on health, health inequalities, and health system costs of ongoing tobacco tax increases (10% annually from 2011 to 2031, compared to no tax increases from 2011 in New Zealand?	The modelling estimated large health gains, health sector cost savings, and health inequality reductions. Additional measures would be needed to achieve faster impacts for the middle- and older-aged population	Country-specific price elasticity estimates by age and social group. The impact of e-cigarettes and smuggling on these elasticities. Synergies between tobacco tax increases and other tobacco control policies (e.g., intensive mass media campaigns) and the joint impact of multiple public health interventions.	Funded by the Health Research Council of New Zealand and the National Health and Medical Research Council of New Zealand
Chaiton, Dubray, Guindon & Schwartz (2021)[66]	Simulation modelling study	Demographic data, sales data, expert panel estimates, other unspecified study designs	Yes	People aged 20–22 living in Ontario, Canada, between 2018 and 2035.	None	What estimated tax and price increases are required to achieve <5% smoking prevalence by 2035 in Ontario, Canada? What impact on tax revenue impact would result from achieving <5% smoking prevalence?	The Ontario SimSmoke Model estimated smoking prevalence to reduce by 8.5% by2035 if the four modelled strategies were implemented. Tobacco tax increases had the greatest impact, decreasing smoking prevalence by 2.8% followed by raising the legal purchase age to 21 years (2.4%), reducing the number of tobacco outlets (1.5%), providing free cessation services (0.7%), and implementing tobacco plain packaging (0.6%). Tobacco tax would need to be increased by more than 20% annually to achieve the Canadian endgame goal.	None stated	Funded by Health Canada Substance Use and Addiction Program
Cobiac, Ikeda, Nghiem, Blakely & Wilson (2014)[64]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	Māori and non-Māori men and women in New Zealand	The study investigates outcomes for Māori men and women	Would regular tobacco tax increases (5%, 10%, 15% and 20%) achieve the 2025 smoke-free Aotearoa goal? What would be the impact on smoking inequalities? How would government tax revenue be impacted over the next 50 years?	The model indicated that a wider range of tobacco endgame interventions are needed beyond tobacco tax increases to achieve <5% smoking prevalence for all social groups. Substantial reductions in smoking prevalence are likely among both Māori and non-Māori populations.	None stated	Funded by the Health Research Council of New Zealand and the National Health and Medical Research Council of New Zealand
Doan, Tan, Dickens, Lean, Yang & Cook (2019)[59]	Simulation modelling study	Demographic data, longitudinal survey data, other unspecified study designs	Yes	The Singapore population	None	What prevalence of nicotine use and quality-adjusted life years (QALYs) are achieved under various alternative scenarios, including 10% tax rises?	Biennial tax increases or prohibiting smoking for the population born after a set year (TFG policy) produced the optimal outcomes.	None stated	Funded by Singapore's Ministry of Health, National Medical Research Council, and National Research Foundation
Laugesen (2012)[65]	Simulation modelling study	Not stated	Yes	Smoking population in New Zealand	None	How would a lower tax rate on very-low nicotine content cigarettes impact excise revenue and consumption of regular nicotine content cigarettes (containing ≥2 mg nicotine per cigarette)?	A lower excise rate for VLNC cigarettes would: (1) facilitate consumers to use a combination of VLNC and regular cigarettes; (2) make VLNC cigarettes available to consumers who continue to smoke; (3) increase the political feasibility of increasing excise on regular cigarettes to reduce their use; and (4) enable consumers to reduce their nicotine addiction before quitting smoking, and potentially increase their quit success.	Research to determine the impact of smoking VLNC cigarettes on brain receptors sometime after smoking regular cigarettes and resultant impact on cravings. Regular analyses of VLNC cigarettes for nicotine content to detect false labelling and excise evasion. Research on the effects of smoking different combinations of regular and VLNC cigarettes on addiction	None

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
								levels and on quitting success.	
Singh, Petrović-van der Deen, Carvalho, Lopez & Blakely (2020)[60]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	Smoking population in the Solomon Islands	None	What are the estimated health- adjusted life years (HALY) gained in the Solomon Islands for the 2016 population over the remainder of their lives, for three interventions: hypothetical eradication of cigarettes; 25% annual tax increases to 2025 such that tax represents 70% of sales price of tobacco; and a tobacco- free generation?	The tax intervention produced faster declines in smoking (especially for younger ages), and delivers 370 HALYs per 1000 population (24.5% of potential health gain). However, the policy is insufficient to achieve the Tobacco- Free Pacific Goal in the Solomon Islands.	Inclusion of both intervention and smoking-attributable disease costs to estimate cost-effectiveness. Disease-specific healthcare expenditures for Solomon Islands with similar data as used in the GBD study	Funded by the Health Research Council of New Zealand
van der Deen, Wilson, Cleghorn, Kvizhinadze, Cobiac, Nghiem & Blakely (2018)[61]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease), unspecified study designs	Yes	All smokers in New Zealand	The authors examined the impact of five tobacco endgame strategies, including 10% annual tobacco tax increases for Māori vs non-Māori smokers. A 10% annual tax increase would reduce smoking prevalence from 34.7%/14.1% for Māori/ non-Māori in 2011 to 16.0%/6.8%.	What are the potential impacts on smoking prevalence, health gains (quality-adjusted life-years (QALYs)) and cost savings of five tobacco endgame strategies, including 10% annual tobacco tax increases?	A 10% annual tax increase implemented in 2011 would reduce inequalities, deliver substantial health gains and health care cost savings by reducing smoking prevalence to 6.8% among non-Māori and 16.0% among Māori New Zealanders by 2025.	Evidence on the effectiveness of the policy implemented according to this proposal.	Funded by from the Health Research Council of New Zealand

GBD: Global Burden of Disease; HALYs: Health-adjusted life years; QALYs: Quality-adjusted life years; TFG: Tobacco-free generation; VLNC: Very low nicotine content

Supplementary Table 11: Characteristics and Findings of Individual Evidence Syntheses: Restrictions on Tobacco Retailer Density/Location/Type/Licensing that Substantially Reduces Tobacco Availability

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
Chaiton, Dubray, Guindon & Schwartz (2021)[66]	Simulation modelling study	Demographic data, sales data, expert panel estimates, other unspecified study designs	Yes	Ontario, Canada population in 2014	None	What are the potential impacts of five tobacco endgame strategies on smoking prevalence in Ontario by 2035?	The combined effect of four strategies is expected to reduce smoking prevalence by 8.5% in 2035. Increasing tobacco taxes had the greatest independent predicted decrease in smoking prevalence (2.8%) followed by raised minimum age for legal purchase to 21 years (2.4%), decreasing tobacco outlets (1.5%), free cessation services (0.7%), and plain packaging (0.6%).	None stated	Funded by Health Canada Substance Use and Addiction Program.
Glasser & Roberts (2021)[74]	Systematic review	Original research (qualitative and quantitative) and systematic reviews from any country	Yes	General population	Some studies included assessed impact of retailer interventions on disparities in retailers between high/low-income areas (mixed findings)	What tobacco retailer density reduction policies have been implemented and formally evaluated? Have these policies been evaluated for their impact on: a) reduction in retailer density (proximal) and b) reduction in tobacco use (distal)?	Tobacco sales bans in pharmacies reduced retailer density, but unclear if equitably. Prohibiting sale of tobacco near schools produced greater density reductions in higher-risk neighbourhoods. Policies in combination were most effective. Density-reduction policies are a promising approach.	Further evidence needed about effectiveness of intervention, including impact on tobacco use and other co-occurring behaviours, effectiveness of retail licensing schemes, and fee amount on both retailer density and tobacco use behaviours, cost-effectiveness, assessment of policy burden on individuals, and policy fairness.	Funded by the US National Cancer Institute
Henriksen (2015)[71]	Traditional (narrative) review	Not stated	No	General population	None	What policies to restrict the quantity, type, and location of tobacco retailers could hasten the endgame?	In the absence of comprehensive marketing restrictions, regulating the number, type and location of tobacco retailers could minimise the impact of retail marketing on initiation, cessation and relapse	Evaluation of existing retailer reduction strategies, such as policies in Hungary and San Francisco. There is also a need for agent-based modelling and other simulations to predict the impact of regulating the built environment on initiation, cessation and tobacco use disparities.	Funded by the US National Cancer Institute, the Tobacco-Related Disease Research Program, and the California Department of Public Health.
Kong & King (2020)[72]	Traditional (narrative) review	Not stated	No	General population	The impact of retailer reduction strategies regarding the impact of the New York tobacco free pharmacy law is described in relation to equity (impact by income level of neighbourhoods).	What is the importance of incorporating strategies focused on the tobacco retailer environment (availability; pricing and promotion; advertising and display; age of sale; and retail licensure) as part of a comprehensive approach to tobacco prevention and control?	Retailer-focused strategies are a complement to, but not a replacement for standard FCTC approaches and should be implemented as part of a comprehensive approach to maximise impact particularly for priority populations with high smoking prevalence. Opportunities exist to reinforce the viability of retailer-focused strategies to address tobacco use and achieve the endgame. Retail-focused strategies may be most impactful when combined together and should be implemented at multiple governmental levels. Adequate enforcement and ensuring compliance is key to achieving impact and equity.	None stated	Author affiliated with the US Office on Smoking and Health at the Centers for Disease Control and Prevention. Funded by the US National Cancer Institute.
Marsh, Vaneckova, Robertson, Johnson, Doscher, Raskind, Schleicher & Henriksen	Systematic review	Cross-sectional, Longitudinal/ cohort	Yes	School-aged youth aged 18 years and under	None	What is the evidence on the density and proximity of tobacco retail outlets to homes, schools and communities and their association with smoking behaviours among youth?	Evidence supports a positive association between tobacco retail outlet density and smoking among youth, particularly for density near youths' homes. Policies that reduce overall density of neighbourhood tobacco retail outlets may be the best approach to reducing smoking rates among youth. Options include: maximizing distance between tobacco retailers, a population-based limit on retailers and	Evidence needed about tobacco retail density and smoking in rural areas. Longitudinal studies needed for better evidence of direction of causality and to strengthen the evidence base for intervention. Research also needed to evaluate	Funded by the Cancer Society of New Zealand, NIH, and the US National, Heart, Lung and Blood Institute.

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
(2021)[73]							creating a more equitable distribution, or restricting tobacco sales to a limited number of government-licensed stores or to age-restricted stores inaccessible to youth.	the impact of density reduction policies on youth smoking and sales to minors, as well as theorized mediators, such as exposure to marketing, price, anti-smoking norms and risk perceptions.	
Pearson, Cleghorn, van der Deen, Cobiac, Kvizhinadze, Nghiem, Blakely & Wilson (2016)[67]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease, for the NZ population), unspecified study designs	Yes	New Zealand population in 2011	Assessed impacts of policies in Māori and non- Māori	What are the potential population-level future health gains and health system costs for four different tobacco retail outlet restriction interventions: (1) reducing the total number of tobacco retail outlets by 95% (2) permitting sales at half the liquor stores (and nowhere else) (3) eliminating sales from outlets within 1 km of schools, and (4) eliminating sales from outlets within 2 km of schools	All 4 interventions led to reductions of >89% of current tobacco outlets after the 10-year phase-in process. The most effective intervention limited sales to half of liquor stores (and nowhere else) at 129 000 QALYs gained over the lifetime of the population (95% UI: 74 100 to 212 000, undiscounted). The per capita QALY gains were up to 5 times greater for Māori compared to non-Māori. All interventions were cost-saving to the health system, with the largest saving for the liquor store only intervention: US$1.23 billion (95% UI: $0.70 to $2.00 billion, undiscounted).	May need longitudinal studies to validate, or recalibrate, the price elasticity methods associated with increased travel to purchase tobacco used in this study.	Funded by the Health Research Council of New Zealand
Pearson, Van der Deen, Wilson, Cobiac & Blakely (2014)[68]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease, for the NZ population), unspecified study designs	Yes	New Zealand population in 2011	None	What is the estimated impact of various interventions that markedly reduce the availability of tobacco retail outlets?	A 95% reduction in outlets led to smoking prevalence of 9.6% by 2025 (compared to 9.9% with no intervention). Permitting tobacco sales at only 50% of liquor stores resulted in the lowest prevalence (9.1%) by 2025. Elimination of outlets within 2 km of schools produced smoking prevalence of 9.3%. Tobacco outlet reduction interventions could modestly contribute to an endgame goal.	Lack of intervention studies on impact of reducing retail outlets.	Funded by the Health Research Council of New Zealand
Petrović-van der Deen, Blakely, Kvizhinadze, Cleghorn, Cobiac & Wilson (2019)[69]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease, for the NZ population), unspecified study designs	Yes	New Zealand population in 2011	Compared modelled outcomes among Māori and non-Māori	What are the potential impacts on future smoking prevalence, population health and health systems costs of restricting tobacco sales to pharmacies only in New Zealand?	Provides modelling-level evidence that restricting tobacco sales to only pharmacies combined with cessation advice in these settings can accelerate progress towards the tobacco endgame, and achieve large population health benefits and cost-savings.	Limited evidence on the effectiveness of restricting sales to pharmacies, and on the effectiveness of brief opportunistic advice provided by pharmacists.	Funded by Health Research Council of New Zealand
Skinner, Walker, Atkinson, Whitehead, Roselli, West, Bright, Heffernan, McDonnell, Veerman, Prodan, Thomas & Burton	Simulation modelling study	Expert elicitation and publications (not study designs not specified)	Yes	Adult daily smokers in the Australian state of Queensland	Potential impacts of interventions on smoking prevalence in Aboriginal and Torres Strait Islander, socio-economically disadvantaged, and regional and remote communities were examined, but no results reported in the manuscript.	What are the potential impacts of a tobacco retailer licensing scheme (where wholesalers and retailers have to apply for a license prior to supplying tobacco products) on adult daily smoking prevalence in the Australian state of Queensland?	Smoking prevalence is projected to reduce by 0.65 and 1.73 percentage points respectively with the introduction of tobacco wholesaler and retailer licensing schemes that either permit or prohibit tobacco sales by alcohol-licensed venues	Effects for this intervention should be considered provisional, as only limited evidence exists for the probable sizes of the direct effects of tobacco licensing on smoking	Authors affiliated with Australia's Sax Institute and Queensland Health. Funded by Queensland Health.

Authors (Year)	Type of evidence synthesis	Types of studies included in evidence synthesis	Study methods detailed?	Population	Equity impacts addressed	Research questions addressed	Authors' conclusions	Evidence gaps noted by authors	Funding and policy actors involved in authoring, or publishing
(2021)[70]									
van der Deen, Wilson, Cleghorn, Kvizhinadze, Cobiac, Nghiem & Blakely (2018)[61]	Simulation modelling study	Demographic data (incidence, prevalence and case-death rates for each disease, for the NZ population), unspecified study designs	Yes	NZ smoking population	Compared outcomes for Māori vs non-Māori populations	What are the estimated impacts on smoking prevalenceQALYs & cost savings of: (1) 10% annual tobacco tax increases (2) a tobacco-free generation (TFG) (3) a substantial outlet reduction strategy **(4)** a sinking lid on tobacco supply and **(5)** a combination of 1, 2 and 3?	Outlet reduction would achieve a non-Māori/Māori smoking prevalence in 2025 of 7.3%/17.8%, with a reduction in ethnic inequalities in smoking and substantive health gain and cost savings.	None stated	Funded by the Health Research Council of New Zealand

FCTC: Framework Convention on Tobacco Control; NIH: National Institutes of Health; NZ: New Zealand; QALYs: Quality-adjusted life years; TFG: Tobacco-free generation; US: United States

References

[1] Malone RE. The race to a tobacco endgame. *Tob Control* 2016;**25**(6):607-608.
[2] Malone RE. Imagining things otherwise: new endgame ideas for tobacco control. *Tob Control* 2010;**19**(5):349-350.
[3] Thomson G, Edwards R, Wilson N*, et al.* What are the elements of the tobacco endgame? *Tob Control* 2012;**21**(2):293-295.
[4] van der Eijk Y. Development of an integrated tobacco endgame strategy. *Tob Control* 2015;**24**(4):336-340.
[5] McDaniel PA, Smith EA, Malone RE. The tobacco endgame: a qualitative review and synthesis. *Tob Control* 2016;**25**(5):594-604.
[6] Houghton F, Houghton S, O'Doherty D*, et al.* The tobacco endgame: the importance of targets and geography. *Can J Public Health* 2018;**109**(5-6):900-901.
[7] Smith EA, Malone RE. An argument for phasing out sales of cigarettes. *Tob Control* 2020;**29**(6):703-708.
[8] Ministry of Health. Smokefree Aotearoa 2025 Action Plan. Wellington: New Zealand Government 2021. https://www.health.govt.nz/system/files/documents/publications/hp7801_-_smoke_free_action_plan_v15_web.pdf (accessed 4 January 2022).
[9] Cabinet Office and Department of Health and Social Care. Advancing our health: prevention in the 2020s. United Kingdom: United Kingdom Government 2019.
[10] Scottish Government. Tobacco Control Strategy - Creating a Tobacco-Free Generation. Scotland: Scottish Government 2013.
[11] Healthy Ireland, Department of Health. Tobacco Free Ireland. Ireland: Department of Health 2019.
[12] Office of Disease Prevention and Health Promotion. Reduce current cigarette smoking in adults — TU-02. *Health People 2030*. Rockville, MD: U.S. Department of Health and Human Services 2021.
[13] Government of Canada. Canada's Tobacco Strategy. Canada: Government of Canada 2020. https://www.canada.ca/en/health-canada/services/publications/healthy-living/canada-tobacco-strategy.html (accessed 2 Dec 2021).
[14] Department of Health. National Preventive Health Strategy. Canberra: Australian Government 2021-2030. https://www.health.gov.au/resources/publications/national-preventive-health-strategy-2021-2030 (accessed 4 January 2022).
[15] Library of Congress. Sweden: New rules on smoking in public places and sale of tobacco enter into force https://www.loc.gov/item/global-legal-monitor/2019-09-25/sweden-new-rules-on-smoking-in-public-places-and-sale-of-tobacco-enter-into-force/ (accessed 2 Dec 2021).
[16] World Health Organization Regional Office for Europe. Strong legislation helps defeat e-cigarettes in Finland. Geneva, Switzerland: World Health Organization 2020. https://www.euro.who.int/en/countries/finland/news/news/2020/5/strong-legislation-helps-defeat-e-cigarettes-in-finland (accessed 2 Dec 2021).
[17] Ministry of Social Affairs and Health. Roadmap to a Tobacco-Free Finland: Action Plan on Tobacco Control. Finland: Ministry of Social Affairs and Health, 2014. https://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/70305/URN_ISBN_978-952-00-3513-6.pdf (accessed 2 Dec 2021)
[18] Government of the People's Republic of Bangladesh. Sustainable Development Goals: Bangladesh Progress Report 2020. Dhaka, Bangladesh: Bangladesh Planning Commission 2020. https://www.bd.undp.org/content/bangladesh/en/home/library/democratic_governance/bangladesh-sustainable-development-goals--sdgs--progress-report-.html (accessed 2 Dec 2021).
[19] Cornell University Library. A Guide to Evidence Synthesis: Types of Evidence Synthesis. Ithaca, NY: Cornell University Library 2021.
[20] Alper BS, Haynes RB. EBHC pyramid 5.0 for accessing preappraised evidence and guidance. *Evid Based Med* 2016;**21**(4):123-125.
[21] Graham ID, Logan J, Harrison MB*, et al.* Lost in knowledge translation: time for a map? *J Contin Educ Health Prof* 2006;**26**(1):13-24.
[22] Greenhalgh T, Thorne S, Malterud K. Time to challenge the spurious hierarchy of systematic over narrative reviews? *Eur J Clin Invest* 2018;**48**(6):e12931.
[23] Whitty CJ. What makes an academic paper useful for health policy? *BMC Med* 2015;**13**:301.
[24] Peters M, Godfrey C, McInerney P*, et al.* Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z, eds. *JBI Manual for Evidence Synthesis*: JBI 2020.
[25] Tricco AC, Lillie E, Zarin W*, et al.* PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018;**169**(7):467-473.
[26] Puljevic C. Closing the gaps in tobacco endgame evidence: a scoping review and gap analysis. Open Science Framework 2021. https://doi.org/10.17605/OSF.IO/H85AT (accessed 2 Dec 2021).
[27] Sutton A, Clowes M, Preston L*, et al.* Meeting the review family: exploring review types and associated information retrieval requirements. *Health Info Libr J* 2019;**36**(3):202-222.
[28] Ferris Wayne G, Donny E, Ribisl KM. A global nicotine reduction strategy: state of the science. In: WHO Study Group on Tobacco Product Regulation, ed. *Report on the Scientific Basis of Tobacco Product Regulation: Seventh Report of a WHO Study Group*. Geneva: World Health Organization 2019. https://apps.who.int/iris/handle/10665/161512 (accessed 2 Dec 2021).
[29] WHO Study Group on Tobacco Product Regulation. Advisory note: Global nicotine reduction strategy. In: WHO study group on tobacco product regulation, ed. *Report on the Scientific Basis of Tobacco Product Regulation: Fifth Report of a WHO Study Group*. Geneva: World Health Organization 2015. https://apps.who.int/iris/rest/bitstreams/848180/retrieve (accessed 2 Dec 2021).
[30] Institute of Medicine. Ending the Tobacco Problem: A Blueprint for the Nation. Washington, DC: The National Academies Press 2007.
[31] Tait P, Saunders C, Rutherford P. Quota Management Policy for New Zealand Tobacco Supply. Auckland: New Zealand Tobacco Control Research Tūranga, University of Auckland 2013.
[32] Benowitz NL, Henningfield JE. Reducing the nicotine content to make cigarettes less addictive. *Tob Control* 2013;**22**:i14-17.
[33] Dermody SS, Donny EC. The predicted impact of reducing the nicotine content in cigarettes on alcohol use. *Nicotine Tob Res* 2014;**16**(8):1033-1044.
[34] Donny EC, Hatsukami DK, Benowitz NL*, et al.* Reduced nicotine product standards for combustible tobacco: building an empirical basis for effective regulation. *Prev Med* 2014;**68**:17-22.
[35] Gaalema DE, Miller ME, Tidey JW. Predicted impact of nicotine reduction on smokers with affective disorders. *Tob Regul Sci* 2015;**1**(2):154-165.
[36] Henningfield JE, Benowitz NL, Slade J*, et al.* Reducing the addictiveness of cigarettes. Council on Scientific Affairs, American Medical Association. *Tob Control* 1998;**7**(3):281-293.
[37] Kurti AN. Reducing tobacco use among women of childbearing age: contributions of tobacco regulatory science and tobacco control. *Exp Clin Psychopharm* 2020;**28**(5):501-516.
[38] Sofuoglu M, LeSage MG. The reinforcement threshold for nicotine as a target for tobacco control. *Drug Alcohol Depen* 2012;**125**(1-2):1-7.
[39] Smith TT, Hatsukami DK, Benowitz NL*, et al.* Whether to push or pull? Nicotine reduction and non-combusted alternatives - two strategies for reducing smoking and improving public health. *Prev Med* 2018;**117**:8-14.
[40] Tidey JW, Davis DR, Miller ME*, et al.* Modeling nicotine regulation: a review of studies in smokers with mental health conditions. *Prev Med* 2018;**117**:30-37.
[41] Tidey JW, Muscat JE, Foulds J*, et al.* Reducing the nicotine content of cigarettes: effects in smokers with mental health conditions and socioeconomic disadvantages. *Nicotine Tob Res* 2019;**21**(Suppl 1):S26-S28.

[42] Villanti AC, Byron MJ, Mercincavage M*, et al.* Misperceptions of nicotine and nicotine reduction: the importance of public education to maximize the benefits of a nicotine reduction standard. *Nicotine Tob Res* 2019;**21**(Suppl 1):S88-S90.
[43] Walker N, Bullen C, McRobbie H. Reduced-nicotine content cigarettes: is there potential to aid smoking cessation? *Nicotine Tob Res* 2009;**11**(11):1274-1279.
[44] White CM, Pickworth WB, Sved AF*, et al.* Using product standards to render the most harmful tobacco products minimally addictive: maximum nicotine level, non-nicotine constituents, and scope. *Nicotine Tob Res* 2019;**21**:S13-S15.
[45] White CM, Hatsukami DK, Donny EC. Reducing the relative value of cigarettes: considerations for nicotine and non-nicotine factors. *Neuropharm* 2020;**175**:108200.
[46] Ahmad S, Billimek J. Estimating the health impacts of tobacco harm reduction policies: a simulation modeling approach. *Risk Analysis* 2005;**25**(4):801-812.
[47] Apelberg BJ, Feirman SP, Salazar E*, et al.* Potential public health effects of reducing nicotine levels in cigarettes in the United States. *NEJM* 2018;**378**(18):1725-1733.
[48] Levy DT, Cummings KM, Heckman BW*, et al.* The public health gains had cigarette companies chosen to sell very low nicotine cigarettes. *Nicotine Tob Res* 2021;**23**(3):438-446.
[49] Tengs TO, Ahmad S, Savage JM*, et al.* The AMA proposal to mandate nicotine reduction in cigarettes: a simulation of the population health impacts. *Prev Med* 2005;**40**(2):170-180.
[50] Berman ML, Glasser AM. Nicotine reduction in cigarettes: literature review and gap analysis. *Nicotine Tob Res* 2019;**21**:S133-S144.
[51] Johnston V, Westphal DW, Glover M*, et al.* Reducing smoking among Indigenous populations: new evidence from a review of trials. *Nicotine Tob Res* 2013;**15**(8):1329-1338.
[52] Keith DR, Kurti AN, Davis DR*, et al.* A review of the effects of very low nicotine content cigarettes on behavioral and cognitive performance. *Prev Med* 2017;**104**:100-116.
[53] Hatsukami DK, Perkins KA, Lesage MG*, et al.* Nicotine reduction revisited: science and future directions. *Tob Control* 2010;**19**(5):e1-e10.
[54] Abrams DB, Glasser AM, Villanti AC*, et al.* Managing nicotine without smoke to save lives now: Evidence for harm minimization. *Prev Med* 2018;**117**:88-97.
[55] Brandon TH, Goniewicz ML, Hanna NH, et al. Electronic nicotine delivery systems: a policy statement from the American Association for Cancer Research and the American Society of Clinical Oncology. *J Clin Oncol* 2015;**33**(8):952-63..
[56] England LJ, Bunnell RE, Pechacek TF, *et al.* Nicotine and the developing human: a neglected element in the electronic cigarette debate. *Am J Prev Med* 2015;**49**(2):286-93.
[57] Levy DT, Borland R, Lindblom EN*, et al.* Potential deaths averted in USA by replacing cigarettes with e-cigarettes. *Tob Control* 2018;**27**(1):18-25.
[58] Mendez D, Warner KE. A magic bullet? The potential impact of e-cigarettes on the toll of cigarette smoking. *Nicotine Tob Res* 2021;**23**(4):654-661.
[59] Doan TTT, Tan KW, Dickens BSL*, et al.* Evaluating smoking control policies in the e-cigarette era: a modelling study. *Tob Control* 2020;**29**(5):522-530.
[60] Singh A, Petrović-van der Deen FS, Carvalho N*, et al.* Impact of tax and tobacco-free generation on health-adjusted life years in the Solomon Islands: a multistate life table simulation. *Tob Control* 2020;**29**(4):388-397.
[61] van der Deen FS, Wilson N, Cleghorn CL*, et al.* Impact of five tobacco endgame strategies on future smoking prevalence, population health and health system costs: two modelling studies to inform the tobacco endgame. *Tob Control* 2018;**27**(3):278-286.
[62] van der Eijk Y, Porter G. Human rights and ethical considerations for a tobacco-free generation. *Tob Control* 2015;**24**(3):238-242.
[63] Blakely T, Cobiac LJ, Cleghorn CL*, et al.* Health, health inequality, and cost impacts of annual increases in tobacco tax: multistate life table modeling in New Zealand. *PLoS Medicine* 2015;**12**(7):e1001856-e1001856.
[64] Cobiac LJ, Ikeda T, Nghiem N*, et al.* Modelling the implications of regular increases in tobacco taxation in the tobacco endgame. *Tob Control* 2015;**24**(e2):e154-160.
[65] Laugesen M. Modelling a two-tier tobacco excise tax policy to reduce smoking by focusing on the addictive component (nicotine) more than the tobacco weight. *N Z Med J* 2012;**125**(1367):35-48.
[66] Chaiton M, Dubray J, Guindon GE*, et al.* Tobacco endgame simulation modelling: assessing the impact of policy changes on smoking prevalence in 2035. *Forecasting* 2021;**3**:267-275.
[67] Pearson AL, Cleghorn CL, van der Deen FS*, et al.* Tobacco retail outlet restrictions: health and cost impacts from multistate life-table modelling in a national population. *Tob Control* 2017;**26**:579–585.
[68] Pearson AL, van der Deen FS, Wilson N*, et al.* Theoretical impacts of a range of major tobacco retail outlet reduction interventions: modelling results in a country with a smoke-free nation goal. *Tob Control* 2014;**24**(e1):e32-38.
[69] Petrović-van der Deen FS, Blakely T, Kvizhinadze G*, et al.* Restricting tobacco sales to only pharmacies combined with cessation advice: a modelling study of the future smoking prevalence, health and cost impacts. *Tob Control* 2019;**28**:643-650.
[70] Skinner A, Walker P, Atkinson JA*, et al.* Policy options for endgame planning in tobacco control: a simulation modelling study. *Tob Control* 2021;**30**:77-83.
[71] Henriksen L. The retail environment for tobacco: a barometer of progress towards the endgame. *Tob Control* 2015;**24**(e1):e1-e2.
[72] Kong AY, King BA. Boosting the Tobacco Control Vaccine: recognizing the role of the retail environment in addressing tobacco use and disparities. *Tob Control* 2020.
[73] Marsh L, Vaneckova P, Robertson L*, et al.* Association between density and proximity of tobacco retail outlets with smoking: A systematic review of youth studies. *Health Place* 2021;**67**:102275.
[74] Glasser AM, Roberts ME. Retailer density reduction approaches to tobacco control: a review. *Health Place* 2021;**67**:102342.
[75] Food and Drug Administration. Tobacco product standard for nicotine level of combusted cigarettes: a proposed rule. Fed Reg. 2018;83:11818–11843. https://www.federalregister.gov/documents/2018/03/16/2018-05345/tobacco-product-standard-for-nicotine-level-of-combusted-cigarettes. Accessed 4 January 2022.
[76] Department of Health. Towards a Smokefree Generation: A Tobacco Control Plan for England. London: UK Government 2017. https://www.gov.uk/government/publications/towards-a-smoke-free-generation-tobacco-control-plan-for-england (accessed 2 Dec 2021).
[77] Levy DT, Tam J, Sanchez-Romero LM*, et al.* Public health implications of vaping in the USA: the smoking and vaping simulation model. *Popul Health Metr* 2021;**19**(1):19.
[78] Cancer Intelligence Team Cancer Research UK. Smoking prevalence projections for England, Scotland, Wales, and Northern Ireland, based on data to 2018/19. London: Cancer Research UK 2020. https://www.cancerresearchuk.org/sites/default/files/cancer_research_uk_smoking_prevalence_projections_february_2020_final.pdf (accessed 2 Dec 2021)
[79] Ministry of Health. Proposals for a Smokefree Aotearoa 2025 Action Plan. Auckland: New Zealand Government 2021. https://www.health.govt.nz/publication/proposals-smokefree-aotearoa-2025-action-plan (accessed 2 Dec 2021).
[80] Gottlieb S, Zeller M. A Nicotine-Focused Framework for Public Health. *N Engl J Med* 2017;**377**(12):1111-1114.

[81] Walters EH, Barnsley K. Tobacco-free generation legislation. *Med J Aust* 2015;**202**(10):509-510.
[82] de Leon K, Sarita JT. The Philippines: pioneering the tobacco endgame. *Tob Control* 2020.
[83] Cromar A. Tobacco-free generation: Brookline passes new restriction aiming to phase out tobacco sales to young smokers. *Bostoncom*. Boston, MA 2020.
[84] Givel MS. History of Bhutan's prohibition of cigarettes: implications for neo-prohibitionists and their critics. *Int J Drug Policy* 2011;**22**(4):306-310.
[85] McDaniel PA, Malone RE. Tobacco industry and public health responses to state and local efforts to end tobacco sales from 1969-2020. *PLoS One* 2020;**15**(5):e0233417.
[86] World Health Organization. Hungary – new regulation of tobacco sales introduced. WHO Framework Convention on Tobacco Control 2013.
[87] Bonevski B, Borland R, Paul CL*, et al.* No smoker left behind: it's time to tackle tobacco in Australian priority populations. *Med J Aust* 2017;**207**(4):141-142.
[88] Clegg LX, Reichman ME, Miller BA*, et al.* Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. *Cancer Causes Control* 2009;**20**(4):417-435.
[89] Hoe C, Kennedy RD, Spires M, *et al*. Improving the implementation of tobacco control policies in low-and middle-income countries: a proposed framework. *BMJ Glob Health* 2019;4:e002078.