The potential impact of policies and structural interventions in reducing cardiovascular disease and mortality: a systematic review of simulation-based studies

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Disclosure of interests

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Abstract

The potential impact of policies and structural interventions in reducing cardiovascular disease and mortality: a systematic review of simulation-based studies

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Background: The aim of the study was to investigate the potential effect of different structural interventions for preventing cardiovascular disease.

Methods: Medline and EMBASE were searched for peer-reviewed simulation-based studies of structural interventions for prevention of cardiovascular disease. We performed a systematic narrative synthesis.

Results: A total of 54 studies met the inclusion criteria. Diet, nutrition, tobacco and alcohol control and other programmes are among the policy simulation models explored. Food tax and subsidies, healthy food and lifestyles policies, palm oil tax, processed meat tax, reduction in ultra-processed foods, supplementary nutrition assistance programmes, stricter food policy and subsidised community-supported agriculture were among the diet and nutrition initiatives. Initiatives to reduce tobacco and alcohol use included a smoking ban, a national tobacco control initiative and a tax on alcohol. Others included the NHS Health Check, WHO 25 × 25 and air quality management policy.

Future work and limitations: There is significant heterogeneity in simulation models, making comparisons of output data impossible. While policy interventions typically include a variety of strategies, none of the models considered possible interrelationships between multiple policies or potential interactions. Research that investigates dose–response interactions between numerous modifications as well as longer-term clinical outcomes can help us better understand the potential impact of policy-level interventions.

Conclusions: The reviewed studies underscore the potential of structural interventions in addressing cardiovascular diseases. Notably, interventions in areas such as diet, tobacco, and alcohol control demonstrate a prospective decrease in cardiovascular incidents. However, to realize the full potential of such interventions, there is a pressing need for models that consider the interplay and cumulative impacts of multiple policies. Rigorous research into holistic and interconnected interventions will pave the way for more effective policy strategies in the future.

Study registration: The study is registered as PROSPERO CRD42019154836.

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List of supplementary material

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/NMFG0214).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

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Plain language summary

This study aimed to explore the potential effects of various policy changes on the prevention of heart disease. By searching two large medical databases, we identified studies that employed computer models to estimate the impact of these policies on heart disease rates. In total, 54 studies matched our criteria. These studies considered a diverse range of policy interventions. Some delved into food and nutrition, investigating aspects like unhealthy food taxes, healthy food subsidies, stricter food regulations, and nutritional assistance programs. Others examined the impact of policies targeting tobacco and alcohol, encompassing smoking bans, nationwide tobacco control measures, and alcohol taxation. Further policies assessed included routine health checkups, global health goals, and measures to enhance air quality.

One significant challenge lies in the varied approaches and models each study employed, making direct comparisons difficult. Furthermore, there's a gap in understanding how these policies might influence one another, as the studies did not consider potential interactions between them. While these policies show promise in the computer models, more comprehensive research is needed to fully appreciate their combined and long-term effects on heart health in real-world scenarios. As of now, we recognize the potential of these interventions, but further studies will determine their true impact on reducing heart disease rates.

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Introduction

Cardiovascular disease (CVD) is a term that describes a family of diseases with a common set of risk factors that result from atherosclerosis (furring or stiffening of artery walls), particularly coronary heart disease (CHD), stroke and peripheral arterial disease.[1] As a major cause of disability and premature death throughout the world, CVD contributes substantially to the escalating costs of health care.[2] CVD affects around seven million people in the UK and is a significant cause of disability and death, affecting individuals, families and communities. Although rates have been reducing recently, CVD is responsible for one in four premature deaths in the UK.[1]

Most CVD cases are preventable. Risk factors, such as high blood pressure, smoking, high cholesterol, diabetes, physical inactivity, obesity, poor diet and excessive drinking can all be reduced through lifestyle or medical interventions to reduce a person's risk of CVD.[3] However, there is a strong consensus amongst public health communities about the powerful role of population-level policies. These are suggested to be more effective, cost saving and more equitable when compared with individual-level interventions.[3] Determining the best population-level intervention modality, delivery method and resource allocation, is complex because although they tend to cut across traditional government department boundaries, health policy and decision-makers must weigh the costs and benefits of structural interventions. Furthermore, such interventions often cannot be tested in clinical trials because of multiple environmental, sociocultural and health system factors that negate the feasibility and safety of trials. Researchers and decision-makers have increasingly relied on simulation models to evaluate structural interventions for primary prevention of CVD. Simulation models have been applied to a broad range of areas in health care to predict outcomes, unintended consequences and costs of proposed interventions, thereby offering an invaluable decision aid for policy-makers and health-care leaders.[4–6] The extent to which simulation modelling has provided decision-makers with evidence to facilitate decision-making in CVD prevention is unknown.[7] Simulation modelling has the potential to provide strong evidence for multiple aspects of informed decision-making at the policy and health system level, including a proposed intervention's resource utilisation, cost-effectiveness, feasibility, sustainability, potential impact and acceptance among stakeholders.[8,9]

No systematic review has investigated simulation models developed to comprehensively assess the impact of structural interventions on prevention of CVD. The most recent systematic reviews have addressed bans on individual topic areas, such as smoking in public places[10] and policies to reduce trans-fat consumption.[11] Therefore, in this systematic review we aim to evaluate the potential impact of structural interventions for preventing CVD.

This publication on the systematic review of effectiveness of policies and structural interventions in reducing CVD and mortality is part of a series of publications on 'Determining optimal strategies for primary prevention of CVD: systematic review, network meta-analysis and cost-effectiveness review (NIHR/HTA: 17/148/05)'. Other publications in this series include:

1. Interventions for primary prevention of cardiovascular: umbrella review of systematic reviews.
2. Increasing Comprehensiveness and Reducing Workload in the preparation of a Systematic Review of Complex Interventions using Automated Machine Learning.
3. Determining optimal primary prevention interventions for major CVD events and all-cause mortality – findings from systematic review and hierarchical network meta-analysis of randomised controlled trials (RCTs).
4. How conclusive is the evidence for interventions in primary prevention of CVD: a trial sequential analysis?
5. Mind the gap! A multilevel analysis of factors associated with variation in published CVD primary prevention interventions effect estimates within and between countries.
6. Determining optimal strategies for primary prevention of CVD: Systematic review of cost-effectiveness analyses in the UK.

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The findings from all the workstreams, including those from the systematic review of modelling studies, will be summarised in a synopsis paper to be published alongside this series.

Methods

This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the following number: CRD42019154836. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).[12]

Eligibility criteria

Type of population

Adult populations (≥ 18 years of age), where interventions may or may not be targeted at moderate/high CVD risk groups (such as hypertension, obesity, hyperlipidaemia, type 2 diabetes or a combination of these).

Type of interventions

Any form of structural and policy-based interventions (population-wide interventions) aimed at the primary prevention of CVD, including, but not limited to: taxation and subsidies, mass media campaigns, food and menu labelling, local food environment, worksite wellness programmes, marketing restrictions, quality standards, healthy local environment or addressing air pollution.

Study design

Studies that used any form of simulation model, including but not limited to system dynamics, Monte Carlo, Markov chain model, agent-based model or discrete event, to investigate the perceived value and efficacy of policy-level interventions for the prevention of CVD. Simulation and modelling studies are important tools in supporting evidence for the effectiveness of primary prevention of CVD. These types of studies allow researchers to investigate the potential impact of interventions on population health, without having to conduct large, costly and time-consuming randomised controlled trials (RCTs). However, we excluded other observational studies. Observational studies are often excluded in systematic reviews of primary prevention of CVD due to their inherent limitations, such as potential for bias and measurement errors, and the high volume of evidence to go through. These limitations make it challenging to draw valid conclusions from observational studies, and they are considered less informative than RCTs.

Comparator

There was no restriction on the comparator. The model or simulation could compare the results of all feasible options in relation to each other and/or to current practices.

Types of outcomes

All-cause mortality [deaths prevented or postponed (DPP)], CVD DPP, major cardiovascular events (MACEs) [defined as fatal and non-fatal myocardial infarction (MI), sudden cardiac death, revascularisation, fatal and non-fatal stroke and fatal and non-fatal heart failure], CHD (fatal and non-fatal MI and sudden cardiac death, excluding silent MI).

Information sources and search strategy

A systematic search was performed to identify all relevant studies that satisfied our selection criteria within the following databases from inception to March 2021: Medline, Embase, Web of Science and the Cochrane Library. Additionally, we checked the reviews that we identified for further studies. The search strategy is included as *Report Supplementary Material 1*.

Selection process

After removing duplicates, two authors independently screened titles and abstracts followed by full-text articles. Any disagreements between the two reviewers were resolved through discussions. However, if a disagreement persisted, it was resolved through consultations involving a third author.

Data extraction

Two reviewers independently extracted data using these forms. Disagreements were resolved through discussions between the two reviewers, and in cases in which no agreement was reached, a third author intervened.

Data items

The following data were extracted from each study: (1) overview of study characteristics, (2) model structure and (3) sources of evidence for model parameters.

Risk of bias in individual studies

The validation of a simulation model is an important determinant of the risk of bias and applicability of a simulation model. All models were assessed in accordance with the guidelines of the International Society for Pharmacoeconomics and Outcomes Research-Society for Medical Decision Making report.[7] For each study, we assessed face validity (wherein experts evaluate model structure, data sources, assumptions and results), verification or internal validity (check accuracy of coding), cross validity (comparison of results with other models analysing the same problem), external validity (comparing model results with real-world results) and predictive validity (comparing model results with prospectively observed events).[7]

Data synthesis

We performed a systematic narrative synthesis to present a critical appraisal of the methodological quality and risk of bias of the selected modelling studies and of their results.

Results

Study selection and characteristics

Figure 1 shows the study selection flow diagram. The literature search yielded 1997 articles. After review, 99 articles were selected for critical reading. Forty-five studies did not meet the inclusion criteria and were excluded. The other 54 studies were included. *Table 1* presents the characteristics of the included studies. The studies were published between 2007 and 2021. Most of the studies were from the USA (n = 23, 42.6%), followed by the UK (n = 10, 18.5%). Most of the studies were based on the USA the Cardiovascular Disease Policy Model for Risk, Events, Detection, Interventions, Costs, and Trends (CVD PREDICT)[13–17] and the UK Infliximab Multinational Psoriatic Arthritis Controlled Trial (IMPACT) Coronary Heart Disease (CHD) Policy Model.[18–24] The majority of the studies were full-text articles (n = 48, 88.9%), and only six were conference abstracts. When reported, the time horizon ranged from 3 years to as much as 50 years. Microsimulation (n = 32, 59.3%) was the most frequently used method for developing the policy simulation models, followed by Markov chain models (n = 11, 20.4%). Most studies conducted probabilistic sensitivity analysis (PSA) (n = 30, 56%). Fourteen studies conducted one-way sensitivity analysis. The policy simulation models can be broadly categorised into diet and nutrition, tobacco and alcohol control initiatives and other initiatives. Diet and nutrition initiatives included: national salt reduction initiatives, fruit and vegetable subsidies, sugar-sweetened beverage (SSB) taxes, elimination of industrial trans-fatty acids, food taxes and subsidies, healthy food and lifestyles policies, palm oil taxes, processed meat taxes, reduction in ultra-processed foods, a supplementary nutrition assistance program, stricter food policy and subsidised community-supported agriculture. Tobacco and alcohol control initiatives included smoking and alcohol, smoke-free policies,

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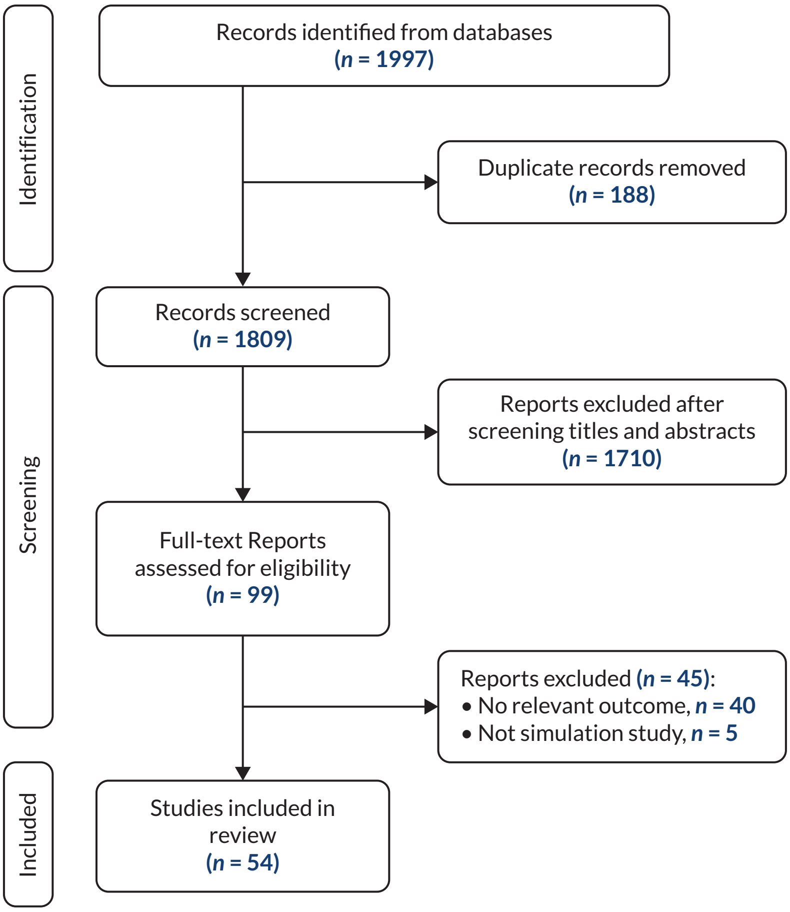

FIGURE 1 Study selection flow.

national tobacco control initiatives and alcohol pricing policies. Other initiatives included the NHS Health Check, the WHO 25 × 25 initiative and air quality management policies.

Percentage reduction in cardiovascular disease mortality

Six studies reported a percentage reduction in CVD mortality (see *Figure 2*).[30,35,36,53,55,64] Three studies were from the USA, one each from the Republic of South Korea, Argentina and Costa Rica. Face validation was adequate for all the studies. Internal validation was adequate in four studies and unclear in the remaining two studies (see *Table 2*). None of the studies reported cross-validation. External validation of the models was performed in only study and none of the studies did not perform predictive validation. The studies were published between 2010 and 2018 and the following policy-level interventions were modelled: national salt reduction initiatives (*n* = 3), air quality management policy (*n* = 1), food and tax subsidy (*n* = 1) and one multicomponent intervention (*n* = 1). The reported potential percentage reduction in CVD mortality varied across interventions modelled, from 0.1% for air quality management policy in the Republic of Korea to 39% for a national salt reduction initiative in Costa Rica. The potential benefit of a national salt reduction initiative varied across countries and periods, from a 2.5% reduction in CVD mortality in Argentina to a 39% reduction in Costa Rica. Three studies modelled different interventions among the US population.[30,36,53] Multicomponent interventions demonstrated the largest percentage reduction in CVD mortality (20%),[36] followed by food tax and subsidy (8.0%)[53] and a national salt reduction initiative (5.4%).[30]

Percentage reduction in cardiovascular disease cases

Four studies reported a percentage reduction in CVD cases (see *Figure 3*).[28,31,44,52] Three studies were from the USA[31,44,52] and one from India.[28] Face validation was adequate for all the studies. Internal validation was adequate in three studies and unclear in one study (see *Table 2*). None of the studies reported cross-validation. External validation of the models was

TABLE 1 Characteristics of included studies

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Asaria[25]	Multicountry	2007	–	Full-text article	2006–15	10	Microsimulation	National Salt Reduction Initiative, National tobacco control initiative	Adult population	Deaths averted	One-way	–
Basu[26]	USA	2020	–	Full-text article			Microsimulation	Subsidised community-supported agriculture	Adult	DALYs	One-way	Longitudinal US cohort data sets
Basu[27]	India	2013	–	Full-text article	2014–23	10	Microsimulation	Palm oil tax	Adult, nationally representative population	mortality due to myocardial infarction and stroke	One-way	Externally validated the model
Basu[28]	India	2013	–	Full-text article	2013–22	10	Microsimulation	National tobacco control initiative	Adult population	Overall mortality trend for myocardial infarctions	One-way	The model's predictions of deaths were validated against Global Burden of Disease estimates for myocardial infarction, stroke and other deaths for the years 2004 and 2008
Bibbins-Domingo[29]	USA	2010	CHD Policy Model	Full-text article	2010–19	10	Markov chain model	National Salt Reduction Initiative	US residents 35 years of age or older	Rates and costs of CVD in subgroups defined by age, sex and race	Monte Carlo simulations	
Choi[30]	USA	2016	–	Full-text article	2015–24	10	Microsimulation	National Salt Reduction Initiative	US population aged 18–85 years	Myocardial infarction and stroke, as well as associated mortality	One-way	National Health and Nutrition Examination Survey (NHANES)

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TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Choi[31]	USA	2017	–	Full-text article	2015		Microsimulation	Supplementary nutrition assistance program	US population, Americans aged 0–85 years	Incidence of major cardiovascular events	Monte Carlo simulation	Centers for Disease Control and Prevention estimates
Cobiac[32]	UK	2017	PROMISE	Full-text article	2013–20	8	Dynamic population modelling	WHO 25 × 25 initiative	UK Population	Mortality and morbidity (years lived with disability) from non-communicable diseases (NCDs) that are averted or delayed	-	-
Collins[18]	England	2014	IMPACT CHD	Full-text article	2010–20	10	Microsimulation	National Salt Reduction Initiative	UK population	Life-year gain	PSA	Calibrated for the English population
Dehmer[33]	USA	2020	–	Full-text article	2018–20	3	Microsimulation	National Salt Reduction Initiative	US Population	Major cardiovascular events	One-way	representative of U.S. population and scaled to the US population aged ≥35 years
Dilley[34]	USA	2012		Full-text article	2000–9	10	Linear regression	National tobacco control initiative	Washington State's Behavioral Risk Factor Surveillance System from 1990 to 2009 to describe the state prevalence of adult cigarette smoking	Hospitalisations	–	National Health Interview Survey from 1990 to 2008
Gillespie[19]	England	2015	IMPACT SEC (Socieconomic differentials)	Full-text article			Microsimulation	National Salt Reduction Initiative	England, population	CHD Death	Monte Carlo simulation	Validated

TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Han[35]	Republic of Korea	2018		Full-text article	2005–14	10	Interrupted time series	Air quality management policy		CVD mortality	One-way	–
Homer[36]	USA	2010	–	Full-text article	1990–2040	50	Systems dynamics	Multicomponent interventions	US population	MACE	One-way	–
Hurley[37]	Australia	2008		Full-text article	1997–2000	4	Markov chain model	National tobacco control initiative		Major cardiovascular events	One-way	–
Kheirbek[37]	USA	2014	–	Full-text article			Microsimulation	Air quality management policy	New York City	Premature deaths, hospital admissions for respiratory and CVD	–	–
Konfino[38]	Argentina	2013		Full-text article	2013–23	10	Markov chain model	National Salt Reduction Initiative	Argentina	Major cardiovascular events	–	–
Konfino[39]	Argentina	2014	CHD Policy Model	Full-text article	2012–20	9	Markov chain model	National tobacco control initiative	Population of Argentina aged 35–84 years in the year 2010	Major cardiovascular events	Monte Carlo simulations	–
Kypridemos[21]	England	2017	IMPACT-NCD	Full-text article	2016–30	15	Microsimulation	National Salt Reduction Initiative	Non-institutionalised population of England	CVD mortality	Probabilistic sensitivity analyses	Model validated well against observed CVD and gastric cancer incidence and mortality in real populations, even when multiply stratified
Kypridemos[20]	UK	2018	IMPACT NCD	Full-text article	2017–40	25	Microsimulation	NHS Health Check	Liverpool population	CVD cases	Second-order Monte Carlo simulation	Validated S1

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TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Lee[13]	USA	2020	CVD-PREDICT	Full-text article			Microsimulation	Sugar-sweetened beverage tax	US adults 35–80 years of age	CVD cases	Probabilistic sensitivity analyses	Validated microsimulation model
Liu[14]	USA	2020	CVD-PREDICT	Full-text article	2018–23	5	Microsimulation	National menu calorie labelling law	US adults aged 35–80 years	CVD cases	Probabilistic sensitivity analyses	Validated microsimulation model
Lloyd-Williams[40]	EU	2008	–	Full-text article	–		Spreadsheet	Subsidized Community Supported Agriculture	EU population	CVD cases	Probabilistic sensitivity analyses	–
Manyema[41]	South Africa	2016	–	Full-text article	20 years	20	Markov chain model	Sugar-sweetened beverage tax	Adult population	CVD cases	Probabilistic sensitivity analyses	–
Marklund[42]	Australia	2020	–	Full-text article	10 years	10	Markov chain model	Eliminating industrial trans-fatty acids	Adult population	CVD cases	Probabilistic sensitivity analyses	Outcomes were compared between a reference population with TFA intake of the Australian population before the intervention and an intervention population with identical characteristics
Mason[43]	Multicountry	2014	IMPACT-CHD	Full-text article	10 years	10	Microsimulation	National Salt Reduction Initiative	Four Eastern Mediterranean Countries	Life years gained	One-way	–
Mekonnen[44]	USA	2013	CVD Policy Model	Full-text article	2013–22	10	Microsimulation	Sugar-sweetened beverage tax	All Californians and California subpopulations	CVD cases	One-way	NHANES and California Health Interview Survey (CHIS) for participants whose self-report of race and ethnicity and family income

TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Moreira[22]	UK	2015	IMPACT Food Policy model	Full-text article	2010–30	20	Microsimulation	Reduction in ultra-process foods	UK	CVD cases	Probabilistic sensitivity analyses	UK population
Mozaffarian[15]	USA	2018	CVD-PREDICT	Full-text article	2013–18	5	Microsimulation	Supplementary nutrition assistance program	NHANES, US adults aged 35–80 years	CVD cases prevented	Probabilistic sensitivity analyses	Validated microsimulation model
Mhurchu[45]	NZ	2015	–	Full-text article	2006–10	5	Markov chain model	Food tax and subsidy	NZ (2.3 million adults, aged 35+ years)	Deaths prevented or postponed (DPP)	One-way	–
Nilson[46]	Brazil	2020	–	Full-text article	2017		Markov chain model	National Salt Reduction Initiative	Brazilian population was 30 years of age or older	CVD mortality	Probabilistic sensitivity analyses	–
Nnoaham[47]	UK	2009	–	Full-text article	-		Spreadsheet	Food tax and subsidy	UK population	CVD mortality	–	–
O'Flaherty[48]	UK	2012	–	Full-text article			Spreadsheet	Stricter food policy	Adults aged 25–84 years	CVD mortality	Probabilistic sensitivity analyses	–
O'Keeffe[23]	Ireland	2013	IMPACT Food Policy Model	Full-text article	-		Microsimulation	Food tax and subsidy	Irish adults aged 25–84 years	CVD mortality	Probabilistic sensitivity analyses	Validated IMPACT Food Policy Model
Pearson-Stuttard[49]	USA	2017	US IMPACT Food Policy Model	Full-text article	2015–30	15	Microsimulation	Fruit and vegetable subsidy	The US population was stratified by age (10-year age groups, 25 to ≥85 years) and sex	CVD death	Probabilistic sensitivity analyses	validated IMPACT methodology

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TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Pearson-Stuttard[50]	USA	2017	US IMPACT Food Policy Model	Full-text article	2015–30	15	Microsimulation	Food tax and subsidy	(Involving 44.5 million individual adults and children) nationwide	CVD mortality	Probabilistic sensitivity analyses	Validated model
Eom[51]	USA	2020	SHINE CVD Model	Abstract	-		Microsimulation	Fruit and vegetable subsidy	New York City (NYC) population, NYC Health and Nutrition Examination Survey	CVD cases	–	–
Garney[52]	USA	2019	–	Abstract	10 years	10	Agent-based model	Smoke-free policy	Arlington and Mesquite, Texas population	CVD cases averted	–	–
Wilde[17]	USA	2018	CVD-PREDICT	Abstract			Microsimulation	Sugar-sweetened beverage tax	US adults 35+ years	CVD cases	Probabilistic sensitivity analyses	Validated
Sy[53]	USA	2018	-	Abstract	2015–35	20	Microsimulation	Food tax and subsidy	US, 35-year olds	CVD death	–	–
Pearson-Stuttard[54]	USA	2018	US IMPACT Food Policy Model	Abstract			Microsimulation	Food tax and subsidy	Entire US population	DPP	Probabilistic sensitivity analyses	Validated
Mejia[55]	Argentina	2011	CHD Model	Abstract			Microsimulation	National Salt Reduction Initiative	Adult population	CVD cases	–	–
Pearson-Stuttard[56]	USA	2018	US IMPACT Food Policy Model	Full-text article	2017–36	20	Microsimulation	National Salt Reduction Initiative	US population	CVD cases	Probabilistic sensitivity analyses	Previously validated US IMPACT Food Policy Model

TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Peñalvo[57]	USA	2017	–	Full-text article			Comparative risk assessment	Food tax and subsidy	Nationally representative data	Cardiometabolic diseases	–	–
Purshouse[58]	England	2010	–	Full-text article	–		Epidemiological mathematical model	Alcohol pricing policy	General Household Survey	Illness prevented	One-way	Validation against historical data
Sahan[59]	Turkey	2016	IMPACT model	Full-text article	2008–25	18	Microsimulation	Healthy food and lifestyles policy	Projected population in 2025 (aged 25–84) of 54 million in Turkey	CVD death	Probabilistic sensitivity analyses	Validated by comparing the model-predicted CHD death rates in 2008 with observed CHD deaths (ICD-10 codes I20–I25) in 2008, stratified by age and gender
Salgado[60]	Argentina	2020	CVD Policy Model-Argentina	Full-text article	2015–24	10	Microsimulation	Sugar-sweetened beverage tax	Adult population	CVD deaths	Probabilistic sensitivity analyses	Validated for use in Argentina
Sanchez-Romero[61]	Mexico	2016	CVD Policy Model–Mexico	Full-text article			Markov chain model	Sugar-sweetened beverage tax	Mexican adults aged 35–94 years	CVD cases	Probabilistic sensitivity analyses	Validated CVD simulation model adapted to describe the population of Mexico, using multiple Mexican national data sources
Schönbach[62]	Germany	2018	DYNAMO-HIA	Full-text article	10 years	10	Dynamic population modelling	Process meat tax	Adult population	CVD cases	Probabilistic sensitivity analyses	–

continued

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TABLE 1 Characteristics of included studies (*continued*)

Study	Country	Year	Model name	Type of publication	Time period	Horizon	Type of model	Type of policy	Setting	Measurements	Sensitivity analysis	Validation
Seferidi[24]	England	2018	IMPACT Food Policy model	Full-text article			Microsimulation	Sugar-sweetened beverage tax	Adults aged 25 years or older.	CVD deaths	Probabilistic sensitivity analyses	Validated
Smith-Spangler[63]	USA	2010		Full-text article			Markov chain model	National Salt Reduction Initiative	US adults aged 40–85 years	CVD cases	One-way	–
Vega-Solano[64]	Costa Rica	2021	PRIME	Full-text article	–		Microsimulation	National Salt Reduction Initiative	Costa Rican population	CVD cases	Probabilistic sensitivity analyses	–
Wang[65]	China	2016	–	Full-text article	2010–19	10	Markov chain model	National Salt Reduction Initiative	Chinese adults	CVD cases	Probabilistic sensitivity analyses and one way	Validation is detailed in S1 File
Wilde[16]	USA	2019	CVD-PREDICT	Full-text article	–		Microsimulation	Sugar-sweetened beverage tax	US adults aged 35–85 years	CVD cases	Probabilistic sensitivity analyses	Validated microsimulation model

DALYs, disability-adjusted life years; ICD-10, *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision; NZ, New Zealand; PRIME, preventable risk integrated model; SHINE, simulations for health improvement and equity; TFA, trifluoroacetic acid.

TABLE 2 Risk of bias of included studies

Study	Year	Face validation	Internal validation	Cross-validation	External validation	Predictive validation
Asaria[25]	2007	Yes	Yes	No	No	No
Basu[26]	2020	Yes	Yes	No	Yes	No
Basu[27]	2013	Yes	Yes	No	Yes	No
Basu[28]	2013	Yes	Yes	No	Yes	Yes
Bibbins-Domingo[29]	2010	Yes	Yes	No	Unclear	No
Choi[30]	2016	Yes	Yes	No	Yes	No
Choi[31]	2017	Yes	Yes	No	Yes	No
Cobiac[32]	2017	Yes	Yes	No	Unclear	No
Collins[18]	2014	Yes	Yes	No	Yes	No
Dehmer[33]	2020	Yes	Yes	No	Yes	No
Dilley[34]	2012	Yes	Unclear	No	Unclear	No
Gillespie[19]	2015	Yes	Yes	No	Yes	No
Han[35]	2018	Yes	Yes	No	Unclear	No
Homer[36]	2010	Yes	Yes	No	Unclear	No
Hurley[37]	2008	Yes	Yes	No	No	No
Kheirbek[66]	2014	Yes	Unclear	No	No	No
Konfino[38]	2013	Yes	Yes	No	No	No
Konfino[39]	2014	Yes	Yes	No	Unclear	No
Kypridemos[21]	2017	Yes	Yes	No	Yes	Unclear
Kypridemos[20]	2018	Yes	Yes	No	Yes	Unclear
Lee[13]	2020	Yes	Yes	Unclear	Yes	No
Liu[14]	2020	Yes	Yes	No	Yes	No

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TABLE 2 Risk of bias of included studies (*continued*)

Study	Year	Face validation	Internal validation	Cross-validation	External validation	Predictive validation
Lloyd-Williams[40]	2008	Yes	Yes	No	Unclear	No
Manyema[41]	2016	Yes	Yes	No	Unclear	No
Marklund[42]	2020	Yes	Yes	No	Yes	No
Mason[43]	2014	Yes	Yes	No	Unclear	No
Mekonnen[44]	2013	Yes	Yes	No	Yes	No
Moreira[22]	2015	Yes	Yes	No	Yes	No
Mozaffarian[15]	2018	Yes	Yes	No	Yes	No
Mhurchu[45]	2015	Yes	Yes	No	Unclear	No
Nilson[46]	2020	Yes	Yes	No	Unclear	No
Nnoaham[47]	2009	Yes	Yes	No	No	No
O'Flaherty[48]	2012	Yes	Yes	No	Unclear	No
O'Keeffe[23]	2013	Yes	Yes	No	Yes	No
Pearson-Stuttard[49]	2017	Yes	Yes	No	Yes	No
Pearson-Stuttard[50]	2017	Yes	Yes	No	Yes	No
Eom[51]	2020	Yes	Unclear	No	Unclear	No
Garney[52]	2019	Yes	Unclear	No	Unclear	No
Wilde[17]	2018	Yes	Yes	No	Yes	No
Sy[53]	2018	Yes	Unclear	No	Unclear	No
Pearson-Stuttard[54]	2018	Yes	Yes	No	Yes	No
Mejia[55]	2011	Yes	Unclear	No	Unclear	No
Pearson-Stuttard[56]	2018	Yes	Yes	No	Yes	No
Peñalvo[57]	2017	Yes	Yes	No	No	No
Purshouse[58]	2010	Yes	Yes	No	Yes	No

continued

TABLE 2 Risk of bias of included studies (*continued*)

Study	Year	Face validation	Internal validation	Cross-validation	External validation	Predictive validation
Sahan[59]	2016	Yes	Yes	No	Yes	No
Salgado[60]	2020	Yes	Yes	No	Yes	No
Sanchez-Romero[61]	2016	Yes	Yes	No	Yes	No
Schönbach[62]	2018	Yes	Yes	No	Unclear	No
Seferidi[24]	2018	Yes	Yes	No	Yes	No
Smith-Spangler[63]	2010	Yes	Yes	No	Unclear	No
Vega-Solano[64]	2021	Yes	Yes	No	Unclear	No
Wang[65]	2016	Yes	Yes	No	Yes	No
Wilde[16]	2019	Yes	Yes	No	Yes	No

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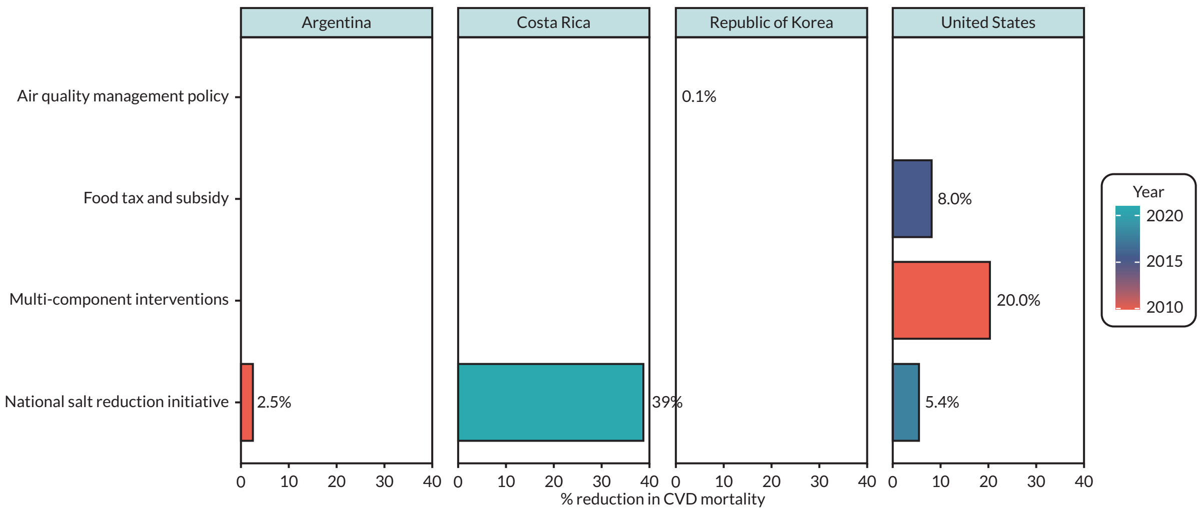

FIGURE 2 Effects of policies and structural interventions on percentage reduction in CVD mortality.

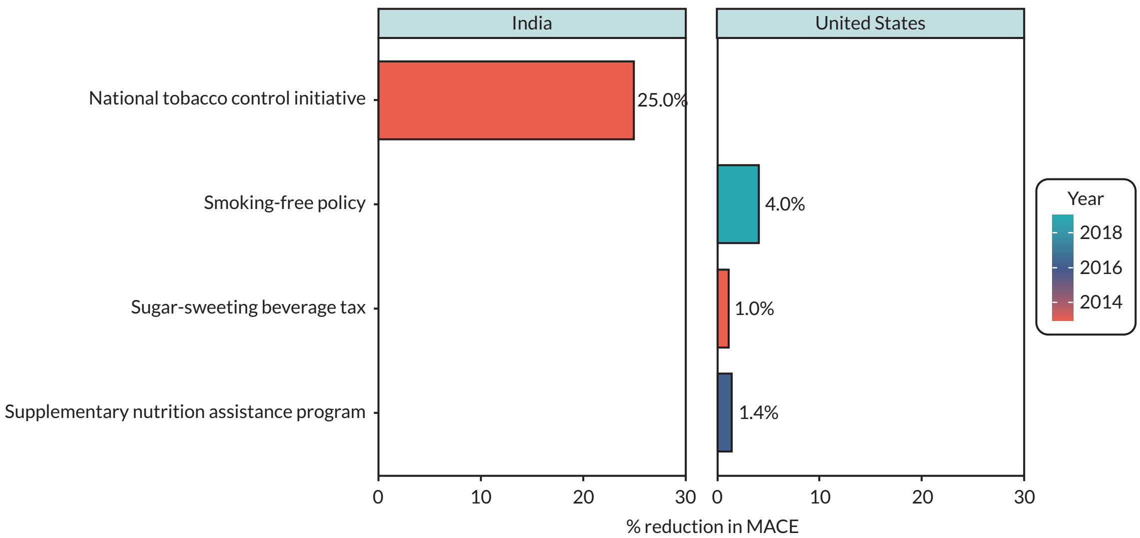

FIGURE 3 Effects of policies and structural interventions on percentage reduction in MACE cases.

performed in three studies and none of the studies did not perform predictive validation. The studies were published between 2013 and 2019 and the following policy-level interventions were modelled: national tobacco control initiative (*n* = 1), smoking-free policy (*n* = 1), SSB tax (*n* = 1) and supplementary nutrition assistance programme (*n* = 1). The reported potential percentage reduction in CVD cases ranged from 1% for a SSB tax in the USA to 25% for a national tobacco control initiative in India. Three studies modelled different interventions among the US population.[31,44,52] A smoke smoking-free policy demonstrated the largest percentage reduction in CVD cases (4%),[52] followed by a supplementary nutrition assistance programme (1.4%)[31] and a SSB tax (1.0%).[31]

Number of deaths prevented or postponed per year

Twenty-six studies reported the number of DPP per year (see *Figure 4*).[19,21–24,27,29,32,33,38–42,45–50,54,57,59,60,65,66] There were seven studies each from the USA and the UK, three from Argentina, and one each from Australia, Brazil, China, India, Ireland, New Zealand, South Africa and Turkey. One was a multicountry study. Face validation was adequate for all the studies. Internal validation was adequate in most studies (*n* = 25, 96%) and unclear in one study (see *Table 2*). None of the studies reported cross-validation. External validation of the models was performed by 14 studies (54%), not performed by 4 studies (15%) and unclear in the remaining 8 studies (31%). Most of the studies did not perform predictive validation

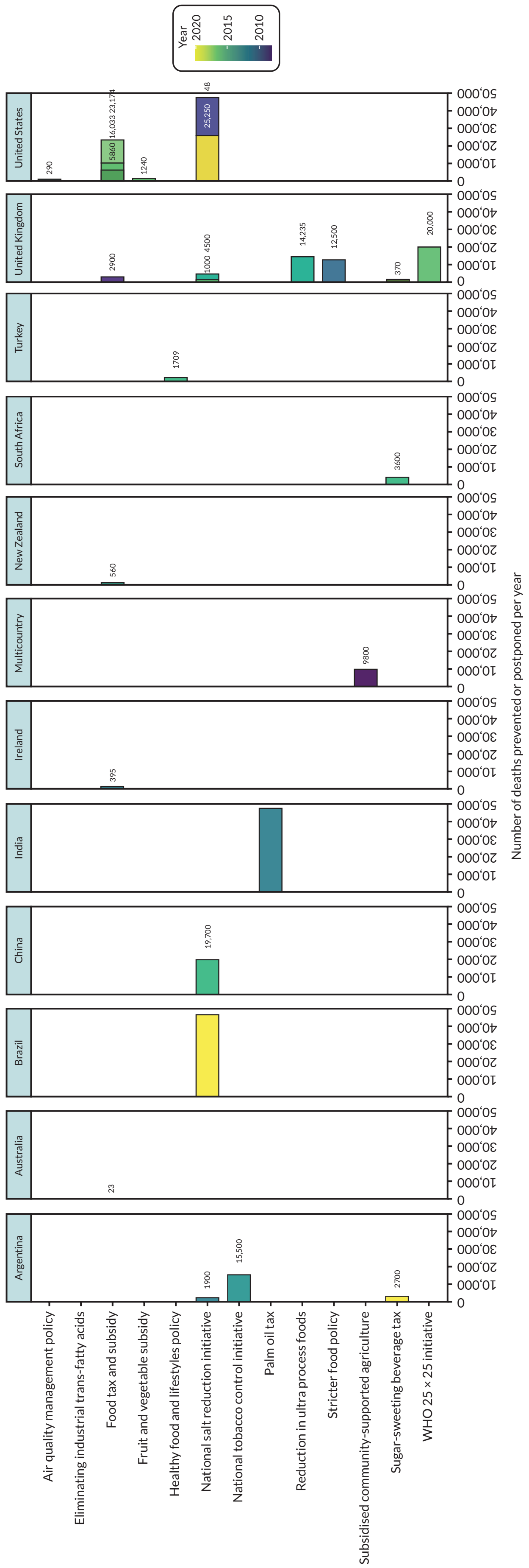

FIGURE 4 Effects of policies and structural interventions on number of deaths prevented or postponed per year.

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(n = 24, 92%). The studies were published between 2008 and 2020, and the following policy-level interventions were modelled: food tax and subsidy (n = 7), national salt reduction initiative (n = 7), food and beverage tax (n = 3), air quality management policy (n = 1), eliminating industrial trans-fatty acids (n = 1), fruit and vegetable subsidy (n = 1), healthy food and lifestyle policy (n = 1), national tobacco control initiative (n = 1), palm oil tax (n = 1), reduction in ultra-processed foods (n = 1), stricter food policy (n = 1), Subsided Community Supported Agriculture (n = 1) and WHO 25 × 25 initiative (n = 1).

The number of DPP depended on the size of population affected but ranged from just 23 per year for eliminating industrial trans-fatty acids in Australia[42] to as many as 48,000 per year for a national salt reduction initiative in the USA.[29] Evidence from Argentina[38,39,60] showed that a national tobacco control initiative could prevent or postpone the largest number of deaths (15,500 deaths per year), followed by a SSB tax (2700 deaths per year) and a national salt reduction initiative (1900 deaths per year). Evidence from the USA[29,33,49,50,54,57,66] showed that a national salt reduction initiative could prevent or postpone the largest number of deaths (48,000 deaths per year), while air quality management could prevent or postpone the least number of deaths (290 deaths per year). Evidence from the UK[19,21,22,24,32,47,48] showed that the WHO 25 × 25 initiative could prevent or postpone the largest number of deaths (20,000 deaths per year), while a SSB tax could prevent or postpone the least number of deaths (370 deaths per year).

Number of CVD cases prevented or postponed per year

Ten studies reported the number of CVD cases prevented or postponed per year (see *Figure 5*).[14,15,20,37,51,54,58,61–63] Five studies were from the USA, two from the UK, and one each from Australia, Germany and Mexico. Face validation was adequate for all the studies. Internal validation was adequate in most studies (n = 9, 90%) and unclear in one study (see *Table 2*). None of the studies reported cross-validation. External validation of the models was performed by six studies (60%), not performed by one study (10%) and unclear in the remaining three studies (30%). Most of the studies did not perform predictive validation (n = 9, 90%). The studies were published between 2008 and 2020, and the following policy-level interventions were modelled: national salt reduction initiative (n = 2), alcohol pricing policy (n = 1), fruit and vegetable subsidy (n = 1), national menu calorie labelling law (n = 1), NHS Health Check (n = 1), processed meat tax (n = 1), SSB tax (n = 1) and supplementary nutrition assistance program (n = 1). The number of CVD cases prevented or postponed ranged from just 750 per year for the NHS Health Check in the UK[20] to as many as 45,000 per year for the national salt reduction initiative in the USA.[54] Five studies modelled different interventions among the US population.[14,15,51,54,63] The national salt reduction initiative demonstrated the largest number of CVD cases prevented or postponed per year (45,000 CVD cases per year prevented), followed by supplementary nutrition

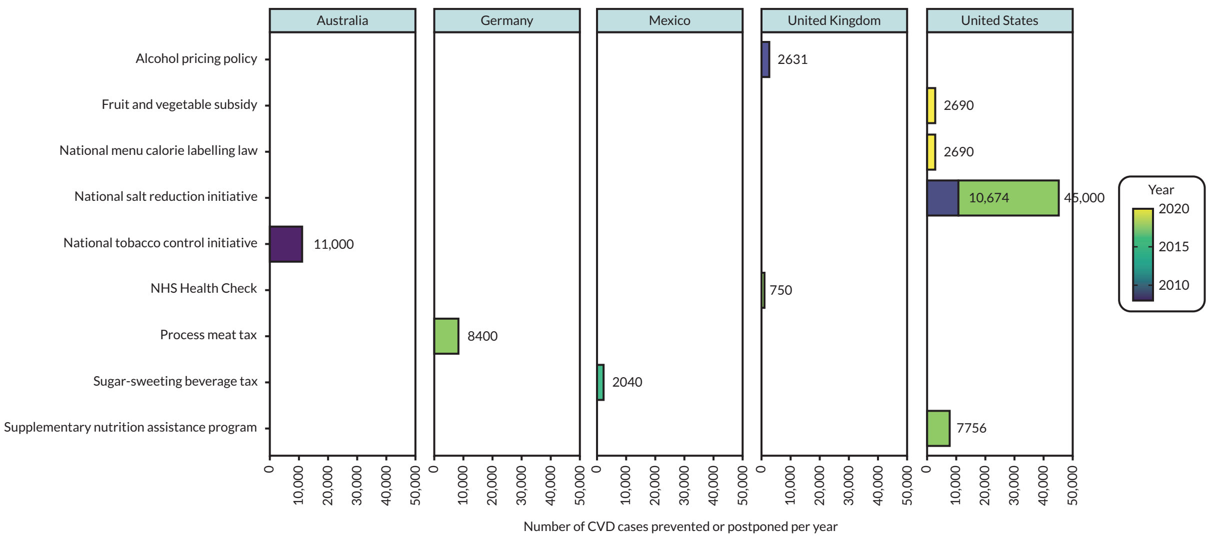

FIGURE 5 Effects of policies and structural interventions on number of CVD cases prevented or postponed per year.

assistance programmes (7756 CVD cases per year prevented), fruit and vegetable subsidies (2690 CVD cases per year prevented) and the national menu calorie labelling law (2690 CVD cases per year prevented). In the UK, a larger number of CVD cases could be prevented by alcohol pricing policy than through NHS Health Check (2631 vs. 750 CVD cases per year prevented).

Discussion

Main findings

The importance of population-level policies is becoming more widely recognised in the public health community.[67] When compared to individual-level interventions, they are more effective, cost-effective and equitable.[67] Policy-makers and the public health community must make further efforts towards shifting the focus of prevention away from individuals and towards populations.[67] Evidence about the potential benefits of a particular intervention is frequently available from a variety of sources. We included well-conducted simulation studies to examine the potential impact of structural and policy interventions at the national level. We identified 54 simulation-based studies finding that there is good evidence that population-wide strategies could reduce the burden of CVD. The modelling studies we included suggest that these interventions could bring population-wide reductions in the burden of CVD.

Diet and nutrition, tobacco and alcohol control, and other programmes are among the policy simulation models explored. The diet and nutrition initiatives included food taxes and subsidies, healthy food and lifestyles policies, palm oil tax, processed meat tax, reduction in ultra-processed foods, supplementary nutrition assistance programmes, stricter food policy and subsidised community-supported agriculture. Initiatives to reduce tobacco and alcohol use included a smoking ban, a national tobacco control initiative and a tax on alcohol. The other programmes we identified included the NHS Health Check, WHO 25 × 25 and air quality management policy. Our review shows that taxation on tobacco, salt, sugar and alcohol is the most potential impactful structural intervention to reduce CVD events and mortality at the population level.

Simulation and modelling studies are important tools in supporting evidence for the effectiveness of primary prevention of CVD.[68–71] These types of studies allow researchers to investigate the potential impact of interventions on population health, without having to conduct large, costly and time-consuming RCTs.[72] One advantage of simulation and modelling studies is that they can be used to estimate the potential impact of an intervention on a population level.[68–71] For example, a simulation study could be used to estimate the number of CVD cases that would be prevented by increasing physical activity levels in a population. This information can be used to inform public health policy and decision-making. Another advantage of simulation and modelling studies is that they can be used to investigate the impact of interventions in subpopulations that may be difficult to study in RCTs. For example, a modelling study could be used to investigate the impact of a dietary intervention on CVD risk in older adults. Simulation and modelling studies also can combine multiple interventions and assess their joint effect on population health; this is a critical aspect for primary prevention of CVD as it often involves multifactorial interventions. Overall, simulation and modelling studies are an important complementary tool to RCTs in providing evidence for the effectiveness of primary prevention of CVD.[68–71]

Strengths and limitations

This systematic review has several advantages. Firstly, our study's main strength was that we conducted a thorough up-to-date overview of the status of policy-level intervention models internationally, using search of the published literature to undertake a comprehensive review of their potential impact on primary prevention of CVD. Second, using appropriate validated tools, two reviewers independently checked all papers and assessed quality. Third, we documented the effect size used in each modelling paper, as well as the source reference. Finally, the studies included a wide range of interventions across

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a wide range of countries, providing highly useful estimates of potential impact and information to design future policies and action.

This review however has some limitations. Simulation and modelling studies are important tools in supporting evidence for the effectiveness of primary prevention of CVD, but they also have limitations that should be considered.[73–77] One limitation of simulation and modelling studies is that they rely on assumptions and estimates. For example, a simulation study may assume that a certain percentage of the population will respond to an intervention in a certain way. If these assumptions are not accurate, the results of the simulation may not be valid. Additionally, the accuracy of the simulation is dependent on the quality and availability of data used to input the model. Another limitation of simulation and modelling studies is that they may not capture all the complex interactions that occur in real-world settings. Additionally, simulation and modelling studies are mostly based on observational data, which is subject to the same limitations as observational studies. Observational studies are often excluded in systematic reviews of primary prevention of CVD due to their inherent limitations. One of the main limitations is the potential for bias, such as selection bias and confounding variables, which can make it difficult to determine causality between the intervention and the outcome.[73–77] This can make it challenging to draw valid conclusions from observational studies and make them less informative compared to RCTs which have a higher level of evidence. Moreover, observational studies are often subject to measurement errors, which can lead to inaccurate results. This can further decrease the validity and generalisability of the results.

We have been unable to undertake a formal meta-analysis because the studies were so diverse. Publication bias is still a possibility, which could lead to an overestimation of the real effects of some interventions. Furthermore, the positive effects of policy changes may appear to be greater when favourable underpinning secular trends are not formally considered. There is significant heterogeneity in simulation models, making output data significantly incomparable between models; thus, the studies in the analysis may not be necessarily comparable. While policy interventions typically include a variety of strategies, none of the models considered interrelations between multiple policies and potential interactions. Different aspects of these policies may have varying effects.

Another important limitation of the studies reviewed is that they primarily reported on major cardiovascular events, such as heart attacks and strokes, but did not report on other CVD outcomes such as cardiomyopathies. By not reporting on these outcomes, the studies may not provide a comprehensive understanding of the impact of the interventions on CVD. Furthermore, it may make it difficult to draw conclusions about the effectiveness of the interventions in preventing different types of CVD. This limitation should be taken into consideration when interpreting the results of the studies and considering the implications for public health policy and clinical practice.

Implications for future research and policy

Our research uncovered a number of evidence gaps that merit additional investigation. First, no real-world policy impact studies were uncovered. Though we discovered that policies and structural interventions aimed at reducing CVD could reduce the burden of CVD and save money if implemented over time, the feasibility of implementing policy changes also warrants further investigation. Many elements, including political feasibility and stakeholder engagement, can help or hinder successful policy formulation.

In a number of other areas, more research is required. Longitudinal studies, for example, are required to increase the evidence base and to aid in the identification of precise combinations of interventions that have the greatest impact on deaths avoided or postponed. These longitudinal studies need to be broader and more representative of target populations likely to benefit. In addition, the adoption of common measures to compare different initiatives and communities would help to boost such evaluation efforts. A standardised evaluation system across various policy-level interventions would be immensely valuable and might serve as a policy lever at the regional or national levels, inspiring greater action. Future study on the effectiveness of policy-level interventions in various populations and settings, as well as intervention effectiveness among different communities or populations with differing demography, would be beneficial. Finally, research that investigates dose–response and interactions between numerous modifications as well as longer-term clinical outcomes can help us better understand the potential impact of policy-level interventions.

Patient and public involvement

Drawing on INVOLVE guidance and support for best practice, we worked closely with three dedicated patient and public involvement advisors, and we welcomed guidance and support from our advisors during the preparatory phase of the project.

Conclusion

We found from simulation studies that there is evidence that population-wide strategies could reduce the burden of CVD. There was no RCT evidence to support effectiveness of multifactorial 'high-risk' strategies for reducing stroke and CVD incidence and mortality. Policy-makers, politicians and public health professionals should continue to work to prioritise these population-wide strategies for CVD prevention.

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Acknowledgements

Contributions of authors

Olalekan A. Uthman (https://orcid.org/0000-0002-8567-3081) (Professor, Evidence Synthesis) contributed to the protocol, study selection, data extraction, validity assessments and synthesis of the included studies. He developed the classifiers and undertook the analyses. He also contributed to the interpretation of the results and the writing of the report and had overall responsibility for the project.

Rachel Court (https://orcid.org/0000-0002-4567-2586) (Information Specialist) contributed to the protocol development, developed the search strategies, and wrote the sections of the report relating to the literature searches. She also contributed to the protocol and interpretation of the results and commented on drafts of the report.

Seun Anjorin (https://orcid.org/0000-0003-0187-6410) (Research Associate) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. He also contributed to the interpretation of the results and the writing of the report.

Jodie Enderby (https://orcid.org/0000-0002-1446-7512) (Research Associate) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. She also contributed to the interpretation of the results and the writing of the report.

Lena Al-Khudairy (https://orcid.org/0000-0003-0638-583X) (Associate Professor, Evidence Synthesis) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. She also contributed to the interpretation of the results and the writing of the report.

Chidozie Nduka (https://orcid.org/0000-0001-7031-5444) (Senior Research Fellow, Evidence Synthesis) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. He also contributed to the interpretation of the results and the writing of the report.

Hema Mistry (https://orcid.org/0000-0002-5023-1160) (Associate Professor, Health Economics) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. She also contributed to the interpretation of the results and the writing of the report.

G. J. Melendez-Torres (https://orcid.org/0000-0002-9823-4790) (Professor, Evidence Synthesis) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. He also contributed to the interpretation of the results and the writing of the report.

Sian Taylor-Phillips (https://orcid.org/0000-0002-1841-4346) (Professor, Evidence Synthesis) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. She also contributed to the interpretation of the results and the writing of the report.

Aileen Clarke (https://orcid.org/0000-0001-8299-3146) (Professor, Evidence Synthesis) contributed to the protocol, study selection, validity assessments and synthesis of the included studies. She also contributed to the interpretation of the results and the writing of the report.

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Ethics statement

This work is a systematic review of accessing, processing and analysing data that has already been published and is available to the public. As a result, no patient data were processed; and patient consent and/or registration via human research ethics committees were, therefore, not relevant.

Data-sharing statement

No new data have been created in the preparation of this article and therefore there is nothing available for access and further sharing. All queries should be submitted to the corresponding author.

Consent for publication

Not applicable.

This article

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This article reports on one component of the research award The potential impact of policies and structural interventions in reducing cardiovascular disease and mortality: a systematic review of simulation-based studies. For more information about this research please view the award page [https://www.fundingawards.nihr.ac.uk/award/17/148/05]

List of abbreviations

CHD	coronary heart disease
CVD	cardiovascular disease
DPP	deaths prevented or postponed
IMPACT	infliximab multinational psoriatic arthritis controlled trial
MACE	major cardiovascular event
MI	myocardial infarction
PSA	probabilistic sensitivity analysis
RCT	randomised controlled trial
SSB	sugar-sweetened beverage

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