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The long-term effectiveness and cost-effectiveness of public health interventions; how can we model behavior? A review

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Abstract

The effectiveness and cost of a public health intervention is dependent on complex human behaviors, yet health economic models typically make simplified assumptions about behavior, based on little theory or evidence. This paper reviews existing methods across disciplines for incorporating behavior within simulation models, to explore what methods could be used within health economic models and to highlight areas for further research. This may lead to better-informed model predictions. The most promising methods identified which could be used to improve modeling of the causal pathways of behavior-change interventions include econometric analyses, structural equation models, data mining and agent-based modeling; the latter of which has the advantage of being able to incorporate the non-linear, dynamic influences on behavior, including social and spatial networks. Twenty-two studies were identified which quantify behavioral theories within simulation models. These studies highlight the importance of combining individual decision making and interactions with the environment and demonstrate the importance of social norms in determining behavior. However, there are many theoretical and practical limitations of quantifying behavioral theory. Further research is needed about the use of agent-based models for health economic modeling, and the potential use of behavior maintenance theories and data mining.

KEYWORDS

cost effective, health behavior, inequality, mathematical models, microeconomic behavior, psychology, public health, public policy, simulation modeling

1 | INTRODUCTION

Public health interventions often aim to change human behavior, such as physical activity or dietary behaviors, yet few attempts have been made to incorporate evidence-based models of the causes of health behaviors within health economic models (Kelly, 2019; Squires et al., 2016). Bates et al. (2020) undertook a systematic review of methods to predict body mass index (BMI) trajectories in health economic models of behavioral weight-management programs. Six different assumptions were made across the included studies to estimate what would happen due to the intervention following the trial, ranging from

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assuming weight-loss is maintained over an individual's lifetime to regaining the weight immediately. These assumptions were based on no or limited evidence or theory. The authors showed that predictions about the long-term effectiveness of the intervention fundamentally affected the model results and hence may affect resource allocation decisions. It is therefore essential to base such modeling decisions upon existing theory or evidence.

Within health economic modeling, a key outcome of interest to policy makers is the difference between the comparator and the intervention(s) over the long term. Public health intervention effectiveness evidence is generally only available over a relatively short time frame (typically two or three data points over 6 or 12 months follow up) and, currently, within public health economic evaluations little attention is spent describing the causal mechanisms of the interventions that influence long-term effectiveness and cost-effectiveness (Bardach et al., 2019; Kwon et al., 2022; Leao et al., 2018; Zanganeh et al., 2019; Zhou et al., 2020). Without understanding the mechanisms of public health interventions, it becomes difficult to project effects beyond the data collection period. This is particularly important if the mechanisms of the interventions being compared are different; for example, some interventions may be more likely to result in behavior maintenance or changing social norms than others.

Kelly et al. (2005) suggest that from a policy perspective it is important for a model to address what aspects of an intervention make it successful or unsuccessful, in order to help decision-makers understand whether interventions may be generalizable in other settings, since public health interventions generally interact with their context. The causal mechanisms of public health interventions are non-linear and dynamic, with much evidence that behavior is influenced by social networks and the environment (Christakis & Fowler, 2007, 2008; Saarloos et al., 2009), yet health economic models typically focus upon the non-interacting individual in a vacuum.

Standard methods of extrapolation applied for the assessment of clinical interventions are thus generally not feasible for public health interventions due to data limitations, and may not be appropriate due to: (i) the non-linear impacts of influences upon behavior over time; and (ii) the types of questions policy makers want to answer, for example, who should be targeted with this intervention for it to be effective and cost-effective and to reduce inequalities?

The aims of this review are therefore to identify existing methods that have been used across disciplines for incorporating health-related behaviors within simulation models, and to assess which methods could usefully be applied within health economic models. The purpose is to lead to better-informed model predictions to support the fair allocation of scarce healthcare resources. More specifically, the objectives are to:

- (1) identify the range of methods for incorporating potential causes of behavior into simulation models across disciplines;
- (2) identify how behavioral theories have been incorporated within simulation models;
- (3) assess the advantages and limitations of each method and theory;
- (4) consider the relevance and feasibility for application to health economic modeling; and
- (5) highlight areas for further research.

2 | METHODS

2.1 | Stage 1: Iterative literature search

Stage 1 of the review involved an iterative search strategy, where the reviewing process was used to enhance understanding, rather than having a narrowly defined set of methods to review a priori. This is because some methods may have been unknown to the authors at the outset, so it was important that the literature search was sufficiently broad to be able to identify all potentially relevant methods for incorporating potential causes of health-related behavior within simulation models. As such, key behavioral operational research (Barnabe & Davidsen, 2020; Kunc et al., 2016), behavioral economics (Kahneman, 2012; Thaler, 2016), health economics (Bates, 2021; Kruger et al., 2012), computational science (Adibuzzaman, 2020; Coveney, 2016), public health (Kelly, 2019; Skivington et al., 2021), sociology (Bianchi & Squazzoni, 2015; Gilbert, 2020) and psychology literature (Michie et al., 2014) were explored to provide an initial broad understanding. Citation searching, reference searching and key author searching was used to inform subsequent iterations. Through this searching process, a range of methods were identified and were critically reviewed.

Stages 2 and 3 of the review involved investigating agent-based modeling (ABM) and the quantification of behavioral theory in more depth via formal literature searches because of the potential of these methods for incorporating behavior within health economic models of public health interventions, identified from stage 1.

2.2 | Stage 2: Search for agent-based modeling reviews applied to public health

The goal of this search was to understand the current state of the art for incorporating behavior within ABMs applied to public health topics. Agent-based modeling is an individual-level simulation approach which uses “rules” to define the interactions between agents and their environment (Gilbert, 2020). A key advantage to this approach is that individual decision-making can be programmed, including how this impacts on, and is impacted upon, by social networks and spatial elements. Due to the large number of ABMs that have been developed, a search for reviews of ABMs applied to public health behaviors was undertaken, using terms for ABMs and public health behaviors. This was limited to reviews published since 2014 since the current state of the art would not be captured by earlier reviews. Papers identified during stage 1 of the review which discussed methodological challenges of using ABMs were also drawn upon where they provided additional relevant information.

2.3 | Stage 3: Search for simulations incorporating behavioral theory

The goal of this search was to understand how behavioral theories have been quantified within simulation models. Behavioral theories attempt to explain why, when and how an intervention does or does not change behavior, and may draw upon psychology, sociology, anthropology and/or behavioral economics (Michie et al., 2018). Incorporation of such theories within health economic models could help decision makers to understand the potential generalizability of the impact of an intervention and to decide which subgroups to target with an intervention, as well as helping to explore the long-term impacts of interventions. Existing known case studies utilizing psychological variables within population health and healthcare models (Bates, 2021; Brailsford & Schmidt, 2003; Kruger et al., 2012; Purshouse et al., 2014) were used to help inform a broad formal search for simulation case studies utilizing behavioral theories for health-related behaviors, using search terms for behavior, theory, individual-level simulations and health. Studies were included if they reported health-related simulations incorporating some theory for describing behavior, with some element of individual decision-making. Studies of non-individual level model types were excluded since these are less flexible for incorporating heterogeneity and answering policy questions about whom to target with an intervention. In addition, studies were excluded if events were based only on global probabilities (e.g., individual infection based only on a probability), or if the theories were not incorporated within a simulation model (e.g., based on an experimental study).

For all stages of the review, all of the retrieved literature was screened at title and abstract level for potential relevance, and full papers were retrieved where insufficient detail was provided within the abstract to determine potential relevance. The search was completed in April 2022. The full search strategy is shown in Supplementary Material S1. For all included papers, a data extraction form was used which was developed based upon the aims of the review, in order to inform a narrative synthesis of the literature.

3 | RESULTS

The results of the searches are shown in Figure 1.

The results are arranged into two cross-cutting themes: the methodological approaches identified (drawing upon all identified studies) and the application of behavioral theory within simulation models (based upon stage 3, the 22 included studies from the behavioral theory search).

3.1 | Methodological approaches

3.1.1 | Econometric techniques within simulation models

Econometrics uses statistical techniques, underpinned by a behavioral theory, to assess economic relationships. Several simulation models have included the relationship between price and consumption using regression analysis, where changes to pricing strategies have been an intervention of interest (Basu et al., 2014; Purshouse et al., 2010). This regression analysis requires data on purchasing and consumption by relevant subgroups as well as price elasticities of demand. It is limited by the variables included within the regression equation, and assumes that consumption can mainly be explained by price, controlling for socio-demographic factors.

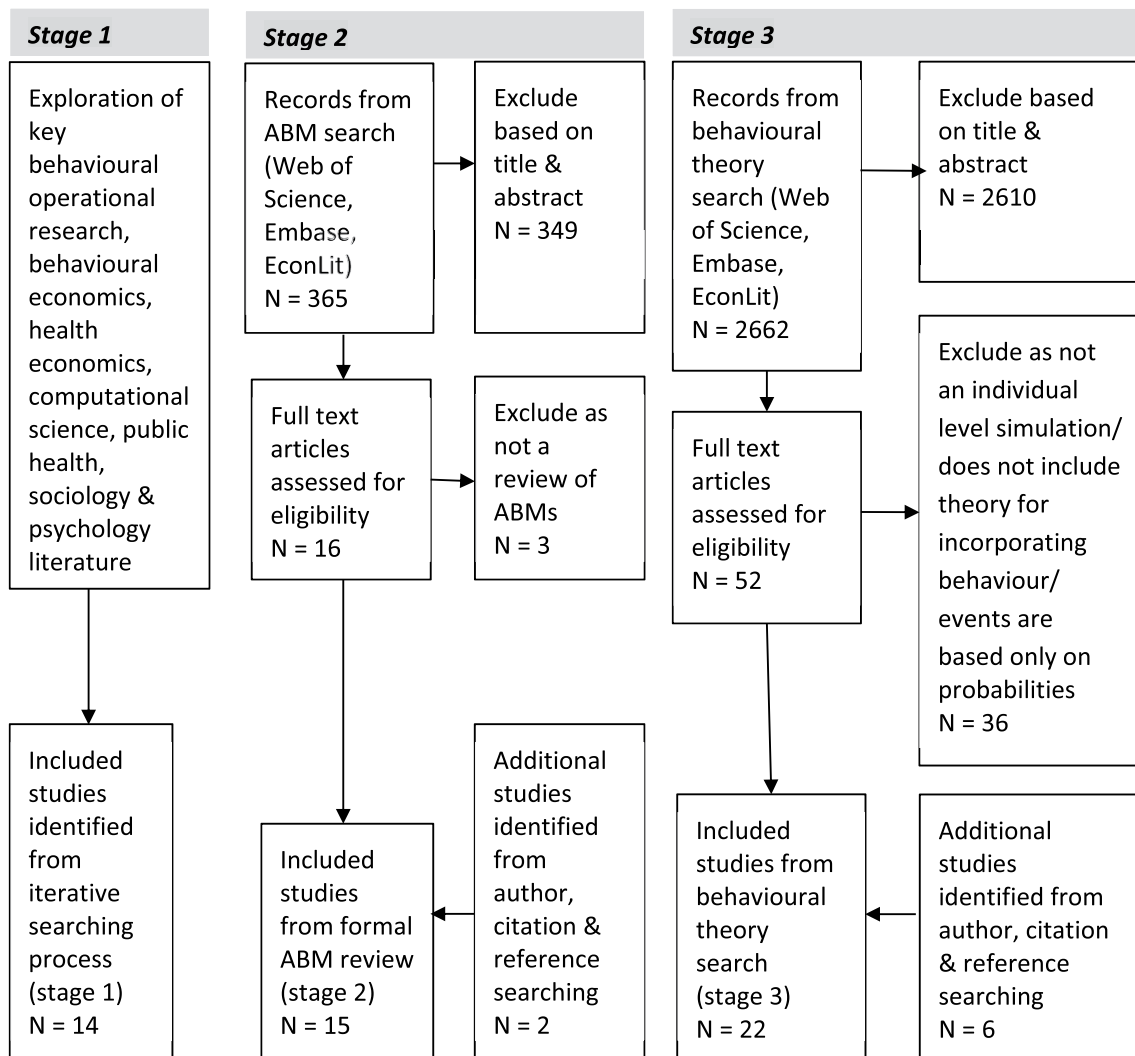


FIGURE 1 PRISMA diagram of search strategy.

Sullivan explored the importance of relationships between two health behaviors for an economic evaluation of behavior-change strategies using econometric techniques and rational choice theory, focusing on a case study between smoking cigarettes and drinking alcohol (Sullivan, 2014). The author used a longitudinal data set because it has been shown that past alcohol (smoking) use is associated with current alcohol (smoking) use. Modeling the relationship between these two behaviors is being explored further within an ongoing research program by Gillespie et al. (2021). This work suggests that it is important to consider whether there are other behaviors which either influence or are influenced by the behavior of interest that should be included in a health economic model. However, relevant datasets would need to include variables for each behavior. All other studies within this review consider a single behavior in isolation.

3.1.2 | Structural equation modeling applied within microsimulations

Structural equation modeling (SEM) includes a set of methods which use statistical models to assess the causal relationships between a set of unobservable (latent) and observable variables (Beran & Violato, 2010). They involve setting out the expected structural relationships between these variables using a path diagram, and then testing the relationships (and the hypothesized overall model) using statistical analyses. One such method is latent growth curve modeling, which was used by Bates (2021) to explore the relationship between weight-reduction interventions and BMI via psychological mechanisms of action (dietary restraint, habit strength, autonomous diet self-regulation). A review by the authors showed that other studies included only two data points, thus assuming a linear relationship. The authors allowed non-linear modeling of the relationships by using four

time points from a randomized controlled trial of the interventions. They described the relationships being explored using a path diagram and the analyses showed that dietary restraint, habit strength and self-regulation were found to moderate the relationship between the interventions and BMI; that is, the psychological variables could explain the decrease in BMI resulting from the interventions. The model did not explicitly include the modifiable behaviors. The authors subsequently incorporated the psychological variables and their relationship with the interventions and BMI within a health economic microsimulation of diabetes and CVD prevention. This is a novel approach and an important advance in the use of psychological variables to explain outcomes of behavioral interventions within a health economic model. It allows modeling of the relationship between the interventions and BMI at the individual level; however, it did not draw upon existing behavioral theories, and the authors highlight that the three psychological variables collected within the trial may not fully explain weight loss. It would therefore be beneficial to understand which variables can explain weight loss a priori based upon an existing theory, although the analysis would be dependent upon data availability. In this case study, the results suggested no predictive advantage to incorporating the psychological mechanisms; however it does enable subgroup analyses to be performed in terms of the included mechanisms, which could inform intervention targeting. Such analyses may also be used for pre-trial modeling.

3.1.3 | Behavioral system dynamics modeling

System dynamics models capture the “stocks” (a quantity of a variable at a given point in time) and “flows” (rates of change of the stocks), including positive and negative feedback loops within a system over time, to capture the behavior of the system. A systems map, or causal loop diagram, of these elements is developed, before they are quantified using differential equations within a simulation model. Such models can represent the physical world relevant to the decision problem, as well as the behavior of the actors within the system. The relationships between the variables can be used to incorporate the fact that decisions within one part of the model will not be based upon full information of the entire system, thus incorporating bounded rationality (Serman, 2000). System dynamics models have been used to replicate human behavior and decision making (Barnabe & Davidsen, 2020). However, system dynamics models are a cohort-modeling approach. Since one of the goals of public health decision making is to reduce inequities between individuals, it may be useful to incorporate a relationship between demographic and socioeconomic characteristics and behavior, as well as being able to report outcomes by these subgroups. Subgroup-stratified system dynamics would be possible, although as the number of subgroups of interest increases the more cumbersome this type of modeling would be. Moreover, within any dynamically complex system, the heterogeneity between individuals is important in determining outcomes, and thus being able to model this heterogeneity and interactions between individuals is beneficial (Weston et al., 2018). It is possible to incorporate these elements within a differential equation model (e.g., Luo et al. (2018)), although this would require substantial mathematical expertise to formulate appropriately, and these types of models lend themselves less well to incorporating geographical data and other types of Big Data.

3.1.4 | Agent based modeling (ABM) and social network analysis

Compared with model types typically employed in health economic modeling, the key advantage of ABM is that individuals can interact with each other and with their environment. Within dynamically complex systems, these interactions can lead to unexpected macro level patterns of behaviors that are difficult to predict. Public health behaviors have been shown to influence each other (Christakis & Fowler, 2007, 2008), and ABMs can incorporate these influences, including potential tipping points where a behavior becomes an accepted social norm. In addition, heterogeneity about the individual's environment can be incorporated, which could inform intervention targeting, since the effectiveness of public health interventions is highly dependent upon context (Skivington et al., 2021).

Fifteen reviews of ABMs or systems simulations related to public health behaviors were identified (Duan et al., 2015; Frerichs et al., 2019; Giabbanelli & Crutzen, 2017; Ku, 2019; Langellier, Bilal, et al., 2019; Langellier, Yang, et al., 2019; Li et al., 2016; Lorig et al., 2021; Morshed et al., 2019; Nianogo & Arah, 2015; Smith et al., 2018; Tracy et al., 2018; Willem et al., 2017; Xue et al., 2018; Yang, 2019) and an additional four ABM methodological papers from the iterative search process were drawn upon (Balke, 2014; Christakis & Fowler, 2007, 2008; Will et al., 2020). Of the 15 ABM reviews identified, four included infectious disease transmission (Duan et al., 2015; Lorig et al., 2021; Smith et al., 2018; Willem et al., 2017), five included obesity or related behaviors (Frerichs et al., 2019; Giabbanelli & Crutzen, 2017; Langellier, Bilal, et al., 2019; Morshed et al., 2019; Xue et al., 2018), one included mental health behaviors (Langellier, Yang, et al., 2019), and five considered behaviors related to non-communicable diseases (Li et al., 2016; Nianogo & Arah, 2015; Yang, 2019) or public health

more generally (Ku, 2019; Tracy et al., 2018). In all areas, the use of ABM has gradually increased over the past decade, with hundreds of infectious disease transmission models developed, particularly more recently with COVID-19, whilst between three (mental health) and 22 (diet) ABMs have been developed for non-communicable behaviors. The models are mainly US-based.

The behavioral rules of the agents

Several (non-mutually exclusive) approaches for the behavioral rules were identified within the reviews:

- 1) utility maximization (the weighted combination of a set of criteria for choosing between options);
- 2) econometric analyses for modeling the relationship between price and consumption;
- 3) game theory (mathematical theory to describe outcomes when multiple people are cooperating or competing for a payoff);
- 4) fixed behavioral patterns based on empirical data or schedules of the agent type;
- 5) behavior change is more likely, or occurs if some threshold is exceeded, depending on number of contacts, (perceived) behavior of contacts and/or distance to location, as well as other variables such as past experience and sociodemographic characteristics;
- 6) follow-the-average, where behavior is adjusted to the average behavior of the social network or model population;
- 7) other heuristics for decision making, based on price, distance, habits, preferences and/or neighbor behavior;
- 8) quantified behavioral theory;
- 9) using existing cognitive architectures which focus upon the inner workings of the brain.

The first three of these approaches assume individuals are rational, assessing all relevant options and able to determine the best one based on some criteria. The remainder assume bounded rationality, which may be more appropriate within public health systems, since evidence suggests people use simple heuristics to make decisions in complex systems (Kunc et al., 2016). Balke T. (2014) set out different architectures for ABMs, from simple If...Then... rules to normative architectures and cognitive architectures, and they suggest that for models of habitual human behavior (which public health behaviors generally are), hybrid approaches which allow for heuristics to override deliberation may be the most suitable approach. It has also been shown that peer influence and social norms are important in determining behavior, and the “follow-the-average” heuristic inherently incorporates social norms, although they can also be included within all other approaches, excluding fixed behavioral patterns. The majority of the ABMs assumed that behavior was affected by the influence of their neighbors.

It is not always explicit what evidence the rules are based upon, but evidence includes secondary literature, survey data (including contact patterns), statistical analyses/data mining of Big Data, formal qualitative research, engaging stakeholders in participatory modeling which may include fuzzy cognitive mapping, and expert elicitation.

Social and spatial networks

The ability to capture influences on behavior from other individuals is one of the key advantages of an ABM. Some of the ABMs did not incorporate explicit networks, assuming random interactions within the population (Lorig et al., 2021). This may be appropriate for exploratory analyses to begin to understand a system, but it would not provide good predictions as is expected within health economic modeling; in the real world it has been shown that a few people have lots of contacts whilst most people have few contacts in their networks (Lopez et al., 2020).

The reviews highlighted two main types of networks that could influence behavior in different ways: physical/spatial networks and information networks. These were implemented by: assuming a random probability of interaction between all agents; using simple random networks, scale free networks (where a few people are connected to lots of individuals), small world networks (most individuals are linked by short pathways of connections), gravity models (estimates agent interaction between two locations based on population size and distance between the two locations), transportation network data, or based on individual-level data from social questionnaires, diaries and wearable sensors. The majority of studies only included one network type, and this was often dependent on which types of interventions were being modeled (Lorig et al., 2021). Most networks were static, but a small number of studies allowed networks to change over time (Morshed et al., 2019; Wrzus et al., 2013; Xue et al., 2018), as would occur in the real world. It has been shown that behavior is affected both by selection of friendships with people who have similar characteristics and the influence of peers (McMillan et al., 2018).

Social network analysis, which uses longitudinal statistical models based on individual level data, has been used to explore the spread of health behaviors and associated outcomes within a population (Christakis & Fowler, 2007, 2008), and this be incorporated within an ABM. Yang (2019) suggests that more realistic social networks can be used to understand which people within the network to target with the intervention to maximize benefits. However, Morshed et al. (2019) reported that there have been mixed results about whether targeting highly connected individuals is better than random targeting within the

population. Health economic models considering alternative targeting policies within a network would be useful to help policy makers decide the most cost-effective group for whom to deliver interventions given scarce resources.

The physical environment

Large scale ABMs have been developed using census data and/or Geographic Information Systems (GIS) to represent geographical areas, mainly for infectious disease modeling (Duan et al., 2015), to enable the assessment of the impact of interventions changing aspects of the physical environment. Frerichs et al. (2019) undertook a scoping review of simulation modeling of the built environment and physical activity, and found that of 16 studies, only 7 were real-world applications (5 US, 1 France, 1 Colombia). Whilst the incorporation of the physical environment within ABMs of public health interventions has received relatively little attention, this is not due to data limitations. Giabbanelli and Crutzen (2017) state that there are spatial datasets of food behaviors which have been used in geography, but have had little use in public health to date, and some datasets also provide travel diaries, which describe how individuals interact with their food environment. The authors also highlight that the University of Cambridge's Fenland Study dataset includes thousands of participants who have worn a GPS for 1 week. They suggest that this could be combined with a GIS using the Points of Interest data collected in England to provide a pre-programmed pathway of activity for agents to follow. The behavior change literature highlights the importance of the physical environment on habits (Kwasnicka et al., 2016), and hence, this could be an important program of research, however, to our knowledge this has not yet been applied in practice.

3.1.5 | Data mining

Data mining techniques can be used within large individual level datasets to extract patterns from the data, including relationships between individual characteristics, environmental variables and health behaviors. In this way, data mining methods have been used to derive the rules of the agents within ABMs (Giabbanelli & Crutzen, 2017). In contrast with SEM which requires hypotheses about the relationships between variables, data mining analyses are generally not grounded in theory. Hence whilst patterns may be found in that dataset, they may be found by chance and could not be generalized. However, Giabbanelli and Crutzen (2017) state that rules obtained from datasets can be combined with rules informed by theory, as well as calibration to travel diaries and surveys for example, which would overcome this limitation. Neural networks are a type of data mining technique which allow data to be classified into categories, and these have been used to predict whether behavioral intention will or will not be exhibited based upon psychological factors, past experience and social influence (Orr et al., 2013). Data mining techniques, alongside the use of theory, have the potential to help make use of Big Data to inform health economic models.

3.2 | The application of theory within health-related simulation models

Twenty-two simulation case studies formally incorporating behavioral theories within health-related simulation models were identified, the majority of which utilized ABMs.

3.2.1 | Theories

Table 1 shows the theory used for each behavior type in the models, divided into normative, (simple) cognitive and neurologically-inspired models, as categorized by Balke T. (2014). Given that Michie et al. (2014) identified 83 behavior change theories which could be used for intervention development, Table 1 shows that the simulation studies have utilized only a small proportion of these theories. Most studies provide little justification within the paper for the theory used, although there are some exceptions to this.

Four studies used models which allowed the incorporation of social norms and assumed rational behavior (Andrews & Bauch, 2015; Chao et al., 2019; Du et al., 2021; Pakravan & MacCarty, 2021). Chao et al. (2019) have modeled smoking behavior using utility maximization, where an individual's choice to smoke is determined by their individual utilities associated with smoking/not smoking, and the prevalence of smoking in their close network and in the population, weighted by their attitude toward conventional and electronic cigarettes. Each cycle the smoking status of each agent is updated to influence each agent's behavior within the next cycle. Similarly, within the model by Pakravan and MacCarty (2021), if the number of people who have adopted clean technology in the person's network is below some threshold, then the person does some rational utility

TABLE 1 Theories quantified within simulation models.

Theory	Behavior								
	Infectious disease prevention	Alcohol	Smoking	Physical activity/healthy eating	Cancer screening	Child mal-treatment	General public health behavior	Adoption of clean technologies	Advance care planning behavior
Normative theories									
Subjective expected utility theory	Andrews & Bauch, 2015		Chao et al., 2019					Pakravan & MacCarty, 2021	
DeGroot learning	Du et al., 2021								
Social norm theory		Probst et al., 2020							
		Vu et al., 2019							
		Vu, Probst, et al., 2020							
Role theory		Vu, Probst, et al., 2020							
		Vu, Buckley, et al., 2020							
Cognitive theories									
Health belief model	Karimi et al., 2015				Brailsford and Schmidt, 2003				
Theory of planned behavior	Pirolli et al., 2020	Purshouse et al., 2014			Brailsford et al., 2012	Hu & Keller, 2015		Pakravan & MacCarty, 2021	
		Buckley et al., 2022							
Theory of reasoned action							Orr et al., 2013		
							Orr & Plaut, 2014		
Self-efficacy theory						Hu & Keller, 2015			
Transtheoretical model				Garcia et al., 2018					Ernecoff et al., 2016
Continuous opinions and discrete actions model				Garcia et al., 2018					
PECS architecture					Brailsford & Schmidt, 2003				

TABLE 1 (Continued)

Theory	Behavior								
	Infectious disease prevention	Alcohol	Smoking	Physical activity/healthy eating	Cancer screening	Child mal-treatment	General public health behavior	Adoption of clean technologies	Advance care planning behavior
Non-specified cognitive theory	Guo et al., 2015								
Neurologically inspired theories									
Cognitive architecture for example, ACT-R	Lopez et al., 2020 Pirolli et al., 2020								
Dual process theory		Buckley et al., 2022							

maximization to determine whether or not to adopt. The utility maximization function is based on the Theory of Planned Behavior, which is discussed in more detail below. Andrews and Bauch (2015) used subjective expected utility theory to model whether each individual decides to adopt a non-pharmaceutical intervention (NPI) (e.g., social distancing) and vaccination given their perception of influenza prevalence and susceptibility. The total utility is the weighted sum of utilities for becoming infected and vaccinated, and for behavior that is perceived to inhibit disease spread and lead to infection of a neighbor. Whilst these models attempt to incorporate the dynamic nature of individual behavior and population-level/neighbor behavior, all individuals are assumed to be rational and have the same ethical beliefs and access to information, which are likely to be far too simplistic for modeling public health interventions effectively.

Du et al. (2021) base an agent's opinion of infection risk upon (i) global information, (ii) social media (using the DeGroot model where opinions are updated according to communication with other connected agents); and (iii) neighbor observations (average of whether neighbors are infected, weighted by the influence of each other agent on the agent), weighted by region, time and agent. The Widrow-Hoff machine learning rule, where the difference between the agent's past opinion and new information on epidemic risk is weighted by their willingness to change their opinion given new information, is used at each time step. This model allows opinions to influence behavior which influences outcomes which influences opinions. However, it does not include any cognition of the agents.

The most used theory within the identified studies was the Theory of Planned Behavior. This links attitude, subjective norms and perceived behavioral control to behavioral intentions (Ajzen, 1991). The advantage of this theory is that it has been widely tested and is relatively simple. Brailsford et al. (2012) chose the Theory of Planned Behavior to model cancer screening attendance based on a literature review of predictive behavioral theories which could be applied to health, which showed it is a popular model where relationships between the variables are clearly defined. In addition, it has been used to model alcohol consumption (Purshouse et al., 2014), child maltreatment (Hu & Keller, 2015) and adoption of clean technologies (Pakravan & MacCarty, 2021). However, it has been criticized within the psychology literature because the four constructs have been shown to be insufficient to explain behavior (Sniehotta et al., 2014). Buckley et al. (2022) attempt to address this using Dual Process Theory, where there is a conscious reflective system and an automatic impulsive system, by including a “habitual” pathway and an “intentional” pathway. The intentional pathway is based on the Theory of Planned Behavior, whilst the habitual pathway updates the probability of drinking based on the person's history of drinking. Each individual has an “automaticity” parameter which determines how likely they are to follow their intentions versus their existing habits. This is consistent with much of the psychology literature which describes a reflective and habitual process (Kahneman, 2012). Similarly, whilst Hu and Keller utilize the Theory of Planned Behavior to model child maltreatment, they combined it with Self-efficacy Theory (an individual's belief in their capacity to undertake a behavior effectively (Bandura, 1997)) and models of parenting stress (Hu & Keller, 2015). This paper clearly describes why these theories were chosen, based on the literature and input from domain experts, and attempts to model the gap between intention and behavior.

Orr and Plaut (2014) aimed to provide a proof-of-concept that “quantum health behavior” that is, behavior that is governed by dynamic non-linear processes that are difficult to predict, can be conceptualized in terms of cognitive science (individuals with mental constructs), health behavior theory (using the Theory of Reasoned Action as an exemplar) and complex systems (ABM). However, the health behavior theory used is the Theory of Reasoned Action, which was a predecessor to the Theory of Planned Behavior but without perceived behavioral control, hence has been subject to criticism about its predictive ability. Within another study, Orr et al. (2013) also used artificial neural networks to determine whether or not an individual will exhibit a behavioral intention, which was a novel approach; however this was also based on the Theory of Reasoned Action.

Karimi et al. (2015) chose the Health Belief Model to model vaccination and social distancing behavior because it is an established theory. The Health Belief Model links perceived susceptibility and severity of disease, and perceived benefits and barriers of a behavior, as well as a cue to action with the adoption of a behavior (Rosenstock et al., 1988). Brailsford and Schmidt (2003) combined the Physical conditions, Emotional state, Cognitive capabilities, and Social status (PECS) architecture with the Health Belief Model to model cancer screening attendance, with the physical, emotional, cognitive and educational status of the individuals in the model affecting their perceptions and cues to action. These measurable individual characteristics could be used to help inform intervention targeting to encourage screening attendance by those that would otherwise be expected to be non-attenders. However, as Brailsford et al. (2012) state, the relationship between the variables within the Health Belief Model are not clearly defined, hence there is substantial structural uncertainty within the mathematical model.

Enecoff et al. (2016) use the Transtheoretical Model of behavior change for Advance Care Planning. Within this model there are 4 stages: (1) Precontemplation; (2) Contemplation; (3) Preparation; and (4) Action-maintenance, and individuals can progress and regress between them. This allows for the incorporation of behavior maintenance and relapse, and for different interventions to be given/have different efficacy at different stages. The Transtheoretical model has been widely used as a theoretical framework, however like the Theory of Planned Behavior, health psychologists have criticized it, partly because of

the poor relationship between contemplation/preparation and behavior change, as well as the focus upon conscious decision making and planning rather than habits and situational determinants of behavior (West, 2005). Ernecoff et al. (2016) do attempt to incorporate these situational determinants by including the influence of barriers and facilitators of the behavior within the ABM; however, they do not incorporate a habitual pathway within the model.

Garcia et al. (2017b) and Rahmani et al. (2021) present conceptual models of leisure time physical activity and healthy eating behaviors based upon an iterative process over 2 years of literature reviewing and input from an expert group of multi-disciplinary experts across multiple countries. These studies highlight the importance of undertaking conceptual modeling to understand the complex relationships associated with these public health behaviors and they set out a transparent and systematic framework for conceptual modeling of these behavioral models. Garcia et al. (2018) also present the implemented ABM based upon the conceptual model, which merges several behavioral theories. Guo et al. (2015) define a mathematical function of the relationship between individual cognition and external information and self-awareness to model influenza prevention behavior; however the paper does not explain the basis upon which the mathematical function was developed.

There are three studies which attempt to model the internal mental processes which lead to a behavior (Buckley et al., 2022; Lopez et al., 2020; Pirolli et al., 2020). As described previously, Buckley et al. (2022) use Dual Process Theory to model an intentional and habitual pathway, with an automaticity parameter to determine which pathway is followed, which helps to close the intention-behavior gap. Lopez et al. (2020) use fuzzy cognitive maps to model mental processing for individual infectious disease prevention behavior. The authors highlight that human behavior is affected by a combination of factors including media, communication, emotions and perceptions, and that neurologically-inspired architectures have been developed to imitate the dynamic between these. Within a case study in the paper, the authors use a model by Mei et al. (2014) which linked primary, secondary and senior emotions and information acquired from the agent's neighborhood to individual behavior. Within this paper, however, the benefit of including this detail is unclear.

Pirolli et al. (2020) use the Adaptive Control of Thought—Rational (ACT-R) architecture which is a computational formulation of the inner workings of the brain and the Theory of Planned Behavior “to develop psychologically valid agents” for COVID-19 infection reduction. The authors state that this enables interventions to be targeted at specific individuals or groups, which became particularly important during the coronavirus pandemic. However, the necessity to model this complexity in order to target interventions at specific (groups of) individuals will be dependent upon the goals of the model and data availability.

3.2.2 | Data, calibration and validation

The identified studies spanned from proof-of-concept based on theory and no or very limited data (Brailsford & Schmidt, 2003; Du et al., 2021; Ernecoff et al., 2016; Hu & Keller, 2015; Orr et al., 2013; Orr & Plaut, 2014) to models which were based upon both substantial data and theory (Brailsford et al., 2012; Buckley et al., 2022; Karimi et al., 2015; Pakravan & MacCarty, 2021; Probst, 2018; Purshouse et al., 2014; Vu et al., 2019; Vu, Buckley, et al., 2020; Vu, Probst, et al., 2020). The proof-of-concept studies were used to demonstrate that it is feasible to undertake such analyses, to build understanding, and/or to recognize data requirements for such a model. For example, Hu and Keller utilized substantial theory and stakeholder input to develop their ABM; however the parameters were not evidence-based (Hu, and Keller, 2015). They state that future work is to calibrate and validate the model with real data. Most of the simulations used secondary literature to inform some model parameters.

Where individual-level datasets were utilized, they were from the UK or the US, including: The Health Survey for England; British Household Panel Survey; The Offending, Crime and Justice Survey (UK); the National Youth Tobacco Survey (US); Behavioral Risk Factor Surveillance System (US); US National Alcohol Survey; and COVID-19 datasets. Most studies which utilized an individual-level dataset did not describe why they used that particular dataset or how it was identified. Survey data do not always report the exact variables needed for the behavioral theories, and hence proxy variables were required within many of the studies. For example, Purshouse et al. (2014) used the Theory of Planned Behavior, but subjective norms were represented by the number of types of people with which a person drinks, whilst perceived behavioral control was represented by the number of locations at which the person drinks. Weights in the logistic regression linking attitude, norms and controls to intention were calibrated using 7 years of data from the Health Survey for England, with an additional year of data used for validation of the model prediction for the same year. This was the first published simulation study identified by this review attempting to utilize data to both calibrate parameters of a behavioral theory and then validate the prediction made by the model. The later alcohol modeling studies (Buckley et al., 2022; Probst et al., 2020; Vu et al., 2019; Vu, Buckley, et al., 2020; Vu, Probst, et al., 2020) build upon this work with similar calibration and validation approaches.

In most studies where survey data was available, linear or logistic regression models were used to fit the relationship between psychological variables and the behavior. However, Vu et al. (2019) explore alternative forms of the relationship between

variables associated with social norm theory by modelers stating where the structural relationships between the variables are uncertain and specifying the space of possible alternative relationships. Alternative model structures were then systematically computationally tested for fit to the specified outcomes within the calibration. The model was a much better fit to the data when social norms were included, suggesting it is important to include social norms in such models. Vu, Probst, et al. (2020) also developed an object-oriented architecture using Unified Modeling Language (UML), which allows the incorporation of multiple psychological theories, with the ability to test alternative model parameters and structures. The authors present a case study which uses social norm theory and role theory to show how social mechanisms can be represented, compared and integrated in order to attempt to explain population level behavior. These methods are comprehensive, although they require substantial computational time to run the calibration and alternative model structures. Notably, none of the studies use SEM to represent theory within their models.

Some studies collected data to inform the modeling as part of the project. Karimi et al. (2015) collected survey data to parameterize the Health Belief Model which was incorporated within the ABM. The authors collected data on students' perceptions of influenza and the factors that impact individual intention to engage in vaccination and social distancing behaviors, with and without the intervention (an educational program). Similarly, Pakravan and MacCarty (2021) undertook a survey of households to inform the Theory of Planned Behavior parameters for their model of adoption of clean technologies. These surveys had smaller sample sizes than the individual-level datasets; however it meant they had the exact data needed for model development, and could understand the impact of the interventions, being assessed, though they did not discuss validation of the outcomes.

Only one of the included studies (Pirolli et al., 2020) used online media for model parameterization. Within this study, attitudes and beliefs toward the intervention (mask wearing) were parameterized based upon textual data from individuals' blogs, articles, tweets and Reddit posts. The authors argue that this is cheaper than conducting their own survey and less prone to bias; however, it could be that people with stronger views are more likely to post their attitudes and beliefs. Given the extensive data already collected within online media, this is potentially a useful resource, however the analysis of such online text requires an additional skill set.

3.2.3 | Model time horizon, outcomes, behavior maintenance and interventions

Health economic models typically need to follow individuals over a lifetime to fully capture the differences between costs and outcomes of alternative interventions, hence how these aspects have been dealt with within the models are of interest.

The time horizons of the models span from 60 days to patient lifetimes, depending on the model purpose. It has been argued that it is not possible to make reasonable predictions far into the future within a complex system (Gilbert, 2020). The included alcohol model showed that it is possible to explain historical data over 15 years (Probst, 2018); however, prediction is more challenging because all relevant mechanisms for the behavior may not be included within the model, and this may be overfitted to the data during calibration (Vu, Probst, et al., 2020). All of the infectious disease ABMs reported infection risk/number as the main outcome, whilst all of the studies of non-communicable behaviors, except the Discrete Event Simulation of a cancer screening program by Brailsford et al. (2012) aimed to report the population pattern of behavior, and did not link this behavior to other risk factors and disease outcomes. Purshouse et al. (2014) suggest that the predicted behavioral outcomes could be incorporated within an existing health economic model. However, this would require compatible outcomes to be included within the health economic model, and it would not be possible to incorporate feedback between the disease and the behavior. Garcia et al. (2017b) recognizes that most theories and models do not capture the dynamic nature within which the behavior and environment are shaped, stating that “the independent, adapting nature of the elements and processes involved in maintaining a behavior needs to be taken into account”.

The ABM by Ernecoff et al. (2016) is the only study to explicitly include behavior maintenance by incorporating the Transtheoretical Model of Behavior Change within which behavior maintenance is one of the stages. Such a model with stages of change has great potential for use within health economic models; however, the Transtheoretical Model has been widely criticized within the psychology literature. Within all of the other ABMs, behavior is reassessed and updated at regular time steps, which means that agents could continue or stop doing the behavior based on a behavioral theory with updated parameters. The limitation of this approach is that the determinants of behavior change have been shown to be different to those of behavior maintenance (Kwasnicka et al., 2016). Thus, these models may produce flawed predictions about behavior over the longer term.

Individuals are likely to maintain a behavior if they are intrinsically motivated with regular gratification, partake in ongoing self-regulation with sufficient resources in a conducive environment, and the behavior becomes habitual (Kwasnicka et al., 2016). Buckley et al. (2022) specifically include an intentional pathway and a habitual pathway, with an automaticity

parameter which determines how likely a person is to continue with a habit or form a new intention. For the habitual pathway, the drinking history (percentage of days in each drinking category over the past year) is used to represent the probability of drinking on that day, and this is then stochastically sampled. Each individual is allocated, through the calibration process, a number of days for a behavior to become habitual, and drinking history is updated at this time point. Research on habit formation was used to inform the ranges this parameter could take.

Only the infectious disease models and six other studies (Brailsford et al., 2012; Ernecoff et al., 2016; Hu & Keller, 2015; Pakravan & MacCarty, 2021; Probst, 2018) attempted to assess the impact of an intervention upon outcomes; the majority of which used none evidence-based efficacy. This is because the purpose of most of the models was more exploratory, rather than to make long term predictions about the impact of the interventions.

4 | DISCUSSION

Within health economic modeling, the goal is to predict the impact of healthcare interventions compared with current practice over the long term. Ultimately, if there is very limited evidence about the effectiveness of the intervention(s) that is, typically less than 3 data points, 6 or 12 months follow up and aggregated results, then it is difficult to predict the long-term impacts of the intervention(s). Given limited intervention effectiveness data, it will be important to understand the theory utilized to develop the intervention where available, as well as obtaining behavioral science and public health expertise, in order to inform extrapolation beyond the study follow up period. Further research should involve collaboration between behavioral scientists and health economic modelers, not only to inform modeling methods development, but also data collection. The uncertainties associated with predicting in a dynamically complex system and with short term study data should be highlighted by health economic modelers, with substantial sensitivity analyses undertaken.

Behavioral theories could help to inform decisions about which individuals to target with which interventions via their use with health economic models. However, all of the psychological theories utilized within the included case studies have been criticized within the literature; two of which (the Theory of Planned Behavior and the Transtheoretical Stages of Change Model) have had calls to be retired (Sniehotta et al., 2014; West, 2005). A key issue with current theory is the inconsistent use of terminology across different theories and the lack of consensus about which are the most appropriate theories to use (Noar & Zimmerman, 2005). Improvements to current theories could be made by using standardized ontologies to describe the entities and relationships that are contained within each theory (Hale et al., 2020; West et al., 2019) and undertaking longitudinal data collection and analyses to test theories empirically.

The studies identified generally incorporated theories of behavior change, with only one considering behavior maintenance explicitly. Yet for non-communicable disease prevention, maintenance of healthy behaviors is imperative. Thus, in order to improve health economic model predictions, where the important outcome is the difference between the long-term outcomes for the intervention(s) compared with current practice, to model behavior beyond the study data it may be more relevant to utilize behavior maintenance theory than theories of behavior change. The review of behavior maintenance theories by Kwasnicka et al. (2016) would be a useful starting point for inclusion of such theories within health economic models, though the review highlighted weaknesses of the limited theories developed to date and these have mostly not been quantified. Further research would be needed to inform how these could be utilized within a health economic model.

SEM may be useful to evaluate the causal mechanisms acting between the interventions and behaviors, drawing upon behavior maintenance theory to develop the path analysis. If individual level data of the relevant variables at multiple time points were available, latent growth curve modeling could be used to describe the trajectories over time, making it possible to understand which individuals to target with which interventions.

However, quantifying behavioral theories is highly time consuming and data intensive, with data collection generally not designed for this purpose. In addition, they tend to focus on the individual rather than the broader determinants of health and health behaviors, such as work, transport, housing, and education, although some do include social norms and social structure (Michie et al., 2014). Gigerenzer and Gaissmaier (2011) argue that in complex systems where there is uncertainty, simple heuristics may outperform more complex models. Future research could compare outcomes of simulations using heuristics to predict behavior, which may include the broader determinants of health behaviors, with those which have incorporated formal behavioral theories.

ABM has the advantage of being able to incorporate the dynamic influences of other individuals and health outcomes upon behavior over time. ABM does not offer a set approach for prediction; it can use a range of approaches for setting the rules of the agents and their interactions with the environment. Ideally it would be possible to develop an ABM to assess the cost-effectiveness of public health interventions, utilizing behavioral theory to develop the rules of the agents and incorporating

the influence of social networks and/or spatial elements. From a theoretical perspective, the issue is in being able to make useful predictions within a complex system over a set of individuals' lifetimes, as is expected within a health economic model when an intervention affects a chronic disease. Gilbert (2020) and Tornberg (2018) suggest that ABMs are useful for theory-generation to explain macro level behavior that has been observed, but that accurate predictions may not be possible within complex systems. However, it is not possible to change the complexity of the system, and therefore the fundamental expectations of health economic modeling may need to be revised, or we need to be explicit about the complexity and uncertainty associated with the predictions (Bicket et al., 2020).

From a practical perspective, time, resources, data, expertise and skill requirements to develop these sorts of models may be constraining factors, and hence they may not be appropriate where decisions are needed quickly, and there are no existing relevant models or data. Most of the included models were developed and run by teams of people over several years. Model sharing using online open-source software repositories (e.g., GitLab) and adopting modular approaches could help to increase model reuse and adaptations so that such modeling is more feasible, as well as making it more transparent. Ideally individual level data is required for calibration and parameterization of the agent-based model. The data available will vary according to topic. However, an advantage of ABM is that it is possible to synthesize a wider collection of knowledge and evidence than is possible with data-driven approaches like SEM. Guidance on when to use complex systems models, including ABM, has been published to help analysts decide when the additional complexity offered by such models is worthwhile (Breeze et al., 2023).

Currently, few studies have attempted to utilize Big Data and data mining methods to inform the rules of the agents which could be explored within further research. However, there are also advantages to using qualitative research, in addition to quantitative evidence, to inform the rules of the agents within an ABM (Yang, 2019). Few of the included ABM reviews reported the use of qualitative data; however qualitative research provides an approach to understanding the behavior of individuals which could be very informative for the rules of the agents and long-term assumptions about intervention effectiveness, particularly given the current challenges in quantifying behavioral theory. Future health economic modeling of public health interventions should consider mixed methods approaches to model development.

Another important practical consideration is the acceptance of more complex modeling methods by stakeholders. It is good practice to obtain input from stakeholders, including policy makers, throughout model development (Squires et al., 2016). Conceptual modeling involving stakeholders could be used to understand the causal pathways of the behavior change interventions (Garcia et al., 2017a) and this will inform decisions about appropriate modeling methods and, if feasible, complementary primary data collection, as well as increasing model credibility. Indeed, it will be important to demonstrate the benefits of the additional complexity within case studies to improve model credibility so that decision makers use the model to help inform policy.

Within epidemiology there are a number of risk equations which have been developed to link risk factors to disease outcomes (Hippisley-Cox & Coupland, 2015, 2017; Hippisley-Cox et al., 2017), however these generally do not include behavioral risk factors apart from in some of the models smoking (yes/no) and alcohol consumption. This means there is no readily available direct relationship between most behaviors and disease. This is therefore an important area of research to inform health economic models which can incorporate these behaviors.

All of the included studies considered only the behavior of the individuals undertaking an unhealthy behavior. However, there is a large program of ongoing research that is exploring the impact of industry behaviors on outcomes using geographical analysis for food, alcohol and tobacco (Horton et al., 2021). Given the importance of the context upon behavior, the findings of this research could be important for consideration within a health economic model.

5 | CONCLUSIONS

This review set out to explore all relevant methods and approaches which could be used to model the causes of health-related behaviors within simulation models to consider their use within health economic modeling of public health interventions, with the aim to improve model predictions and inform intervention targeting. A range of methods were identified which could be drawn upon, including econometric analyses, SEMs, data mining and agent-based modeling, which has the advantage of incorporating social and spatial networks. Many theoretical and practical limitations of quantifying behavioral theory were identified, such that the use of simpler heuristics may be preferable within health economic models.

Studies have shown that social norms and networks affect behavior and thus the cost-effectiveness of public health interventions may be underestimated if these are not considered. Where there is clear evidence that social networks affect behavior which could lead to a tipping point in population behaviors or where targeting interventions toward highly connected individuals may be an option, it would be useful to capture these interactions within an ABM. Where interventions being assessed relate

to access to venues such as food outlets or green spaces, it may be preferable to incorporate spatial information within an ABM. These elements are not easily captured by alternative methods.

Initial steps to improve current approaches within health economic modeling could be a more multidisciplinary approach, collaborating with behavioral scientists, both to inform data collection and for behavioral scientists to inform model assumptions, as well as consulting with policy makers and experts in geographical analyses. Further research is needed around:

- 1) The feasibility and requirements for developing ABMs for health economic modeling, including social networks and the built environment;
- 2) The use of heuristics within health economic models;
- 3) The potential use of behavior maintenance theories in health economic models;
- 4) The use of data mining methods and theory for the analyses of Big Data to inform health economic models;
- 5) The inclusion of behavioral risk factors within disease risk equations;
- 6) Guidance for health economic modelers about when and how to use each of these methods;
- 7) Consistent reporting of the way in which behavior is incorporated within health economic models.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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REFERENCES

- Adibuzzaman, M. G. P. M. (2020). Big data in health care delivery. In T. L. S. E. Woo & R. W. Proctor (Eds.), *Big data in psychological research*. American Psychological Association.
- Ajzen, I. (1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes*, 50(2), 179–211. [https://doi.org/10.1016/0749-5978\(91\)90020-t](https://doi.org/10.1016/0749-5978(91)90020-t)
- Andrews, M. A., & Bauch, C. T. (2015). Disease interventions can interfere with one another through disease-behaviour interactions. *PLoS Computational Biology*, 11(6), e1004291. <https://doi.org/10.1371/journal.pcbi.1004291>
- Balke, T. G. N., & Gilbert, N. (2014). How do agents make decisions? *A Survey. Journal of Artificial Societies and Social Simulation: JASSS*, 17(4). <https://doi.org/10.18564/jasss.2687>
- Bandura, A. (1997). *Self-efficacy: The exercise of control* (1st ed.). Worth Publishers.
- Bardach, A. E., Alcaraz, A. O., Ciapponi, A., Garay, O. U., Riviere, A. P., Palacios, A., Cremonte, M., & Augustovski, F. (2019). Alcohol consumption's attributable disease burden and cost-effectiveness of targeted public health interventions: A systematic review of mathematical models. *BMC Public Health*, 19(1), 1378. <https://doi.org/10.1186/s12889-019-7771-4>
- Barnabe, F., & Davidsen, P. I. (2020). Exploring the potentials of behavioral system dynamics: Insights from the field. *Journal of Modelling in Management*, 15(1), 339–364. <https://doi.org/10.1108/jm2-03-2019-0081>
- Basu, S., Seligman, H., & Winkleby, M. (2014). A metabolic-epidemiological microsimulation model to estimate the changes in energy intake and physical activity necessary to meet the healthy people 2020 obesity objective. *American Journal of Public Health*, 104(7), 1209–1216. <https://doi.org/10.2105/ajph.2013.301674>
- Bates, S. (2021). Incorporating psychological mechanisms of action in a health economic model of obesity. Retrieved from: <https://etheses.whiterose.ac.uk/29411/>
- Bates, S., Bayley, T., Norman, P., Breeze, P., & Brennan, A. (2020). A systematic review of methods to predict weight trajectories in health economic models of behavioral weight management programs: The potential role of psychosocial factors. *Medical Decision Making*, 40(1), 90–105. <https://doi.org/10.1177/0272989x19889897>
- Beran, T. N., & Violato, C. (2010). Structural equation modeling in medical research: A primer. *BMC Research Notes*, 3(1), 267. <https://doi.org/10.1186/1756-0500-3-267>

- Bianchi, F., & Squazzoni, G. (2015). Agent-based models in sociology. *WIREs Computational statistics*, 7(4), 284–306. <https://doi.org/10.1002/wics.1356>
- Bicket, M., Christie, I., Gilbert, N., Hills, D., Penn, A., & Wilkinson, H. (2020). Magenta book 2020 supplementary guide: Handling complexity in policy evaluation. Retrieved from: <https://www.gov.uk/official-documents>
- Brailsford, S., Harper, P. R., & Sykes, J. (2012). Incorporating human behaviour in simulation models of screening for breast cancer. *European Journal of Operational Research*, 219(3), 491–507. <https://doi.org/10.1016/j.ejor.2011.10.041>
- Brailsford, S., & Schmidt, B. (2003). Towards incorporating human behaviour in models of health care systems: An approach using discrete event simulation. *European Journal of Operational Research*, 150(1), 19–31. [https://doi.org/10.1016/s0377-2217\(02\)00778-6](https://doi.org/10.1016/s0377-2217(02)00778-6)
- Breeze, P. R., Squires, H., Ennis, K., Meier, P., Hayes, K., Lomax, N., Shiell, A., Kee, F., de Vocht, F., O'Flaherty, M., Gilbert, N., Purshouse, R., Robinson, S., Dodd, P. J., Strong, M., Paisley, S., Smith, R., Briggs, A., Shahab, L., ... Brennan, A. (2023). Guidance on the use of complex systems models for economic evaluations of public health interventions. *Health Economics*, 32(7), 1603–1625. <https://doi.org/10.1002/hec.4681>
- Buckley, C., Field, M., Vu, T. M., Brennan, A., Greenfield, T. K., Meier, P. S., Nielsen, A., Probst, C., Shuper, P. A., & Purshouse, R. C. (2022). An integrated dual process simulation model of alcohol use behaviours in individuals, with application to US population-level consumption, 1984–2012. *Addictive Behaviors*, 124, 107094. <https://doi.org/10.1016/j.addbeh.2021.107094>
- Chao, D. D., Hashimoto, H., & Kondo, N. (2019). Social influence of e-cigarette smoking prevalence on smoking behaviours among high-school teenagers: Microsimulation experiments. *PLoS One*, 14(8), 11. <https://doi.org/10.1371/journal.pone.0221557>
- Christakis, N. A., & Fowler, J. H. (2007). The spread of obesity in a large social network over 32 years. *New England Journal of Medicine*, 357(4), 370–379. <https://doi.org/10.1056/nejmsa066082>
- Christakis, N. A., & Fowler, J. H. (2008). The collective dynamics of smoking in a large social network. *New England Journal of Medicine*, 358(21), 2249–2258. <https://doi.org/10.1056/nejmsa0706154>
- Coveney, P. D. E. H. R. (2016). *Big data need big theory too* (p. 374). Philosophical Transactions of the Royal Society A.
- Du, E., Chen, E., Liu, J., & Zheng, C. (2021). How do social media and individual behaviors affect epidemic transmission and control? *Science of the Total Environment*, 761, 144114. <https://doi.org/10.1016/j.scitotenv.2020.144114>
- Duan, W., Fan, Z., Zhang, P., Guo, G., & Qiu, X. (2015). Mathematical and computational approaches to epidemic modeling: A comprehensive review. *Frontiers of Computer Science*, 9(5), 806–826. <https://doi.org/10.1007/s11704-014-3369-2>
- Ernecoff, N. C., Keane, C. R., & Albert, S. M. (2016). Health behavior change in advance care planning: An agent-based model. *BMC Public Health*, 16(1), 193. <https://doi.org/10.1186/s12889-016-2872-9>
- Frerichs, L., Smith, N. R., Lich, K. H., BenDor, T. K., & Evenson, K. R. (2019). A scoping review of simulation modeling in built environment and physical activity research: Current status, gaps, and future directions for improving translation. *Health and Place*, 57, 122–130. <https://doi.org/10.1016/j.healthplace.2019.04.001>
- Garcia, L., Roux, A., Martins, A., Yang, Y., & Florindo, A. (2017a). Development of a dynamic framework to explain population patterns of leisure-time physical activity through agent-based modeling. *International Journal of Behavioral Nutrition and Physical Activity*, 14(1), 111. <https://doi.org/10.1186/s12966-017-0553-4>
- Garcia, L., Roux, A., Martins, A., Yang, Y., & Florindo, A. (2017b). Development of a dynamic framework to explain population patterns of leisure-time physical activity through agent-based modeling. *International Journal of Behavioral Nutrition and Physical Activity*, 14(1), 111. <https://doi.org/10.1186/s12966-017-0553-4>
- Garcia, L. M. T., Roux, A. V. D., Martins, A. C. R., Yang, Y., & Florindo, A. A. (2018). Exploring the emergence and evolution of population patterns of leisure-time physical activity through agent-based modelling. *International Journal of Behavioral Nutrition and Physical Activity*, 15(1), 112. <https://doi.org/10.1186/s12966-018-0750-9>
- Giabbanelli, P. J., & Crutzen, R. (2017). Using agent-based models to develop public policy about food behaviours: Future directions and recommendations. *Computational and Mathematical Methods in Medicine*, 2017, 1–12. <https://doi.org/10.1155/2017/5742629>
- Gigerenzer, G., & Gaissmaier, W. (2011). Heuristic decision making. *Annual Review of Psychology*, 62(1), 451–482. <https://doi.org/10.1146/annurev-psych-120709-145346>
- Gilbert, N. (2020). *Agent-based models* (Vol. 2nd ed.). SAGE Publications Inc.
- Gillespie, D., Hatchard, J., Squires, H., Gilmore, A., & Brennan, A. (2021). Conceptualising changes to tobacco and alcohol policy as affecting a single interlinked system. *BMC Public Health*, 21(1), 17. <https://doi.org/10.1186/s12889-020-10000-3>
- Guo, D., Li, K. C., Peters, T. R., Snively, B. M., Poehling, K. A., & Zhou, X. (2015). Multi-scale modeling for the transmission of influenza and the evaluation of interventions toward it. *Scientific Reports*, 5(1), 8980. <https://doi.org/10.1038/srep08980>
- Hale, J., Hastings, J., West, R., Lefevre, C. E., Direito, A., Bohlen, L. C., Godinho, C., Anderson, N., Zink, S., Groarke, H., & Michie, S. (2020). An ontology-based modelling system (OBMS) for representing behaviour change theories applied to 76 theories. *Wellcome Open Research*, 5, 177. <https://doi.org/10.12688/wellcomeopenres.16121.1>
- Hippisley-Cox, J., & Coupland, C. (2015). Development and validation of risk prediction algorithms to estimate future risk of common cancers in men and women: Prospective cohort study. *BMJ Open*, 5(3), 1–25. <https://doi.org/10.1136/bmjopen-2015-007825>
- Hippisley-Cox, J., & Coupland, C. (2017). Development and validation of QDiabetes-2018 risk prediction algorithm to estimate future risk of type 2 diabetes: Cohort study. *BMJ*, 359, j5019. <https://doi.org/10.1136/bmj.j5019>
- Hippisley-Cox, J., Coupland, C., & Brindle, P. (2017). Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: Prospective cohort study. *BMJ*, 357.
- Horton, M., Perman-Howe, P. R., Angus, C., Bishop, J., Bogdanovica, I., Brennan, A., Britton, J., Brose, L. S., Brown, J., Collin, J., Dockrell, M., Friel, S., Gillespie, D., Gilmore, A. B., Hill, S. E., Knai, C., Langley, T., Martin, S., & Bauld, L. (2021). The SPECTRUM consortium: A new

- UK Prevention Research Partnership consortium focussed on the commercial determinants of health, the prevention of non-communicable diseases, and the reduction of health inequalities. *Wellcome Open Research*, 6, 6. <https://doi.org/10.12688/wellcomeopenres.16318.1>
- Hu, X., & Keller, N. (2015). Agent-based modeling and simulation of child maltreatment and child maltreatment prevention. *The Journal of Artificial Societies and Social Simulation: JASSS*, 18(3), 6. <https://doi.org/10.18564/jasss.2783>
- Kahneman, D. (2012). *Thinking, fast and slow*. Penguin Books Ltd.
- Karimi, E., Schmitt, K., & Akgunduz, A. (2015). Effect of individual protective behaviors on influenza transmission: An agent-based model. *Health Care Management Science*, 18(3), 318–333. <https://doi.org/10.1007/s10729-014-9310-2>
- Kelly, M., McDaid, D., Ludbrook, A., & Powell, J. (2005). *Economic appraisal of public health interventions*. Health Development Agency, Issue.
- Kelly, M. P. (2019). Cognitive biases in public health and how economics and sociology can help overcome them. *Public Health*, 169, 163–172. <https://doi.org/10.1016/j.puhe.2019.02.012>
- Kruger, J., Brennan, A., Thokala, P., Cooke, D., Bond, R., & Heller, S. (2012). Accounting for psychological determinants of treatment response in health economic simulation models of behavioural interventions: A case study in type 1 diabetes. *Value in Health*, 15(4), A191. <https://doi.org/10.1016/j.jval.2012.03.1031>
- Ku, C. (2019). *Healthcare seeking behaviour as a link between tuberculosis and socioeconomic factors*. The University of Sheffield. Retrieved from: <https://etheses.whiterose.ac.uk/25352/1/Thesis%2C%20Chu-Chang%20Ku.pdf>
- Kunc, M., Malpass, J., & White, L. (2016). *Behavioural operational research: Theory, methodology and practice*. Palgrave Macmillan.
- Kwasnicka, D., Dombowski, S. W. M., & Sniehotta, F. (2016). Theoretical explanations for maintenance of behaviour change: A systematic review of behavioural theories. *Health Psychology Review*, 10(3), 277–296. <https://doi.org/10.1080/17437199.2016.1151372>
- Kwon, J., Squires, H., Franklin, M., Lee, Y., & Young, T. (2022). Economic models of community-based falls prevention: A systematic review with subsequent commissioning and methodological recommendations. *BMC Health Services Research*, 22(1), 316. <https://doi.org/10.1186/s12913-022-07647-6>
- Langellier, B., Bilal, U., Montes, F., Meisel, J., Cardoso, L., & Hammond, R. (2019). Complex systems approaches to diet: A systematic review. *American Journal of Preventive Medicine*, 57(2), 273–281. <https://doi.org/10.1016/j.amepre.2019.03.017>
- Langellier, B., Yang, Y., Purtle, J., Nelson, K., Stankov, I., & Roux, A. (2019). Complex systems approaches to understand drivers of mental health and inform mental health policy: A systematic review. *Administration and Policy in Mental Health and Mental Health Services Research*, 46(2), 128–144. <https://doi.org/10.1007/s10488-018-0887-5>
- Leao, T., Kunst, A. E., & Perelman, J. (2018). Cost-effectiveness of tobacco control policies and programmes targeting adolescents: A systematic review. *The European Journal of Public Health*, 28(1), 39–43. <https://doi.org/10.1093/eurpub/ckx215>
- Li, Y., Lawley, M. A., Siscovick, D. S., Zhang, D., & Pagan, J. A. (2016). Agent-based modeling of chronic diseases: A narrative review and future research directions. *Preventing Chronic Disease*, 13, 150561. <https://doi.org/10.5888/pcd13.150561>
- Lopez, L., Fernandez, M., Gomez, A., & Giovanini, L. (2020). An influenza epidemic model with dynamic social networks of agents with individual behaviour. *Ecological Complexity*, 41(13), 100810. <https://doi.org/10.1016/j.ecocom.2020.100810>
- Lorig, F., Johansson, E., & Davidsson, P. (2021). Agent-based social simulation of the covid-19 pandemic: A systematic review. *Jasss-the Journal of Artificial Societies and Social Simulation*, 24(3). Article 5. <https://doi.org/10.18564/jasss.4601>
- Luo, J., Wang, J. P., Zhao, Y. L., & Chen, T. Q. (2018). Scare behavior diffusion model of health food safety based on complex network. *Complexity*, 14, 1–14. <https://doi.org/10.1155/2018/5902105>
- McMillan, C., Felmlee, D., & Osgood, W. (2018). Peer influence, friend selection, and gender: How network processes shape adolescent smoking, drinking, and delinquency. *Social Networks*, 55, 86–96. <https://doi.org/10.1016/j.socnet.2018.05.008>
- Mei, S., Zhu, Y., Qui, X., Zhou, X., Zu, Z., Boukhanovsky, A. V., & Sloat, P. M. A. (2014). Individual decision making can drive epidemics: A fuzzy cognitive map study. *IEEE Transactions on Fuzzy Systems*, 22(2), 264–273. <https://doi.org/10.1109/TFUZZ.2013.2251638>
- Michie, S., Carey, R. N., Johnston, M., Rothman, A. J., de Bruin, M., Kelly, M. P., & Connell, L. E. (2018). From theory-inspired to theory-based interventions: A protocol for developing and testing a methodology for linking behaviour change techniques to theoretical mechanisms of action. *Annals of Behavioral Medicine*, 52(6), 501–512. <https://doi.org/10.1007/s12160-016-9816-6>
- Michie, S., West, R., Campbell, R., Brown, J., & Gainforth, H. (2014). *ABC of behaviour change theories*. Silverback Publishing.
- Morshed, A. B., Kasman, M., Heuberger, B., Hammond, R. A., & Hovmand, P. S. (2019). A systematic review of system dynamics and agent-based obesity models: Evaluating obesity as part of the global syndemic. *Obesity Reviews*, 20(S2), 161–178. <https://doi.org/10.1111/obr.12877>
- Nianogo, R. A., & Arah, O. A. (2015). Agent-based modeling of noncommunicable diseases: A systematic review. *American Journal of Public Health*, 105(3), E20–E31. <https://doi.org/10.2105/ajph.2014.302426>
- Noar, S. M., & Zimmerman, R. S. (2005). Health behavior theory and cumulative knowledge regarding health behaviors: Are we moving in the right direction? *Health Education Research*, 20(3), 275–290. <https://doi.org/10.1093/her/cyg113>
- Orr, M. G., & Plaut, D. C. (2014). Complex systems and health behavior change: Insights from cognitive science. *American Journal of Health Behavior*, 38(3), 404–413. <https://doi.org/10.5993/ajhb.38.3.9>
- Orr, M. G., Thrush, R., & Plaut, D. C. (2013). *The theory of reasoned action as parallel constraint satisfaction: Towards a dynamic computational model of health behavior*. Figshare. Retrieved from: <http://dx.doi.org.sheffield.idm.oclc.org/10.1371/journal.pone.0062490.s001>
- Pakravan, M. H., & MacCarty, N. (2021). An agent-based model for adoption of clean technology using the theory of planned behavior. *Journal of Mechanical Design*, 143(2). Article 021402. <https://doi.org/10.1115/1.4047901>
- Pirolli, P., Bhatia, A., Mitsopoulos, K., Lebiere, C., & Orr, M. (2020). Cognitive modeling for computational epidemiology SBP-BRIMS.
- Probst, C. (2018). Can normative mechanisms explain the changes in female drinking patterns over the past decades? An agent-based model. *Alcoholism: Clinical and Experimental Research*, 42(Supplement 1), 331A. <https://doi.org/10.1111/acer.13748>

- Probst, C., Vu, T. M., Epstein, J., Nielsen, E., Buckley, C., Brennan, A., Rehm, J., & Purshouse, R. C. (2020). The normative underpinnings of population-level alcohol use: An individual-level simulation model. *Health Education & Behavior, 47*(2), 224–234. <https://doi.org/10.1177/1090198119880545>
- Purshouse, R. C., Ally, A. K., Brennan, A., Moyo, D., & Norman, P. (2014). *Evolutionary parameter estimation for a theory of planned behaviour microsimulation of alcohol consumption dynamics in an English birth cohort 2003 to 2010*. [Gecco'14: Proceedings of the 2014 genetic and evolutionary computation conference]. *16th genetic and evolutionary computation conference (GECCO)*. Vancouver.
- Purshouse, R. C., Meier, P. S., Brennan, A., Taylor, K. B., & Rafia, R. (2010). Estimated effect of alcohol pricing policies on health and health economic outcomes in England: An epidemiological model. *Lancet, 375*(9723), 1355–1364. [https://doi.org/10.1016/S0140-6736\(10\)60058-X](https://doi.org/10.1016/S0140-6736(10)60058-X)
- Rahmani, J., Razaz, J. M., Kalantari, N., Garcia, L. M. T., Shariatpanahi, S. P., Bawadi, H., Thompson, J. Y., Ryan, P. M., Santos, H. O., & Roudsari, A. H. (2021). Dynamic conceptual framework to investigate adoption of healthy diet through agent-based modelling. *British Food Journal, 123*(8), 2743–2755. <https://doi.org/10.1108/bfj-09-2020-0828>
- Rosenstock, I. M., Strecher, V. J., & Becker, M. H. (1988). Social learning theory and the health belief model. *Health Education Quarterly, 15*(2), 175–183. <https://doi.org/10.1177/109019818801500203>
- Saarloos, D., Kim, J. E., & H. T. (2009). The built environment and health: Introducing individual space-time behavior. *International Journal of Environmental Research and Public Health, 6*(6), 1724–1743. <https://doi.org/10.3390/ijerph6061724>
- Skivington, K., Matthews, L., Simpson, S. A., Craig, P., Baird, J., Blazeby, J. M., Boyd, K. A., Craig, N., French, D. P., McIntosh, E., Petticrew, M., Rycroft-Malone, J., White, M., & Moore, L. (2021). A new framework for developing and evaluating complex interventions: Update of Medical Research Council guidance. *BMJ, 374*, n2061. <https://doi.org/10.1136/bmj.n2061>
- Smith, N. R., Trauer, J. M., Gambhir, M., Richards, J. S., Maude, R. J., Keith, J. M., & Flegg, J. A. (2018). Agent-based models of malaria transmission: A systematic review. *Malaria Journal, 17*(1), 299. <https://doi.org/10.1186/s12936-018-2442-y>
- Sniehotta, F. J. P., V. A.-S., & Araújo-Soares, V. (2014). Time to retire the theory of planned behaviour. *Health Psychology Review, 8*(1), 1–7. <https://doi.org/10.1080/17437199.2013.869710>
- Squires, H., Chilcott, J., Akehurst, R., Burr, J., & Kelly, M. P. (2016). A framework for developing the structure of public health economic models. *Value in Health, 19*(5), 588–601. <https://doi.org/10.1016/j.jval.2016.02.011>
- Sterman, J. (2000). *Business dynamics: Systems thinking and modeling for a complex world*. McGraw-Hill.
- Sullivan, W. (2014). *Exploring the importance of links between health behaviours for economic evaluations of behaviour-change strategies: A case study considering the link between smoking cigarettes and drinking alcohol*. University of Sheffield. White Rose Online. Retrieved from: <https://etheses.whiterose.ac.uk/6971/>
- Thaler, R. H. (2016). Behavioral economics: Past, present and future. *The American Economic Review, 106*(7), 1577–1600. <https://doi.org/10.1257/aer.106.7.1577>
- Tornberg, A. (2018). Abstractions on steroids: A critical realist approach to computer simulations. *Journal for the Theory of Social Behaviour, 49*, 127–143.
- Tracy, M., Cerda, M., & Keyes, K. M. (2018). Agent-based modeling in public health: Current applications and future directions. In J. E. Fielding, R. C. Brownson, & L. W. Green (Eds.), *Annual review of public health* (Vol. 39, pp. 77–94). <https://doi.org/10.1146/annurev-publhealth-040617-014317>
- Vu, T. M., Buckley, C., Bai, H., Nielsen, A., Probst, C., Brennan, A., Shuper, P., Strong, M., & Purshouse, R. (2020). Multiobjective genetic programming can improve the explanatory capabilities of mechanism-based models of social systems. *Complexity, 1*–19.
- Vu, T. M., Probst, C., Epstein, J. M., Brennan, A., Strong, M., & Purshouse, R. C. (2019). Toward inverse generative social science using multi-objective genetic programming. In *Genetic and evolutionary computation conference*.
- Vu, T. M., Probst, C., Nielsen, A., Bai, H., Buckley, C., Meier, P., Strong, M., Brennan, A., & Purshouse, R. (2020). A software architecture for mechanism-based social systems modelling in agent-based simulation models. *The Journal of Artificial Societies and Social Simulation: JASSS, 23*(3), 1. <https://doi.org/10.18564/jasss.4282>
- West, R. (2005). Time for a change: Putting the transtheoretical (stages of change) model to rest. *Addiction, 100*(8), 1036–1039.
- West, R., Godinho, C. A., Bohlen, L. C., Carey, R. N., Hastings, J., Lefevre, C. E., & Michie, S. (2019). Development of a formal system for representing behaviour-change theories. *Nature Human Behaviour, 3*(5), 526–536. <https://doi.org/10.1038/s41562-019-0561-2>
- Weston, D., Hauck, K., & Amlot, R. (2018). Infection prevention behaviour and infectious disease modelling: A review of the literature and recommendations for the future. *BMC Public Health, 18*(1), 336. <https://doi.org/10.1186/s12889-018-5223-1>
- Will, M. G. J., Frank, K., Maller, B., & Müller, B. (2020). Combining social network analysis and agent-based modelling to explore dynamics of human interaction: A review. *Socio-Environmental Systems Modelling, 2*, 16325. <https://doi.org/10.18174/sesmo.2020a16325>
- Willem, L., Verelst, F., Bilcke, J., Hens, N., & Beutels, P. (2017). Lessons from a decade of individual-based models for infectious disease transmission: A systematic review (2006–2015). *BMC Infectious Diseases, 17*(1), 612. <https://doi.org/10.1186/s12879-017-2699-8>
- Wrzus, C., Hanel, M., Wagner, J., & Neyer, F. J. (2013). Social network changes and life events across the life span: A meta-analysis. *Psychological Bulletin, 139*(1), 53–80. <https://doi.org/10.1037/a0028601>
- Xue, H., Slivka, L., Igusa, T., Huang, T. T., & Wang, Y. (2018). Applications of systems modelling in obesity research. *Obesity Reviews, 19*(9), 1293–1308. <https://doi.org/10.1111/obr.12695>
- Yang, Y. (2019). A narrative review of the use of agent-based modeling in health behavior and behavior intervention. *Translational Behavioral Medicine, 9*(6), 1065–1075. <https://doi.org/10.1093/tbm/iby132>

- Zanganeh, M., Adab, P., Li, B., & Frew, E. (2019). A systematic review of methods, study quality, and results of economic evaluation for childhood and adolescent obesity intervention. *International Journal of Environmental Research and Public Health*, 16(3), 485. <https://doi.org/10.3390/ijerph16030485>
- Zhou, X., Siegel, K. R., Ng, B. P., Jawanda, S., Proia, K. K., Zhang, X., Albright, A. L., & Zhang, P. (2020). Cost-effectiveness of diabetes prevention interventions targeting high-risk individuals and whole populations: A systematic review. *Diabetes Care*, 43(7), 1593–1616. <https://doi.org/10.2337/dci20-0018>

SUPPORTING INFORMATION

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