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# A Framework for Developing the Structure of Public Health Economic Models

*Hazel Squires, PhD[1,*], James Chilcott, MSc[1], Ronald Akehurst, MSc[1,2], Jennifer Burr, PhD[1], Michael P. Kelly, PhD[3]*

[1]School of Health and Related Research, University of Sheffield, Sheffield, UK; [2]Bresmed, Sheffield, UK; [3]Primary Care Unit, Institute of Public Health, University of Cambridge, Cambridge, UK

A B S T R A C T

**Background:** A conceptual modeling framework is a methodology that assists modelers through the process of developing a model structure. Public health interventions tend to operate in dynamically complex systems. Modeling public health interventions requires broader considerations than clinical ones. Inappropriately simple models may lead to poor validity and credibility, resulting in suboptimal allocation of resources. **Objective:** This article presents the first conceptual modeling framework for public health economic evaluation. **Methods:** The framework presented here was informed by literature reviews of the key challenges in public health economic modeling and existing conceptual modeling frameworks; qualitative research to understand the experiences of modelers when developing public health economic models; and piloting a draft version of the framework. **Results:** The conceptual modeling framework comprises four key principles of good practice and a proposed methodology. The key principles are that 1) a systems approach to modeling should be taken; 2) a documented understanding of the problem is imperative before and alongside developing and justifying the model structure; 3) strong communication with stakeholders and members of the team throughout model development is essential; and 4) a systematic consideration of the determinants of health is central to identifying the key impacts of public health interventions. The methodology consists of four phases: phase A, aligning the framework with the decision-making process; phase B, identifying relevant stakeholders; phase C, understanding the problem; and phase D, developing and justifying the model structure. Key areas for further research involve evaluation of the framework in diverse case studies and the development of methods for modeling individual and social behavior. **Conclusions:** This approach could improve the quality of Public Health economic models, supporting efficient allocation of scarce resources.

***Keywords:*** conceptual modeling, guidance, methods, public health.



## Introduction

Conceptual modeling is the abstraction of elements of reality at an appropriate level of simplification for the problem [1]. It is the first part of a modeling project, which guides and affects all other stages. If done poorly, the subsequent analysis, no matter how mathematically sophisticated, is unlikely to be useful for decision makers [2]. The absence of formal conceptual modeling may lead to a plethora of errors including answering the wrong (or less useful) question; poor validity and credibility; no basis for model verification, structural uncertainty analysis, or specification of key areas for further research; poor transparency for stakeholders and model reuse; ignorance of system variation; and inefficient model development.

In 2011 Chilcott et al. [3] highlighted the lack of formal methods for health economic model development. Given the scientific rigor of technical methods such as probabilistic sensitivity analysis (PSA) for representing parameter uncertainty and the importance placed on these approaches for health care decision making [4], methods for the development of the model structure are relatively underdeveloped. If the model structure is inadequate, the PSA will provide misleading results, leading to inappropriate policy decisions. The lack of formal conceptual modeling approaches is particularly problematic for economic models of public health interventions. Public health economic models are models of any intervention preventing disease, prolonging life, or promoting health. A key objective of public health is sometimes to reduce inequities rather than maximize the health of the society. In addition, public health interventions tend to operate in dynamically complex social systems that include the social determinants of health [5]. The modeling described in this article seeks to capture the complexities involved. Key challenges associated with

The views expressed in this article are those of the authors and not necessarily those of the National Health Service, the National Institute for Health Research, or the Department of Health.

* *Address correspondence to:* Hazel Squires, School of Health and Related Research (ScHARR), University of Sheffield, Regent Court, 30 Regent Street, Sheffield, South Yorkshire S1 4DA, UK.

E-mail: h.squires@sheffield.ac.uk.



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developing the structure of public health economic models are described in detail by the authors in an existing article [6].

This article aims to provide a conceptual modeling framework for developing models of public health interventions, that is, a methodology that helps to guide modelers through the development of a model structure, from developing and describing an understanding of the decision problem to the abstraction and nonsoftware-specific description of the quantitative model, using a transparent approach that enables each stage to be shared and questioned. It is intended to be used by any modeler undertaking public health economic evaluations. It also provides a standardized approach that will help stakeholders to input into and use the model developed.

During the development of this framework an important obstacle had to be confronted. Given the lack of guidance on conceptual modeling in health economic evaluation more generally, we did not have a platform on which to build the additional considerations and differences for public health. Thus, the aim to present a conceptual modeling framework for developing the structure of public health models necessarily involved developing guidance that was general and also outlining specific public health considerations that may otherwise be overlooked. While our work has been underway, the lack of conceptual modeling guidance has been recognized as an issue within the wider health economics community, with the International Society for Pharmacoeconomics and Outcomes Research and the Society for Medical Decision Making (ISPOR-SMDM) Joint Modeling Good Research Practices Task Force developing guidance to inform conceptual modeling for health economics [7]. The ISPOR guidance describes *what* modelers should do, but it does not describe *how* they might do it. Thus all parts of the framework are new in that they describe methods to help health economic modelers develop model structures, whilst specific public health considerations are mainly outlined in those areas of the framework dealing with developing an understanding of the decision problem. When methods or processes in the framework are established we provide references to key literature. Methods or processes are outlined in detail if they have not been described previously for health economic modeling.

The parallel development of our framework and the ISPOR guidance highlights the importance and timely nature of this work. We intend that this guidance will complement and add to the ISPOR conceptual modeling guidance by helping modelers think about their approach to model development. It is not intended to provide a checklist for developing "good" model structures. Given its purpose, it is necessary to provide a good deal of detail.

## Methods for Developing the Conceptual Modeling Framework

The conceptual modeling framework was informed by two literature reviews, qualitative research with modelers, including in-depth interviews, observation of modeling practice and focus groups with key experts, and a pilot study. The literature reviews aimed to 1) describe the key challenges in public health economic modeling and 2) review conceptual modeling frameworks in the broader modeling literature. The qualitative research aimed to understand the experiences of modelers when developing public health economic model structures and their views about the barriers and benefits of using a conceptual modeling framework. These are each described briefly here, although a more detailed description of the methods is available in the doctoral thesis by Squires [8].

### *Review of Key Challenges in Public Health Economic Modeling*

An iterative search process was undertaken to identify literature describing the key challenges in public health economic evaluation. Articles relating to economic evaluation resulting from the work of the Public Health Excellence Centre at the National Institute for Health and Care Excellence (NICE) were identified by searching for key people from the NICE website as authors in MEDLINE, publications written by the Public Health Research Consortium [9] were handsearched, and a MEDLINE search for terms relating to problems in public health economic modeling was undertaken. Key public health journals were subsequently searched using search terms relating to economic evaluation. The review included methodological articles on economic modeling in public health. It excluded case studies of economic evaluations, methods for valuing equity or health outcomes (as against the incorporation of these in a model), and "gray literature" if the content was already published in a peer-reviewed journal. After the initial searching process, additional targeted searches were undertaken to develop more in-depth knowledge about the key challenges identified from relevant discipline-specific literature. Further details of this review are described in a paper by Squires et al. [6].

### *Review of Existing Conceptual Modeling Frameworks*

Existing conceptual modeling frameworks were identified via an iterative search process following the NICE Technical Support Document Guidance, including citation, reference, and key author searching in MEDLINE, Scopus, and Web of Science in 2011 [10]. Three sets of search terms were combined with "AND": 1) terms for conceptual models (limited to title with the aim of ensuring that this is the main focus of the article); 2) terms for quantitative models (to help to limit studies to those in which the aim of the conceptual model is to develop a quantitative model); and 3) terms for development (to help focus the search on methods for the development of conceptual models rather than on case studies reporting the output of a conceptual model). Searches were not limited by discipline, study type, publication date, or language. After article retrieval, the key characteristics of the methods described in the articles were identified using a data extraction form that was specifically developed for this review.

### *Qualitative Research*

The qualitative research involved 1) tracking the development of a specific public health economic model including observing key meetings and undertaking in-depth interviews with the two modelers involved; 2) systematically analyzing notes from a previous modeling project assessing the cost-effectiveness of interventions to encourage young people to use contraceptives; and 3) holding a focus group meeting with modelers from five different UK centers. The participants were identified purposively for their varied experience in public health economic modeling projects so that the views presented would be relevant, varied, and comprehensive. Topic guides were developed for the interviews and the focus group, and the sessions were audio-recorded and subsequently transcribed. The focus group aimed to capture both agreement and disagreement between modelers. Analysis involved copying each sentence of the transcripts and notes systematically to an MS Excel (Microsoft) spreadsheet into emergent categories, which were then grouped into themes. A reflexive approach was taken (in which meaning was developed on the basis of the complex relationship between the understanding of the participants and the researchers before the research combined with the additional meaning gained from the research), and alternative meanings for each piece of data and opposing views were actively considered.

### *Diabetes Pilot Study*

The literature reviews and qualitative research led to the development of a wide range of specific requirements for a conceptual modeling framework in public health economic evaluation (see Appendix Table in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011, which shows which method led to each finding). On the basis of these, a draft version of the conceptual modeling framework was developed. This was piloted in a project funded by the National Institute for Health Research School for Public Health assessing the cost-effectiveness of interventions for diabetes screening and prevention [11] and its use was critically reflected upon, which led to further improvements to the framework.

## The Conceptual Modeling Framework

The conceptual modeling framework is underpinned by four key principles of good practice in developing valid, credible, and feasible models. These principles were derived from the two literature reviews and the qualitative analysis and are described in the next section, before the methodology of the framework is presented. Detailed process suggestions and an example to illustrate the methods on the basis of the diabetes prevention pilot study are provided in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011, although aspects of the diabetes example are drawn upon throughout the article.

### *Key Principles of Good Practice*

Four key principles of good practice emerged from a triangulation of the methods described earlier: 1) a systems approach to public health modeling should be taken; 2) a documented understanding of the problem is imperative before and alongside developing and justifying the model structure; 3) strong communication with stakeholders and members of the team throughout model development is essential; and 4) a systematic consideration of the determinants of health is central to identifying key impacts of the interventions in public health economic modeling. These are each described here.

#### *Key principle of good practice 1: A systems approach to public health modeling should be taken*

Public health economic modeling generally involves understanding dynamically complex systems [12]. This means that these systems are typically nonlinear in which the whole is not equal to the sum of the parts. They are history-dependent; there is no clear boundary around the system being analyzed, heterogeneity and self-organization have an impact on the outcomes, and people affected by public health interventions may learn and adapt over time and change their behavior accordingly [13]. In complex systems there may be positive feedback loops, whereby if factor A increases [decreases], the number of factor B increases [decreases], which leads to factor A increasing [decreasing] further, which would lead to exponential growth [decay] if no other factors were present [13]. For example, an increase in obesity might lead to an increase in depression, which, in turn, might lead to an increase in obesity, and so on. There may also be negative feedback loops, in which an increase [decrease] in factor A leads to an increase [decrease] in factor B, which, in turn, leads to a decrease [increase] in factor A [11]. For example, an increase in eating will lead to an increase in weight gain (all other things being equal), which may lead to a decrease in eating. When both positive and negative feedback loops exist in a system, this may produce counterintuitive behavior, often occurring over a long period of time [13]. In these dynamically complex systems, factors are constantly changing over time, and a sudden modification in behavior may arise as a result of a number of smaller heterogeneous changes. Taking action in such a system on the basis of simple cause and effect may lead to unexpected and unwanted outcomes.

A systems approach, or systems thinking, is suited to modeling these dynamically complex public health systems. It is a holistic way of thinking about the interactions between parts in a system and with its environment [14]. In systems thinking there are multiple system levels, whereby the system of interest is subjectively defined and there is always a higher level system in which it belongs and a lower level system that describes detailed aspects. The challenge in health economic modeling is to determine which level will represent that of the system of interest (the model), by demonstrating sufficient knowledge about the higher level system (the broader understanding of the problem), and subsequently defining an appropriate level of detail for the system of interest. In systems thinking, the importance of not considering one aspect of a system in isolation is emphasized to avoid ignoring unintended consequences. In addition, the culture and politics of the system cannot be ignored because these will affect the process by which decisions are made and the objectives of stakeholders and the environment they operate in, as recognized by soft systems methodology [15].

#### *Key principle of good practice 2: A documented understanding of the problem is imperative before and alongside developing and justifying the model structure to develop valid, credible, and feasible models*

It is valuable to have an initial understanding of the problem and to document this understanding before making simplifications when developing the model structure for both theoretical and practical reasons. Theoretically, it provides a basis for validation by facilitating the specification of an appropriate model scope and transparent structural assumptions, and for increasing credibility by supporting stakeholder involvement and producing clear documentation throughout the development of the model structure [3]. We learn by building upon what we already know, and our vision of the world or construction of a problem is constrained by our previous "knowledge" [16]. As such, if a model is data-led and/or based on only the analyst's interpretation of the data, it may lead to a narrow view of what should be included in the model. Documenting an understanding of the problem before analyzing available data sets allows that understanding to be reflected upon and shared. This reduces the risk of ignoring something that may be important to the model outcomes, which may be particularly important given the likely dynamic complexity of the system. In terms of systems thinking (see key principle of good practice 1), documenting an understanding of the problem (the higher level system) allows the modeler to be able to define the boundary of the system of interest for modeling. This description of the understanding of the problem should also help the modeler to understand the impact of potential simplifying assumptions they might use in the model.

Practically, if the problem is not sufficiently understood, an inappropriate model structure may be developed which may be inefficient to correct in the computer software retrospectively, particularly if an alternative model type needs to be developed (e.g., a discrete event simulation rather than a Markov model). Thus, taking time at the beginning of the project to understand the problem could reduce overall time requirements. Documenting the understanding of the problem also enables communication with stakeholders and the project team (see key principle of good practice 3). An additional benefit is that the documentation of the understanding of the problem could be used (alongside any logic models developed) to help stakeholders understand potential impacts of the interventions. Finally, documenting the understanding of the problem will enable researchers and policymakers who are not involved in the project to understand the problem and the basis for decisions about the model structure.

Thus, as also proposed by Roberts et al. [7] and Kaltenthaler et al. [17] in the context of clinical economic modeling, it is recommended that the model structure be developed in two phases. The first is to develop an understanding of the decision problem that is sufficiently formed to tackle the aforementioned theoretical and practical issues; this exercise should not be limited by the empirical evidence available. The second is to specify a model structure for the decision problem that is feasible within the constraints of the decision-making process. The understanding of the problem will inevitably continue to form during model development; this initial documented understanding, however, provides a basis for comparison and any major changes to this understanding can subsequently be documented.

### *Key principle of good practice 3: Strong communication with stakeholders and members of the team throughout model development is essential for model transparency, validity, and credibility*

The literature suggests that stakeholders can encourage learning about the problem (including geographical variation of health care provision and stakeholders' values and preferences), help to develop appropriate model objectives and requirements, facilitate model verification and validation, help to develop credibility and confidence in the model and its results, guide model development and experimentation, encourage creativity in finding a solution, and facilitate model reuse [7, 17–22]. In addition, stakeholders can help to define the meaning of subject-specific terminology, which has a different lay meaning. Pidd [1] has used the metaphor of taking a photograph of a scene, whereby each person involved might see different aspects of the scene and frame the photo differently. The more frames provided by people with different interests, the better the discussion regarding the perspectives and the richer our understanding.

The modeler should question the assumptions of the stakeholders [23] and the project team throughout the model development process to uncover inconsistent, biased, and invalid assumptions. In topics for which the project team has existing "knowledge," it is important to be aware of the tendency to anchor to initial beliefs and be open to new theories to develop valid models [14, 24]. Effective ways of communicating information, such as using clear diagrams, should be used to share information and describe assumptions.

### *Key principle of good practice 4: A systematic consideration of the determinants of health is central to identifying key impacts of the interventions in public health economic modeling*

The determinants of health that include the social, economic, and physical environment, as well as a person's individual characteristics, are central to the consideration of public health interventions. There are a large number of classifications of the determinants of health; many of them, however, comprise similar factors. Perhaps the most well-known is that of Dahlgren and Whitehead [25], shown in Figure 1, which shows individual-, community-, and population-level factors that impact on and are impacted by health. Individual behaviors (such as buying certain food) impact on the social determinants of health (such as social class and access to amenities), which, in turn, impact on individual behaviors [26]. Thus, it is important to consider broader determinants of health to predict the full impact of interventions on health outcomes. In addition, classifications of the determinants of health could be used to facilitate identification of nonhealth costs and outcomes associated with the interventions, such as those in transport or employment, and of potential intervention types to assess in the model. This includes those that might impact on individual health through making community- and population-level changes, such as food production, as well as those that might impact on health through changing individual lifestyle factors. Similarly, subpopulations that might benefit from the intervention could be identified, for example, low-income areas where there are high levels of unemployment and lack of education. Finally, the consideration of social network effects could affect the analytical model type chosen, and subsequently the predicted impact of the interventions. It is unlikely to be appropriate or feasible to include all the determinants of health in a model; nevertheless, they should be systematically reflected upon during the understanding of the problem phase to consider which determinants it might be important to include in the model so that all important mechanisms and outcomes of the interventions can be captured.

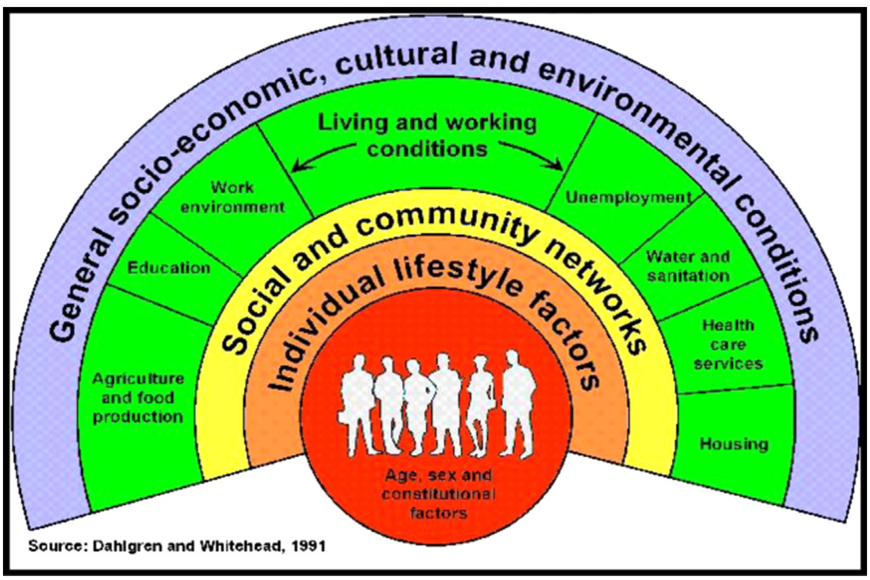


**Fig. 1 – Determinants of health by Dahlgren and Whitehead [25] (reproduced with permission).**

### The Conceptual Modeling Framework Methodology

The conceptual modeling framework consists of four key phases: Phase A: Aligning the framework with the decision-making process; Phase B: Identifying relevant stakeholders; Phase C: Understanding the problem; and Phase D: Developing and justifying the model structure (as shown in Fig. 2). The entire model development process is inherently iterative, as shown by the arrows in Figure 2. Evidence identification is not described as a separate activity (apart from reviewing existing models) because it is required in most of the outlined stages. Iterations, however, are inevitable between appropriate conceptualization and data collection because there is unlikely to be the exact evidence available that has been specified by the conceptual model. Each stage of the conceptual modeling framework is described here.

#### Phase A: Aligning the framework with the decision-making process

The conceptual modeling framework is intended to be applicable across different decision-making contexts, which means that decisions about how to use the framework in a specific process are required. For example, the project team may need to operate differently according to the nature of the engagement with decision makers (people whom the model supports) and clients (people who sponsor the modeling) in the project. Key decisions during this phase relate to the relevant modes of stakeholder engagement, the approach to evidence searching, and the time and resources available for the modeling project and each stage of the framework. A deliverable of this phase may be a protocol document outlining the project plan with headings for each stage in the conceptual modeling framework, including detailed project time scales. This document can be used as a basis for discussion between the project team and the stakeholders and should be approved by the client. This helps the clients to understand whether the project is planned to run appropriately and the project team in ensuring feasibility of the project.

#### Phase B: Identifying relevant stakeholders

There are a number of different types of stakeholders, defined as any person who impacts on or is impacted upon in the system, in any public health project. The choice of stakeholders involved with the development of the model will inevitably affect the model developed and the interventions assessed. For instance, stakeholders help define the model scope, make value judgments, use their expertise to recommend structural assumptions such as extrapolating short-term trial data over the long-term, and choose which interventions to assess in the model. In some projects, the stakeholders who inform the model development are chosen by the modeling team, whereas in other projects a group of experts is chosen by a decision-making body, such as in the NICE process (see phase A). There is, however, usually the opportunity to involve additional experts chosen by the project team, which is useful for providing alternative perspectives.

On the basis of soft systems methodology [15] and a conceptual modeling article by Roberts et al. [7], the types of stakeholders to involve are as follows:

1. Customers of the interventions, including patient representatives and lay members;
2. Actors in the system, including clinical and epidemiologic experts for all relevant diseases and methods experts; and
3. System owners, that is, those with the power to stop public health activity (including problem owners).

The relationships between the customers, actors, and system owners can be considered to identify relevant stakeholders. For

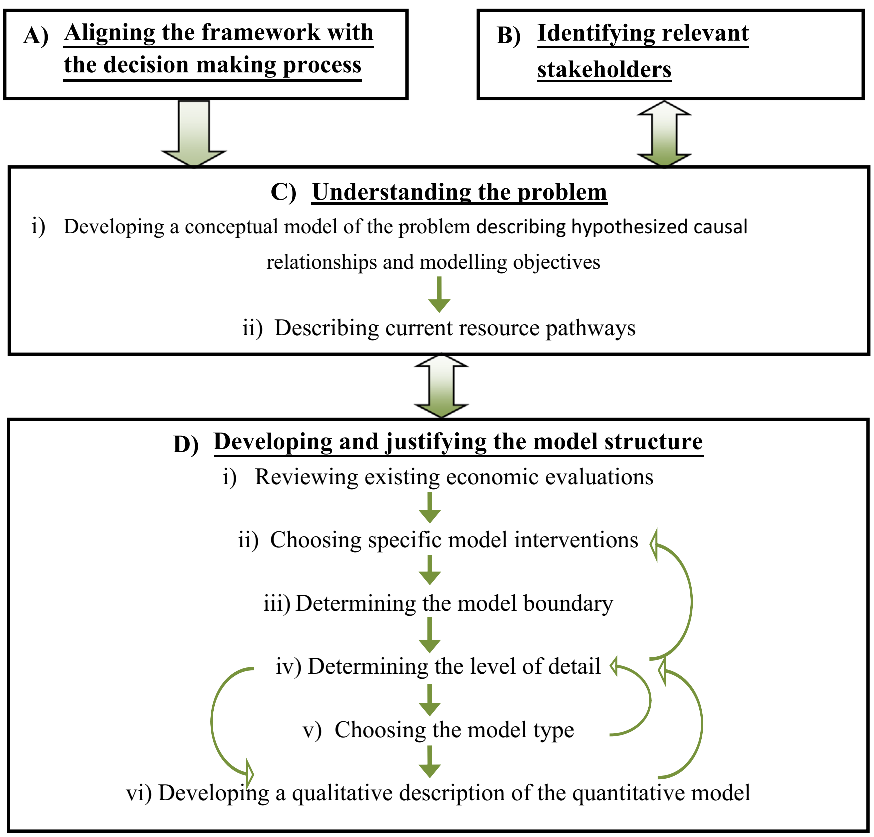


**Fig. 2 – Overview of conceptual modeling framework for public health economic modeling.**

the diabetes example, if a general practitioner (actor) has been identified as a stakeholder, this could help identify the patient (customer). The person with the power to stop the actor giving the customer a service might be the local commissioner (system owner). A table of stakeholders and their roles could be included in the report/appendices (see diabetes example in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011). Stakeholders should be involved during the understanding of the problem phase and the development and justification of the model structure phase. If time and resources allow, this could be through a series of workshops, although modelers should be aware that these are subject to their own dynamics. Practically, the approach to stakeholder communication needs to be flexible. We discuss stakeholder involvement further in phases C and D.

### *Phase C: Understanding the problem*

The whole of phase C is about *problem* formulation rather than *model* formulation. Developing and documenting an understanding of the problem is at the core of being able to develop an appropriate model structure (see key principle of good practice 3). This is about understanding what is relevant to the problem, and should not be limited by what empirical evidence is available [17]. The understanding of the problem phase in Figure 2 comprises 1) developing a conceptual model of the problem describing hypothesized causal relationships (as described in steps 1–4), including specifying a clear research question, and 2) describing present resource pathways. A diagram depicting the understanding of the problem (see Fig. 3 for an illustrative example) and a diagram showing key resource use in the system, both with accompanying notes, can be included in a report. An example of the development of these diagrams using the diabetes pilot study is shown in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011.

*Developing a conceptual model of the problem describing hypothesized causal relationships*. This section outlines a methodology for developing a conceptual model of the problem by using the notation of causal diagrams, borrowing some of the methods from cognitive mapping [27], and ensuring that the worldview of each of the stakeholders is considered [15, 27]. This methodology provides a systematic approach for developing an understanding of the problem at an appropriate and manageable level of relevance. A causal diagram depicts the relationships between factors by arrows, using a "+" or "–" sign to indicate a positive or a negative causal relationship. Causal diagrams allow feedback loops to be described that depict the dynamic complexity of the system. Each factor is a quantity such that one factor leads to an increase or decrease in another factor. For example,

$$\text{CVD event} \xrightarrow{+} \text{Cost and CVD event} \xrightarrow{-} \text{Quality of life}$$

means an increase in cardiovascular disease (CVD) events leads to an increase in costs and a decrease in quality of life, respectively. The hypothesized causal relationships associated with the problem can be depicted using this notation, bringing together the understanding of relevant diseases, human behavior, and societal influences.

*Step 1: What is the problem?*. The first step, on the basis of cognitive mapping [27], is to ask "What is the problem?" This is the key problem from the decision makers' perspective and could be based on the project scope if available. The cause of the problem described should include a potentially modifiable component. Describing the key problem as the starting point encourages a focused boundary around the understanding of the problem.

*Step 2: Why is this a problem?*. The modeler can then ask "Why is this a problem?" and continue to ask "Why?" or "What are the implications of this?" until no more factors are identified, again on the basis of the methods of cognitive mapping [27]. The goal may be to maximize net benefits by maximizing health and minimizing costs, or equity may be considered of primary importance, as is often the case in public health [28].

*Step 3: Developing additional causal links*. A set of questions that may help develop the diagram further has been constructed, as given in Table 1. The development of the understanding of the problem is iterative, and hence it may be useful to continually revisit these questions. The meaning of topic-specific terminology should be clearly described.

*Step 4: Incorporating types of intervention*. In dynamically complex systems such as public health systems, the possible types of interventions may not be easily definable at the start of the project before developing a sufficient understanding of the problem. Thus, the modeler can ask how to avoid or reduce the impact of the described problem. It is useful to know what is considered to be the present practice. Potential types of interventions can then be added on the basis of the project scope, any effectiveness studies identified, and by considering in the diagram when interventions may be beneficial. One way of doing this is to consider which of the potentially modifiable determinants of health (individual lifestyle factors; living and working conditions and access to essential goods; and general socioeconomic, cultural, and environmental conditions) affect the decision problem. Combinations of individual, community, and population interventions may be considered because simultaneous implementation is likely to be most effective [29]. It is not expected that the final interventions being assessed in the model will have been chosen at this stage. It is, however, important to define the types of interventions that might be assessed in the model so that their impact on model factors, including those not already incorporated into the diagram, may be considered.

A set of questions that may be useful for considering the impacts of the interventions has been constructed, as given in Table 2. These should be considered in the context of each type of intervention potentially assessed in the model.

*The research question*. A research question should be agreed upon and clearly specified during the development of the understanding of the problem, and may comprise the types of interventions being assessed, their outcomes, and the population(s) of interest. For example, "What is the effectiveness and cost-effectiveness of intervention *x* which might decrease outcome *y* in population *z*?" The research question should be regularly referred to during the design-oriented conceptual modeling phase (see phase D) so that the model is built for purpose. In addition, as Roberts et al. [7] suggest, the policy context of the modeling project needs to be clear, particularly in terms of the funder, the policy audience, and whether the model is planned to be for single or multiple use.

*Sources of evidence*. The proposed diagram can provide an explicit description of our hypotheses about causal relationships and the challenge is to be able to justify the causal assumptions made. The causal hypotheses can be developed on the basis of a range of sources including the project scope, literature (which may involve perspectives from several disciplines including considering existing models in biology, psychology, sociology, and behavioral economics), stakeholder input, the team's previous work, and any other diagrams developed by the project team or decision makers to depict their understanding of the problem. By developing the diagram with input from stakeholders, it allows their assumptions and beliefs to be made explicit so that they can be agreed upon or questioned. Developing the diagram using all these sources of evidence will be an iterative process, providing multiple opportunities to question and adapt the causal assumptions.

An illustrative example of a conceptual model of the problem for the diabetes pilot project is shown in Figure 3.

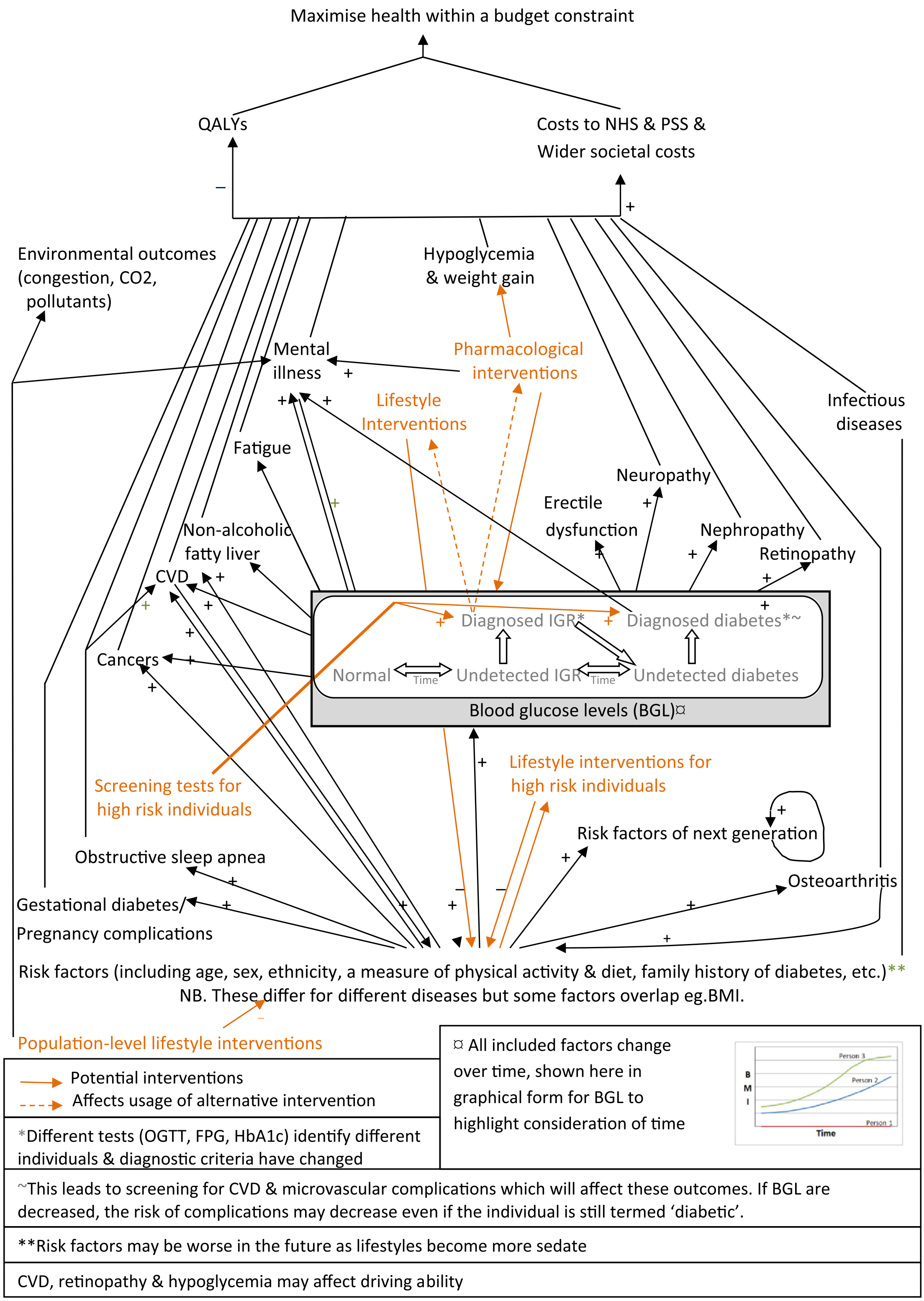


**Fig. 3 – Example conceptual model of the problem (with interventions). BGL, blood glucose level; CVD, cardiovascular disease; FPG, fasting plasma glucose; $HbA_{1c}$, glycated hemoglobin $A_{1c}$; IGR, impaired glucose regulation; NHS, National Health Service; OGTT, oral glucose tolerance test; PSS, Personal Social Services; QALYs, quality-adjusted life-years.**

**Table 1 – Questions about the decision problem to help with developing the diagram.**

1. *Questions relating to the disease and the determinants of health:*
- Have any relevant disease natural histories been captured?
- Are the following determinants of health (taken from the study by Dahlgren and Whitehead [25]) important in determining effects and in what way?
  - Age, sex, and other inherent characteristics of the population of interest
  - Individual lifestyle factors (including diet, physical activity, smoking, alcohol/drug misuse)
  - Social and community networks (including friends, family including intergenerational impacts, wider social circles)
  - Living and working conditions and access to essential goods and services (including unemployment, work environment, agriculture and food production, education, water and sanitation, health care services, housing)
  - General socioeconomic, cultural, and environmental conditions (including economic activity, government policies, climate, built environment including transportation, crime)

2. *Question to help ensure that the understanding of the problem is sufficiently broad:*
- Are there any other (positive or negative) consequences of each factor?

3. *Questions to ensure that the dynamic complexity of the system has been captured:*
- Could there be any other factors that explain two outcomes, for links that may not be causal, but correlated?
- Are there any other possible causal links between the factors? (with the aim of establishing whether there are any feedback loops)
- Are there interactions between people that affect outcomes? (see social networks earlier)
- Is timing/ordering of events important?

**Table 2 – Questions about the interventions and their impacts.**

1. *Questions relating to the constraints of the decision-making process:*
- Are there constraints on the project scope? (e.g., Are we constrained by the types of interventions we are assessing? What about the population?)

2. *Questions relating to the goals and mechanisms associated with the interventions:*
- What are all the outcomes (positive and negative) of the interventions?
- What would happen in the absence of the interventions vs. as a result of the interventions—would outcomes be prevented or delayed?
- What evidence exists to describe the outcomes of the intervention/comparator over time? Are behavioral outcomes important? If so, do any relevant models of behavior from psychology, sociology, or behavioral economics exist to help describe the behavior resulting from the intervention or the comparator? This will require additional targeted literature searches.
- Are there any determinants of health reported by the effectiveness studies that are not included in the causal diagram? Can such a relationship be described?

3. *Questions relating to the dynamic complexity of the system:*
- Might a third party act to reduce the impact of interventions?
- Are there any substantial impacts of social and/or community networks on intervention effectiveness? Will these impacts be captured over the long term in the effectiveness evidence?
- Are there any substantial impacts of the interventions on other lifestyle factors?
- Might the interventions have other impacts not already considered?

*Describing present resource pathways.* A detailed description of resource use at this stage is not necessary because some factors in the conceptual model of the problem will be excluded from the quantitative model. Nevertheless, a broad consideration of resource use at this stage may help the modeler choose which factors to include and exclude from the model when choosing the model boundary (see phase D, "Determining the model boundary" section). For example, a factor that is unlikely to affect the model results substantially on the effect side but requires substantial resources may be included, whereas one that is also unlikely to substantially impact on the cost side may be excluded. Practically, it is useful to begin to establish resource use with stakeholders at this early stage because this usually requires several iterations. Flow diagrams, tables, and/or a textual description of the resource pathways can be useful.

### *Phase D: Developing and justifying the model structure*

This section aims to outline an approach for specifying an appropriate model structure that is feasible, valid, and credible to develop into a quantitative model, which may be described as the design-oriented conceptual modeling phase [17]. As outlined in Figure 2, this phase includes 1) reviewing existing health economic models; 2) choosing model interventions and comparators; 3) determining the model boundary (deciding what factors are included in the model rather than being part of its external environment); 4) determining the level of detail (the breakdown of what is included for each factor in the model boundary and how the relationships between factors are defined); 5) choosing the model type (the analytic modeling technique used, e.g., a Markov model); and 6) developing a qualitative description of the quantitative model. A method for each of these stages is subsequently described. Documenting each of these stages aids in transparency and model verification, validation, and reuse, and suggested ways of doing this are described. As for the understanding of the problem phase, a practical example is shown for the diabetes pilot study in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011. The understanding of the problem, the review of existing economic evaluations, and the review of intervention effectiveness can be used to facilitate decisions around the model boundary, level of detail, and model type, as shown in Figure 4. This figure provides the linkages between each stage. The subsequent sections then provide more detail about how each stage informs the other.

*Reviewing existing health economic models.* It is standard practice in health economic evaluation to undertake a systematic review of existing health economic models in the same area [30, 31]. Some existing models may have been used to develop the understanding of the problem, but a systematic review of models at this stage can be used in a number of ways [32]:

1. To compare and contrast how other modelers have chosen to structure the model and estimate key variables, and how the model results differ on the basis of these choices;
2. To identify which variables are important in influencing model results (including any that have not been highlighted during the understanding of the problem phase) and which do not substantially affect the differences in outcomes between the interventions and comparators;

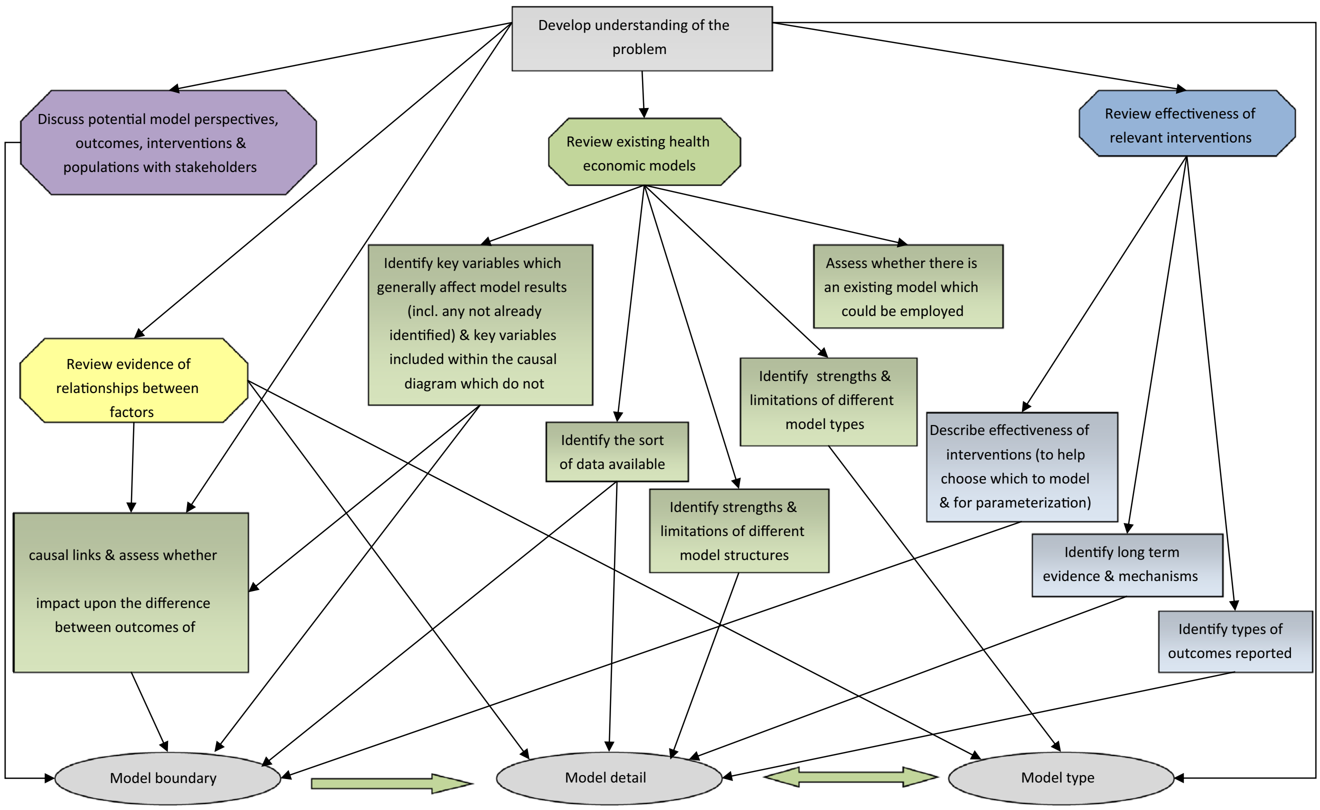


**Fig. 4 – Defining the model boundary, level of detail, and model type.**

3. To provide an insight into the types of data available that may inform the model level of detail;
4. To consider the strengths and limitations of existing economic evaluations, to inform model development;
5. To determine whether there is an existing model that could be used, either in part or as a whole.

*Choosing model interventions and comparators.* The decision makers (with consideration of the clients' needs if they are not the decision makers) should define which specific interventions to model, with reference to the intervention effectiveness evidence, and according to expertise from other stakeholders. The decision makers may limit interventions to be assessed on the basis of the evidence available, including relevant populations, outcomes, and potential biases in the trials. It is possible that one good study or a number of studies can be used to estimate the short-term effectiveness. As far as possible, the comparator can be based on the same studies as the interventions if this is representative in practice. If practice is substantially different, then an adjustment on the effectiveness estimate would be required. Context is important for the effectiveness of public health interventions. Given that economic evaluation is a comparative analysis, the model results are meaningful only in relation to the comparators chosen [7].

*Determining the model boundary.* Determining the model boundary is about deciding, on the basis of the understanding of the problem, what factors should be judged as relevant for inclusion in the model and which can be excluded given the time and resource constraints of the decision-making process. The boundary of the model must differ from the boundary of the understanding of the problem to be able to make informed judgments about what is important to include in the model structure. The model boundary should be defined such that all important interactions between the elements of the system identified in the understanding of the problem are captured [23].

*Model population and subgroups.* The model populations can be discussed with the stakeholders, informed by the populations in the intervention effectiveness evidence. The modeling team and the stakeholders could consider whether there is a bigger problem in a particular subgroup or whether the intervention is likely to be more effective in a particular subgroup and whether there is sufficient data to undertake any subgroup analysis. These might be based on the determinants of health shown in Figure 1, including age, sex, and other inherent characteristics of the population of interest, individual lifestyle factors, living and working conditions and access to essential goods, and general socioeconomic, cultural, and environmental conditions.

*Model perspectives and outcomes.* Often in health economic evaluation, a health sector perspective is used [30]. Nevertheless, in public health economic modeling, other perspectives are likely to be relevant because substantial costs and benefits may extend beyond these sectors. Alternative perspectives include (but are not limited to) a societal perspective, a public sector perspective, or the perspective of the particular agencies involved in the system. Of particular importance will be the perspectives of the system owners identified in phase B of the framework. For example, if employers are considered to be system owners, then an employer perspective would be useful. It should be noted that there are at present unresolved issues around using these alternative perspectives in terms of 1) whether it is possible or desirable to make social value judgments associated with the value of health relative to the

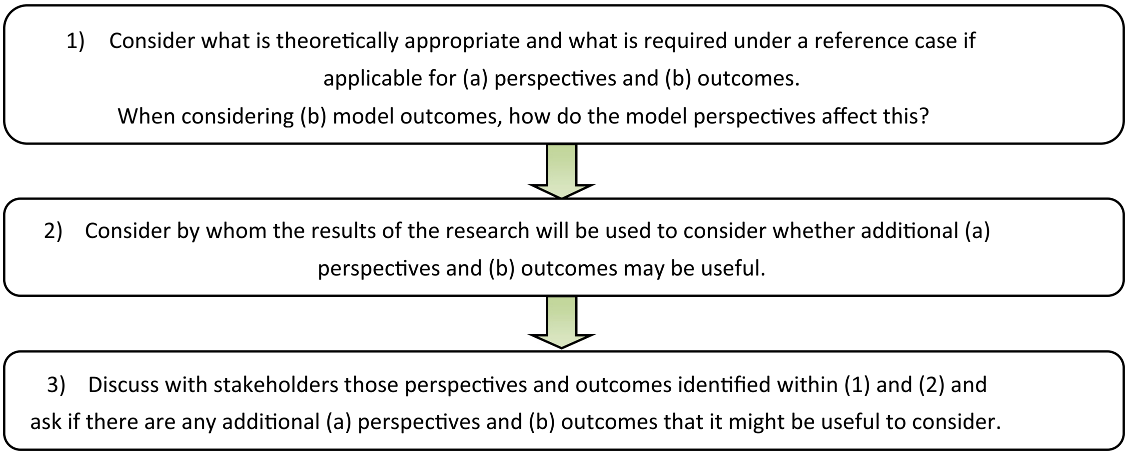


**Fig. 5 – Method for choosing appropriate modeling perspectives and outcomes.**

value of other costs and benefits and 2) the practicality of transferring costs and benefits between sectors [33]. Nonetheless, if substantial costs and benefits are expected to fall outside of the National Health Service and the Personal Social Services (PSS), presenting these alternative perspectives is likely to be informative for decision makers.

To be able to compare interventions across different populations in terms of health costs and outcomes, the incremental cost per quality-adjusted life-year may be used [34]. When the model boundary extends beyond health, it may be useful to understand the modeling requirements in other sectors so that relevant outcomes may be presented. A cost-benefit analysis may be considered theoretically superior given the scope of public health interventions and outcomes [35]; nevertheless, there are at present practical issues associated with monetary valuation of outcomes. One way of presenting multiple outcomes for different sectors is to present a cost-consequence analysis alongside the cost-effectiveness analysis [36–38]. A method for choosing model outcomes and perspectives has been outlined in Figure 5.

*Other model boundary considerations*. An algorithm to help define the model boundary is shown in Figure 6 and can be considered for each factor in the conceptual model of the problem. In Figure 6, the question "Does the factor have many causal links?" aims to identify which factors are central and should be included in the model, even in the absence of data (lots of links), and which factors are less important (not many links to other factors). Formal approaches for assessing importance or centrality in extensive causal chains are available and implemented in computer software [27]. The question of whether the impact of a factor is substantially captured by other factors attempts to exclude any double counting.

Subsequent questions in Figure 6 encourage the modeler to think about whether it is worthwhile including noncentral factors given the expected results of the model and the anticipated direction of effect of the factor on those results, as well as the differential impacts of the interventions on that factor. If different interventions impact on the factor through different mechanisms, then including or excluding the factor may lead to different incremental analysis conclusions. The question in Figure 6 about whether the factor is likely to have a substantial impact on the difference between costs and effects of the interventions entails having an understanding of the magnitude of the cost and outcomes associated with the factor and the extent to which the interventions might change these. Such subjective judgments will inevitably be considered in the context of the time available for modeling and the potential future uses of the model. The model boundary stage, however, should not be overly dependent on the evidence or time available because this can be accommodated by the level of detail incorporated. It is likely to be more appropriate to crudely include a factor that is expected to substantially affect the model results than to exclude it from the model completely. Finally, to maintain model credibility, stakeholders can be asked whether they are happy, given these justifications, with the exclusion of factors. One way of reporting this stage is to produce a table stating whether each factor is included or excluded and the justification for exclusion, as suggested by Robinson [39].

*Determining the level of detail*. The *level of detail* is defined as the breakdown of what is included for each factor in the model boundary and how the relationships between factors are defined. A decision about which parts of the model are likely to benefit from a more detailed analysis can be made a priori to avoid situations in which the modeler focuses on specific parts of the model because they are more easily dealt with and subsequently run out of time to develop other parts in detail. Essentially, the modelers can weigh up, on the basis of the documented understanding of the problem and the defined model boundary, whether the time required to do one analysis at a specific level of detail in the model is likely to have more of an impact on the model results compared with comparative time spent on other analyses, given the present evidence available and the overall time constraints. During model analysis, more detail can be incorporated if part of the model is shown to substantially affect the results. Table 3 summarizes key questions for the modeler to help choose an appropriate level of detail.

*Searching for evidence*. Data for inclusion for specifying the model structure and its parameters will need to be identified at this point if they have not been already. This could be based on literature identified during the development of the conceptual model of the problem for which specific literature was noted as useful, although additional specific searches may also be required. Data collection and the development of a description of the level of detail for the model will be a highly iterative process. Sufficient evidence is required to be able to justify why the modeling choices have been made [10]. It is important to note that elements for which there is a lack of empirical data and which are considered to have key differential impacts on the comparator(s) and the intervention(s) may be informed by expert

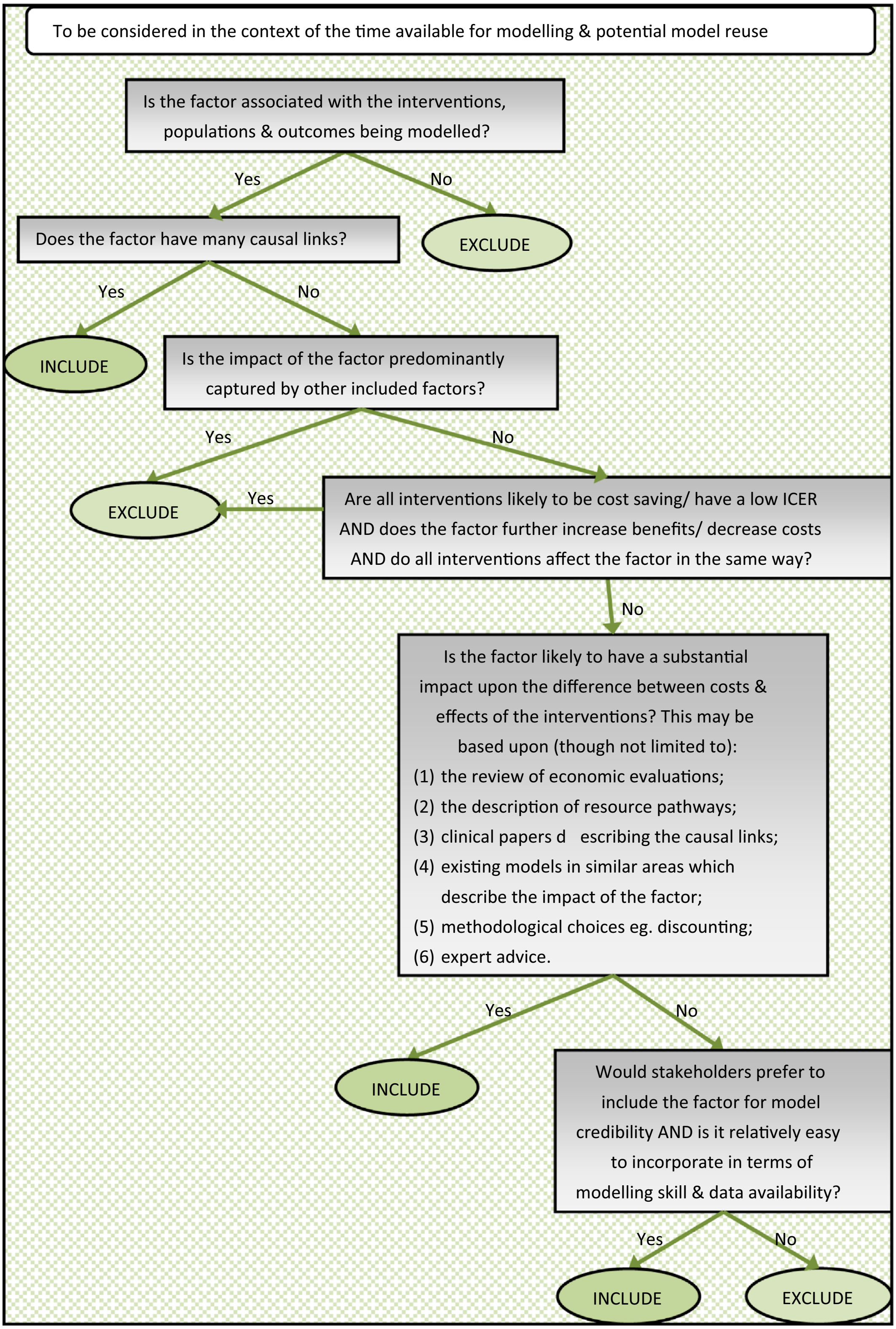


**Fig. 6 – Defining the model boundary. ICER, incremental cost-effectiveness ratio.**

elicitation. One consideration at this stage is likely to be the derivation of the disease natural history parameters, which may be taken from existing studies or calibrated using statistical methods.

*Expressing structural uncertainty.* It is likely to be preferable to limit the development of different model structures in policy analysis, and conceptual modeling can be used to do so. Nevertheless, when there is more than one plausible assumption that

**Table 3 – Questions to help in making judgments about the model level of detail.**

1. *General question:*
   - Is the time required to do the analysis at a specific level of detail likely to have more of an impact on the model results than the same time period spent on other analyses, given the evidence available and the overall time constraints?
2. *Questions to describe the relationship between the included factors over time:*
   - What outcomes are reported in the review of intervention effectiveness? (to help choose which causal links to include)
   - What evidence is available to model the causal links and the outcomes of the factor? (to avoid relying on the first available evidence)
   - What do other economic evaluations suggest are the strengths and limitations of different mathematical relationships between model factors?
   - Which determinants of health are key drivers of the problem according to relevant theory?
3. *Questions to help extrapolate study outcomes:*
   - What outcomes are reported in the review of intervention effectiveness?
   - What evidence is available for long-term follow-up?
   - Is there sufficient evidence and time available to model social networks given the expected impact on model results (on the basis of the understanding of the problem)?
4. *Questions about the level of detail used to describe each included factor:*
   - Which are the specific aspects of each factor that are likely to have a substantial impact on the model results?
     - Is all costly resource use captured?
     - Are all substantial health benefits and disbenefits captured using measures acceptable to the decision maker given the available evidence?
   - Are impacts included in both costs and benefits where appropriate?
5. *Questions about how interventions will be implemented in practice:*
   - What do the effectiveness studies describe?
   - What do stakeholders suggest would happen in practice and is this likely to lead to different estimates of effectiveness to those in the study?

may substantially affect the results, it may be appropriate to develop model structures for each assumption to undertake posterior analysis of structural uncertainty, for example, model averaging. This would be undertaken by creating a parameter to be included in the PSA to represent the probability of each structure being appropriate. This parameter and its distribution could then be estimated by elicitation with experts [40].

*Reporting level of detail.* A document can be developed that describes and explains the key model simplifications and assumptions for discussion with stakeholders, ideally during a second workshop. Writing these down with justification provides a mechanism for systematically questioning the simplifications and assumptions with stakeholders and the project team to improve model validity and credibility. It also facilitates the development of models in future projects. The level of detail will be affected by the model type chosen, and hence it will be an iterative process between identifying an appropriate level of detail and choosing the model type.

*Choosing the model type*

*Most appropriate model type given the characteristics of the problem.* It is important to understand the most appropriate method given the characteristics of the problem, even if it is not practical to develop this model type, so that the simplifications being made are clear. A number of existing articles outline taxonomies for deciding on appropriate model types given the characteristics of the problem for health economic modeling [41–43]. Although decision trees and Markov models are most often used when modeling clinical interventions [42], because of the complexity associated with public health systems it is likely that alternative model types may be more appropriate. Agent-based simulation (ABS) is not included in existing taxonomies; it may, however, be useful for modeling dynamically complex public health systems. ABS is a bottom-up approach in which the behavior of the system is a result of the defined behavior (based on a set of rules) of individual agents and their interactions in the system [44]. Thus, ABS may be preferable when the interactions between heterogeneous agents and their environment are important. ABS more easily allows the analyst to capture spatial aspects to model appropriate interactions (e.g., family and friend networks for transmission of a contagious disease) [44]. Studies have shown strong social network impacts of behaviors such as dietary habits [45].

*Most appropriate model type on the basis of broader considerations.* It may not always be practical to use the model type that is most appropriate for the characteristics of the problem. Figure 7 provides an outline of how the modeler might decide on the most appropriate model type according to broader practical issues.

*Qualitative description of the quantitative model.* A qualitative diagram of the quantitative model alongside the development of the model structure can facilitate clear communication of the final model structure to stakeholders, other members of the team, and people who may want to understand the model in the future. Standard diagrams associated with each model type can be developed. Although the design-oriented conceptual modeling can be described before the quantitative model development, it may be iteratively revised according to data availability and/or inconsistencies identified during the development of the quantitative model [17,19,20,39]. These modifications should be documented throughout so that there is transparent justification for the final model developed.

## Discussion and Conclusions

A conceptual modeling framework has been developed as a helpful tool for modelers of public health economic models. The recent development of two conceptual modeling frameworks for assessing the cost-effectiveness of clinical interventions highlights the importance and timely nature of this work [7, 17]. The conceptual modeling framework developed here complements and adds to these existing frameworks by focusing on public health economic modeling and providing practical approaches for the modeler to follow throughout the conceptual modeling process. The main contribution of this research is that it draws upon several disciplines to provide a systematic approach for developing public health model structures and, in particular, systematic consideration of:

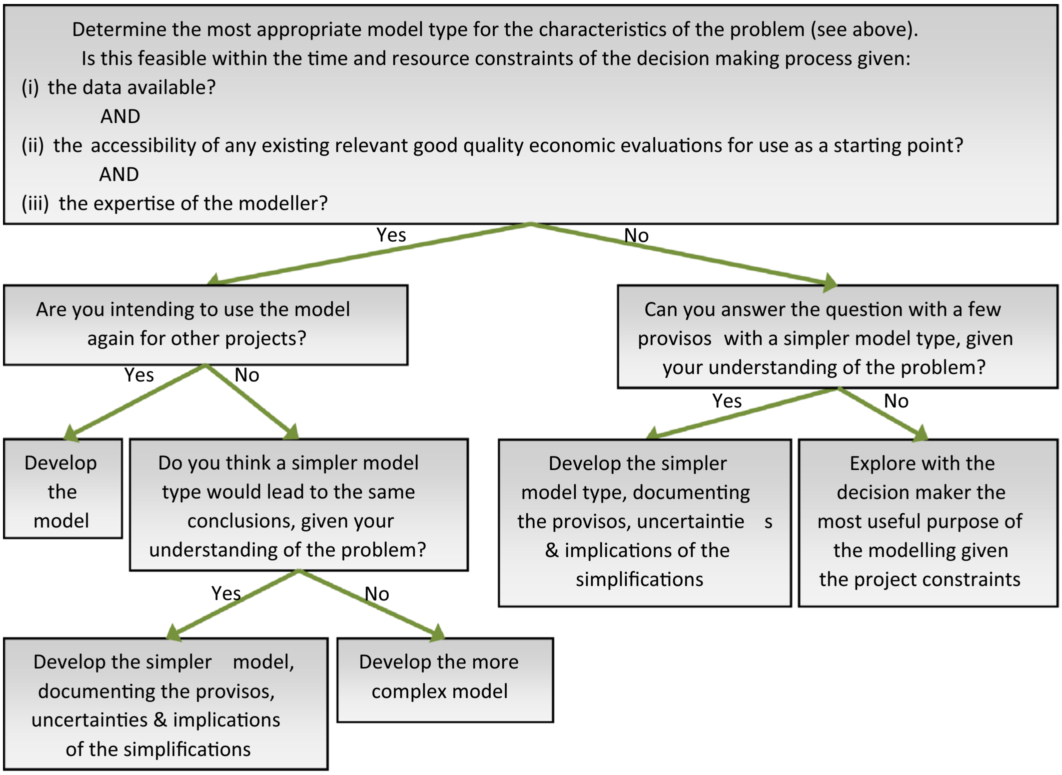


**Fig. 7 – Choosing the model structure.**

1. the social determinants of health;
2. the dynamic complexity (feedback loops, unintended consequences);
3. the understanding of the problem;
4. moving from an understanding of the problem to the model structure; and
5. stakeholder involvement.

The aim of this systematic approach is to help to improve the quality of public health economic models to support the efficient allocation of scarce resources and contribute to improved health and well-being.

The use of the conceptual modeling framework requires a shift in the way some modelers who are used to developing models of clinical interventions approach decision problems, both in terms of the planning and reporting process and the consideration of the broader determinants of health and dynamic complexity. This shift is essential if model development in public health economic evaluation is to be improved. There are typically time constraints around the decision-making process, and an important practical consideration is that if the modelers are spending time justifying the model structure, then they are not spending time on other modeling activities. Phase A of the framework relates to adapting the framework according to the specific requirements of the project. Model justification is always good practice; nevertheless, less time will be required for conceptual modeling for a simpler problem. In the present practice, the model type developed is often based on that which is familiar to the modeler or one previously used in that area. Training may be required for some modelers to expand their skills beyond developing decision trees and Markov models to allow a shift in the approach for public health modeling.

Forrester [46] states that "any worthwhile venture emerges first as an art, and as such the outcomes are special cases and are poorly transferable, but that this can then be transformed into a science by understanding the foundations of the art, making it more useful to new situations." The research presented here aims to improve and make transparent the present understanding of conceptual modeling in public health economic evaluation to take the first step in moving from an art to a science. Because this is the first framework of this kind, it provides modelers in public health economic evaluation with a conceptual modeling process that they are able to critique, which has not existed before this research.

Although this conceptual modeling framework was developed by drawing upon different types of decision problems and contexts, it has not yet been applied in multiple case studies. The Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.011 provide an illustration of the methods applied to the diabetes prevention pilot project. The use of the framework in this case study suggested that it is a potentially useful method. The diabetes project was complex in terms of the problem, the relevant stakeholders, and the mathematical model developed. The conceptual modeling framework provided an approach for the team to follow to help deal with this complexity. It is intended that as the conceptual modeling framework is applied in different projects and as developments in other related research areas are made, it will be continually improved. Thus, its use in case studies and future developmental suggestions are encouraged. Key areas for further research involve evaluation of the framework in diverse case studies and the development of methods for modeling individual and social behavior drawing upon sociology, psychology, and public health.

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## Supplementary Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2016.02.011 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

## REFERENCES


[1] Pidd M. Tools for Thinking: Modelling in Management Science. Chichester, UK: John Wiley and Sons, Ltd., 2009.
[2] Ackoff RL. The future of operational research is past. J Oper Res Soc 1979;30:93–104.
[3] Chilcott J, Tappenden P, Rawdin A, et al. Avoiding and identifying errors in health technology assessment models. Health Technol Assess 2010;14:iii–iv, ix–xii, 1–10.
[4] Claxton K, Sculpher M, McCabe C, et al. Probabilistic sensitivity analysis for NICE technology assessment: not an optional extra. Health Econ 2005;14:339–47.
[5] Kelly MP, Doohan E. The social determinants of health. In: Merson MH, Black RE, Mills AJ,eds. Global Health: Diseases, Programs, Systems and Policies. Burlington, MA: Jones & Bartlett, 2012: 75–113.
[6] Squires H, Chilcott J, Akehurst R, et al. A systematic literature review of the key challenges for developing the structure of public health economic models. Int J Public Health [Epub ahead of print] January 8, 2016.
[7] Roberts M, Russell L, Paltiel D, et al. Conceptual modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force—2. Med Decis Making 2012;32:678–89.
[8] Squires H. A methodological framework for developing the structure of public health economic models. 2014. Available from: http://etheses.whiterose.ac.uk/5316/. [Accessed April 1, 2015].
[9] Public Health Research Consortium. 2013. Available from: http://phrc.lshtm.ac.uk/. [Accessed June 1, 2013].
[10] Paisley S. Identifying Evidence to Inform Decision-Analytic Models of Cost-Effectiveness: A Qualitative Study of Information Seeking Processes and Behaviour. PhD Thesis, University of Sheffield, UK, 2012.
[11] Breeze P, Preston L, Squires H, et al. Modelling the economics of type 2 diabetes mellitus prevention: a literature review of methods. Appl Health Econ Health Policy 2014;12:239–53.
[12] Shiell A, Hawe P, Gold L. Complex interventions or complex systems? Implications for health economic evaluation. BMJ 2008;336: 1281–3.
[13] Sterman JD. Learning from evidence in a complex world. Am J Public Health 2006;96:505–14.
[14] Von Bertalanffy L. General System Theory: Foundations, Development, Applications. New York, NY: George Brazillier, Inc., 1968.
[15] Checkland P. Soft Systems Methodology: A 30-Year Retrospect. Chichester, UK: John Wiley & Sons, Ltd., 1999.
[16] Sterman JD. Business Dynamics: Systems Thinking and Modeling for a Complex World. Jeffrey J. Shelstad, USA, 2000.
[17] Kaltenthaler E, Tappenden P, Paisley S, Squires H. Identifying and reviewing evidence to inform the conceptualisation and population of cost-effectiveness models. National Institute for Health and Care Excellence (NICE) DSU Technical Support Documents, 2011.
[18] Robinson S. Conceptual Modeling for Simulation. New York, NY: Wiley, 2011.
[19] Howick S, Eden C, Ackermann F, Williams T. Building confidence in models for multiple audiences: the modelling cascade. Eur J Oper Res 2008;186:1068–83.
[20] Rodriguez-Ulloa R, Paucar-Caceres A. Soft system dynamics methodology (SSDM): combining soft systems methodology (SSM) and system dynamics (SD). Syst Pract Action Res 2005;18:303–32.
[21] Fernández I, Kekäle T. Better models with Delphi and analytic hierarchy process approaches: the case of reverse logistics. Int J Logistics Syst Manag 2008;4:282–96.
[22] Vennix JAC, Gubbels JW. Knowledge elicitation in conceptual model building: a case study in modeling a regional Dutch health care system. Eur J Oper Res 1992;59:85–101.
[23] Flood R, Jackson M. Creative Problem Solving: Total Systems Intervention. Chichester, UK: John Wiley & Sons, Ltd., 1991.
[24] Plous S. The Psychology of Judgement and Decision Making. New York, NY: McGraw-Hill, 1993.
[25] Dahlgren G, Whitehead M. Policies and strategies to promote social equity in health (Mimeo). Stockholm, Sweden: Institute for Future Studies, 1991.
[26] Kelly MP. The individual and the social level in public health. In: Killoran A, Kelly MP,eds. Evidence Based Public Health: Effectiveness and Efficiency. Oxford, UK: Oxford University Press, 2009.
[27] Eden C, Ackermann F. Making Strategy: The Journey of Strategic Management. London: Sage, 1998.
[28] Cookson R, Drummond M, Weatherly H. Explicit incorporation of equity considerations into economic evaluation of public health interventions. Health Econ Policy Law 2009;4:231–45.
[29] National Institute for Health and Clinical Excellence. Behaviour Change at Population, Community and Individual Levels. NICE Public Health Guidance, 2007. https://www.nice.org.uk/guidance/ph6. [Accessed June 1, 2013].
[30] Briggs A, Claxton K, Sculpher M. Decision Modelling for Health Economic Evaluation. New York, NY: Oxford University Press, 2006.
[31] National Institute for Health and Clinical Excellence. A Guide to the Methods of Technology Appraisal. London: National Institute for Health and Clinical Excellence, 2008.
[32] Anderson R. Systematic reviews of economic evaluations: utility or futility? Health Econ 2010;19:350–64.
[33] Claxton K, Sculpher M, Culyer A. Mark versus Luke? Appropriate methods for the evaluation of public health interventions. Working Papers from Centre for Health Economics, University of York, 2007.
[34] Drummond MF. Methods for the Economic Evaluation of Healthcare Programmes. (3rd ed). Oxford, UK: Oxford University Press, 2005.
[35] Edwards RT, Charles JM, Lloyd-Williams H. Public health economics: a systematic review of guidance for the economic evaluation of public health interventions and discussion of key methodological issues. BMC Public Health 2013;13:1001.
[36] Kelly MP, McDaid D, Ludbrook A, Powell J. Economic Appraisal of Public Health Interventions. London: National Institute for Health and Clinical Excellence, 2005.
[37] Weatherly H, Drummond M, Claxton K, et al. Methods for assessing the cost-effectiveness of public health interventions: key challenges and recommendations. Health Policy 2009;93:85–92.
[38] Anderson R. Modelling and evidence synthesis: challenges, value and issues for discussion. Presented at: Workshop in Methods of Economic Evaluation in Public Health Research, Public Health Research Consortium, University of York, July 13, 2010.
[39] Robinson S. A Framework for Simulation Conceptual Modeling: Conceptual Modeling for Discrete-Event Simulation. Boca Raton, FL: Taylor & Francis Group, 2011; 73–101.
[40] Bojke L, Claxton K, Sculpher M, Palmer S. Characterizing structural uncertainty in decision analytic models: a review and application of methods. Value Health 2009;12:739–49.
[41] Brennan A, Chick SE, Davies R. A taxonomy of model structures for economic evaluation of health technologies. Health Econ 2006;15: 1295–310.
[42] Barton P, Bryan S, Robinson S. Modelling in the economic evaluation of health care: selecting the appropriate approach. J Health Serv Res Policy 2004;9:110–8.
[43] Cooper K, Brailsford S, Davies R. Choice of modelling technique for evaluating health care interventions. J Oper Res Soc 2007;58:168–76.
[44] Siebers PO, Macal CM, Garnett J, et al. Discrete-event simulation is dead, long live agent-based simulation! J Simul 2010;4:204–10.
[45] Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. N Engl J Med 2007;357:370–9.
[46] Forrester J. Industrial Dynamics. New York, NY: Wiley, 1961.