

**Title: Designing and Undertaking a Health Economics Study of Digital Health Interventions**

**Authors:**

**Paul McNamee, PhD.** Health Economics Research Unit, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK.

**Elizabeth Murray, FRCGP, FRCP, PhD.** eHealth Unit, Research Department of Primary Care and Population Health, University College London, London, UK.

**Michael P. Kelly, Hon FRCP, FRCPE, FFPH, PhD.** Primary Care Unit, Institute of Public Health, University of Cambridge, Cambridge, UK.

**Laura Bojke, PhD.** Centre for Health Economics, University of York, York, UK.

**Jim Chilcott, MSc.** Health Economics and Decision Science, School of Health and Related Research, University of Sheffield, Sheffield, UK.

**Alastair Fischer, PhD.** Public Health and Social Care Section, National Institute for Health and Care Excellence, London.

**Robert West, PhD.** Health Behaviour Research Centre, Department of Epidemiology and Public Health, University College London, London.

**Lucy Yardley, PhD.** Department of Psychology, University of Southampton, Southampton, UK.

**Corresponding Author:**

Paul McNamee, PhD

Health Economics Research Unit

Institute of Applied Health Sciences

University of Aberdeen

Aberdeen, UK

AB25 2ZD

Tel: 01224 437169

Fax: 01224 437195

Email: [p.mcnamee@abdn.ac.uk](mailto:p.mcnamee@abdn.ac.uk)

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## Abstract

This paper introduces and discusses key issues in the economic evaluation of digital health interventions. The purpose is to stimulate debate so that existing economic techniques may be refined or new methods developed. The paper does not seek to provide definitive guidance on appropriate methods of economic analysis for digital health interventions.

We describe existing guides and analytical frameworks that have been suggested for the economic evaluation of health care interventions. Using selected examples of digital health interventions, we assess how well existing guides and frameworks align to digital health interventions. We show that digital health interventions may be best characterised as complex interventions in complex systems. Key features of complexity relate to intervention complexity, outcome complexity and causal pathway complexity, with much of this driven by iterative intervention development over time and uncertainty regarding likely reach of the interventions amongst the relevant population. These characteristics imply that more complex methods of economic evaluation are likely to be better able to capture fully the impact of the intervention on costs and benefits over the appropriate time horizon. This complexity includes wider measurement of costs and benefits, and a modelling framework that is able to capture dynamic interactions between the intervention, the population of interest and the environment. We recommend that future research should develop and apply more flexible modelling techniques, to allow better prediction of the inter-dependency between interventions and important environmental influences.

## Background

The purpose of economic evaluations of digital health interventions (DHIs) is to inform decision-makers about the relative value for money of those interventions against specified alternatives. With resource scarcity, it is argued that use of resources will be more efficient if these are allocated to interventions where the magnitude of additional benefits relative to the magnitude of additional costs is greatest, subject to an identified budget constraint.

There are several ways to conduct an economic evaluation of health interventions. One of the most common is Cost-Utility analysis. This measures benefits in terms of Quality Adjusted Life Years (QALYs), which is a measure of length of life weighted by quality of life to reflect desirability of that life (scaled from 0 to 1, where 0=dead and 1=perfect health). Other analyses include Cost-Effectiveness Analysis, which measures benefits in terms of clinical units, such as whether an individual is free of symptoms, and Cost-Consequences Analysis, an extended form of Cost-Effectiveness Analysis, where multiple benefits are measured and reported separately. Within other public policy fields, such as environment and transport appraisal, the technique of Cost-Benefit Analysis is the most common type of evaluation, with the benefits of programs being measured in monetary terms.

Several sets of guidelines for the design and conduct of economic evaluation exist for studies in health care,<sup>1</sup> but the extent to which these are relevant to DHIs has received little attention. The term ‘digital health interventions’ in this paper refers to interventions that employ digital technology to promote and maintain health, through supporting behaviour change or decision making of the general public, patients or healthcare practitioners. Interventions are typically automated, interactive and personalized, employing user input or sensor data to tailor feedback or treatment pathways (e.g. a smartphone app to promote greater levels of physical activity

would be one example). In telemedicine and telecare, which may be component parts of some DHIs, systematic reviews suggest there is a lack of good evidence regarding costs and therefore cost-effectiveness,<sup>2,3</sup> and this partly arises through lack of methodological rigour within the original published studies.<sup>4</sup>

The paper does not seek to provide definitive guidance on appropriate methods of economic analysis for DHIs, but instead aims to highlight key issues in the economic evaluation of DHIs, in order to stimulate debate so that refined economic tools and methods may in due course be developed. The paper is organised along the following lines. First, we describe existing guides and analytical frameworks suggested for the economic evaluation of interventions applied to complex interventions. Second, using selected examples of DHIs, we assess how well existing guides and frameworks map to DHIs. Third, we propose key decision points in the design and conduct of economic evaluations.

## Existing Analytical Frameworks

### 1. ISPOR Good Research Practice Guide

To enhance the conduct and reporting of trial-based economic evaluation studies applied to new medicines, medical devices and procedures, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has published an updated good research practice guide.<sup>1</sup> This re-emphasises the need to base economic evidence on effectiveness rather than efficacy, the benefits from direct data collection on resource use and health states (or other measures of effectiveness) from study participants rather than indirectly (such as mapping), and recognising that study designs such as randomised controlled trials (RCTs) are complementary to model-based evaluations. These recommendations appear salient for evaluation of DHIs. For example, there is already recognition that RCTs are not always appropriate as a means to establish effectiveness,<sup>5</sup> and a similar argument holds for evaluation of cost-effectiveness.

In some specific areas however, the recommendations may be less appropriate for DHIs. For example, where interventions are designed in order to bring about health behaviour change, it can be argued that they differ from medicines, devices and procedures in terms of intended mechanisms of action. Here notions of mechanism of action confined to biological interactions within single individuals have been significantly developed and refined,<sup>6-9</sup> to accommodate importance of interaction with the health and social care system, or the wider social environment.

One area in particular where there may be a need for a different approach relates to the use of intermediate (surrogate) measures of benefit. The ISPOR guide recommends that the use of “intermediate (or surrogate)” measures should be avoided in the measurement of benefit wherever possible. However, when the expected effects of an intervention are only likely to be observed in the long-term, the guide suggests that surrogate measures are appropriate, as long as the relationship to “final” measures (e.g. mortality, health related quality of life, or well-being) is firmly established. A focus on surrogate measures may not be sufficient in circumstances where intervention adapt and change over time, where the mechanisms of action are unclear and where effectiveness and cost-effectiveness is theorised to relate closely to the system or environment in which it is placed. In short, existing guidelines such as the ISPOR guide, which are available for medicines, devices and procedures, may require amendment for many DHIs.

## **2. MRC Framework for Complex Interventions**

DHIs can be characterised as ‘complex interventions’ in a complex system.<sup>10-12</sup> Within the MRC Framework for the Evaluation of Complex Interventions,<sup>13</sup> a complex intervention is one that “contains several interacting components, and other characteristics, such as the number and difficulty of behaviours required by those delivering or receiving the intervention”. Complexity may also refer to features of the system in which an intervention is implemented, as well as the intervention itself. Shiell et al<sup>12</sup> note that “a complex system is one that is adaptive to changes in its local environment, is composed of other complex systems, and behaves in a non-linear fashion (i.e. change in outcome is not proportional to change in input)”. Petticrew et al<sup>14</sup> outline this further by drawing distinctions between intervention complexity, outcome complexity and causal pathway complexity:

- **Intervention complexity:**

- Multiple, interacting components
- Likely to be tailored, adapt or change over time

- **Outcome complexity:**

- Spillovers and externalities, i.e. outcomes go beyond the immediate recipient of the intervention, such as influencing the behaviour or health of other family members
- Feedback loops, i.e. the uptake of the intervention may be affected by uptake by others, “social contagion” effect

- **Causal pathway complexity:**

- Multiple moderators and mediators of the relationship between intervention and outcomes, in particular strong influence of system characteristics (i.e. the setting/context of the intervention is important and likely to generate heterogeneity in costs and benefits, through differences in resource availability, culture, beliefs, attitudes, interpersonal relationships)
- Non-linear relationships between intervention resource inputs and multiple outputs, “phase” changes, i.e. sudden, unpredictable tipping points

A key question is the extent to which DHIs map to the above types of complexity. Clearly some may align with the above classification more than others; for example, consider a health app for the management of type 2 diabetes - if additional input from health care staff is required according to individual patient goals or preferences, or if the intervention partly comprises an element of feedback from health care staff, then this gives rise to *intervention complexity* – the intervention is highly individualised and heterogeneous. There may also be *outcome*



complexity, e.g. if the individual needs to change food and alcohol intake, then other household members may also have to change, but may be resistant to this. Further, if the app includes the option of information exchange with other users, e.g. electronic posting of goals achieved, this could affect behaviour in a positive or negative way. Finally, there may need to be a set of necessary conditions in place for the intervention to be effective, especially in the longer-term; these could relate to a set of motivational factors, such as prior diabetes history, other patient characteristics (education, income, and time preference in terms of willingness to invest time and effort today in order to achieve additional benefits later) and wider contextual factors, such as an individual being within a social network where members already undertake “healthy behaviours”. These conditions give rise to *causal pathway complexity*. Taken together, it could be argued that the health app intervention is a complex intervention in a complex system. Conversely, other DHIs for the same condition may exhibit less complexity, for example, if there is little or no interaction with health care professionals or other recipients, then *causal pathway complexity* is likely to be smaller.

Taking forward these notions, Shiell et al<sup>12</sup> draw out some lessons for economic evaluation; it is argued that, where a complex intervention lacks significant interaction with the setting, i.e. where the casual pathway is relatively simple, current methods of economic evaluation might be sufficient, i.e. identifying, measuring and valuing resource use and weighing that against the value of health or other outcomes that are produced. However, where there is significant interaction with setting, there are potentially additional challenges for economic evaluation. These include more difficult choices regarding what measures of effectiveness should be included, how consequences should be valued, and how evaluation should be conducted. More fundamentally, there may be significant challenges associated with historicity or path dependence. For instance, the past twenty years have seen a marked change in public

acceptability of smoking and use of mobile devices, so it may be hypothesised that a DHI intervention to encourage smoking cessation may have achieved very different effects at any point during that period. These challenges may lead therefore to a need to conduct a “complex economic evaluation”, e.g. attempting to estimate cost-effectiveness for sub-groups according to the extent of interaction with the system or with each other. (Note however that it is still legitimate to conduct “simple” evaluations of complex interventions, by addressing “simple” questions,<sup>14</sup> e.g. what is the average change in health and costs after intervention receipt, relative to usual care?). Ultimately, the type of evaluation conducted will depend on the research question, as well as extent of interaction, between intervention and system/setting, or between individuals, and the importance this has for generating heterogeneity in costs and benefits.

To illustrate what a complex economic evaluation might look like, consider Zhang et al,<sup>15</sup> who used an agent-based model of social network interactions to examine the effect of different policy instruments in changing dietary behaviours (Figure 1). Based on a multi-level theory of population health that encompasses habitual behaviours,<sup>16</sup> behaviours are influenced by standard economic incentives, such as price, but also affected by cognitive habits that are subject to social norms. The model simulated potential policy impacts (e.g taxation), and could be extended by incorporating data from natural experiments and health administrative records, to examine influences on health, well-being and costs to the health care system.

Whether simple or complex, a key factor in economic evaluation relates to judgement regarding the time frame for the expected effects to occur. This creates a challenge for DHIs as the content of many interventions evolves over time, and there may be a protracted period before benefits are observed. Conventional approaches have usually been built on the randomised

controlled trial (RCT). The RCT is designed to determine whether the relationship between a constant (the independent variable) and the outcome of the interaction it has with the environment into which it is applied is free from bias. So long as the intervention is constant, then this is appropriate. But some DHIs are not constant, with many evolving as they are implemented. As a result, the artificial nature of RCTs may mean that they are not good vehicles to indicate the potential impact of DHIs.

If trials with randomisation at the individual level are potentially problematic, what are the alternative options? Aside from cluster-randomisation, other study designs such as natural experiments are possible.<sup>17</sup> For example, the five test bed sites within NHS England provide a vehicle to examine effectiveness and cost-effectiveness on a large scale.<sup>18</sup> However, use of quasi-experimental or observational study designs to demonstrate effectiveness also carries limitations, such as inability to control for unobserved variables.<sup>17</sup> More fundamentally, in many cases an evaluation will be needed by decision-makers before the DHI has been trialled, and in cases where a trial does proceed, by the time it is nearing completion, both its effectiveness and cost effectiveness will already be ‘known’ with sufficient accuracy before real-world data are available. This may then provide disincentives for the future use of real-world data to examine effectiveness and cost-effectiveness. This suggests that a decision-theoretic approach will be required (and may be sufficient by itself) in some circumstances, such as where the intervention could not conceivably cause harm, and where the likely effect size would produce an estimate of cost-effectiveness that is well below currently acceptable thresholds.<sup>19,20</sup> For example, the PRIMIT handwashing intervention was designed for use in a flu pandemic;<sup>21</sup> here, international dissemination of a fully automated digital intervention to reduce spread of respiratory infection would likely result in healthcare savings and wider health and socio-economic benefits so great that the cost of the intervention becomes negligible.

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252 Within the framework of complex interventions in complex systems, a critical factor driving  
 253 effectiveness may be the extent of uptake by a social network or other relevant population. The  
 254 argument here is that changes in health behaviour can be spread or transmitted from one  
 255 individual to another within a social network; the parallel is earlier work on obesity and the  
 256 idea that this is partly a social disease, through a clustering effect.<sup>22</sup> In similar fashion, the  
 257 effectiveness and cost-effectiveness of DHIs may depend on diffusion through social networks  
 258 for uptake and effect. For example, an internet-delivered hand washing intervention resulted  
 259 in reductions in respiratory infection in the user and also in family members who had not  
 260 engaged with the intervention directly,<sup>21</sup> and smaller effects could spread more widely. In  
 261 addition, there may be feedback loops and potentially non-linear relationships, such as  
 262 effectiveness at the individual level being partly dependent on nature of uptake at the group  
 263 level (e.g. ‘The GCC challenge’ [www.gettheworldmoving.com](http://www.gettheworldmoving.com)).<sup>23</sup>

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265 Since Christakis & Fowler<sup>22,24,25</sup> there has been an explosion of epidemiological studies using  
 266 social network analytical methods for describing and understanding network effects.<sup>26</sup>  
 267 However, there have been far fewer published attempts to use such methods as the basis for  
 268 the design and evaluation of DHIs.<sup>27,28</sup> This may be because development of experimental  
 269 methods in social networks analysis is still at a relatively early stage,<sup>29,30</sup> and there is need to  
 270 develop the wider use of modelling techniques for predicting social network effects.<sup>31</sup>

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272 **Implications of Applying the Complexity Framework for Economic Evaluation of Digital**  
 273 **Health Interventions**

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275 In situations where it is judged that applying standard methods of economic evaluation may  
276 not be optimal, there are implications for costs as well as for benefits, and also major challenges  
277 for selection of the appropriate modelling framework. We turn to these issues below, by  
278 discussing implications in three areas: *inclusion of development costs, measurement of benefits*  
279 *and resource use impacts*, and the *appropriate modelling framework*.

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## 1. Inclusion of development costs plus maintenance & running costs, or only the latter?

The vast majority of costs are incurred during development. Development costs may include:

- Literature reviews, summarising available evidence on:
  - The condition addressed by the DHI (causes, treatments);
  - Interventions likely to be effective if delivered digitally (e.g. tailored content, behaviour change techniques, emotional support);
- *De novo* research identifying user “wants and needs”
- Costs of content development (this will vary with the intended goal of the DHI, but may include information provision, behaviour change interventions, decision support, emotional or psychological interventions, opportunities to interact online with peers or health care professionals)
- Costs of design features (navigation, images, videos, graphics)
- Costs of software features (interactivity, algorithms, tailoring)
- Costs of user experience testing

These costs can be substantial, ranging from £20,000 (for a simple one session intervention)<sup>32</sup> to £500,000 (or more) for a longitudinal, highly interactive intervention with extensive content, tailored to many different variables.<sup>33</sup> Many of these costs relate to iterative development and evaluation of the intervention to maximise acceptability and feasibility.<sup>34,35</sup> In contrast, maintenance costs can be very low. The minimum maintenance cost is hosting. Costs of hosting vary according to complexity of DHI and levels of security and response times required.

Although the issue of whether to include development costs, and other costs such as training costs and future costs of related diseases and treatments is not specific to DHIs, there are three additional considerations that may be peculiar to DHIs:

- Most DHIs require regular updating to remain “the same”, e.g. where the DHI promises to deliver up-to-date information. Updating is required for: a) content; b) navigation and visuals; and c) software. As mainstream software manufacturers update their products, DHIs that are not updated will cease to function.
- As outlined in Yardley et al,<sup>36</sup> there is good evidence that DHIs alone are often not as effective as DHI + human support or facilitation, where the human input focuses on getting the patient (user) to use the DHI as intended.<sup>37,38</sup> Unlike all other costs associated with DHIs, which are fixed, these facilitation costs are variable as they increase with each additional user.
- Many interventions are likely to evolve unpredictably over time. Such change makes reproducibility more challenging, and also data collection difficult if the change was quick and no measurement of resource use was planned. Where change is planned as part of the intervention, this knowledge should be built into the cost estimates, otherwise there is a danger that the costs incurred in a research study may not be fully reflective of resource use outside of that setting.<sup>35</sup>

The issue of perspective, i.e. whether the evaluation is conducted from a payer perspective, societal perspective or some other perspective, is also important in judging the importance of inclusion of development costs. From the perspective of a national health regulator such as NICE, the decision may be whether to develop a DHI *de novo* and make it available as a public

good, i.e. once it is provided to at least one individual, it can be provided to an unlimited number of other people at no further cost. Here, good estimates of fixed costs of development are important, alongside knowledge regarding resources required for storage, data retrieval, and encryption. The payer (the NHS) would then agree a price with the manufacturer to cover these costs, together with a potential mark-up to protect intellectual property. However, other perspectives than those of a national regulator can be adopted, and other factors, such as whether the DHI is a modification of an existing product, will have implications for the inclusion or exclusion development costs within the evaluation. For example, for evaluation of existing products, prior development costs would usually be excluded, as these are “sunk costs” as there is no further resource impact for decision-makers going forward, but resources required for modification would be included. Further, likely product reach and future costs of updating as technology changes are both highly unpredictable, and may be further affected by regulatory changes. Information on reach is important in estimation of cost-effectiveness as the marginal costs per additional user will tend to zero as the population size. This is not a trivial task, requiring additional effort and data analysis.<sup>39</sup>

## **2. Measurement of benefits and resource use impacts**

The measurement of benefit should relate to the purpose of the individual technology – what is it trying to achieve over a particular time frame? This is important because it acts as the key guide to how benefits are measured. The main categories of benefit include the following:

- health effects in their natural units, e.g. number of cancer cases avoided;
- generic measures of healthy time and/or other outcomes, e.g. Quality Adjusted Life Years (QALYs);
- monetary valuation of healthy time and/or other outcomes, e.g. willingness to pay to gain % increase in healthy life years;



Less common approaches include measurement of changes in well-being, e.g. capability, the extent to which an individual feels it is possible for them to live a meaningful life,<sup>40</sup> or measures of life satisfaction.

It is clear that different interventions are designed to achieve different objectives, some of which may relate to reductions in service use. For example, DHIs for diabetes and for patients receiving warfarin<sup>41</sup> are intended to reduce the need for monitoring visits with NHS staff. Outcomes have been measured as change in utilisation of health care resources, patient satisfaction and maintained control of symptoms. For such DHIs it seems plausible to maintain an NHS perspective for costs and outcomes, i.e. only health effects, and health and social care costs may be deemed relevant for evaluation. (However, even here, it could be argued that a wider perspective is warranted, as patient monitoring of symptoms may increase reassurance and empowerment, but may also lead to adverse effects, such as anxiety and intrusiveness). For other DHIs however, the range of benefits may be much wider and individual health effects may take longer to occur. These include internet based programs and apps to encourage a lifestyle change, such as weight loss, exercise or sleep behaviour, which may result in health changes as well as other effects, such as greater social inclusion and productivity changes.

Finally, an important issue relates to safety. There may be unintentional and intentional harms. For example, a weight loss mobile app shared among teenage girls may give rise to unintended consequences such as an increase in smoking. Digital apps also exist to help individuals to commit suicide. Some provide advice that is opposite to existing guidelines. National regulation is therefore important. Equally, regulation is appropriate to protect consumers from fraudulent apps, such as those purporting to measure Blood Alcohol Concentration, but with no capacity to do so.<sup>42</sup> Further, harm may occur if information or advice in a DHI is inaccurate

or out of date, or through misinterpretation by the user. DHIs may also cause anxiety or feelings of inadequacy if users feel burdened by them.<sup>43</sup>

### **3.Appropriate modelling framework**

Finally, there is the challenge of bringing costs and benefits together in the appropriate modelling framework. In order to conduct evaluation that accounts for the degree of complexity that is relevant to the intervention and setting, it is vital that economic modellers develop or apply better tools to encapsulate individual and population level interactions, rather than impose highly simplified assumptions or heuristics about the nature of human behaviour.<sup>44</sup> These models and the techniques to develop them should be more widely embraced in economic analysis of DHIs.<sup>45</sup> As highlighted earlier,<sup>15,16</sup> there appears a role for agent-based modelling.<sup>46,47</sup> Within this approach, individuals make decisions autonomously, as well as interacting with others and with their environment using individually tailored “behavioural rules”. These rules can be non-linear (e.g. discontinuous) and time-dependent (e.g. agents adapt and learn from previous experience).

There is ample scope for methodological development in economic modelling in this field. A possible starting point may be a critical review of existing interventions and development of novel case studies. For example, an ongoing EU collaboration, INTEGRATE-HTA, is examining aspects of complexity relevant to complex interventions in complex settings.<sup>48</sup> Many of these aspects are potentially relevant when considering DHIs; including the impact of multiple interacting agencies involved in the intervention and the wider system, problems with defining the intervention due to characteristics like flexibility, tailoring, self-organization, adaptivity and evolution over time, and issues of historicity or path dependence, whereby the

evolution of the system through series of irreversible and unpredictable events means that generalizability and repeatability of an intervention is problematic.

## **Concluding Comments - Key Decision Points in the Design & Conduct of Economic Evaluations for DHIs**

There is considerable scope for variation in how a particular DHI is delivered to a potential user, and the way in which that user then interacts with that intervention and the wider environment. Moreover, feedback mechanisms may be critical to the success of that intervention, such that the wider environment has a strong effect on how a recipient uses a particular intervention. In short, many DHIs may be best characterised as complex interventions within a complex system, and within the class of complex interventions, they may hold special characteristics that require key questions to be addressed when planning the design of an economic evaluation, outlined in Table 1:

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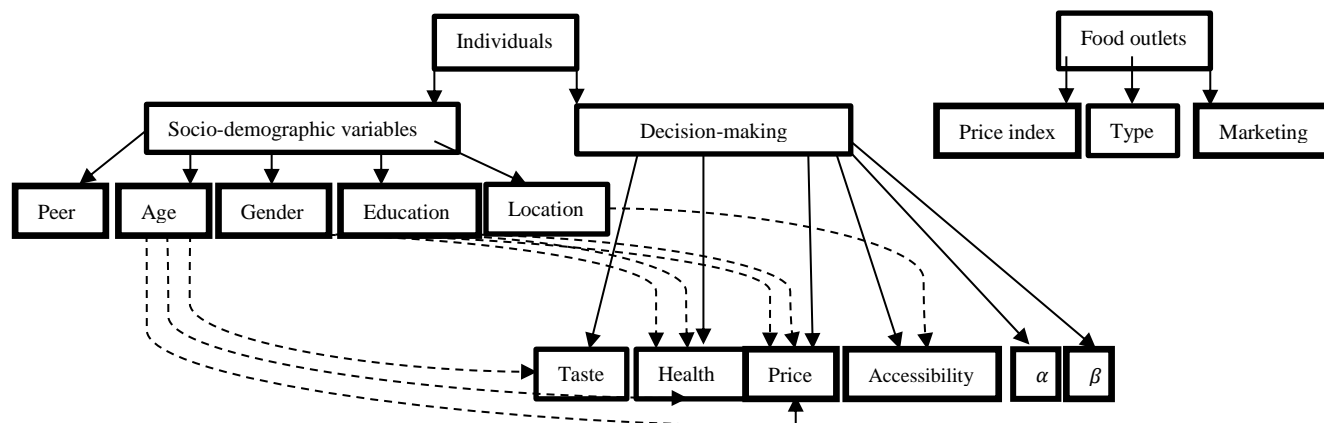
418 **Table 1.** Key guidance points and priority topics for future research**Guidance points based on existing research**

- Assess whether an intervention is complex, e.g. does it involve adaptive intervention components or interaction with other people? Is the causal pathway from intervention to outcomes complex? i.e. are there multiple mediators or moderators of outcomes?
- Consider whether a complex economic evaluation is appropriate. (e.g. can the research question be addressed using “standard” methods of economic evaluation which do not require modelling of patient-system-network relationships to generate robust cost and benefit estimates?)
- For a given study perspective, identify the relevant and important costs that should be included in an economic evaluation. (e.g. should all the resources used in the development of the DHI be included? Alternatively, is it acceptable to focus solely on measurement of the health care resources and any other resources required in future maintenance and support of DHIs?)
- For a given study perspective, identify the relevant and important benefits that should be included in an economic evaluation. (e.g. benefits are likely to be multi-faceted and potentially span beyond health, creating a challenge for measurement, e.g. does engagement with DHIs facilitate future employment prospects for some individuals? Are there other spin-offs? Are there negative effects? What effect does the DHI have on the wider environment, and what effect does the environment have on the DHI?)

**Priority topics for future research**

- Critical review of existing economic evaluations of digital health interventions, with particular focus on comparative studies that have undertaken different modelling approaches
- Validation of agent-based models that capture dynamic interactions between the intervention, the population of interest and environment
- Further interrogation of existing datasets to permit better estimates of reach and uptake of new digital health interventions
- Exploration of how best to incorporate economic factors into intervention design and re-design

Figure 1. Model of Unhealthy Dietary Behaviours. Reproduced from Zhang et al (2014).



### Explanatory Note:

The aim of the model is to compute probabilities of healthy and unhealthy food consumption from the estimated regression coefficients ( $\alpha$  &  $\beta$ ). The agent-based model comprises 2 agents: individuals and food outlets. Individuals make dietary choices, and food outlets adapt to those choices.

Individuals are assigned demographic characteristics (age, gender, educational attainment) to match the demographic profile of the local area. Individuals are assigned a home location and a set of friends, both constant throughout the modelling period.

Food outlets were categorized as selling fresh fruit and vegetables (FV), or fast food (FF). Individuals chose to consume FV or FF each period on the basis of taste preferences, health beliefs, a food-price index, price sensitivity, food accessibility, and demographic factors (age, gender, and education). The weight assigned to each factor is based on data derived from an attitudinal & behavioural survey, supplemented by other empirical studies. Taste preferences and health beliefs are updated in each period according to prior habits, social network influences and food marketing strategies.

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