Title

Analytical frameworks and outcome measures in economic evaluations of digital health interventions: a methodological systematic review

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All the data used is publicly available in the sources mentioned within the manuscript.

Abstract

Background

Digital health interventions (DHIs) can improve the provision of healthcare services. To fully account for their effects in economic evaluations, traditional methods based on measuring health-related quality of life may not be appropriate, as non-health and process outcomes are likely to be relevant too.

Purpose

This systematic review identifies, assesses and synthesises the arguments on the analytical frameworks and outcome measures used in the economic evaluations of DHIs. The results informed recommendations for future economic evaluations.

Data Sources

We ran searches on multiple databases, complemented by grey literature, backward and forward citation searches.

Study Selection

We included records containing theoretical and empirical arguments associated with the use of analytical frameworks and outcome measures for economic evaluations of DHIs. Following title/abstract and full-text screening, our final analysis included 15 studies.

Data extraction

The arguments we extracted related to analytical frameworks (14 studies), generic outcome measures (5 studies), techniques used to elicit utility values (3 studies), disease-specific outcome measures and instruments to collect health states data (both from 2 studies).

Data synthesis

Rather than assessing the quality of the studies, we critically assessed and synthesised the extracted arguments. Building on this synthesis, we developed a three-stage set of recommendations where we encourage the use of impact matrices and analyses of equity impacts to integrate traditional economic evaluation methods.

Limitations

Our review and recommendations explored but not fully covered other potentially important aspects of economic evaluations which were outside our scope.

Conclusions

This is the first systematic review that summarises the arguments on how the effects of DHIs could be measured in economic evaluations. Our recommendations will help design future economic evaluations.

Highlights

- Using traditional outcome measures based on the health-related quality of life (like the quality-adjusted life-year) may not be appropriate in economic evaluations of digital health interventions, which are likely to trigger non-health and process outcomes.
- This is the first systematic review that investigates how the effects of digital health interventions could be measured in economic evaluations.
- We extracted and synthesised different arguments from the literature, outlining advantages and disadvantages associated with different methods used to measure the effects of digital health interventions.
- We propose a methodological set of recommendations where: 1) we suggest that researchers consider the use of impact matrices and cost-consequence analysis; 2) we discuss the suitability of analytical frameworks and outcome measures available in economic evaluations; 3) we highlight the need for analyses of equity impacts.

Introduction

The role of technology in healthcare is ever-growing. Technological innovations have introduced new treatments and diagnostic tests impacting on people's quality of life and life expectancy. They are also changing how healthcare services are used, allowing individuals to be empowered in monitoring and managing their own care[1-3].

Digital health is a wide-encompassing term which includes multiple and diverse interventions based on information and communications technologies, spanning over mobile health (or mHealth), telemedicine and telehealth[4]. Reducing transportation costs, inefficiencies, hospital stays and time to diagnosis are some of the potential gains attributable to digital health interventions (DHIs)[5-7]. DHIs can widen accessibility to healthcare services, extending their reach to remote areas or, as in the COVID-19 pandemic, to people in self-isolation. However, these benefits come at a price, for example the costs of the new technologies or adapting to new processes[8]. Quality of care may decrease if the new DHIs are not a perfect substitute for the existing alternative, or if users and healthcare professionals struggle to fully adapt to the new procedures[8]. These drawbacks potentially affect the safety, acceptability and effectiveness of the new technologies. Inequality and ethical issues may also arise, since individuals are likely to differ in the way they access and accept the use of a digital health technology[8-10].

As with any new intervention, the natural trade-offs in DHIs call for economic evaluations estimating their costs and consequences[9]. The effects triggered by DHIs on accessibility, acceptability, quality and costs[8, 11] increases the number of key outcomes to consider. Process outcomes are likely to emerge[6] (e.g. number of face-to-face visits) and outweigh the value of health-related quality of life (HRQoL) outcomes, which sometimes share only a tenuous link with DHIs[12]. Consequently, the ability of standard outcome measures based on HRQoL, such as the quality-adjusted life-year (QALY), to capture all the relevant outcomes of DHIs is a matter of debate[13].

While the simplicity of the QALY contributes to its wide acceptance and key role in healthcare decision-making[14], limitations have emerged. These have ranged from theoretical issues (such as the lack of correspondence between QALY-underlying expected utility and actual individuals' behaviour[14-18]) to more methodological aspects (e.g. diverging utility values obtained from adopting different eliciting techniques[15-17, 19, 20]). Equity concerns have also been voiced, particularly when interventions not likely to substantially improve life expectancy nor health conditions (and thus yielding lower QALYs) may still be important for specific populations[15-17, 21].

Specific problems arise in the context of DHIs too. DHIs are multi-dimensional in the way they produce multiple effects to numerous stakeholders. The most common examples pertain to the user's perspective, ranging from more tangible effects, like those related to reduced waiting or travel time, faster diagnosis and better access to healthcare services[5-7, 12], to less tangible ones, like the sense of reassurance or anxiety triggered by the flow of information on personal health[6, 22]. The perspectives of healthcare professionals and managers can also be taken into account (e.g. how do they accept or are they willing to use a DHI? Which educational effects can be reaped?), as well as the perspective of the whole healthcare system (e.g. how can the implementation of a DHI be scaled up?)[13, 23]. Further perspectives which go beyond the interaction between users and healthcare professionals may be considered relevant, such as those of caregivers or other users[22].

In addition, DHIs can be applied to multiple health areas. This affects the generalisability of their evaluations, which may also fail to capture the long-term and evolving effects of

DHIs[5,22,24]. The demand of healthcare services may also change over time, as the use of DHIs can uncover needs that traditional interventions are not able to meet[23].

These challenges indicate that one-size-fits-all rules for economic evaluations of DHIs may not be sensible. In the complexity of interactions created by DHIs[25, 26] HRQoL-informed QALYs and other generic outcome measures may not fully capture externalities (e.g. effects on caregivers), non-health factors (e.g. travel time), network effects (e.g. as the number of users increases the overall digital health technology improves) and other process outcomes[5, 6, 22, 27].

Economic evaluations of DHIs and systematic reviews assessing their quality and findings[28, 29] have proliferated, while suggestions addressing methodological challenges are emerging (Gomes et al., 2022[30]). However, to our knowledge no review has synthesised arguments on how the effects of DHIs could be measured in economic evaluations, including whether HRQoL-informed QALYs and other generic outcome measures could be valid metrics in this field. In this review we intend to address this gap by collecting, assessing and synthesising arguments on how to measure the effects of DHIs in economic evaluations, as we focus on the arguments on the choice and use of analytical frameworks and outcome measures. Then, we use the findings to create a set of methodological recommendations which can guide future economic evaluations of DHIs.

Methods

The systematic review process followed a predetermined protocol (registered on PROSPERO as CRD42021243636) and standard reporting guidance[31] (Table S1).

Search strategy

We searched five electronic databases, specifically: MEDLINE (Ovid); Embase (Ovid); Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (Cochrane Library); International Health Technology Assessment Database; and the NHS Economic Evaluation Database. Search terms used included ‘digital health’ and common alternatives terms (e.g. telemedicine, eHealth, telehealth, mHealth), along with ‘economic’, ‘quality-adjusted life-year’, ‘value’ and ‘outcome’. The search strategies used are in Tables S2 to S6. The searches were run on 22nd February 2021 and no date limits were applied.

Grey literature searches were conducted on health economic websites, including: International Society for Pharmacoeconomics and Outcomes Research (ISPOR); international Health Economics Association (iHEA); and the Office of Health Economics (OHE). The websites were searched via the Google search engine, due to limitations in search functionality on the websites themselves. These searches were run by two of the co-authors on 26th March (LF) and 31st March 2021 (VB) using key synonyms for ‘digital health’ (Table S7).

Backward citation searches were also conducted by checking the references of the studies included in the analysis following the initial searches and screening. References citing the studies included in the analysis were identified by running forward citation searches in Scopus, Web of Science and Google Scholar on 17th June 2021.

Study selection

The main criterion for study inclusion was the presence of a discussion of theoretical and empirical challenges of, and/or the advantages and disadvantages associated with, the measurement, valuation and use of outcome measures, including the choice of analytical frameworks, for economic evaluations of DHIs. This represented our Outcome in an adapted version of the Population (general population), Intervention (any DHIs), Comparator (any) and Outcome model (PICO). We considered any empirical and non-empirical studies (e.g.

systematic reviews, economic evaluations, theoretical and methodological studies), except abstracts. Only records in English were included.

Those records retrieved by the multi-database searches were de-duplicated and then screened. To determine eligibility, four co-authors (VB, LF, CHa, JS) used a pre-piloted screening tool (Table S8) as part of a two-stage screening process managed in EndNote:

1) Records were split in four batches, with the title and abstract of each record screened by one co-author, and a random sample (20% of the batch size) cross-screened by another co-author;
2) The full text of selected records was then screened independently by two co-authors.

Data extraction

The same four co-authors extracted data from the selected studies, and validated each other's extractions, using a pre-piloted Excel template which focused on:

- Aim and design;
- Arguments on measurement, valuation and use of outcome measures, including:
    - instruments to collect health states data;
    - techniques used to elicit utility values or weights; and,
    - generic and disease-specific outcome measures;
- Other arguments on outcome measures (e.g. analysis and interpretation of results) or analytical frameworks.

This list was updated during the data extraction process as new relevant items were identified. Any discrepancy in the study selection was resolved through discussions, with oversight by another co-author (AC). The protocol and this manuscript were reviewed by a public adviser (CHi), whose involvement is detailed in Table S9.

Quality assessment

As our review focused on the arguments presented in the studies, a traditional assessment of the overall study quality was out of scope. Traditional checklists which focus on the quality of the studies' design and methodology may not be appropriate to review theoretical or qualitative evidence[32, 33]. Therefore, the arguments were qualitatively assessed in our data synthesis.

Data synthesis

We undertook a narrative synthesis of the arguments presented in the included studies by relevant methodological areas. This synthesis informed the development of a three-stage set of recommendations which can help designing future economic evaluations of DHIs.

Role of funding source

The funder source had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Results

Search results

We identified 15,050 results of which 3,641 were duplicates. Thirty-nine records were selected for full-text screening. Further records were screened through backward (n=16) and forward (n=718) citation searching, and grey literature searching (n=212). From those, an additional 19 records were selected for full-text screening (thus 58 in total).

Following full-text screening, 15 studies were included in the analysis, as summarised in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart[31] (Figure 1). The reasons for the exclusion of the other 43 records are listed in Table S10.

[Figure 1 here]

Overall summary of included studies

The included studies were published between 1997 and 2021. All had a theoretical or methodological design: six were (or included) reviews of the literature[5, 7, 13, 24, 25, 34], six were theoretical studies or had a theoretical component[6, 12, 22, 26, 27, 35], two proposed theoretical frameworks[36, 37] and one was a methodological guideline[23].

The arguments extracted from the included studies pertained to: analytical frameworks (from 14 studies, equal to 93%); generic outcome measures (5 studies, 33%); techniques used to elicit utility values (3 studies, 20%); disease-specific outcome measures and instruments to collect health states data (2 studies, 13%). The characteristics of the included studies are summarised in Table 1.

[Table 1 here]

Synthesis of arguments

Analytical frameworks

Economic evaluations in digital health are challenging, as DHIs can be complex, involve multiple stakeholders[25, 26] and produce time-changing effects[22, 34]. As their impact on health outcomes may be indirect, using surrogate outcome measures may be necessary, although they may be weakly associated with health outcomes, as underlined by Ohinmaa et al. (2001)[23].

While the use of traditional frameworks for economic evaluations is advocated in methodological guidelines, as in the guideline by the National Institute for Health and Care Excellence (NICE) in the UK[37], alternatives exist to deal with the diversity of outcomes and corresponding measurement challenges[22].

Below we summarise the arguments we extracted from the included studies, organised by each analytical framework which can be adopted in economic evaluations of DHIs.

<u>Cost-Consequence Analysis (CCA) (n=3 studies)</u>

The use of CCAs is suggested by NICE (2018)[37] when DHIs trigger non-health outcomes. According to McIntosh and Cairns (1997), CCAs can act as a 'balance sheet'[6] which: highlights the variety of outcomes attributable to DHIs; identifies data gaps and critical variables for sensitivity analyses; and helps in deciding on the appropriate units of analysis when monetary and non-monetary outcomes exist[6]. The authors emphasised that in CCAs the relevance of the trade-offs between the different costs and consequences is not evident[6], and relies on the decision-makers' judgment, as underlined by Snoswell et al. (2017)[12].

<u>Cost-Benefit Analysis (CBA) (n=7 studies)</u>

The use of monetary metrics, which facilitates cross-area comparisons, is considered an important advantage of CBAs by Reardon (2005)[24]. Another advantage considered by this author is the possibility of capturing a broad range of costs and outcomes associated with DHIs[24]. These can be captured by eliciting the willingness to pay (WTP) of digital health users on factors such as access to health services, ability to measure their own health status, reduced time for appointments, productivity and efficiency gains[12, 25, 35].

However, other studies point to the limits of using CBAs. As shown by Davalos et al. (2009) and Bongiovanni-Delaroziere and Le Goff-Pronost (2017), asking users to supply information about their WTP for different factors and attempting to convert health outcomes into monetary units can be challenging[5, 34]. Unlike other types of tradable commodities, health outcomes are not typically attached to a visible price, which may complicate the valuation of health improvements generated by DHIs, as stressed by Reardon (2005) and Angjellari-Dajci et al. (2017)[24, 36].

Cost-Effectiveness Analysis (CEA) (n=3 studies)

Reardon (2005)[24] provided insights on the importance of choosing the outcome measure in CEAs. For example, measuring access to care using the number of appointments may overlook how DHIs trigger fewer appointments in the first place[24]. Another well-known limitation of CEAs pointed out by Reardon (2005), not confined to digital health, is the lack of cross-area comparability of their findings[24].

Besides cost-effectiveness, LeFevre et al. (2017) argued that the financial impact and equitable distribution of costs and consequences across the users of DHIs are relevant[35]. According to these authors, extended cost-effectiveness analyses (ECEAs) can investigate these equity impacts by exploring the role of different health and social determinants across sub-groups[35]. For example, McIntosh and Cairns (1997) emphasised how, in measuring the value of improving access to healthcare services, a greater weight can be placed on the gains of those living in remote areas[6].

Cost-Utility Analysis (CUA) (n=1 study)

The cross-area comparability of QALYs is regarded as an advantage for CUAs over CEAs by Bergmo (2015)[26]. Nevertheless, Bergmo (2015) also recognised that the typical estimation of QALYs using HRQoL utility values can be a limitation where non-health effects are relevant, as in DHIs (e.g. changes in access to services, time management and healthcare provision)[26].

As a part of any of the above frameworks, the use of the net benefit regression framework (NBRF) can provide a platform to develop sensitivity analysis, as discussed by LeFevre et al. (2017)[35]. Within the NBRF, the sensitivity of the results can be tested against the maximum WTP amount for one additional QALY, obtaining a range of probabilities where a DHI may be more cost-effective than its alternatives. Investigating associations between subgroup differences (e.g. in gender, age and ethnicity) and the net monetary benefit can reveal potential determinants of cost-effectiveness[35].

Other frameworks (n=4 studies)

As outlined by McNamee et al. (2016)[22], agent-based modelling can capture the complex (i.e. multi-faceted behaviours are assumed by those delivering or receiving the intervention) and time-changing (e.g. individuals adapt and learn from previous experience) components of DHIs. In this framework, individuals follow non-linear and adaptive behaviour rules that reflect how decisions are taken autonomously and collectively in the context of DHIs.

McIntosh and Cairns (1997)[6] discussed the use of conjoint analysis, where DHIs users determine the relative importance of different levels of the features of the interventions through pairwise choices. These features do not only relate to health outcomes but also to non-health and process outcomes[6], which can be central in digital health.

Kolasa and Kozinski (2020)[13] delved into the use of multi-criteria decision-making, where the multi-faceted features of digital health are explored, as weights are assigned to the (at times conflicting) preferences elicited from the different stakeholders.

Lastly, Le Goff-Pronost and Sicotte (2010)[27] presented a five-step framework for economic evaluations of DHIs, where: (i) a traditional economic evaluation is integrated with longitudinal and stakeholder analyses; (ii) a break-even point measures the volume of services needed to cover the fixed costs; (iii) a net present value is calculated to discount future costs and consequences; (iv) social benefits are estimated (e.g. network effects whereby the entry of new users increases the network's overall value); and, (v) sensitivity analyses test the impact of different factors on the results.

Instruments to collect health states data and techniques used to elicit utility values

While the use of the EuroQol Five Dimension descriptive system (EQ-5D) in economic evaluations of DHIs is recommended in methodological guidelines[37], generic HRQoL instruments may not be suitable to measure non-health effects of DHIs, as underlined by Mistry (2012) and Bongiovanni-Delaroziere and Le Goff-Pronost (2017)[7, 34]. Moreover, Bergmo (2014) warned that, given the different eliciting techniques available, different utility values for similar health states may arise[25]. For example, McIntosh and Cairns (1997)[6] recommended the WTP method to elicit utility values, but Snoswell et al. (2017)[12] recognised that different ways to ask the WTP from digital health users (e.g. multiple choice or open-ended questions) may influence the responses and corresponding utility values. Overall, users need to see the full picture of what they are valuing[12], which includes the changing nature of DHIs and the range of services or effects produced (health and non-health outcomes).

Discrete choice experiments (DCEs) could reflect this dynamic nature. According to Snoswell et al. (2017), the DCEs trade-off questions allow users to make choices around variations of DHIs, creating a preference-based ranking of the different aspects and characteristics (e.g. waiting time, clinical interaction, technological options) that form the overall WTP value[12].

Generic outcome measures

Since DHIs can trigger indirect effects on health outcomes, as pointed out by McIntosh and Cairns (1997)[6], Ohinmaa et al. (2001) indicated that the use of QALYs and other generic outcome measures could miss shorter-term and process outcomes which are still important in digital health[23].

Bergmo (2014) explained how the estimation of QALYs through generic HRQoL instruments, like the EQ-5D, may miss disease-specific factors of relevance, or underestimate the value of interventions for people whose improvements in health status or life expectancy will not be substantial[25]. Bergmo (2015) also underlined that in digital health other impacts could be relevant, for example how digital health users feel secure and empowered[26].

Moreover, Kolasa and Kozinski (2013) argued that the typical HRQoL-based estimation of QALYs ignores the perspectives of digital health stakeholders beyond the patients (e.g. clinicians, healthcare managers and funding bodies) and may fail to capture the full value of clinical and organisational effects[13].

Disease-specific outcome measures

As disease-specific outcome measures may better capture the health-related effects triggered by DHIs on users, the common criticism over their lack of cross-area comparability is nevertheless echoed in the DHI field (see Bergmo, 2014[25]).

As with generic outcome measures, incorporating indirect effects of DHIs can be complex when using disease-specific outcome measures. For example, Davalos et al. (2009) explained how identifying and measuring the benefits of DHIs which indirectly help improve medication

adherence is not straightforward, even if the subsequent effects on patients' outcomes may seem apparent[5].

Supplementary narrative synthesis on costs and non-health outcomes

By presenting the above arguments, we focused on the traditional methodological areas that characterise the analytical frameworks and the measurement of outcomes in economic evaluations of any healthcare intervention. Nevertheless, we recognise that other methodological areas are important in economic evaluations in general, such as how to measure and value costs, and in economic evaluations of DHIs in particular, such as how to measure and value non-health outcomes. As such, we also explored whether the included studies provided any arguments on how to measure and value costs and non-health outcomes in a supplementary narrative synthesis included in Appendix S1. Despite the assessment of costs being out of the scope of our systematic review, we believe that this supplementary narrative synthesis enriches our review by providing evidence on how to capture the wide range of costs and consequences triggered by DHIs.

Discussion

Place in the literature

To our knowledge, this is the first systematic review to investigate how the effects of DHIs could be measured in economic evaluations. Reviews such as those by Rojas and Gagnon (2008)[38] and Bergmo (2009)[28] identified indicators for costs and effectiveness used to assess telemedicine interventions, and commented on the lack of a common set of indicators which would facilitate cross-area comparability. However, unlike our review, those reviews did not evaluate the suitability of the analytical frameworks and outcome measures in economic evaluations of DHIs, and therefore were not included in our final analysis. Another review by Bergmo (2014)[25], included in our review, explored the use of health state utilities to generate QALYs and transparency of methods in economic evaluations of DHIs. Jankovic et al. (2021)[39] discussed the significance of the perspective for the identification of outcomes, and the lack of clear trade-offs between health gains and costs when disease-specific outcome measures are used. Kolasa and Kozinski (2020)[13], also included in our review, developed recommendations on how the value assessment of digital health interventions should be carried out, recognising that QALYs may not be appropriate to capture the multi-dimensional character of DHIs. Lastly, an ongoing systematic review by Hariz et al. (2020)[40] is set to identify the methodological choices made in economic evaluations of internet-based e-health interventions (e.g. time horizon, perspective, choice of costs and outcomes), and to assess the impact of these choices on the results of economic evaluations.

Despite the useful findings of these systematic reviews, their inclusion criteria are limited to a few study designs, such as applied economic evaluations or guidelines. This narrow scope limits the number and range of findings obtained. Our review's scope was more inclusive, as we also considered studies with a theoretical or methodological design. Our focus was not on identifying *which analytical frameworks and outcome measures were used* within the DHI economic evaluations, but on identifying, assessing and summarising arguments on *how analytical frameworks and outcome measures could be used,* which gives our systematic review a more methodological basis. Compared with previous studies, we intended to provide a more in-depth discussion around the choices needed to measure the effects of DHIs. In this sense, we use our findings to formulate a set of recommendations which aims to help researchers in designing economic evaluations of DHIs. Similar tools exist in the literature, such as the flowchart proposed by LeFevre et al. (2017)[35] for the economic evaluations of any healthcare interventions, or the recommendations proposed by Kolasa and Kozinski (2020)[13] for the economic evaluations of DHIs. Compared with LeFevre et al. (2017)[35], our

recommendations focus specifically on economic evaluations of DHIs while, compared with Kolasa and Kozinski (2020)[13] who systematically reviewed DHIs guidelines, we base our recommendations on a wider evidence base. Our recommendations intend to address researchers' challenges in designing economic evaluations. However, they are not prescriptive nor represent a one-size-fits-all approach. On the contrary, they are an aiding tool where the suggested analyses and tasks can be adapted to (or even excluded in consideration of) the individual DHI context (specific health area, setting, and type of decision maker), timeframe for DHI implementation and resources devoted to a specific economic evaluation.

Set of recommendations for measuring effects of DHIs in economic evaluations

Below we describe our three-stage set of recommendations which is illustrated in Figure 2.

[Figure 2 here]

1. Development of impact matrix and CCA

Given the multi-dimensional effects of DHIs, we suggest the use of a matrix to list these potential effects. For example, in Le Goff-Pronost and Sicotte (2010)[27] and Bongiovanni-Delarozière and Le Goff-Pronost (2017)[34], impact matrices reveal the expected effects of DHIs on different stakeholders (e.g. patients and caregivers, healthcare professionals and institutions, governments) in terms of accessibility, organisation, quality and safety of care, and costs[41].

This could be a preparatory activity which helps developing a CCA, the analysis suggested by NICE when DHIs impact on non-health outcomes[37]. The CCA would present the expected effects as listed in the impact matrix for the DHI and its competing alternatives, together with their measurement in natural or monetary units[6].

2. Incorporation of outcome measures in economic evaluations

The CCA could then be used to prepare a more methodologically complex economic evaluation. However, a consensus seems lacking on which analytical framework would best suit an economic evaluation of DHIs. The issues around converting outcomes in monetary units in CBAs[5, 34], the lack of generalisability of area-specific outcomes of interest in CEAs[24], and the limited ability of outcome measures estimating healthy years (typically QALYs) in capturing all relevant effects in CUAs, are challenges that should be considered[26].

Similarly, there does not seem to be a consensus on which outcome measures could be used. The use of QALYs in economic evaluations of healthcare interventions is backed by methodological guidelines[42], but their use has been debated in digital health[13]. However, arguments favouring the use of alternative outcome measures are lacking in the digital health literature. The typical arguments against the use of QALYs seem to focus on the limited ability of HRQoL instruments, such as EQ-5D, to capture a wider range of effects. Theoretically, the QALY construct ensures flexibility in terms of the dimensions that could be included in the underlying social welfare function, which may include non-health dimensions too, but this is somewhat unexplored in practice[43]. The use of disease-specific outcome measures may help in capturing area-specific dimensions and effects that generic HRQoL instruments may miss. To increase the generalisability of the findings, mapping algorithms can be used to convert the scores obtained from disease-specific outcome measure into EQ-5D utility values[44]. Direct methods to elicit utility values have also been discussed in the literature. For instance, DCEs could estimate the values attached to variations in the features of DHIs (e.g. different levels of access to healthcare services, or health information received), to find the most valued combination by users[12].

3. Assessment of impacts on equity

With their application to multiple health areas, DHIs naturally share equity-related concerns which are common in other healthcare interventions. However, some equity concerns can be considered specific to DHIs. For example, DHIs may facilitate access to healthcare services for people with existing limited access (e.g. those living in remote areas)[5]. At the same time, reaching familiarity with DHIs may not be straightforward for all users, and the lack of face-to-face interaction with healthcare professionals may depersonalise the provision of healthcare[9]. Healthcare settings may differ on how receptive they are or how much they can invest in DHIs, which could limit a widespread geographical implementation. Consequently, existing health inequalities may potentially be widened by the introduction of DHIs.

Where possible, we encourage the use of ECEAs to integrate traditional economic evaluations with an investigation of how equitable the distribution of the costs and effects of DHIs is[35]. This can be carried out by formally analysing the effects of DHIs on different sub-groups through the NBRF, exploring the role played by socio-economic, educational and clinical differences[35].

Some recommendations (e.g. impact matrices and CCAs) are encouragingly shared by Gomes et al. (2022)[30]. Distinctively, our recommendations emerge from a systematic approach and cover more elements, like utility values and equity impacts. To flesh out how to operationalise the recommendations, we built a case study presenting separate examples from studies which adopted approaches in line with the three stages above (Appendix S2).

Strength and limitations

The primary strength of our systematic review is the identification, assessment and synthesis of arguments on how to measure the effects of DHIs in economic evaluations which, to our knowledge, represents a first attempt in the literature. Moreover, we used our findings to inform a three-stage set of recommendations which can help practitioners in designing economic evaluations in this field.

One limitation lies in the underlying structural problem of systematic review processes, which are always prone to miss relevant studies. However, we believe that, by integrating our initial searches with backward and forward citation searching, and grey literature searches, we are likely to have identified the relevant studies.

In this review we focused on the analytical frameworks and outcome measures used in economic evaluations of DHIs, specifically looking at ways which have been used to try and overcome the limitations of using traditional approaches (e.g. HRQoL-informed QALYs). We recognise that other aspects of economic evaluations are potentially important and were not investigated here as out of our scope, such as the choice of the time horizon and modelling techniques. Similarly, our review was not specifically designed to search for studies including arguments on the identification and measurement of costs or on the choice of perspective (e.g. consideration of non-health outcomes). We did synthesize the arguments found from our included studies on costs and non-health outcomes in Appendix S1 to supplement our narrative synthesis.

Lastly, the generalisability of our proposed set of recommendations may be limited as DHIs tend to be applied to multiple health areas with diverse characteristics. However, we believe that our set of recommendations also addresses some of the issues inherent in DHIs, such as the multi-dimension of outcomes, which could be assessed using impact matrices and analyses of equity impacts, as suggested.

Further research

How to best measure outcomes in economic evaluations of DHIs is not straightforward, as specific features of digital health may make the application of traditional economic evaluation methods not suitable. Future research may focus on providing general guidance for DHI evaluations along the lines of our set of recommendations as well as specific guidance for health areas which are likely to trigger different effects (e.g. teleradiology vs telepsychiatry). Applying this guidance on ad hoc economic evaluations will prove useful too (as in Gomes et al., 2022[30]).

Moreover, one of the key takeaways of our review is that no analytical framework nor outcome measure on their own may be able to fully capture the effects of DHIs. Future research may explore how a combination of different analytical approaches and outcome measures could be operationalised.

Conclusions

The effects of DHIs can be varied and can go beyond the health outcomes of their users. In this systematic review, we searched for arguments on how these varied effects of DHIs could be measured in economic evaluations. The findings indicate that traditional frameworks (like CBAs, CEAs or CUAs) and commonly used outcome measures (such as QALYs) may not appropriately determine the full value of DHIs[13].

We used these findings to develop a three-stage set of recommendations. Using impact matrices to list the multi-dimensional effects of DHIs on different stakeholders, and developing analyses to capture the equity impacts, can enrich traditional economic evaluations based on the estimation of cost-effectiveness. Despite the lack of generalisability which hinders economic evaluations in digital health[5], we believe that the recommendations could help the design of future economic evaluations in this field.

Acknowledgments

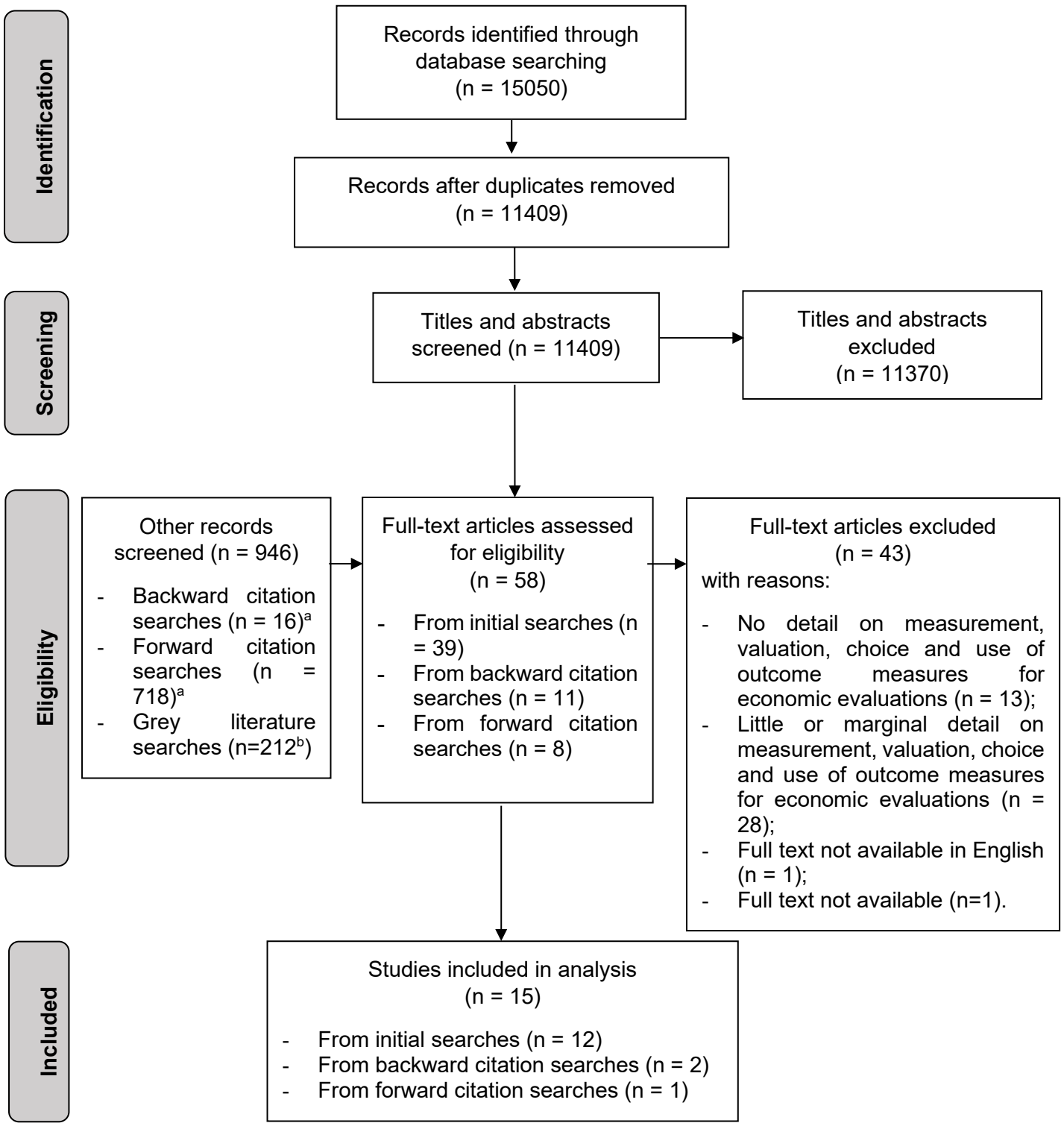
See Title Page for Acknowledgements.

Conflict of Interests

The Authors declare that there is no conflict of interest.

Tables and figures

Figure 1. Flowchart reporting search and screening processes identifying included studies [31]



[a] Records identified through the backward and forward citation searches were screened firstly in terms of their title/abstract and, if relevant, also in terms of their full text.
[b] This figure is approximate as the number of results retrieved by the Google search engine tends to rapidly vary.

Table 1. Summary of included studies (n=15)

First author (year)	Aim	Design	Were any of the extracted arguments relevant to …				
			Analytical frameworks?	Instruments to collect health states data?	Techniques used to elicit utility values?	Generic outcome measures?	Disease-specific outcome measures?
Angjellari-Dajci (2013)[36]	To provide a framework for Benefit-Cost Analysis for the economic evaluation of telehealth and face-to-face interventions for people with autism spectrum disorders.	Theoretical framework.	Yes	No	No	No	No
Bergmo (2014)[25]	To review the use of QALYs in economic evaluations of telehealth.	Literature review.	Yes	No	Yes	Yes	Yes
Bergmo (2015)[26]	How to apply economic evaluation methods in the eHealth field.	Theoretical study.	Yes	No	No	Yes	No
Bongiovanni-Delarozière (2017)[34]	To review economic evaluations of telemedicine and define a standardised framework for economic evaluation.	Systematic review / theoretical study.	Yes	Yes	No	No	No
Davalos (2009)[5]	To review the economic literature and research guidelines in telemedicine.	Literature and guidelines review.	Yes	No	No	No	Yes
Kolasa (2020)[13]	To describe the characteristics of specific DHIs guidelines and criteria and methods used in the evaluation of DHIs.	Systematic review of assessment frameworks.	Yes	No	No	Yes	No

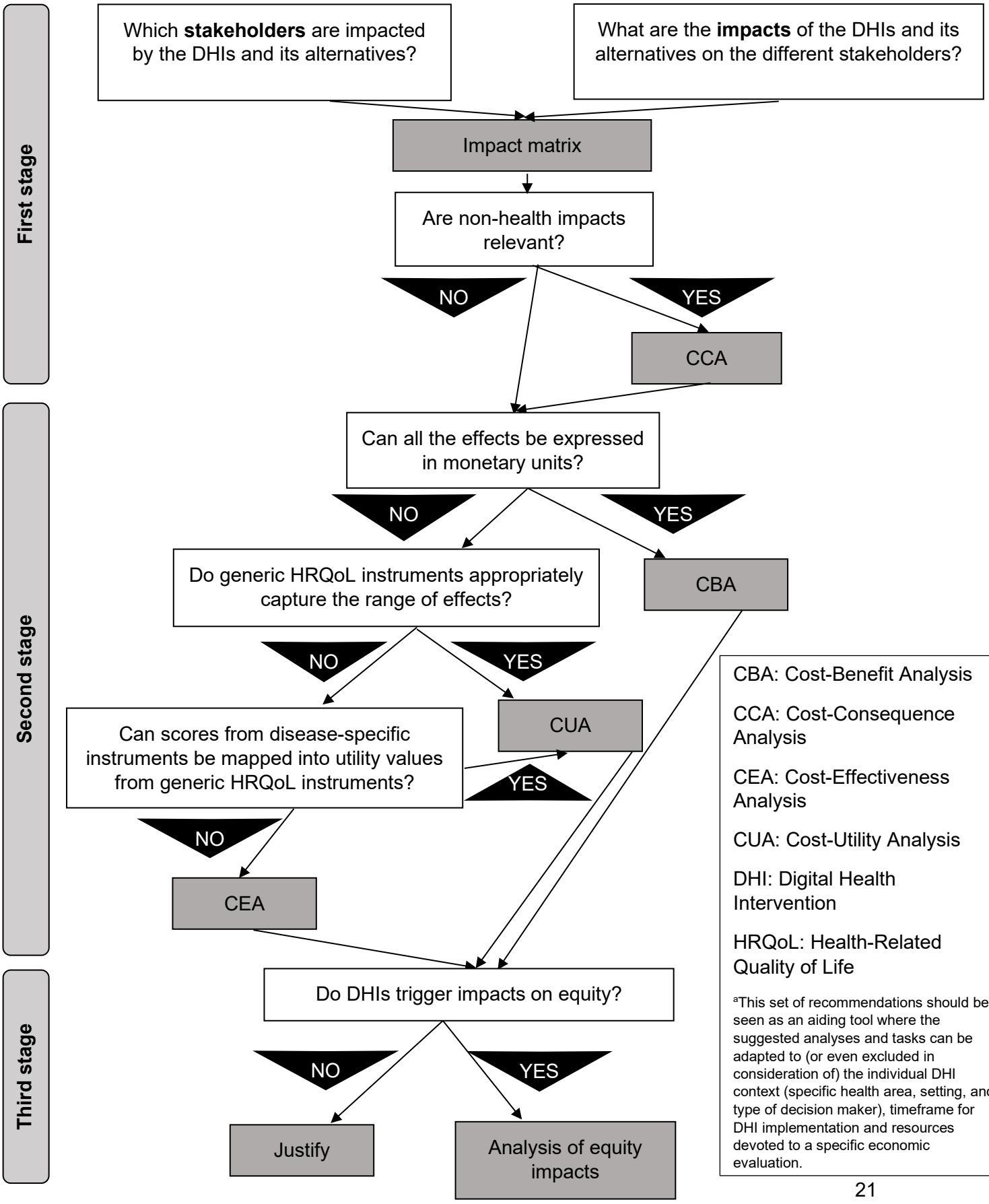
First author (year)	Aim	Design	Were any of the extracted arguments relevant to …				
			Analytical frameworks?	Instruments to collect health states data?	Techniques used to elicit utility values?	Generic outcome measures?	Disease-specific outcome measures?
LeFevre (2017)[35]	How to select methods for economic evaluation and financial evaluation of DHIs.	Guideline / Theoretical study.	Yes	No	No	No	No
LeGoff-Pronost (2010)[27]	To describe a framework for the economic evaluation of telemedicine networks.	Theoretical study with applied case study.	Yes	No	No	No	No

First author (year)	Aim	Design	Were any of the extracted arguments relevant to …				
			Analytical frameworks?	Instruments to collect health states data?	Techniques used to elicit utility values?	Generic outcome measures?	Disease-specific outcome measures?
McIntosh (1997)[6]	To illustrate the challenges in economic evaluations of telemedicine interventions.	Theoretical study.	Yes	No	Yes	Yes	No
McNamee (2016)[22]	To focus on the key issues of economic evaluations of DHIs, by describing guides and analytical frameworks for complex interventions and proposing key decision points.	Theoretical study.	Yes	No	No	No	No
Mistry (2012)[7]	To review economic evaluations of telemedicine interventions and their adherence to reporting guidelines.	Systematic review.	No	Yes	No	No	No
NICE (2018)[37]	To describe the standard evidence used to demonstrate the value of digital health technologies in the UK health and social care system.	Theoretical framework.	Yes	No	No	No	No
Ohinmaa (2001)[23]	To provide an approach for the assessment of telemedicine interventions.	Methodological guideline.	Yes	No	No	Yes	No

First author (year)	Aim	Design	Were any of the extracted arguments relevant to …				
			Analytical frameworks?	Instruments to collect health states data?	Techniques used to elicit utility values?	Generic outcome measures?	Disease-specific outcome measures?
Reardon (2005)[24]	To review literature on economic studies of telemedicine and provide strategies for improvement of future research.	Literature review.	Yes	No	No	No	No
Snoswell (2017)[12]	To describe the methods of economic evaluation of telehealth interventions.	Theoretical study.	Yes	No	Yes	No	No
YES n(%)			14(93)	2(13)	3(20)	5(33)	2(13)

DHIs: digital health interventions. NICE: National Institute for Health and Care Excellence. QALY: quality-adjusted life-year.

Figure 2. Flowchart summarising the set of recommendations for measuring effects of digital health interventions (DHIs) in economic evaluations[a]



[a]This set of recommendations should be seen as an aiding tool where the suggested analyses and tasks can be adapted to (or even excluded in consideration of) the individual DHI context (specific health area, setting, and type of decision maker), timeframe for DHI implementation and resources devoted to a specific economic evaluation.

Supplementary material

Table S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Checklist[45]

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods: Study selection Table S8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods: Search strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Tables S2 to S7
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods: Study selection
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods: Data extraction
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods: Data extraction
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods: Data extraction
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods: Quality assessment
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods: Data synthesis
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods: Data synthesis

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods: Data synthesis
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods: Data synthesis
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods: Data synthesis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods: Data synthesis
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods: Data synthesis
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods: Data synthesis
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods: Data synthesis
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results: Search results Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Table S10
Study characteristics	17	Cite each included study and present its characteristics.	Results: Overall summary of included studies Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Results: Synthesis of arguments
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Results: Overall summary of included studies Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results: Synthesis of arguments Appendices S1 and S2

Section and Topic	Item #	Checklist item	Location where item is reported
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results: Synthesis of arguments
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results: Synthesis of arguments
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Results: Synthesis of arguments
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Results: Synthesis of arguments
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results: Synthesis of arguments
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion: Place in the literature
	23b	Discuss any limitations of the evidence included in the review.	Discussion: Strength and limitations
	23c	Discuss any limitations of the review processes used.	Discussion: Strength and limitations
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion: Set of recommendations for measuring effects of DHIs in economic evaluations Discussion: Further research
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding Methods: Role of funding source
Competing interests	26	Declare any competing interests of review authors.	Conflict of Interests
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Acknowledgments

Table S2. Search strategy used in Medline (Ovid)

Search number	Query
1	exp Telemedicine/
2	Telenursing/
3	Therapy, Computer-Assisted/
4	Computer-Assisted Instruction/
5	(mobile health* or m-health or mhealth or mobile care).ti,ab,kw,kf.
6	(Ehealth or e-health or electronic health* or electronic care or e-rehab* or erehab* or e-care or ecare or e-consult* or econsult* or e-diagnos* or ediagnos* or e-medicine or emedicine or e-nurs* or enurs* or e-psych* or epsych* or e-therap* or etherap*).ti,ab,kw,kf.
7	(telehealth* or tele-health* or telenurs* or tele-nurs* or telemedicine or tele-medicine or teleeducation or tele-education or telecare or tele-care or Telepsych* or tele-psych* or Telemonitor* or tele-monitor* or teleprevention or tele-prevention or teleadvice or Tele-advice or Teleassist* or tele-assist* or Telebased or tele-based or Teletherapy or tele-therapy or Teleconsult* or tele-consult* or Teletriag* or tele-triag* or telerehab* or tele-rehab* or telecoaching or tele-coaching or telemanagement or tele-management or telepharmacy or tele-pharmacy or telesupport or tele-support or teledermatolog* or tele-dermatolog* or telehome* or tele-home* or telescreen* or tele-screen* or telediagnos* or tele-diagnos* or telematic*).ti,ab,kf,kw.
8	((digital or online or on-line or virtual or computer* or web based or web delivered or internet) adj4 (health* or care or medicine or intervention* or therap* or treatment* or educat* or training)).tw.
9	((Remote or digital or video or virtual or wireless or phone* or telephone* or smartphone*) adj4 (consult* or appointment* or conferenc* or triag* or care or monitor* or check up$1 or checkup$1 or support)).tw.
10	(Videoconferenc* or video chat* or video call* or instant messag* or sms or short messaging service or texting or phone messag*).tw.
11	or/1-10
12	(electronic health record* or electronic care record*).ti,ab,kf,kw.
13	11 not 12
14	Health Care Costs/
15	Telemedicine/ec [Economics]
16	Quality-Adjusted Life Years/
17	(economic* adj6 (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)).tw.
18	((preference or cost effectiveness or cost benefit) adj3 measur*).tw.
19	((quality adjusted life year* or qaly*) and (alternative* or method* or utilit* or critici* or limitation* or drawback* or draw back* or problem* or disadvantage* or flaw* or weak* or issue* or disbenefit* or pitfall* or appropriate* or inappropriate* or suitab* or unsuitab*)).tw.
20	(quality adjusted life year* or qaly*).ti.
21	(quality of life adj3 (measur* or evaluat* or assess*)).tw.
22	(value based health or (valu* adj2 health state*)).tw.
23	(valu* adj3 health adj3 (outcome* or measur*)).tw.
24	or/14-23
25	13 and 24
26	limit 25 to english language

Table S3. Search strategy used in Embase (Ovid)

Search number	Query
1	exp telemedicine/
2	telenursing/
3	computer assisted therapy/
4	(mobile health* or m-health or mhealth or mobile care).ti,ab,kw.
5	(Ehealth or e-health or electronic health* or electronic care or e-rehab* or erehab* or e-care or ecare or e-consult* or econsult* or e-diagnos* or ediagnos* or e-medicine or emedicine or e-nurs* or enurs* or e-psych* or epsych* or e-therap* or etherap*).ti,ab,kw.
6	(telehealth* or tele-health* or telenurs* or tele-nurs* or telemedicine or tele-medicine or teleeducation or tele-education or telecare or tele-care or Telepsych* or tele-psych* or Telemonitor* or tele-monitor* or teleprevention or tele-prevention or teleadvice or Tele-advice or Teleassist* or tele-assist* or Telebased or tele-based or Teletherapy or tele-therapy or Teleconsult* or tele-consult* or Teletriag* or tele-triag* or telerehab* or tele-rehab* or telecoaching or tele-coaching or telemanagement or tele-management or telepharmacy or tele-pharmacy or telesupport or tele-support or teledermatolog* or tele-dermatolog* or telehome* or tele-home* or telescreen* or tele-screen* or telediagnos* or tele-diagnos* or telematic*).ti,ab,kw.
7	((digital or online or on-line or virtual or computer* or web based or web delivered or internet) adj4 (health* or care or medicine or intervention* or therap* or treatment* or educat* or training)).tw.
8	((Remote or digital or video or virtual or wireless or phone* or telephone* or smartphone*) adj4 (consult* or appointment* or conferenc* or triag* or care or monitor* or check up$1 or checkup$1 or support)).tw.
9	(Videoconferenc* or video chat* or video call* or instant messag* or sms or short messaging service or texting or phone messag*).tw.
10	or/1-9
11	(electronic health record* or electronic care record*).ti,ab,kw.
12	10 not 11
13	"health care cost"/
14	(exp telemedicine/ or telenursing/ or computer assisted therapy/) and ec.fs.
15	quality adjusted life year/
16	(economic* adj6 (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)).tw.
17	((preference or cost effectiveness or cost benefit) adj3 measur*).tw.
18	((quality adjusted life year* or qaly*) and (alternative* or method* or utilit* or critici* or limitation* or drawback* or draw back* or problem* or disadvantage* or flaw* or weak* or issue* or disbenefit* or pitfall* or appropriate* or inappropriate* or suitab* or unsuitab*)).tw.
19	(quality adjusted life year* or qaly*).ti.
20	(quality of life adj3 (measur* or evaluat* or assess*)).tw.
21	(value based health or (valu* adj2 health state*)).tw.
22	(valu* adj3 health adj3 (outcome* or measur*)).tw.
23	or/13-22
24	12 and 23
25	limit 24 to english language

Table S4. Search strategy used in the Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (Cochrane Library)

Search number	Query
1	MeSH descriptor: [Telemedicine] explode all trees
2	MeSH descriptor: [Telenursing] explode all trees
3	MeSH descriptor: [Therapy, Computer-Assisted] explode all trees
4	MeSH descriptor: [Computer-Assisted Instruction] explode all trees
5	((mobile NEXT health*) or "m-health" or mhealth or "mobile care"):ti,ab,kw
6	(Ehealth or "e-health" or (electronic NEXT health*) or "electronic care" or "e-rehab" or "e-rehabilitation" or erehab* or "e-care" or ecare or "e-consultations" or "e-consulting" or econsult* or "e-diagnosis" or ediagnos* or "e-medicine" or emedicine or "e-nursing" or enurs* or "e-psychiatry" or "e-psychology" or epsych* or "e-therapy" or "e-therapies" or etherap*):ti,ab,kw
7	(telehealth* or (tele NEXT health*) or telenurs* or "tele-nursing" or telemedicine or "tele-medicine" or teleeducation or "tele-education" or telecare or "tele-care" or Telepsych* or "tele-psychiatry" or "tele-psychology" or Telemonitor* or "tele-monitoring" or teleprevention or "tele-prevention" or teleadvice or "Tele-advice" or Teleassist* or "tele-assisting" or "tele assistance" or Telebased or "tele-based" or Teletherapy or "tele-therapy" or Teleconsult* or "tele-consultations" or "tele-consulting" or Teletriag* or "tele-triage" or telerehab* or "tele-rehabilitation" or "tele-rehab" or telecoaching or "tele-coaching" or telemanagement or "tele-management" or telepharmacy or "tele-pharmacy" or telesupport or "tele-support" or teledermatolog* or "tele-dermatology" or telehome* or (tele NEXT home*) or telescreen* or "tele-screening" or telediagnos* or "tele-diagnosis" or telematic*):ti,ab,kw
8	((digital or online or "on-line" or virtual or computer* or "web based" or "web delivered" or internet) NEAR/4 (health* or care or medicine or intervention* or therap* or treatment* or educat* or training)):ti,ab,kw
9	((Remote or digital or video or virtual or wireless or phone* or telephone* or smartphone*) NEAR/4 (consult* or appointment* or conferenc* or triag* or care or monitor* or "check up" or "check ups" or checkup* or support)):ti,ab,kw
10	(Videoconferenc* or (video NEXT chat*) or (video NEXT call*) or (instant NEXT messag*) or sms or "short messaging service" or texting or (phone NEXT messag*)):ti,ab,kw
11	{OR #1-#10}
12	("electronic health record" or "electronic care record" or "electronic health records" or "electronic care records"):ti,ab,kw
13	#11 NOT #12
14	MeSH descriptor: [Health Care Costs] explode all trees
15	MeSH descriptor: [Telemedicine] explode all trees and with qualifier(s): [economics - EC]
16	MeSH descriptor: [Quality-Adjusted Life Years] explode all trees
17	(economic* NEAR/6 (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)):ti,ab,kw
18	((preference or "cost effectiveness" or "cost benefit") NEAR/3 measur*):ti,ab,kw
19	(("quality adjusted life year" or "quality adjusted life years" or qaly*) and (alternative* or method* or utilit* or critici* or limitation* or drawback* or "draw back" or "draw backs" or problem* or disadvantage* or flaw* or weak* or issue* or disbenefit* or pitfall* or appropriate* or inappropriate* or suitab* or unsuitab*)):ti,ab,kw

Search number	Query
20	("quality adjusted life year" or "quality adjusted life years" or qaly*):ti
21	("quality of life" NEAR/3 (measur* or evaluat* or assess*)):ti,ab,kw
22	("value based health"):ti,ab,kw
23	(valu* NEAR/2 ("health state" or "health states")):ti,ab,kw
24	(valu* NEAR/3 health NEAR/3 (outcome* or measur*)):ti,ab,kw
25	{OR #14-#24}
26	#13 AND #25

Table S5. Search strategy used in the International Health Technology Assessment Database

Query
(("Telenursing"[mh]) OR ("Telemedicine"[mhe])) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))
(("mobile care") OR (mhealth) OR ("mobile health")) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))
(Ehealth or "electronic health*" or "electronic care" or erehab* or ecare or econsult* or ediagnos* or emedicine or enurs* or epsych* or etherap*) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))
(telehealth* or "tele-health*" or telenurs* or "tele-nurs*" or telemedicine or "tele-medicine" or teleeducation or "tele-education" or telecare or "tele-care" or Telepsych* or "tele-psych*" or Telemonitor* or "tele-monitor*" or teleprevention or "tele-prevention" or teleadvice or "Tele-advice" or Teleassist* or "tele-assist*" or Telebased or "tele-based" or Teletherapy or "tele-therapy" or Teleconsult* or "tele-consult*" or Teletriag* or "tele-triag*" or telerehab* or "tele-rehab*" or telecoaching or "tele-coaching" or telemanagement or "tele-management" or telepharmacy or "tele-pharmacy" or telesupport or "tele-support" or teledermatolog* or "tele-dermatolog*" or telehome* or "tele-home*" or telescreen* or "tele-screen*" or telediagnos* or "tele-diagnos*" or telematic*) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))
(((digital or online or virtual or computer* or "web based" or "web delivered" or internet) AND (health* or care or medicine or intervention* or therap* or treatment* or educat* or training))[abs]) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))

Query
(((Remote or digital or video or virtual or wireless or phone* or telephone* or smartphone*) AND (consult* or appointment* or conferenc* or triag* or care or monitor* or "check up*" or checkup* or support))[abs]) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))
((Videoconferenc* or "video chat*" or "video call*" or "instant messag*" or sms or "short messaging service" or texting or "phone messag*")[abs]) AND (((valu* AND health AND (outcome* or measur*))[abs]) OR ("value based health") OR ("quality of life" AND (measur* or evaluat* or assess*)) OR ("quality adjusted life year*" or qaly*) OR (((preference or "cost effectiveness" or "cost benefit") AND measur*)[abs]) OR (economic* AND (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) OR ("Quality-Adjusted Life Years"[mh]) OR ("Health Care Costs"[mh]))

Table S6. Search strategy used in the NHS Economic Evaluation Database

Search number	Query
1	MeSH DESCRIPTOR Health Care Costs EXPLODE ALL TREES
2	MeSH DESCRIPTOR Quality-Adjusted Life Years EXPLODE ALL TREES
3	(economic* NEAR6 (aspect* or model* or framework* or frame work* or method* or quality or technique* or outcome* or tool* or concept* or assess*)) IN NHSEED
4	((preference or cost effectiveness or cost benefit) NEAR3 measur*) IN NHSEED
5	(("quality adjusted life year*" or qaly*) AND (alternative* or method* or utilit* or critici* or limitation* or drawback* or "draw back*" or problem* or disadvantage* or flaw* or weak* or issue* or disbenefit* or pitfall* or appropriate* or inappropriate* or suitab* or unsuitab*)) IN NHSEED
6	("quality of life" NEAR3 (measur* or evaluat* or assess*)) IN NHSEED
7	("value based health") IN NHSEED
8	(valu* NEAR2 "health state*") IN NHSEED
9	(valu* NEAR3 health NEAR3 (outcome* or measur*)) IN NHSEED
10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
11	MeSH DESCRIPTOR Telemedicine EXPLODE ALL TREES
12	MeSH DESCRIPTOR Telenursing EXPLODE ALL TREES
13	("mobile health*" or "m-health" or mhealth or "mobile care") IN NHSEED
14	(Ehealth or "e-health" or "electronic health*" or "electronic care" or "e-rehab*" or erehab* or "e-care" or ecare or "e-consult*" or econsult* or "e-diagnos*" or ediagnos* or "e-medicine" or emedicine or "e-nurs*" or enurs* or "e-psych*" or epsych* or "e-therap*" or etherap*) IN NHSEED
15	(telehealth* or "tele-health*" or telenurs* or "tele-nurs*" or telemedicine or "tele-medicine" or teleeducation or "tele-education" or telecare or "tele-care" or Telepsych* or "tele-psych*" or Telemonitor* or "tele-monitor*" or teleprevention or "tele-prevention" or teleadvice or "Tele-advice" or Teleassist* or "tele-assist*" or Telebased or "tele-based" or Teletherapy or "tele-therapy" or Teleconsult* or "tele-consult*" or Teletriag* or "tele-triag*" or telerehab* or "tele-rehab*" or telecoaching or "tele-coaching" or telemanagement or "tele-management" or telepharmacy or "tele-pharmacy" or telesupport or "tele-support" or teledermatolog* or "tele-dermatolog*" or telehome* or "tele-home*" or telescreen* or "tele-screen*" or telediagnos* or "tele-diagnos*" or telematic*) IN NHSEED
16	((digital or online or "on-line" or virtual or computer* or "web based" or "web delivered" or internet) NEAR4 (health* or care or medicine or intervention* or therap* or treatment* or educat* or training)) IN NHSEED
17	((Remote or digital or video or virtual or wireless or phone* or telephone* or smartphone*) NEAR4 (consult* or appointment* or conferenc* or triag* or care or monitor* or "check up*" or checkup* or support)) IN NHSEED
18	(Videoconferenc* or "video chat*" or "video call*" or "instant messag*" or sms or "short messaging service" or texting or "phone messag*") IN NHSEED
19	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18
20	#10 AND #19

Table S7. Websites and search string used in the grey literature searches

Websites	Search string
ispor.org	("mobile health*" OR mhealth OR "mobile care" OR Ehealth OR erehabilitation OR erehab OR telehealth OR telehealthcare OR telemedicine OR telecare OR telenursing)
healtheconomics.org	
ohe.org	

Table S8. Screening tool

Analytical frameworks and outcome measures in economic evaluations of digital health interventions: a methodological systematic review	
Research aim: To systematically identify and assess studies which discuss the challenges, advantages and disadvantages associated to the use of outcome measures such as quality-adjusted life-year (QALY) and its alternatives in economic evaluations of digital health interventions (DHIs)	
Key elements	
Population	**Included:** • General population (i.e. patient or user) and healthcare professionals using a digital health (or similar) intervention.
	Excluded: • General population (i.e. patient or user) and healthcare professionals not using a digital health (or similar) intervention.
Interventions	**Included**: • Any DHI, i.e. delivered using technologies facilitating a remote access and use, and adopted for the purpose of health promotion or improvement, and disease prevention and/or treatment.
	Excluded: • Any non-DHI.
Settings	**Any**
Outcomes	**Included:** • Any study including a discussion of the theoretical and empirical challenges, advantages and disadvantages associated with the measurement, valuation and use of outcome measures (e.g. QALY and its alternatives), including the choice of analytical frameworks, for economic evaluations of DHIs.
	Excluded: • Any study that does not include a discussion of the methodological challenges attached to the use of analytical frameworks and outcome measure for economic evaluations of DHIs (e.g. studies which only list or summarise the outcome measures used in economic evaluations).
Comparison	**Any** (e.g. face-to-face or other DHIs)

Analytical frameworks and outcome measures in economic evaluations of digital health interventions: a methodological systematic review	
Study design	**Included:** • Empirical studies: - systematic reviews (and meta-analyses) of economic evaluations; - scoping reviews of economic evaluations; - qualitative reviews of economic evaluations; - narrative reviews of economic evaluations; - full applied economic evaluations (i.e. which consider both the costs and the consequences of DHIs and their comparators); - observational studies (e.g. cohort and case-control studies); - interventional studies (e.g. pre-post study, non-randomised and randomised controlled trials); • Non-empirical studies: - theoretical or conceptual papers; - economic guidelines and checklists; - position papers; - editorials; - commentaries - letters. **Excluded**: • Abstracts.
Limits	English language studies only.

Table S9. Guidance for Reporting Involvement of Patients and Public (GRIPP2) table[46]

Section and topic	Item
1: Aim of the study	To identify, assess and synthesise the arguments in the literature on how the effects of digital health interventions (DHIs) could be measured in economic evaluations.
2: PPI methods	One public adviser (CHi) was recruited following the circulation of an expression of interest call within the Public Advisers' Forum of the National Institute for Health and Care Research Applied Research Collaboration North West Coast (NIHR ARC NWC). In the call we specified the aim, outline and timescales of the planned systematic review, together with the expected input from the public adviser. In particular, we sought input in terms of reading, reviewing and commenting on the draft protocol and report from the systematic review to inform the presentation, interpretation and application of the results. The call also detailed the type of payment for the public adviser's input.
3: PPI results	Following the recruitment, an initial meeting between one of the co-authors (VB) and CHi was held, where the systematic review was discussed, and reciprocal expectations set out in more detail. The tasks and related time commitment for CHi, as well as the support available from the other co-authors, were outlined and agreed. After the initial meeting, CHi provided feedback to the draft protocol of the systematic review. Valuable comments were provided with focus on the assessment of health inequalities which may arise from the implementation of DHIs (e.g. lack of confidence in using a new technology). This feedback was incorporated in the protocol which was then registered on PROSPERO, with CHi included as one of the co-authors. During the systematic review process, one of the co-authors (VB) sent regular updates to CHi to provide information about the progress of the work and any adjustments in the expected timescale. Once the draft of the manuscript was reviewed by the other co-authors, it was then sent to CHi for feedback. CHi found the descriptions of the systematic review process to be very thorough and clear in terms of the search strategy and literature review. On the other hand, the discussion of analytical frameworks was deemed quite complex due to the use of technical economics language and acronyms. CHi appreciated the inclusion of a specific section dedicated to equity impacts, given her concerns that the increase in digital health provision could exclude disadvantaged and elderly patients, thus potentially contributing to the widening of health inequalities. Lastly, CHi found the draft clear in outlining the potential for further research in light of the increasing use of digital health initiatives and possibility of using a combination of analytical frameworks to measure their outcomes. CHi also reviewed this table, agreeing with the content describing her involvement and the PPI process.

Section and topic	Item
4: Discussion and conclusions	The PPI activities contributed to enhance the systematic review process mainly in two ways. First, CHi provided useful feedback on areas where the synthesis of the findings should focus on, in particular on where differences across digital health users may emerge (e.g. geographical and prior knowledge variation). These differences are likely to trigger health inequalities which may not be necessarily captured by traditional economic evaluations, which focus on an assessment of cost-effectiveness but should incorporate equity assessments too, as we recommend in our proposed set of recommendations on how to measure outcomes of DHIs in economic evaluations. Second, the collaboration with CHi helped us focus on the clarity of the description of the systematic review process in the protocol and manuscript. We strived to minimise the use of technical terms or, where not possible, briefly explain them. However, this is an area where further work is needed, as CHi rightly pointed out in the review of the manuscript. While to some extent the use of technical terms and acronyms is almost inevitable in academic papers, we will certainly keep these concerns in mind when we will prepare presentations and lay summaries of our findings for audiences which are wider than the academic one.
5: Reflections/critical perspective	With the systematic review being methodological in nature, it was our intention to facilitate the understanding of the process and findings of our review to both specialist and non-specialist audiences. Thanks to the input of CHi, we understood the strength and limitations of the manuscript draft. While the clear description of the systematic review process and the inclusion of a section specifically dedicated to equity impacts were well welcomed by CHi, her concerns over the use of acronyms and economic language deserve attention. We will certainly take these concerns on board when preparing presentations and lay summaries from our work. This is a lesson that we would recommend to any researcher involved in writing up and disseminating methodological findings. In relation to the actual PPI process, we thought that clear and regular communication with the public adviser was going to be key throughout the process. As such, we set out our reciprocal expectations clearly from the outset and sent regular updates on our work to keep CHi abreast of our progress. We think it is important to maintain regular contact with the public adviser during the process especially when, as is the case for systematic reviews, the work can be particularly lengthy and subject to change compared with the initially planned timescales. More importantly, our aim was to generate frank discussion with the public adviser about the quality of the work. This can be fostered by finding ways to rise the engagement of the public adviser: regular contacts and creating an environment where everyone's view is valued are some of the methods that we would recommend to other researchers developing PPI activities.

PPI: Patient and Public Involvement.

Table S10. Records excluded following full-text screening (n=43)

First author (year)	Reason for exclusion			
	No detail on measurement, valuation, choice and use of outcome measures for economic evaluations	Little or marginal detail on measurement, valuation, choice and use of outcome measures for economic evaluations	Full text not available in English	Full text not available
Abimbola (2019)[47]		✓		
Bashshur (1995)[11]		✓		
Beecham (2019)[48]		✓		
Berki (1975)[49]				✓
Bertoncello (2018)[50]	✓			
Charrier (2016)[51]	✓			
Crowe (1992)[52]		✓		
Doze (1999)[53]		✓		
Enam (2018)[54]	✓			
Goldstein (2001)[55]	✓			
Griscenko (2012)[56]	✓			
Hailey (1999)[57]		✓		
Hailey (2000)[58]		✓		
Hailey (2003)[59]		✓		
Hailey (2004)[60]		✓		
Hakansson (2000)[61]		✓		
Hughes (2002)[62]	✓			
Iribarren (2017)[63]	✓			
Jankovic (2021)[39]		✓		
Jean (2016)[64]			✓	
Jurkeviciute (2020)[65]		✓		
Kadu (2019)[66]		✓		
Kennedy (2005)[10]		✓		

First author (year)	Reason for exclusion			
	No detail on measurement, valuation, choice and use of outcome measures for economic evaluations	Little or marginal detail on measurement, valuation, choice and use of outcome measures for economic evaluations	Full text not available in English	Full text not available
Kidholm (2010)[67]		✓		
Kidholm (2012)[68]		✓		
Kidholm (2017)[69]	✓			
Kristiansen (2003)[70]	✓			
Lobley (1997)[71]		✓		
Luxton (2013)[72]		✓		
Luzi (2016)[73]		✓		
Mair (2000)[74]		✓		
Ohinmaa (2002)[75]		✓		
Phillips (2017)[76]		✓		
Powell (2020)[77]		✓		
Rojas (2008)[38]		✓		
Ruckdäschel (2006)[78]		✓		
Rudolph (2011)[79]	✓			
Scott (2007)[8]		✓		
Sisk (1998)[80]		✓		
Suzuki (2019)[81]	✓			
Vis (2020)[82]	✓			
Wang (2014)[83]		✓		
Zanaboni (2011)[84]	✓			
n(%)	13(30)	28(65)	1(2)	1(2)

Appendix S1. Supplement to narrative synthesis: arguments from the included studies on the measurement of digital health interventions' costs and non-health outcomes

In this appendix we summarise arguments, identified in the included studies, on how to measure costs and non-health outcomes. Therefore, this appendix focuses on those impacts which are not typically measured by generic and disease-specific outcome measures in economic evaluations, and complements the narrative synthesis presented in our main article.

It is important to note that we focus here on *how to measure costs and non-health outcomes* triggered by digital health interventions (DHIs)*,* rather than on listing *which costs and non-health outcomes* are triggered by DHIs. Such lists abound in the included studies and we refer the reader to the related articles (see for example the lists provided by Angjellari-Dajci et al., 2013[36], Davalos et al., 2009[5], and Le-Goff Pronost and Sicotte, 2010[27]).

It should also be noted that the cost side was not the focus of our systematic review, since our search strategy was specified to capture arguments on how to measure outcomes from DHIs. Consequently, the list of arguments on how to measure costs presented here is only illustrative and should not be seen as exhaustive.

Costs

The study by Bergmo (2015)[26] delineated the standard method to measure and value healthcare costs in economic evaluations of DHIs. This method involves three steps where the different cost categories (such as labour, capital and overheads) are first identified, then measured in physical units (resource use), and finally valued using tariffs (unit costs).

Once the cost categories are identified, resource use data are usually sourced from medical records and case report forms. However, for their actual measurement two approaches can be adopted (in conjunction or separately). With micro-costing, costs are separated into individual components (for example, resource use for investigations, tests or medicines and so on). With gross costing instead, bundles of service use are considered (for example, by measuring bed days or hospital stays)[26].

Then tariffs are applied to each resource use to obtain the total healthcare costs, as recommended by economic guidelines (for example, the guideline by the UK National Institute for Health and Care Excellence on DHIs (2018)[37]). Tariffs can be site-specific or system-specific, with the latter derived from national databases listing unit costs for labour, specific investigations, tests or medicines, diagnosis-related groups and health-resource groups[26]. Equipment costs should be also considered, and their costs annuitized over the lifetime of the equipment to account for depreciation and the opportunity cost of the capital invested[26].

Among the indirect costs, the time taken off work due to illness or to seek care (as a patient), or to care for someone (as a caregiver), is also considered in the study by Bergmo (2015)[26]. Time off work is usually measured by calculating productivity losses. These are valued by referring to gross wages[5, 26] or by adopting the friction cost method, which is based on the time needed to reinstate production at the level it would have been had the patient or caregiver carried on working[26].

Non-healthcare outcomes

As indicated by Bergmo (2015), the measurement of non-healthcare outcomes, such as access to care, sense of empowerment and knowledge transfer may be challenging[26]. Among the included studies, perhaps the most significant source of information on how to measure

non-health outcomes is the study by Davalos et al. (2009)[5], which includes insights on monetising outcomes in the context of cost-benefit analyses (CBAs). Here we focus on some key non-health outcomes, but for more details on other outcomes the reader can refer directly to the article by Davalos et al. (2009)[5].

For some of the non-health outcomes, the methods available to monetise them are rather straightforward. For example, for the reduced travel triggered by a DHI (for patients or users and healthcare professionals alike), the monetary value can be obtained by multiplying the distance to the healthcare site by the mileage allowance rate, or simply by referring to the specific fares of the mode of transport used[5].

For other non-health outcomes, the associated methods of monetisation are more complex. For example, for knowledge transfer among healthcare professionals, Davalos et al. (2009)[5] suggested the estimation of avoided referrals or, alternatively, the training time required to obtain the same knowledge together with the time taken off work to attend training. These would be then monetised by considering the healthcare professionals' specific hourly wage (for the time not spent on the referral or, alternatively, for the time not spent on training and the consequent work time saved) and the patients' avoided costs (for the avoided referrals). Where market values are not available, then a willingness-to-pay analysis may be useful to understand the monetary value placed by individuals on a specific DHI. However, separating out the individual values of specific outcomes (e.g. patient's satisfaction or acquired health knowledge) remains difficult[5].

Appendix S2. Case study on set of recommendations on measuring effects of digital health interventions in economic evaluations: examples from published studies

In this case study, we present examples of published studies which show how our evidence-based recommendations on the measurement of outcomes in economic evaluations of digital health interventions can be operationalised.

1. Development of impact matrix and Cost-Consequence Analysis (CCA)

Impact matrix

A fitting example of a comprehensive impact matrix based on multiple stakeholders and dimensions comes from the study by Le Goff-Pronost and Sicotte (2010)[27]. The authors designed a matrix which intended to describe the potential impacts of telemedicine networks for patients, physicians, hospitals and governments in terms of five attributes, namely: 1) accessibility; 2) acceptability; 3) quality; 4) organisation; and 5) costs and benefits.

Another similar example can be found in Bongiovanni-Delarozière and Le Goff-Pronost (2017)[34]. These authors followed the French National Authority for Health methodological framework in order to create an impact matrix based on a systematic review of economic evaluations of telemedicine interventions. This matrix is set to describe changes in: 1) accessibility; 2) professional practice/care organisation; 3) care quality/safety; and 4) costs. Again, the four attributes can be evaluated by taking into account the separate impacts on patients and family caregivers, physicians/allied health professionals, healthcare institutions, government, health insurance companies and local authorities.

CCA

The study by Snoswell et al. (2019)[85] represents an example of how relevant non-health impacts could be captured and emphasised using CCAs. In this study telehealth was compared with other two modes of delivery to provide specialist clinics to remote Indigenous people with diabetes in Australia. Given the unique and diverse consequences triggered by each mode of delivery, the authors adopted a CCA in order to present the consequences separately, rather than using a composite outcome measure. Among the consequences analysed, non-health consequences for the patients were related to time (such as the time taken away from other activities and the waiting time for consultation), capacity (such as the number of patients that could access each clinic at one time) and place (such as the location of the appointments).

Another example where time-related consequences (on work and travel) were considered is in the study by Noble et al. (2005)[86], whose CCA compared telemedicine and routine GPs appointments for the treatment of minor injuries in the UK.

2. Incorporation of outcome measures in economic evaluations

Cost-Benefit Analysis (CBA)

Langabeer et al. (2017)[87] performed a CBA of a telehealth-based consultation between patients and physicians working in Emergency Medical Services, where the need for patient transportation to a hospital emergency department was evaluated. Averted transportation costs for patients and averted emergency consultations costs were counted as benefits, and then compared against the costs triggered by the intervention. Since the intervention was examined only in terms of efficiency implications, implementing a CBA was a reasonable choice in this case.

However, if the focus also embraces the patients' utility from the intervention, then a willingness-to-pay (WTP) analysis is an option that may need to be explored as part of a CBA. This was the case of the study by Stahl and Dixon (2010)[88], where videoconferencing was compared with face-to-face office visits in primary care. After being examined in both settings, patients were asked about their WTP for videoconferencing, which can be computed based on open-ended questions, binary choices like standard gamble elicitation, or bidding.

Another more sophisticated option to estimate WTP is to use discrete choice experiments (DCEs). This method is more robust to typical stated preference problems, such as strategic answering or hypothetical bias. As an example, Chang et al. (2017)[89] chose to use a DCE to evaluate the benefits obtained by households using online health services. In this DCE, a hypothetical internet network service was evaluated by incorporating both price and online health service elements as attributes, around which the users' preferences were elicited.

Cost-Utility Analysis (CUA)

According to our evidence-based set of recommendations, CUAs can be adopted when generic health-related quality of life (HRQoL) instruments like the EuroQol Five Dimension descriptive system (EQ-5D) are able to capture the relevant range of effects triggered by the interventions under examination. This is the case of the CUA developed by Noben et al. (2017)[90] who compared a web-based employability intervention against usual care (i.e. regular trade union support) for people with work-related disabilities in the Netherlands. Since the focus was on a range of disabilities rather than specific ones, using a generic and non-specific HRQoL instrument like the EQ-5D to then estimate quality-adjusted life years (QALYs) seems sensible.

The approach chosen in the study by Tan et al. (2021)[91] on telestroke in China may be considered as an appropriate example for the use of CUA too. Importantly, the utility scores in this CUA, estimated using the EQ-5D, were assigned differently to patients categorised according to the severity of the consequences of their stroke, as measured by the modified Rankin Scale. The resulting QALYs were reflective of the different degrees of disease-specific disability or dependence of the stroke survivors.

Mapping algorithms

An example of the use of mapping algorithms in economic evaluations of digital health interventions is provided in the study by Naveršnik and Mrhar (2014)[92] who evaluated a web-based depression intervention. The effectiveness of the intervention was measured using the Beck Depression Inventory scale, and the relative scores were then converted into QALY weights. As recognised by the authors, when interventions for people with mental disorders are assessed, generic HRQoL instruments like the EQ-5D may not be sensitive enough to capture the health and quality of life impacts of the patients. In this and other disease areas, existing[93] or *de novo* mapping algorithms should be considered to generate disease-sensitive QALYs.

Cost-Effectiveness Analysis (CEA)

The previously mentioned study by Noben et al. (2017)[90] represents an example of when a CUA and a CEA can co-exist. As the web-based intervention under examination aimed to improved employability of the users, their work ability was assessed in a CEA (in terms of cost per gain in work ability outcome), together with the QALYs analysed in the CUA.

In another CEA, Franzini et al. (2011)[94] evaluated the effect of tele-intensive care unit programmes on patient mortality. As this outcome of interest could not be suitably measured

by HRQoL instruments, a CEA based on the effects of the intervention on mortality was deemed adequate.

3. Assessment of impacts on equity

As mentioned in LeFevre et al. (2017)[35], the use of extended cost-effectiveness analyses to assess equity impacts is limited in economic evaluations. However, we have identified other ways to investigate equity impacts from digital health interventions in the literature. A fitting example comes from a trial which looked at investigating the cost-effectiveness of mHealth and community mobilisation interventions in preventing and controlling Type 2 diabetes mellitus and risk factors for non-communicable diseases in rural Bangladesh[95]. In this trial, the equity analysis was first set out in the protocol of the economic evaluation[96] and then developed[97]. Sub-group analyses were intended to capture how the exposure to and the effects of the interventions differed across participants with different socio-economic characteristics, such as age, gender and wealth[97].

Witt Udsen et al. (2017)[98] provided another example of the use of sub-group analysis. In this study, the incremental QALYs resulting from a tele-healthcare trial for people with chronic obstructive pulmonary disease in Denmark were further investigated by stratifying the population according to their comorbidities, age, gender, prior social care resource use and delivery sites. In particular, geographical stratification is likely to play a key role in the delivery of digital health interventions, which may alter the access to healthcare services for underserved segments of the population (e.g. those living in rural areas). As such, techniques like geospatial assessment, as explored in a study on a virtual urgent care programme in the United States by Khairat et al. (2019)[99], are worth considering as part of a wider analysis on equity impacts.

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