Health technology assessment for digital health technologies

A thesis submitted to fulfil requirements for the degree of Doctor of Philosophy

By

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2023

Statement of originality

This is to certify that, to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes.

I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

Amy Von Huben		Date: 28 February 2023

Authorship attribution statement

This thesis contains material previously published as peer-reviewed journal articles or currently under review for publication. The relevant articles are listed in Appendix B, along with detailed statements of each co-author's relative contributions.

Additionally, we make the following general statement of acknowledgment:

This thesis is principally the work of Amy Von Huben. She is the singular author of the introduction in Chapter 1 and the discussion in Chapter 7. She is the lead and corresponding author for the five component studies presented in Chapters 2 to 6. She was primarily responsible for the design of the project, the performance of the systematic reviews, designing and conducting the preference survey, conducting statistical and economic analyses, and interpreting results. All writing, revising, and creation of tables and figures in the chapters of this thesis were completed by Amy Von Huben.

All supervisors listed below provided substantial support for this project, aiding in conceptualisation and design, interpretation of results, and critical review of all manuscripts and chapters.

Amy Von Huben		Date: 28 February 2023
Dr Martin Howell		Date: 28 February 2023
Associate Professor Sarah Norris		Date: 28 February 2023
Professor Clara K Chow		Date: 28 February 2023
Professor Kirsten Howard		Date: 28 February 2023

Ethical clearance

Ethics approval for the study in Chapter 4 was obtained from The University of Sydney Human Research Ethics Committee. All study participants gave written informed consent for participation in the study.

Abstract

Background

Digital health technologies (DHTs) for the remote or self-management of patients with chronic disease are becoming a ubiquitous component of health service delivery. Accelerated by the recent pandemic, publicly funded healthcare service providers are increasingly making decisions on the funding of these technologies.

The health technology assessment (HTA) process offers a systematic and multidisciplinary approach to assessing the value-for-money and budget impact of new health technologies. While internationally established and commonly used HTA frameworks offer technology-specific content for performing HTA on non-digital health technologies (i.e., *medical and surgical interventions*, *diagnostics*, *pharmaceuticals,* and *screening technologies*), little specific content is provided for DHTs. Specific HTA frameworks for DHTs have recently emerged (e.g., the UK's ESF and DTAC, Germany's DiGA, and Finland's Digi-HTA), but it has not yet been established whether they are suitable for comprehensive HTA, incorporate the issues raised in almost twenty years of DHT evaluation framework literature, or whether their content reflects the relative preferences of a broad cross-section of stakeholders on the most important issues to consider when assessing DHTs for public funding.

Objectives

To develop a literature-informed and stakeholder-prioritised checklist of DHT-specific considerations for DHTs that manage chronic disease that extends internationally established frameworks for HTA: to enable users to perform a DHT-specific and comprehensive HTA and to encourage primary researchers to collect appropriate data to inform this HTA.

Methods

Chapter 2

Identification of DHT-specific content relevant for HTA was performed via a systematic review of international peer-reviewed and grey literature on DHT evaluation frameworks to March 2020. Using the internationally established framework of the EUnetHTA HTA Core Model ("the Core Model") as a scaffold, the most frequently recommended DHT evaluation content from the included frameworks was mapped to the Core Model by domain, topic, and issue to produce "content lists" for a comprehensive and DHT-specific HTA.

Chapter 3

Current trends in primary research were examined via a systematic review of peer-reviewed literature on DHTs that manage chronic disease published from 1 January 2015 to 20 March 2020. The extent to which the primary research covered the content list items was evaluated, and the content list questions were revised for duplication, redundancy, and terminology during the review.

Chapter 4

Stakeholder prioritisation of the content was performed via a best-worst scaling preference study in 2022 with a large sample of patients, carers, health professionals, and general community stakeholders in Australia, Canada, the United Kingdom, and New Zealand. Prior to the preference study, the content items were grouped by issue similarity into non-overlapping attributes of a DHT over several iterations of feedback and a pilot best-worst scaling survey. Stakeholders were asked which DHT attributes were the most and least important to consider in the public funding of DHTs that manage chronic disease. Each participant was randomised to one of eight blocks of twelve choice sets with three attributes per choice set. An arbitrary threshold of a preference score over 50% in at least one

stakeholder group was set to identify "prioritised" attributes for a practical list of DHT content for HTA. Final study results were analysed with multinomial models by stakeholder group, and by latent class to investigate the heterogeneity of preferences that may not be captured in the stakeholder model.

Chapter 5

The content relating to the prioritised DHT attributes was grouped by Core Model (or new DHT-specific) issue ID into a checklist of DHT-specific "clarifications" to extend the Core Model, i.e., the "extended checklist".

Chapters 6 and 7

Finally, a within-trial cost-effectiveness analysis of a self-management DHT for children with urinary incontinence was conducted using the extended checklist recommendations for analysis and reporting. The relevance of, and practicality of finding evidence for, the checklist items was assessed. As Chapter 6 was an evaluation of a DHT prepared for a clinical audience, the assessment of the extended checklist was presented in Chapter 7.

Results

Chapter 2

Forty-four DHT evaluation frameworks were identified, mainly covering clinical effectiveness (n = 30) and safety (n = 23) issues. No DHT evaluation frameworks were identified that consistently covered all DHT-specific issues in the domains of safety, effectiveness, and economic evaluation. The framework authors recommended DHT evaluation content in 28 of the 145 Core Model issues. However, they also recommended a further 22 DHT-specific issues not covered in the Core Model; ten in safety and nine in clinical effectiveness. Seventy-one content items covering the fifty issues were identified and

split into two content lists: 1. DHT-specific content (covering forty-one issues), and 2. Content common to all technologies but essential for DHTs (covering nine issues).

Chapter 3

The systematic review of DHT primary research identified 178 DHT chronic disease remote or self-management interventions, predominantly randomised controlled trials targeting cardiovascular disease and diabetes in high to middle-income countries. A coverage assessment of 112 cardiovascular and diabetes DHT studies revealed less than half covered DHT-specific content in all but the health problem domain. Content common to all technologies but essential for DHTs was better covered, but less than half the studies covered this content in the clinical effectiveness and ethical analysis domains.

Chapter 4

The seventy-one content items were grouped by issue similarity into 24 non-overlapping DHT attributes. In the final best-worst scaling survey of 1,251 stakeholders (576 community members, 543 patients/carers, and 132 health professionals), twelve DHT attributes achieved the predefined threshold for a "prioritised" attribute. These attributes predominantly related to safety but also technical features, effectiveness, ethics, and economics. Results from the latent class model supported this prioritisation. Overall, connectedness with the patient's healthcare team seemed the most important, with *"Helps health professionals respond quickly when changes in patient care are needed"* as the most highly prioritised of all attributes.

Chapter 5

The twelve prioritised attributes mapped to content in sixteen Core Model issues and six new DHT-specific issues, resulting in an extended checklist of 22 DHT-specific clarifications. The clarifications were reported by Core Model (or new DHT-specific) issue ID and issue,

along with literature references and the issue IDs with similar themes in other HTA domains ("Content relations"). To standardise assessment and reporting, recommendations on *evidence data sources* (from peer-reviewed and grey literature*), suggested methods, tools and measures*, and *evidence types* (i.e., narrative or comparative to usual care), were also provided by checklist item.

Chapters 6 and 7

The economic evaluation of a self-management DHT for urinary incontinence in children (eADVICE) found the technology to be cost-saving and beneficial (dominant). In performing the analysis and reporting of the evaluation, the extended checklist items were all found to be relevant for informing the public funding decision for the DHT. However, this case study highlighted the difficulties of finding evidence for the checklist items if the gathering of this evidence was not planned for or prioritised in the clinical trial. It also highlighted the difficulties of reporting the required evidence in the peer-reviewed literature without the widespread routine use of DHT-specific reporting standards for clinical trials.

Conclusions

DHTs that manage chronic disease are increasingly becoming an integral part of healthcare service delivery. There has been a wealth of research on the unique potential benefits and risks of these technologies, and nearly twenty years of research on DHT-specific evaluation content to inform considerations over a nine-domain health technology assessment (HTA).

The research studies in Chapters 2 to 4 confirmed that existing HTA frameworks do not consider all the DHT-specific issues required for the comprehensive HTA of DHTs. In addition, no current DHT evaluation frameworks cover all issues recommended by the DHT evaluation literature or can demonstrate that the included issues are those that are most important to community stakeholders. Furthermore, primary research on DHTs that manage

chronic disease is not generating all the required evidence for DHT-specific and comprehensive HTA.

Much of the content and methodologies of HTA for more established technologies apply to DHTs, but the quality of HTA for DHTs can be improved by including DHT-specific considerations. There is currently a critical need to communicate these considerations and the evidence required for HTA to improve the quality of research so health services can make optimal funding decisions.

This thesis has compiled literature-informed and stakeholder-prioritised DHT-specific considerations for undertaking HTAs of DHTs that manage chronic disease, using internationally accepted HTA terminology and frameworks for ease of adoption in many countries, to enable users to perform a DHT-specific and comprehensive HTA, and encourage primary researchers to collect appropriate data to inform this HTA.

Acknowledgements

Thank you to my supervisors, Dr Martin Howell, Associate Professor Sarah Norris, and Professors Kirsten Howard and Clara Chow, for whom I would have never had the courage nor the resources to start, pursue, or complete this PhD. I am indebted to them for many hours, sharing their ideas, knowledge, and experience with me.

Thank you to Professor Armando Teixeira-Pinto for all the statistical inspiration and for introducing me to the wonderful research community of the Centre for Kidney Research, The Children's Hospital, Westmead. Working with such an encouraging and supportive group of researchers, I was inspired to start this PhD, and I have benefited from their encouragement throughout this journey.

This work would not have been possible but for the financial support of the Postgraduate Scholarship in Health Economics (Patient-Centred Care and Outcomes in Chronic Disease), the School of Public Health, The University of Sydney, and Professor Clara Chow and Senior Biostatistician, Simone Marschner, employing me at the Westmead Applied Research Centre (WARC), University of Sydney, where I gained so much practical experience and learnt so much. I am also grateful for the financial support of a National Health and Medical Research Council (NHMRC) Medical Research Future Fund (MRFF) Grant.

Thanks also go to Associate Professor Patrina Caldwell, Professor Natasha Nassar, Dr Amanda Ampt, the Menzies Kids team, and the Sydney Health Economics Discussion group that have kept me smiling this last year and made me believe it was possible to finish this thesis.

To my parents, Phillipa and Graeme, and big sister, Emma, thank you for always supporting and encouraging me. To my husband, Mark, and son Carl, who ran every step of this marathon with me, thank you for all your love and patience.

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Appendix A

Thesis roadmap

Thesis aim

The aim of this thesis was to develop a literature-informed and stakeholder-prioritised checklist of digital health technology (DHT)-specific considerations that extends internationally established frameworks for health technology assessment (HTA). The purpose of the extended checklist was to enable users to perform a DHT-specific and comprehensive HTA for DHTs that manage chronic disease, and to encourage primary researchers to collect appropriate data to inform this HTA.

Structure of the thesis

To achieve this aim, the following research tasks were undertaken:

1. An investigation to describe the frameworks being used to evaluate and perform HTAs of DHTs internationally and in Australia
2. A systematic review of international peer-reviewed literature and grey literature for DHT evaluation frameworks
3. A detailed analysis of the content recommended by the evaluation frameworks for a DHT-specific and comprehensive HTA
4. A systematic review of primary research on chronic disease remote/self-management DHTs to assess the extent to which this research addresses the content identified for a DHT-specific and comprehensive HTA
5. Research of stakeholder (patients, carers, health professionals, and general community) preferences for the most important attributes of chronic disease remote/self-management DHTs to consider in public funding decisions

6. Application of the quantified stakeholder preferences to adapt and prioritise the content required for a DHT-specific and comprehensive HTA, with a view to extending internationally established frameworks for HTA
7. Testing the relevance and practicality of the recommended content for a DHT-specific and comprehensive HTA through its use in practice in a cost-effectiveness analysis of a DHT

The main body of the thesis has seven chapters, largely comprising published or submitted peer-reviewed publications: a topic introduction (Chapter 1), a series of studies that identify, revise, and prioritise content required for a DHT-specific and comprehensive HTA (Chapters 2 to 4), an adaptation of the content as an "extended checklist" for an internationally accepted HTA framework (Chapter 5), a cost-effectiveness analysis of a DHT as a case study to test the relevance and practicality of the extended checklist (Chapter 6), and synthesis and discussion of the project (Chapter 7). Appendices include supplementary materials (Appendix A) and statements of co-author contributions (Appendix B).

Chapter 1: Introduction

This chapter provides the background to the topic, the research questions, and the thesis aims. It also provides the definitions of key concepts, historical detail, and context required to answer the research questions and essential to achieving the thesis aims. This includes describing the definitions of DHTs and the DHTs that are the focus of this thesis, defining HTA and the components of HTA that are the focus of this thesis, identifying the commonly used HTA frameworks for non-digital technologies, and detailing the development frameworks to evaluate and perform HTAs of DHT internationally and in Australia.

Chapter 2: DHT evaluation frameworks - Identification of content for a DHT-specific and comprehensive HTA

Chapter 2 reports on a systematic review of international peer-reviewed and grey literature on DHT evaluation frameworks. This review was undertaken to identify content for a DHT-specific and comprehensive HTA. DHT-specific content and content that is common to all technologies but critical for an HTA of DHTs were identified. This chapter has been published in the *International Journal of Technology Assessment in Health Care*.

Chapter 3: DHT primary research - Coverage of content required for a DHT-specific and comprehensive HTA

Chapter 3 reports on a systematic review of all primary research (published between 1 January 2015 and 20 March 2020) on the effectiveness and cost-effectiveness of DHTs for managing chronic disease at home. The purpose of this review was to examine how many of the identified HTA content issues were covered by the primary research. The content list questions were also revised for duplication of issues and terminology during this review. This chapter has been published in the *International Journal of Technology Assessment in Health Care*.

Chapter 4: Community preferences for attributes of DHTs to consider in health service funding

Chapter 4 describes a best-worst scaling (BWS) preference study undertaken with patients, carers, health professionals and the general community to elicit the relative preferences on the most important content for a DHT-specific and comprehensive HTA. This chapter has been published in the *International Journal of Technology Assessment in Health Care*.

Chapter 5: An extended checklist for HTA of DHTs that manage chronic disease

Chapter 5 presents an extended checklist for HTA of DHTs that manage chronic disease based on the research described in earlier chapters and using the ontology of the internationally accepted and widely used EUnetHTA Core Model for HTA.

Chapter 6: eADVICE: an economic evaluation of a web-based program for children with incontinence

Chapter 6 presents a within-trial cost-effectiveness analysis of a DHT for managing urinary incontinence in children (eADVICE). The recommendations of the content to be provided to inform a DHT-specific and comprehensive HTA in the extended checklist (Chapter 5) were used to prepare this manuscript. This chapter has been submitted to *Pediatrics* for publication. As this publication is aimed at reporting the evaluation of eADVICE to a clinical audience, the assessment of the relevance and practicality of the extended checklist items for evaluating eADVICE is summarised in Chapter 7.

Chapter 7: Discussion and conclusions

This final chapter synthesizes the findings and recommendations of the previous chapters. Topics of discussion include the summary of study findings, including learnings from the case study (Chapter 6), study strengths and limitations, what the research adds, implications for evaluators, developers, and researchers, and possible directions for future research.

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Chapter 1 Introduction

1.1. Background

Digital health technologies (DHTs) enabling remote monitoring or self-management of patients offer many potential benefits, particularly for patients managing chronic diseases. Examples of potential benefits include reduced travel and clinic waiting times, reduced exposure to and spread of infection, gains in confidence in self-managing conditions, and better patient connection with their healthcare team at critical times (1-3).

However, the use of DHTs as a health intervention can present a significant change in the logistics of health service delivery. Benefits may only be realised if staff are supported with appropriate enablers, e.g., adequate resources and change management support, systems interoperability and adequate data quality management, appropriate funding, and champions of the new intervention within the organisation (3-11).

In addition, with the potential benefits come risks unique to DHTs, such as threats to patient privacy from inadequate cybersecurity (12-14), use of incorrect patient information from poor interoperability/data quality management (2, 4, 14-16), lack of access in areas of poor connectivity/infrastructure (2-4, 6, 10, 14, 16-20), and ethical threats such as a false sense of security from being monitored or incorrect interpretation of test results without clinician supervision (21, 22). Furthermore, DHTs commonly collect a large amount of personal data, and DHTs that promote behavioural change often use this data to develop predictive behaviour algorithms (22). Technology companies may also use transmissions of data with linkable user identifiers from DHTs for undesirable marketing and analytics purposes (13). The resulting threats to privacy from how DHTs are designed are unique challenges for evaluating the risks versus benefits of these technologies. These unique risks must be considered along with risks common to other technologies, e.g., less effective treatments, missed diagnoses, and misclassification of disease severity.

To realise the benefits and minimise risks, a robust evaluation process is essential to inform decision-makers on funding and planning all new health technologies, including DHT interventions. Health technology assessment (HTA) offers a framework for comprehensively evaluating new health technologies (23). Many countries commonly use HTA to ascertain the value-for-money and the budget impact of new health technologies to inform public funding/investment decisions.

1.2. Research questions

Given the acceleration in the development and use of DHTs for remote management and self-management of chronic conditions in the recent pandemic, it is now more common for public health services to evaluate DHT interventions for funding. In countries that use HTA to inform these decisions, the health services assessments will likely use existing HTA frameworks. However, there is a question as to whether existing commonly used and internationally established HTA frameworks, which have been developed through the evaluation of non-digital health technologies, are sufficiently comprehensive to consider the unique risks and benefits of DHTs. Peer-reviewed literature on DHT evaluation frameworks has been evolving since 2004 (24), and checklists for DHT evaluation started appearing on HTA agency websites in 2012 (25). More recently, HTA frameworks explicitly designed for DHT have emerged (6, 26, 27). These developments suggest concerns persist from researchers, governments, and HTA agencies over the adequacy of current HTA frameworks to evaluate DHTs.

Furthermore, if existing HTA frameworks are insufficient for DHT evaluation and the new DHT-specific HTA frameworks are to be used, subsequent questions arise as to whether these new frameworks:

- Are sufficiently comprehensive for HTA

- Have incorporated all the recommendations from almost twenty years of DHT evaluation framework literature
- Include recommendations that reflect the views of a broad cross-section of stakeholders as to the most important issues to consider when evaluating DHTs for public funding

International consensus on the content of these new DHT-specific frameworks has yet to be reached.

Another question is the extent to which primary research on DHTs is generating appropriate evidence for HTA, be it under current HTA frameworks or DHT-specific frameworks. Primary research evaluating DHT safety, effectiveness, and cost-effectiveness has increased with the development and widespread availability of digital technologies. However, systematic reviews of primary research on DHTs have identified a wide variation in scope and methods, limiting the quality and consistency of evidence available to inform funding decisions (28-30). Even if new DHT-specific HTA frameworks are the most appropriate to inform public funding decisions, finding the evidence required to complete the assessment may be challenging. Measures may therefore be required to improve the quality and transparency of evidence generation for DHT-specific HTAs.

1.3. The need for this study

Given these questions and the acceleration in the use of DHTs in health delivery in recent years, it is, therefore, an appropriate time to review the content of current HTA frameworks, emerging DHT-specific HTA frameworks, and DHT primary research against the recommendations of the DHT evaluation framework literature and the preferences of stakeholders as to the most important DHT issues to be considered in HTA. These learnings can then be included in HTA models and guidance.

The work of this thesis in bridging the gap in HTA guidance for the evaluation of DHTs is critical because if health services do not have the required frameworks and evidence to comprehensively evaluate DHTs by considering the risks and benefits unique to DHTs, they will likely make sub-optimal funding decisions.

1.4. The aims of this thesis

This thesis aims to answer the abovementioned research questions and develop a literature-informed and stakeholder-prioritised checklist of DHT-specific considerations that extends internationally established frameworks for HTA to:

- Enable users to perform a DHT-specific and comprehensive HTA
- Encourage primary researchers to collect appropriate data to inform this HTA

To answer these research questions, it is essential to first:

- Detail the various definitions of DHTs and define the DHTs that are in scope for this thesis
- Define health technology assessment (HTA) and the components of the HTA in focus for this thesis
- Identify commonly used and internationally established existing HTA frameworks for non-digital health technologies (i.e., to assess whether they are sufficient for DHTs)
- Describe the development of frameworks to evaluate and perform HTAs of DHTs internationally and in Australia

The remaining sections of this chapter detail this information to provide the definitions, context, and scope for the research studies in subsequent chapters.

1.5. The definition of digital health technology (DHT)

One of the complexities hampering the development of DHT evaluation frameworks has been the vast array of technologies that are labelled as DHTs, e.g., telemedicine, information communication technology for health system infrastructure ("eHealth"), mobile phone applications ("mHealth"), and medical device software (MDSW). These technologies have different risk and benefit profiles dependent on function, purpose, and user, making the development of a common evaluation framework challenging. Furthermore, the terms describing DHT classes (digital devices, mhealth, eHealth) are numerous, not consistently defined, and rapidly changing. Table 1.1 provides a summary of the varying terms and definitions for DHT classes by source encountered when researching DHT evaluation frameworks.

Table 1.1: Terms and definitions for DHT classes

Term	***Definition***	***Source***
digital devices	Human performance and behaviour measurement devices, e.g., sensors and wearables	Caulfield et al. (31)
mHealth	The use of mobile wireless technologies for health. This includes digital devices defined above and either mobile or web-based applications, "Apps"	WHO (32)
mHealth Apps	The subset of mHealth technologies that are mobile or web-based applications ("Apps")	Study defined
eHealth	The use of information and communications technology in support of health and health-related fields. This includes mHealth as defined above	WHO (32)
digital health	A broad umbrella term encompassing eHealth (which includes mHealth), as well as emerging areas, such as the use of advanced computing sciences in "big data", genomics, and artificial intelligence	WHO (32)
medical device software (MDSW)	Software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the medical devices regulation or in vitro diagnostic medical devices regulation	MDCG (33)
AI-based MDSW	MDSW with embedded self-learning algorithms	HAS (17)
digital mental health services	Mental health, suicide prevention, or alcohol and other drug services...in the form of information; digital counselling; treatment (including assessment, triage, and referral); or peer-to-peer service that is delivered to a service user via a digital means	ACSQHC (4)

WHO, World Health Organisation; MDCG, Medical Device Co-ordinating Group; AI, Artificial Intelligence; HAS, Haute Autorité de Santé; ACSQHC, Australian Commission on Safety and Quality in Health Care.

However, the UK National Institute for Health and Care Excellence (NICE), in their Evidence Standards Framework (ESF) for Digital Health Technologies (10), addresses the challenge of a vast number of DHT classes by using a functional classification of technologies and a risk-based approach. DHTs deemed higher risk to patient safety require more evidence to qualify for public funding under the ESF. The French National Authority for Health (HAS) also published a functional classification of DHTs that adds consideration of the DHT's level of user personalisation and autonomy into the classification (34). Although international consensus on these functional classifications of DHTs is yet to be achieved, defining classes of DHTs that have more homogenous risk and benefit profiles to identify the relevant content for HTA is a practical and prudent approach.

1.6. The DHTs in focus for this thesis

The class of DHTs in focus for this thesis has been chosen so they are representative of the most likely technologies to undergo HTA to inform public funding decisions. In countries that use HTA to inform public funding decisions, standard HTA pathways commonly require medical regulator market approval prior to or concurrently applying for public subsidy/reimbursement. In addition, HTA is most utilised for informing decisions on new medical technologies that can demonstrate a direct health outcome to patients. For example, it is uncommon to use HTA to inform decisions on DHTs that provide systemwide efficiencies, such as electronic health records and electronic prescribing. Investments in systemwide health information and communication technologies are more commonly strategic decisions made by governments and health service organisations. Similarly, a large portion of DHTs targeted to the consumer, e.g., Fitbit, and Apple Watch, are less likely to need to apply for public funding. This considerably narrows the range of DHTs that need to be considered for the HTA frameworks that inform public funding decisions.

The DHTs that are the focus of this project are those specifically designed for patients with a diagnosed chronic non-communicable disease for active remote (e.g., home) monitoring or self-management. These technologies are of two main types: 1. Remote monitoring via digital devices and 2. Web-based programs or applications ("apps") for self-management. These DHTs are most likely to be regulated as medical device software (MDSW) under EU medical device regulation (MDR) (33), and so have a standard pathway to gain market approval from a medical device regulator. They also represent a large proportion of current DHT primary research on direct health outcomes to patients, aiming to establish the technology's comparative safety, effectiveness, and cost-effectiveness over existing technologies. Given the similarity in purpose, function, users, and component technologies across this class of DHTs, it has a relatively homogenous risk and benefit profile. In addition, they are classified into the highest-risk evidence tier (Tier C) under the NICE ESF (10). Focusing on a high-risk DHT class should identify a fuller range of DHT-specific content, with the expectation that not all this content will apply to lower-risk DHT classes.

1.7. The definition of health technology assessment (HTA)

The definition of health technology assessment has evolved from the first HTA report by the US Office of Technology Assessment in 1976 (35) to the recent 2020 publication of an internationally accepted definition of HTA (23). Several initiatives have aimed to improve the international consistency of HTA practices over this period, such as the development of the European Union Network for HTA (EUnetHTA) HTA Core Model (36, 37) and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) HTA Council Working Group report on good practices in HTA (38). Still, there remained no international consensus on a definition for HTA. As a result, a task group co-led by the International Network of Agencies for Health Technology Assessment (INAHTA) and Health Technology Assessment International (HTAi) developed the definition shown in Figure 1.1

(23). It differed from previous definitions by emphasising that HTA is a formal, transparent, and multidisciplinary process applicable at different stages of a technology's lifecycle.

HTA is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.

Note 1: A health technology is an intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program, or system (definition from the HTA Glossary; http://htaglossary.net/health+technology)

Note 2: The process is formal, systematic, and transparent, and uses state-of-the-art methods to consider the best available evidence.

Note 3: The dimensions of value for a health technology may be assessed by examining the intended and unintended consequences of using a health technology compared to existing alternatives. These dimensions often include clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, organizational and environmental aspects, as well as wider implications for the patient, relatives, caregivers, and the population. The overall value may vary depending on the perspective taken, the stakeholders involved, and the decision context.

Note 4: HTA can be applied at different points in the lifecycle of a health technology, that is, pre-market, during market approval, post-market, through to the disinvestment of a health technology.

Figure 1.1: The internationally agreed definition of HTA (23)

This definition of HTA is broad, and the assessment may change by the context, purpose, perspective, stakeholders involved, and the point in the lifecycle of health technology. The focus of this thesis is on HTA as a multidisciplinary process (23) to assess and prioritise new technologies against existing healthcare interventions based on comparative safety, clinical effectiveness, cost-effectiveness (39), and other DHT-relevant dimensions of value at the stage in a health technology's lifecycle of investment/public funding decisions. This thesis aims to identify the most important considerations for DHTs to ascertain value-for-money and budget impact to inform investment/public funding decisions.

1.8. Commonly used HTA frameworks for non-digital health technologies

While many HTA agencies publish guidance on HTA methods and procedures, there is only one HTA framework that has been developed for international use over a range of technologies (37), namely the EUnetHTA HTA Core Model ("the Core Model") (36). The ISPOR HTA Council Working Group lists the Core Model as a "good practice" example of a

framework to perform and scope an assessment, i.e., determine the critical research questions and identify information available to address them (38). The model was developed in Europe as a basis for EU HTA agency collaboration and European HTA agencies use the Core Model for joint assessments. INHATA has 32 member countries across six continents, including Australia. As the majority of INHATA members are European countries, the model is highly relevant to this international network of HTA agencies. Even though non-European agencies have their own methodological guidance, this guidance is grounded in at least six of the Core Model domains and often bears many similarities to the model. It is, therefore, a representative model of current good practice HTA internationally.

The Core Model was developed to improve the standard, consistency, and transparency of HTAs by defining common elements, methods, and the reporting structure for HTAs. In addition, given that it was built to enable broad-scoped, multidisciplinary HTA (37), it is comprehensive in the 145 issues it considers. According to the model, nine information domains should be considered within any HTA (Table 1.2). The primary HTA domains were identified by Busse et al (40) with the EUR-ASSESS Working group (41) and these have been slightly modified over time. The Core Model built upon this work and a review of other methodologies being used internationally. Research on international HTA reports shows good coverage of the Core Model domains except for ethical, social, and legal (42).

Table 1.2: Domains of the EUnetHTA HTA Core Model version 3.0 (36)

#	Abbr.	Name	Description
1	CUR	Health problems and current use of technology	Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status
2	TEC	Description and technical characteristics of technology	Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it
3	SAF	Safety	Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers

#	Abbr.	Name	Description
4	EFF	Clinical effectiveness	Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting
5	ECO	Costs and economic evaluation	Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value-for-money judgments
6	ETH	Ethical analysis	Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA
7	ORG	Organisational aspects	Identifies resources to be mobilised or organised to implement the new technology and the consequences (Intra/inter-organisational and health system)
8	SOC	Patient and social aspects	Considers issues related to the new technology relevant to patients, carers, and social groups
9	LEG	Legal aspects	Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

However, the content of the domains was developed based on evaluations of specific types of non-digital technologies, originally medical and surgical interventions and diagnostics, and later screening technologies and pharmaceuticals. No revision of the Core Model has been done considering evaluations of DHTs.

For the reasons mentioned above, the Core Model (37) was identified as the most appropriate HTA framework to use in this thesis as it represents a commonly used and internationally established HTA framework against which to assess the sufficiency of its content to perform HTAs for DHTs.

1.9. Development of frameworks to evaluate and perform HTAs of DHTs

1.9.1. International development

Early attempts at establishing evaluation frameworks for DHT concentrated on telemedicine as a replacement for face-to-face consultation via telephone, internet call, or videoconferencing. Hailey et al. (24) developed a scoring system for study quality assessment. Gagnon and Scott (43) proposed that evaluations should be tailored to the telemedicine application's context, through the lifecycle, and involve stakeholders from multiple relevant disciplines. Kidholm et al. (3) stated that due to a lack of evidence of

effectiveness and inadequate economic evaluations, the European Commission in 2009 funded the authors' development of a telemedicine HTA framework, the Model for Assessment of Telemedicine applications (MAST) (3). This is a three-element model based on the EUnetHTA Core Model (36), a systematic review of reviews on telemedicine (44) and stakeholder workshops.

The World Health Organisation (WHO) also responded to requests of member countries for guidance on how to implement, scale, evaluate and monitor information communication technology (ICT) for health, termed "eHealth", by producing the 2012 National eHealth Strategy Toolkit (45). In 2013, Labrique et al. (46) reported on the "rapid proliferation" of mobile health (mHealth) projects without evidence of effectiveness or cost-effectiveness. They recommended that a mHealth framework be based strategically on health system needs to avoid disconnected and mHealth innovator-led investment. Their work resulted in the 2019 WHO guideline: Recommendations on digital interventions for health system strengthening (32). However, this guideline only covered a subset of DHTs and did not cover DHTs for individual patient use.

In 2011, Eysenbach (21) extended the Consolidated Standards of Reporting Trials (CONSORT) statement to clinical trials of eHealth/mHealth interventions to improve and standardise reporting for appraisal of trial validity. The CONSORT-EHEALTH checklist items are mandatory reporting items for studies to be published in the *Journal of Medical Internet Research*.

The European Commission began a public consultation in April 2014 with the Green Paper on Mobile Health (47) in an effort to remove barriers and resolve issues relating to mHealth deployment. The consultation centred on the themes of safety (patient safety, transparency of information, and data protection), legal framework and liability, social issues such as equity, efficiency issues such as interoperability, and what support structures were required to

stimulate investment and innovation, such as models for reimbursement (47). This led to the establishment of the European Commission's Working Group on mHealth Assessment Guidelines (48). In 2017, the group stated it was unable to issue guidelines after a year of work due to the complexity, lack of consensus between stakeholders, and new developments in other EU regulations, such as the Medical Devices Regulation (MDR) (49) and General Data Protection Regulation (GDPR) (50). However, the work of this group was utilised by the UK National Institute for Health and Care Excellence (NICE) in building their Evidence Standards Framework for Digital Health Technologies (10) and the UK Medicines & Healthcare Products Regulatory Agency (MHPRA) for mHealth products not considered medical devices (51).

On the medical regulation side, given a growing awareness of the inadequacy of existing regulations to address the potential risk of harm to patients of digital technologies, the International Medical Device Regulator Forum (IMDRF) formed a "Software as a Medical Device (SaMD)" working group. This group published guidance on key definitions, a framework for risk categorisation (52), quality management and clinical evaluation for SaMD over the period 2013 to 2017. The risk categorisation framework (52) was formally adopted in guidance by the European Union Medical Device Coordination Group (MDCG) in October 2019 (33), leading to the widening of the scope of medical device regulation to all digital technologies that have a "stated medical purpose" termed "Medical Device Software" (MDSW). These regulations also increased the risk classifications of many digital technologies and hence the level of evidence required for approval. A similar working group was formed to address medical device cybersecurity, issuing a principles and practices document in March 2020 (53).

At the start of this project, because of the IMDRF work, medical technology regulators internationally were quite advanced in communicating criteria for market approval of DHTs.

However, little guidance existed on the criteria for assessing DHTs for public funding. A handful of European HTA agencies had addressed DHTs with published checklist criteria for evaluating health applications on their websites (16, 25), criteria for reimbursement of connected medical devices with a consultation on evaluating automatic learning processes (7, 17), and the UK NICE had just published its first iteration (two subsequent updates during the project) of the *Evidence standards framework (ESF) for digital health technologies (DHTs)* (27). Although the ESF was the most comprehensive guidance identified for HTA agencies, the NICE stated the framework was not designed to describe an evaluation process for a DHT but rather to describe types and levels of evidence for consistent analyses of effectiveness and economic impact. During the project, the *Digi-HTA* framework was implemented to perform assessments in Finland (54), and the *Digital Health Applications Ordinance (DiGAV)* (6) now regulates the reimbursement of digital health applications by statutory public health insurance in Germany. However, none of these recent DHT HTA frameworks that are used for public funding decisions today covers all nine domains recommended by the EUnetHTA Core Model, and, to our knowledge, their content is not informed by studies on the preferences of a broad cross-section of stakeholders on the most important issues to consider when making public funding/reimbursement decisions on DHTs.

1.9.2. Australian development

1.9.2.1. Australia's National Digital Health Strategy

The Australian Digital Health Agency (ADHA) is the peak Australian government entity responsible for digital healthcare. It was established in 2016 to lead the development of the National Digital Health Strategy ("the strategy") and its implementation. The strategy (55) was focused on providing the infrastructure for digital health in Australia, identifying seven priority outcomes to deliver by 2022 to create a safe, seamless, and secure health system. Key deliverables were: 1. a national electronic health record (My Health Record); 2. secure digital

channels for health information exchange; and 3. electronic prescribing and dispensing. Another priority area was to improve data quality and systems interoperability using data standards, common terminologies, and unique identifiers. In addition, a small number of digitally enabled healthcare models were chosen to be tested, measures to ensure a digitally capable healthcare workforce were to be identified, and an assessment framework for mobile health applications was to be developed (55).

The mobile health (mHealth) assessment framework, published in December 2022 (56), is the first initiative by the ADHA to develop an assessment framework for a portion (apps only) of the DHTs that are the focus of this thesis, i.e., remote monitoring and self-management DHTs for patients with chronic disease. However, it is not an evaluation framework to inform public funding decisions but rather a voluntary assurance-focused tool aimed at industry to help promote the development and use of safe and effective health apps. Medical device software apps may be referred to the Therapeutic Goods Administration (TGA) during the assessment, but they do not have to be regulated or have market approval by the regulator. Apps are assessed through a four-stage process against 13 criteria over a maximum of five domains: 1. acceptability, 2. safety and trust, 3. ease of use, 4. privacy and security, and 5. technical quality assurance. Apps passing assessment may be published on the mHealth Apps library with a badge of endorsement or a more detailed assessment with a star rating for each domain. This approach is similar to the development of the UK NHS Digital's DTAC Tool (16) to assess apps for the now-discontinued NHS Apps Library. Endorsement or assessment ratings may encourage individual health services and health professionals to invest in or recommend these apps to patients. However, given that endorsed and assessed apps may not be regulated by the TGA, the onus is on health services and health professionals to check whether the use and recommendation to patients of non-regulated apps are in accordance with the guidelines of the Medical Board and the relevant College, and covered under professional

indemnity insurance. In addition, the onus is on manufacturers of apps to ensure they have complied with MDSW regulations or gained the necessary exclusions or exemptions.

1.9.2.2. State and territory digital strategies

In addition to the ADHA's national digital strategy, all states and territories of Australia have some form of digital health strategy with differing visions, timelines, and outcomes (57). However, similar to the national strategy, they focus on building the infrastructure to enable digital healthcare and not yet the development of DHT evaluation or HTA frameworks. Because the Australian and state/territory governments do not have standalone frameworks or processes for DHT assessment (57), applications for public funding of DHTs can only go through standard HTA pathways.

1.9.2.3. National standard HTA pathways and frameworks

At the Australian government level, the Medical Services Advisory Committee (MSAC) is responsible for assessing technologies (including digital technologies) that are regulated by the TGA (57) for public subsidy. The Prostheses List Advisory Committee (PLAC) is responsible for assessing technologies (including digital technologies) regulated by the TGA and eligible for funding by private insurers. Each entity uses international best practice HTA frameworks and methods to assess the comparative safety, effectiveness, cost-effectiveness, and budget impact of a new technology compared to existing technology (57). However, the DHT-specific guidance in the recently updated MSAC technical guidelines (9) for HTA is limited to fixed (not dynamic) multifactorial algorithms and patient data security.

Furthermore, the ability of a DHT manufacturer or sponsor to apply through national HTA pathways is limited by whether the DHT is regulated by the TGA. Recent exclusions of DHTs by the TGA to medical device regulation (58) have narrowed the range of DHTs eligible for assessment by MSAC. Given the burden of regulating all software with a stated

medical purpose or software that controls or interacts with a medical device internally or externally, the TGA excluded some software-based medical devices from medical device regulation by function (59). Although it is unlikely these exclusions will impact DHTs that are the focus of this thesis (chronic disease active remote monitoring and self-management DHTs), some of the following exemptions may impact components of these digital health interventions, leaving them unregulated with no standard national government HTA pathway:

- Software for self-management of an existing disease or condition that is not serious (provided it does not provide specific treatment or treatment suggestions)
- Digital mental health tools, including cognitive behaviour therapy tools (provided it is based on established clinical practice guidelines that are referenced and displayed in the software)
- Communication software for telehealth consultations, including the transmission of patient information
- Software that provides alerts or additional information to health professionals about patient care (provided the health professional can exercise their judgement in determining whether to action the alert or information)

Clinical decision support software (CDSS) is another DHT likely to be assessed through standard HTA pathways. The TGA maintains that CDSS are medical devices and must meet the essential principles for the safety and performance of medical devices. However, a CDSS that meets specific criteria is exempted by the TGA from medical device regulation. This means the TGA retains some oversight for advertising, adverse events, and notification, but registration on the Australian Register of Therapeutic Goods (ARTG) (60) is not required. Since an exempt CDSS is still regulated by the TGA, this is less likely to impact the ability of exempt CDSS to apply through national HTA pathways for public funding.

Very few DHTs have been assessed through MSAC and PLAC to date. However, twenty-three Medicare Benefits Schedule (MBS) consultation items related to telehealth activities are available to health professionals for publicly funded reimbursement of consults via phone and video under certain conditions.

1.9.2.4. State and territory standard HTA pathways and frameworks

The Australian government shares responsibility for funding public hospitals with state and territory governments, so guidance for conducting HTA also exists at the state and territory level. DHTs excluded from the national HTA pathways may be assessed by jurisdictional governments or Local Health Districts (LHD) to inform investment decisions. The "eADVICE" DHT described in Chapter 6 of this thesis is an example of a DHT seeking funding through this pathway.

However, state and territory HTA frameworks do not include any DHT-specific considerations for assessment. The New South Wales (NSW) HTA framework (61) has a broader definition of new health technologies than the national HTA frameworks, stating that changes to delivering care are considered a new health technology. This broader definition seems more inclusive of new digital health interventions. Given that many DHTs aim to reduce days in hospital by managing patients remotely or encouraging self-management in the community, assessment at the state or district level, where detailed information on benefits and risks can be collected, is appropriate. However, the ability to share the results of these assessments across districts and states is limited, given the strict criteria for nominating locally implemented new health technologies for discussion at the state or national health technology committees (61).

1.9.2.5. Summary of Australian development of HTA frameworks for DHTs

HTA frameworks and pathways for DHTs have yet to be a priority area for national, state, and territory digital healthcare strategies. Australia continues to rely on standard HTA frameworks and pathways for DHTs, and few assessments of DHTs have been conducted at the national level. Although more evaluations have occurred at the state/territory and district level, this may result in variation in the HTA approach, outcomes, and fragmented implementation of DHT across jurisdictions. In addition, little guidance on DHT-specific considerations is found in current Australian HTA frameworks.

1.10. Conclusion

Internationally established sets of technology-specific considerations are available for HTAs in *medical and surgical interventions*, *diagnostics*, *pharmaceuticals*, and *screening.* However, the development of an internationally accepted set of DHT-specific content has been hampered by the wide range of DHTs with varied benefit and risk profiles. By focusing on a class of DHTs that are most likely to be assessed by HTA for public funding and have a relatively homogeneous risk and benefit profile, i.e., DHTs used for active remote monitoring and self-management of chronic diseases, DHT-specific content can be identified from almost twenty years of DHT evaluation framework literature, the content prioritised by stakeholder preferences, and a practical set of DHT-specific content can be developed to with a view to extending existing commonly used and internally established HTA frameworks. The following chapters present the studies that aim to achieve this objective.

1.11. References

1. Bergmo TS. How to measure costs and benefits of eHealth interventions: An overview of methods and frameworks. *J Med Internet Res*. 2015;17(11):e254.
2. European Commission. Synopsis report, consultation: Transformation health and care in the digital single market. Luxembourg City (LU): European Commission, 2018.
3. Kidholm K, Ekeland AG, Jensen LK, Rasmussen J, Pedersen CD, Bowes A, et al. A model for assessment of telemedicine applications: MAST. *Int J Technol Assess Health Care*. 2012;28(1):44.
4. Australian Commission on Safety and Quality in Health Care (ACSQHC). National safety and quality digital mental health standards. Sydney (AU): ACSQHC; 2020.
5. Drury P, Roth S, Jones T, Stahl M, Medeiros D. Guidance for investing in digital health. Manila (PH): Asian Development Bank (ADB), 2018.
6. Regulation on the procedure and requirements for testing the eligibility for reimbursement of digital health applications in the statutory public health insurance, S. Digital Health Applications Ordinance (DiGAV), Federal Ministry of Health (DE) (2019).
7. Haute Autorité de Santé (HAS) [French National Authority for Health]. Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement. Paris (FR): HAS, 2019.
8. Lennon MR, Bouamrane MM, Devlin AM, O'Connor S, O'Donnell C, Chetty U, et al. Readiness for delivering digital health at scale: Lessons from a longitudinal qualitative evaluation of a national digital health innovation program in the United Kingdom. *J Med Internet Res.* 2017;19(2):e42.

9. Medical Services Advisory Committee (AU). Guidelines for preparing assessment reports for the medical services advisory committee. [Pdf] 2021 [updated 18 May 2021]; Available from: http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Documents-for-Applicants-and-Assessment-Groups; Accessed 12 August 2022.

10. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Pdf] 2018 [updated 09 August 2022]; Available from: https://www.nice.org.uk/corporate/ecd7. Accessed 15 August 2022.

11. Rojahn K, Laplante S, Sloand J, Main C, Ibrahim A, Wild J, et al. Remote monitoring of chronic diseases: A landscape assessment of policies in four European countries. *PLoS One*. 2016;11(5):e0155738.

12. European Commission. Draft code of conduct on privacy for mobile health applications. [Pdf] 2016 [updated 07 December 2017]; Available from: https://digital-strategy.ec.europa.eu/en/library/code-conduct-privacy-mhealth-apps-has-been-finalised. Accessed 29 March 2020.

13. Huckvale K, Torous J, Larsen ME. Assessment of the data sharing and privacy practices of smartphone apps for depression and smoking cessation. *JAMA Network Open*. 2019;2(4):e192542.

14. Ruck A, Wagner Bondorf S, Lowe C, Consard Limited. Second draft of guidelines, EU guidelines on assessment of the reliability of mobile health applications, European Commission, Directorate-General of Communications Networks, Content & Technology, 2016.

15. Department of Health & Social Care (UK). A guide to good practice for digital and data-driven health technologies. [Internet]; 2019 [Updated 19 January 2021];

Available from: https://www.gov.uk/government/publications/code-of-conduct-for-data-driven-health-and-care-technology/initial-code-of-conduct-for-data-driven-health-and-care-technology. Accessed 18 August 2022

16. NHS Digital (UK). The digital technology assessment criteria for health and social care (DTAC). [Internet] 2019 [updated 16 April 2021]; Available from: https://transform.england.nhs.uk/key-tools-and-info/digital-technology-assessment-criteria-dtac/. Accessed 18 August 2022
17. Haute Autorité de Santé (HAS) [French National Authority for Health]. Public consultation on the draft analysis grid intended for use by CNEDiMTS to contribute to its evaluation of medical devices embedding decision systems based on automatic learning processes ("Artificial Intelligence"). Paris (FR): HAS, 2019.
18. Lewis TL, Wyatt JC. Mhealth and mobile medical apps: A framework to assess risk and promote safer use. *J Med Internet Res*. 2014;16(9):e210.
19. Moshi MR, Tooher R, Merlin T. Development of a health technology assessment module for evaluating mobile medical applications. *Int J Technol Assess Health Care*. 2020;36(3):252-61.
20. Nielsen S, Rimpiläinen S. Report on international practice on digital apps. Glasgow (UK): Digital Health and Care Institute, 2018.
21. Eysenbach G. Consort-eHealth: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res*. 2011;13(4):e126.
22. Sax M, Helberger N, Bol N. Health as a means towards profitable ends: Mhealth apps, user autonomy, and unfair commercial practices. *J Consumer Policy*. 2018;41(2):103-34.

23. O'Rourke B, Oortwijn W, Schuller T. International Joint Task Group. The new definition of health technology assessment: A milestone in international collaboration. *Int J Technol Assess Health Care*. 2020;36(3):187-90.

24. Hailey D, Ohinmaa A, Roine R. Study quality and evidence of benefit in recent assessments of telemedicine. *J Telemed Telecare*. 2004;10(6):318-24.

25. Andalusian Health Quality Agency (ES). Complete list of recommendations on design, use and assessment of health apps. [Internet] 2012; Available from: http://www.calidadappsalud.com/en/listado-completo-recomendaciones-app-salud/. Accessed 16 August 2020.

26. Haverinen J, Keränen N, Falkenbach P, Maijala A, Kolehmainen T, Reponen J. Digi-HTA: Health technology assessment framework for digital healthcare services. *FinJeHeW*. 2019;11(4).

27. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Pdf] 2019; Accessed 15 August 2020.

28. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mhealth? A systematic review of economic evaluations of mhealth solutions. *PLoS One*. 2017;12(2):e0170581.

29. Kidholm K, Kristensen MBD. A scoping review of economic evaluations alongside randomised controlled trials of home monitoring in chronic disease management. *Appl. Health Econ. Health Policy*. 2018;16(2):167-76.

30. Vukovic V, Favaretti C, Ricciardi W, de Waure C. Health technology assessment evidence on e-health/m-health technologies: Evaluating the transparency and thoroughness. *Int J Technol Assess Health Care*. 2018;34(1):87-96.

31. Caulfield B, Reginatto B, Slevin P. Not all sensors are created equal: A framework for evaluating human performance measurement technologies. *NPJ Digit*. 2019;2(1).

32. World Health Organisation. WHO guideline: Recommendations on digital interventions for health system strengthening. Geneva (CH): 2019.

33. Medical Device Coordination Group. Guidance on qualification and classification of software in regulation (EU) 2017/745 – MDR and regulation (EU) 2017/746 – IVDR. European Commission; 2019.

34. Haute Autorité de Santé (HAS) [French National Authority for Health]. Functional classification, according to their intended use, of digital solutions used in the context of medical and paramedical care. Paris (FR): HAS, 2021.

35. Banta D, Jonsson E. History of HTA: Introduction. *Int J Technol Assess Health Care*. 2009;25(S1):1-6.

36. EUnetHTA Joint Action 2 Work Package 8. HTA core model® version 3.0. [Pdf] 2016; Available from: https://www.htacoremodel.info/BrowseModel.aspx. Accessed 14 August 2022.

37. Kristensen FBMDP, Lampe KMD, Wild CD, Cerbo MM, Goettsch WMP, Becla LM. The HTA core model® —10 years of developing an international framework to share multidimensional value assessment. *Value Health*. 2017;20(2):244-50.

38. Kristensen FB, Husereau D, Huić M, Drummond M, Berger ML, Bond K, et al. Identifying the need for good practices in health technology assessment: Summary of the ISPOR HTA council working group report on good practices in HTA. *Value Health*. 2019;22(1):13-20.

39. Australian Government Department of Health and Ageing. Review of health technology assessment in Australia. Canberra (AU): Commonwealth of Australia, 2009.

40. Busse R, Orvain J, Velasco M, Perleth M, Drummond M, G¨Rtner F, et al. Best practice in undertaking and reporting health technology assessments. Int J Technol Assess Health Care. 2002;18(2):361-422.

41. Liberati A, Sheldon TA, Banta HD. EUR-ASSESS project subgroup report on methodology: Methodological guidance for the conduct of health technology assessment. *Int J Technol Assess Health Care*. 1997;13(2):186-219.

42. Merlin T, Tamblyn D, Ellery B. What's in a name? Developing definitions for common health technology assessment product types of the international network of agencies for health technology assessment (INHATA). Int J Technol Assess Health Care. 2014;30(4):430-7.

43. Gagnon M-P, Scott RE. Striving for evidence in e-health evaluation: Lessons from health technology assessment. *J Telemed Telecare*. 2005;11(2_suppl):34-6.

44. Ekeland AG, Bowes A, Flottorp S. Effectiveness of telemedicine: A systematic review of reviews. *Int J Med Inform*. 2010;79(11):736-71.

45. World Health Organisation. National ehealth strategy toolkit. Gevena (CH): WHO, 2012.

46. Labrique AB, Vasudevan L, Kochi E, Fabricant R, Mehl G. Mhealth innovations as health system strengthening tools: 12 common applications and a visual framework. *Glob health, Sci Pract*. 2013;1(2):160-71.

47. European Commission. Summary report on the public consultation on the green paper on mobile health. Brussels (BE): European Commission, 2015.

48. European Commission. Report of the working group on mhealth assessment guidelines. European Commission, 2016.

49. Regulation (EU) 2017/745 of the European Parliament and of the Council, *Official Journal.* 2017; L117:1-175.

50. Regulation (EU) 2016/679 of the European Parliament and of the Council, *Official Journal;* 2016; L119:1-88.

51. Medicines and Healthcare Regulatory Authority. Guidance: Medical device stand-alone software including apps (including IVDMDS) v1.10. [Pdf] 2014; [updated 8 September 2022]; Available from: https://www.gov.uk/government/publications/medical-devices-software-applications-apps. Accessed 20 February 2023.

52. IMDRF Software as a Medical Device (SaMD) Working Group. "Software as a medical device": Possible framework for risk categorization and corresponding considerations. International Medical Device Regulators Forum (IMDRF), 2014.

53. Medical Device Cybersecurity Working Group. Principles and practices for medical device cybersecurity. International Medical Device Regulators Forum (IMDRF), 2020.

54. Haverinen J, Turpeinen M, Falkenbach P, Reponen J. Implementation of a new Digi-HTA process for digital health technologies in Finland. *Int J Technol Assess Health Care*. 2022;38(1).

55. Australian Digital Health Agency. Australia's national digital health strategy. [Pdf] 2018; Available from: https://www.digitalhealth.gov.au/about-us/strategies-and-plans/national-digital-health-strategy-and-framework-for-action. Accessed 30 August 2019.

56. Australian Digital Health Agency (AU). Assessment framework for mhealth apps. [Pdf] 2022. Available from: https://www.digitalhealth.gov.au/about-us/strategies-and-plans/assessment-framework-for-mhealth-apps. Accessed 5 February 2023.

57. Janssen A, Shah K, Norris S, Shaw T, Wilson A. Australian digital health landscape analysis: Key findings report. Sydney (AU): The University of Sydney, 2022.

58. Department of Health and Aged Care (AU) Therapeutic Goods Administration (TGA). Therapeutic goods act. Is my software regulated? [Pdf] 2021; Available from: https://www.tga.gov.au/sites/default/files/my-software-regulated.pdf. Accessed 5 February 2023.

59. Department of Health and Aged Care (AU) Therapeutic Goods Administration (TGA). How the TGA regulates software based medical devices. [Pdf] 2021; Available from: https://www.tga.gov.au/sites/default/files/how-tga-regulates-software-based-medical-devices.pdf; Accessed 12 February 2023.

60. Department of Health and Aged Care (AU), Therapeutic Goods Administration (TGA), Clinical decision support software, scope and examples. [Pdf] 2021; Available from: https://www.tga.gov.au/sites/default/files/clinical-decision-support-software.pdf. Accessed 12 February 2023.

61. New South Wales (NSW) Health (AU). NSW framework for new health technologies and specialised services: Guideline, NSW Government; 2018.

Chapter 2 Health technology assessment for digital health technologies that manage chronic disease: A systematic review

The material in this chapter has been published as:

Von Huben A, Howell M., Howard K, Carrello J, Norris S. Health technology assessment for digital technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2021;37(1), e66. doi:10.1017/S0266462321000362.

A statement of the specific contribution of the co-authors can be found in Appendix B.

Purpose of chapter

To identify content for a DHT-specific and comprehensive HTA, a systematic review of peer-reviewed and grey literature of DHT evaluation frameworks to 20 March 2020 was undertaken.

2.1. Abstract

Objectives: A growing number of evaluation frameworks have emerged over recent years addressing the unique benefits and risk profiles of new classes of digital health technologies (DHTs). This systematic review aims to identify relevant frameworks and synthesize their recommendations into DHT-specific content to be considered when performing a Health Technology Assessment (HTA) for DHTs that manage chronic non-communicable disease at home.

Methods: Searches were undertaken of Medline, Embase, Econlit, CINAHL, and The Cochrane Library (January 2015 to March 2020), and relevant grey literature (January 2015 to August 2020) using keywords related to HTA, evaluation frameworks, and DHTs. Included framework reference lists were searched from 2010 until 2015. The EUNetHTA HTA Core Model version 3.0 was selected as a scaffold for content evaluation.

Results: Forty-four frameworks were identified, mainly covering clinical effectiveness (n = 30) and safety (n = 23) issues. DHT-specific content recommended by framework authors fell within 28 of the 145 HTA Core Model issues. A further twenty-two DHT-specific issues not currently in the HTA Core Model were recommended.

Conclusions: Current HTA frameworks are unlikely to be sufficient for assessing DHTs. Development of DHT-specific content for HTA frameworks is hampered by DHTs having varied benefit and risk profiles. By focusing on DHTs that actively monitor/treat chronic non-communicable diseases at home, we have extended DHT-specific content to all nine HTA Core Model domains. We plan to develop a supplementary evaluation framework for designing research studies, undertaking HTAs, and appraising the completeness of HTAs for DHTs.

2.2. Introduction

Digital health technologies (DHTs) have the potential to overcome the barrier of geographical location to widen access to health care and improve connectivity between patients and their healthcare team. A DHT's ability to continuously monitor a patient's physiological indicators with preset alert thresholds can expedite treatment compared with traditional office visits.

Chronic diseases are long-lasting conditions with persistent effects, often affecting a patient's social and economic circumstances (1). DHTs that help patients self-manage a long-lasting condition at home and escalate treatment only when required may be particularly suited to these patients. With increasing personal investment in electronic devices, the growing burden of chronic disease, and a limited health budget and workforce, there is potential for DHTs to offer a comparatively safe, effective, and cost-effective treatment pathway for chronic disease.

Terms describing DHT classes (digital devices, mHealth, eHealth) are numerous, not consistently defined, and rapidly changing (see Table 2.1 footnote d for DHT class terms and definitions). The DHTs that are the focus of this review are those specifically designed for patients with diagnosed chronic non-communicable diseases to use at home for active monitoring or treatment, e.g., remote monitoring via implants/wearables, web-based cognitive behavioural therapy treatment programs. These DHTs with a functional classification of "Active monitoring" or "Treat" are classified into the highest risk evidence tier, Evidence Tier 3b, under the United Kingdom's (UK) National Institute for Health and Care Excellence (NICE) Evidence Standards (2) and are regulated as Medical Device Software (MDSW) under the new European Union (EU) Medical Devices Regulation (MDR) (3).

Despite the unique benefits of these DHTs, there are many risks/challenges associated with their use: technical reliability/stability of electronic sensors and data transmissions; transparency of algorithms for autonomous decisions; access and useability; reorganisation of workflows/infrastructure; and security threats in data transmissions and storage. Given patients with chronic disease may already be socially isolated and economically vulnerable, the use of DHTs in this population deserves careful consideration. A tailored approach to the Health Technology Assessment (HTA) of DHTs could assist such considerations by explicitly examining the unique benefits and risks of DHTs for these vulnerable patients.

Although HTA has multiple definitions, for this paper we define HTA as the multidisciplinary process (4) to assess and prioritise new technologies against existing health care interventions based on comparative safety, clinical, and cost-effectiveness (5) at the lifecycle stage of public funding assessment.

Given the topics and issues within established HTA frameworks have evolved to guide the assessment of pharmaceuticals, medical devices, and medical services, it is not clear if such frameworks are fit for purpose in assessing DHTs. The last decade has seen an increase in DHT-specific evaluation frameworks, HTA agency guidance, and improved clarity in DHT regulation (EU MDR (3, 6) and EU General Data Protection Regulation (GDPR) (7)); all important considerations for a DHT-specific HTA framework.

The exponential rise in clinical applications for DHTs has driven an increase in clinical trials of these technologies. Recent systematic reviews (8-11) of HTAs and economic evaluations for DHTs identify a wide variation in scope and methods used, limiting the quality and consistency of evidence available to inform funding decisions. Identifying and defining DHT-specific content within generally accepted HTA frameworks may help researchers collect consistent and robust evidence for decision-makers.

The aim of the current systematic review is twofold: first to identify and synthesize the recommendations of DHT-specific HTA and evaluation frameworks using an established HTA model with a broad scope of content and applicability to multiple jurisdictions as a scaffold, and second, to develop a comprehensive list of DHT-specific content to be considered when undertaking an HTA to inform funding decisions for DHTs that manage chronic non-communicable disease at home.

2.3. Methods

This systematic review was registered with PROSPERO (#CRD42020186888) and is reported in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (12).

2.3.1. Inclusion criteria

This review focuses on HTA frameworks for evaluating comparative effectiveness, cost-effectiveness, and safety for public funding purposes, not on the evaluation of effectiveness or safety for individual interventions. The review is limited to recently published frameworks because of the rapid development of DHTs. Frameworks also have to be suitable for MDSW. For these reasons, peer-reviewed journal articles, dissertations, and theses, HTA agency, and health economic institute publications that discuss methods for performing an HTA, or an assessment of comparative effectiveness, safety, or cost-effectiveness, appropriate for MDSW and published between 2015 and 2020, were eligible for inclusion.

2.3.2. Exclusion criteria

Medline, Embase, Econlit, CINAHL, and The Cochrane Library were searched from 1 January 2015 to 20 March 2020 using keywords related to HTA, evaluation frameworks, and DHT. The full search strategy is presented in Figure A 1. The start date of January 2015 was selected given the rapid development of DHTs and the focus on up-to-date HTA frameworks.

Grey literature was searched using the Canadian Agency for Drugs and Technologies in Health (CADTH)'s Grey Matters (13). Agencies listed under HTA and Health Economics (see Table A 1) were searched for evaluation frameworks published between 1 January 2015 and 31 March 2020 using the keyword searches: "electronic health" or eHealth or "mobile health" or mHealth or telehealth or telemedicine or "digital health" or "digital medicine." The ProQuest Dissertations and Theses Global (PQDT) database was searched using these same keywords. The grey literature search was updated on 31 August 2020 for releases post 31 March 2020.

To reduce the risk of missing DHT-specific content from evaluation frameworks published before 2015 but not subsequently updated, pearling of included frameworks was conducted. The start date of 2010 for pearling was chosen because prior to 2010 DHT evaluation frameworks focused mainly on telecommunications as a replacement for face-to-face consultations (14-18), and these DHTs are out of scope for our review.

2.3.3. Study selection

All authors participated in the title and abstract screening. Full-text screening was undertaken by AvH, with ten percent of full texts reviewed independently by JC and conflicts resolved by SN.

2.3.4. Data extraction

Data extracted for each framework included: First author/institution, year published, country/region that the framework is intended for, website or journal citation, the author's affiliation (e.g., university, HTA agency, government agency), intended audience, the purpose of the framework (and if relevant, the name of the framework), and DHT classes covered.

Data extraction was conducted by AvH and checked by JC.

2.3.5. Content evaluation

The aspects covered by the included frameworks were analysed using the European Network for Health Technology Assessment (EUNetHTA) HTA Core Model version 3.0 ("HTA Core Model") (19). The HTA Core Model was selected as our analytic scaffold because it is used across multiple countries to assess a range of health technologies, includes a wide range of issues for content mapping, and uses internationally accepted HTA terminology. The model has nine domains, with 51 topics and 145 issues (see Table A 2). Each of the 145 issues has a unique assessment element identifier ("issue identifier") and a card that clarifies which content is common to all applications or is specific to applications within a technology class.

Content from the included frameworks was mapped to the 145 issues of the HTA Core Model in a two-stage process. Initially, DHT-specific topics and issues raised by the frameworks but not already included in the model were included to ensure a comprehensive collation of DHT content. For new DHT-specific topics, new topic names were proposed (indicated as NEW in tables), and for new DHT-specific issues, new issue identifiers were assigned using a DHT prefix. Subsequently, all content recommended by each framework was mapped to the extended set of issues. Decisions regarding whether to map content from the included frameworks to new DHT-specific issues or existing HTA Core Model issues were made by AvH and reviewed by SN.

For each included framework, we recorded whether it partially or (near) completely covered each HTA domain and whether it recommended any DHT-specific content in each HTA domain.

2.3.6. Synthesis of results

We calculated the number and proportion of frameworks covering, and recommending DHT-specific content in, each HTA domain.

We summarised the content mapping results into two lists: The first comprises DHT-specific content to be considered when undertaking an HTA; the second comprises existing HTA content (i.e., content common across digital and non-digital technologies) but recommended by the frameworks as essential for undertaking HTAs on DHTs. For both lists, each item of content was reported by HTA domain, topic, issue identifier, and the reference(s) of the framework(s) that recommended it for ease of use and traceability.

Risk of bias and completeness of reporting assessments (beyond comparison with the HTA Core Model) were not relevant for this systematic review.

2.4. Results

2.4.1. Study selection and characteristics

The peer-reviewed literature and grey literature searches resulted in 9,236 unique records (Figure A 2). After applying our inclusion and exclusion criteria, forty-four frameworks were included (Table 2.1 and Table A 3). These frameworks were published between 2011 and 2020, with twenty-three dating from 2018 to 2020. Twenty-two frameworks were indicated as being international, eleven were intended for EU countries, seven for the United Kingdom, and four for the Asia Pacific region. Fifteen frameworks covered digital health, seven were limited to eHealth, fifteen further refined their scope to mHealth, five were strictly intended for MDSW, and two targeted sensors and wearables (digital devices). Twenty-six first authors were affiliated with universities, seven with HTA agencies, and seven with government bodies.

Table 2.1: Summary of coverage and DHT-specific content by HTA domain for each framework

HTA Domains[a]	1. Health problem and current use of technology (CUR)		2. Description and technical character of technology (TEC)		3. Safety (SAF)		4. Clinical effectiveness (EFF)		5. Costs and economic evaluation (ECO)		6. Ethical analysis (ETH)		7. Organisation aspects (ORG)		8. Patients and Social aspects (SOC)		9. Legal aspects (LEG)		DHT class[d] covered by framework
Frameworks	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	
Eysenbach 2011 (35)	◗		✓	D	◗	D	◗	D	×		◗	D	×		×		×		eHealth
Andalusian Health Quality Agency (AHQA) 2012 (36)	◗		◗	D	◗	D	◗	D	×		◗	D	×		×		◗	D	mHealth Apps
Kidholm et al. 2012 (20)	✓		✓	D	✓	D	◗	D	◗	D	◗		✓		◗	D	✓	D	eHealth
Haute Autorité de Santé (HAS) 2013 (22)	×		×		×		◗		×		×		×		×		×		MDSW
Khoja 2013 (37)	×		×		×		◗	D	◗		◗		◗		×		×		eHealth
Lewis and Wyatt 2014 (38)	×		×		◗	D	×		×		×		×		×		×		mHealth
Bergmo 2015 (29)	×		×		×		×		✓	D	×		×		×		×		eHealth
Mohr et al. 2015 (39)	×		×		×		◗	D	×		×		×		×		×		digital health
Mookherji et al. 2015 (24)	×		×		×		◗		×		×		×		×		×		mHealth
Steventon et al. 2015 (40)	×		×		×		◗	D	×		×		×		×		×		digital health
EU Draft Consard Ltd 2016 (41)	◗		✓	D	◗	D	◗	D	◗		◗	D	×		×		◗	D	mHealth Apps
Gorski 2016 (42)	◗		×		×		×		◗	D	×		×		×		×		mHealth
McMillan et al. 2016 (43)	×		×		◗	D	◗	D	×		×		×		×		×		mHealth (behaviour intervention)

HTA Domains[a]	1. Health problem and current use of technology (CUR)		2. Description and technical character of technology (TEC)		3. Safety (SAF)		4. Clinical effectiveness (EFF)		5. Costs and economic evaluation (ECO)		6. Ethical analysis (ETH)		7. Organisation aspects (ORG)		8. Patients and Social aspects (SOC)		9. Legal aspects (LEG)		DHT class[d] covered by framework
Frameworks	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	
McNamee et al. 2016 (27)	×		×		×		×		◗	D	×		×		×		×		digital health
Murray et al. 2016 (44)	◗		◗	D	◗	D	◗	D	◗	D	×		×		×		×		digital health
Rojahn et al. 2016 (34)	×		×		×		×		◗		×		◗	D	×		×		MDSW
IRB Advisor 2017 (45)	×		×		×		×		×		◗	D	×		×		×		mHealth
Lennon et al. 2017 (33)	×		×		×		×		×		×		◗	D	×		×		digital health
Maar et al. 2017 (46)	×		×		×		◗		×		×		×		×		×		mHealth
Michie et al. 2017 (47)	×		×		◗	D	◗	D	◗	D	×		×		×		×		digital health
Philpott et al. 2017 (25)	×		×		×		◗	D	×		×		×		×		×		mHealth Apps
Drury et al. 2018 (32)	◗	D	◗	D	×		×		✓	D	×		◗	D	×		×		digital health
European Commission (EC) 2018 (48)	×		◗	D	◗	D	×		◗	D	✓	D	◗	D	◗		◗	D	digital health
Hogaboam 2018 (49)	×		✓	D	◗	D	◗	D	◗	D	×		◗	D	◗	D	×		digital devices
Jurkeviciute 2018 (50)	×		×		×		◗	D	×		×		×		×		×		eHealth
Nielsen and Rimpiläinen/ The Digital Health & Care Institute 2018 (51)	×		◗	D	◗	D	◗	D	×		×		×		×		◗	D	mHealth Apps
Sax et al. 2018 (30)	×		×		×		×		×		◗	D	×		×		◗	D	mHealth

HTA Domains[a]	1. Health problem and current use of technology (CUR)		2. Description and technical character of technology (TEC)		3. Safety (SAF)		4. Clinical effectiveness (EFF)		5. Costs and economic evaluation (ECO)		6. Ethical analysis (ETH)		7. Organisation aspects (ORG)		8. Patients and Social aspects (SOC)		9. Legal aspects (LEG)		DHT class[d] covered by framework
Frameworks	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	
UK Academy of Medical Sciences 2018 (52)	×		×		◗	D	×		×		◗	D	×		×		×		digital health
Wyatt 2018 (26)	×		×		×		◗	D	×		×		×		×		×		mHealth Apps
Beintner et al. 2019 (53)	×		×		×		◗	D	×		×		×		×		×		eHealth
Caulfield et al. 2019 (54)	◗		✓	D	◗	D	◗	D	◗	D	×		×		×		◗	D	digital devices
UK Dept Health & Social Care 2019 (55)	◗		◗	D	◗	D	◗		◗		×		×		◗		◗	D	digital health
HAS 2019 (23)	✓		◗	D	◗	D	◗		◗		×		◗	D	×		×		MDSW
Draft HAS 2019 (56)	◗		◗	D	◗	D	◗	D	×		×		×		×		×		AI-based MDSW
Huckvale et al. 2019[b] (31)	×		×		◗	D	×		×		◗	D	×		×		×		mHealth Apps
NICE 2019 (2)	◗	D	◗	D	◗	D	✓	D	✓		◗		✓	D	◗		◗	D	digital health
NHS Digital 2019 (57)	✓		◗	D	◗	D	◗		×		×		×		×		×		digital health
Rajan et al. 2019 (58)	×		×		×		×		◗	D	×		◗	D	×		×		eHealth
Draft Australian commission on safety and quality in health care (CSQHC) 2020 (21)	×		◗	D	✓	D	◗	D	×		◗	D	◗		◗	D	◗	D	digital mental health services
Dick et al. 2020(59)	×		×		×		◗	D	×		×		×		×		×		mHealth

HTA Domains[a]	1. Health problem and current use of technology (CUR)		2. Description and technical character of technology (TEC)		3. Safety (SAF)		4. Clinical effectiveness (EFF)		5. Costs and economic evaluation (ECO)		6. Ethical analysis (ETH)		7. Organisation aspects (ORG)		8. Patients and Social aspects (SOC)		9. Legal aspects (LEG)		DHT class[d] covered by framework
Frameworks	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	**Coverage**	**DHT specific**	
Draft Federal Ministry of Health Germany 2020 (60)	◗		◗		◗	D	◗	D	×		×		◗		×		◗	D	digital health
Health Information and Quality Authority (HIQA) Ireland 2020 (61)	×		×		×		×		×		×		×		×		◗	D	digital health
Draft Aust. Medical Services Advisory Committee MSAC 2020[c] (62)	✓		◗		◗	D	✓		✓		✓		✓		◗		✓		digital health
Moshi et al. 2020 (63)	◗	D	✓	D	✓	D	◗	D	◗	D	◗	D	◗	D	◗	D	◗	D	mHealth

✓ Majority coverage; ◗ Partial coverage (less than two-thirds of topics covered); × No coverage of HTA domain; D DHT-specific content;
DHT, Digital Health Technology; HTA, Health Technology Assessment

[a] From HTA Core Model version 3.0 (19)

[b] While this paper does not strictly meet the evaluation framework inclusion criteria, it provides DHT-specific content on data privacy relevant to the Safety and Ethical Analysis domains

[c] Note this is a draft version of the technical guidelines for MSAC applications that includes DHT-specific content. There exist two in-force technical guidelines: One for investigative and one for therapeutic technologies that do not include digital specific content

[d] Terms and definitions for DHT classes

Term	*Definition*	*Source*
digital devices	Human performance and behaviour measurement devices, e.g., sensors and wearables	Caulfield et al.(54)
mHealth	The use of mobile wireless technologies for health. This includes digital devices defined above and either mobile or web-based applications "Apps."	WHO(64)
mHealth Apps	The subset of mHealth technologies that are mobile or web-based applications ("Apps")	Study defined
eHealth	The use of information and communications technology in support of health and health-related fields. This includes mHealth as defined above	WHO(64)
digital health	A broad umbrella term encompassing eHealth (which includes mHealth), as well as emerging areas, such as the use of advanced computing sciences in 'big data', genomics and artificial intelligence	WHO(64)
medical device software (MDSW)	Software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the medical devices regulation or in vitro diagnostic medical devices regulation	MDCG(3)
AI-based MDSW	MDSW with embedded self-learning algorithms	HAS(56)
digital mental health services	Mental health, suicide prevention, or alcohol and other drug services...in the form of information; digital counseling; treatment (including assessment, triage, and referral); or peer-to-peer service that is delivered to a service user via a digital means	ACSQHC(21)

WHO, World Health Organisation; MDCG, Medical Device Co-ordinating Group; HAS, Haute Autorité de Santé; ACSQHC, Australian Commission on Safety and Quality in Health Care

2.4.2. HTA domain coverage and recommended HTA content from included frameworks

Table 2.1 presents a summary of coverage and DHT-specific content by HTA domain for each framework, and Table 2.2 reports the number and proportion of frameworks covering, and recommending DHT-specific content for, each HTA domain.

As stated in Methods, we created two lists of HTA content recommended by the frameworks. Table 2.3 presents the list of DHT-specific content to be considered when undertaking an HTA. Table 2.4 presents the list of existing HTA content common across digital and non-digital technologies but recommended as essential for undertaking an HTA on DHTs. A more detailed listing of the recommended content can be found in Table A 4.

The included frameworks recommended DHT-specific content in 28 of 145 issues (18 of the 51 topics) and all nine domains of the HTA Core Model (See Table 2.3). Another twenty-two issues (eight topics) not included in the HTA Core Model are recommended in six HTA domains; predominantly Domain 3: Safety (SAF) and Domain 4: Clinical effectiveness (EFF).

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Table 2.2: Summary of EUnetHTA HTA Core Model version 3.0[a] domain coverage and Digital Health Technology (DHT) specific content of frameworks in review

Domains within the HTA Core Model[a]			Frameworks (N=44)			
			Frameworks covering the domain	Full or near full coverage	Partial coverage	Discusses DHT-specific content
			n (%)	n (%)	n (%)	n (%)
1	CUR	Health problem and current use of technology	16 (36%)	4 (9%)	12 (27%)	3 (7%)
2	TEC	Description and technical characteristics of technology	19 (43%)	6 (14%)	13 (29%)	17 (39%)
3	SAF	Safety	23 (52%)	3 (7%)	20 (45%)	23 (52%)
4	EFF	Clinical effectiveness	30 (68%)	2 (5%)	28 (63%)	23 (52%)
5	ECO	Costs and economic evaluation	19 (43%)	4 (9%)	15 (34%)	12 (27%)
6	ETH	Ethical analysis	14 (32%)	2 (5%)	12 (27%)	10 (23%)
7	ORG	Organisational aspects	14 (32%)	3 (7%)	11 (25%)	9 (20%)
8	SOC	Patient and social aspects	8 (18%)	0 (0%)	8 (18%)	4 (9%)
9	LEG	Legal aspects	14 (32%)	2 (5%)	12 (27%)	13 (30%)

HTA, health technology assessment; DHT, digital health technology
Frameworks covering the domain: Framework provides any coverage of the domain
Full or near-full coverage: Framework covers more than two-thirds of topics in the domain
Partial coverage: Framework covers less than two-thirds of topics in the domain
[a]Rows of the table are the domains of the EUNetHTA HTA Core Model version 3.0(19):

CUR: Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status
TEC: Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it
SAF: Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers
EFF: Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting
ECO: Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value for money judgments
ETH: Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA
ORG: Identifies resources to mobilise or organise to implement the new technology and the consequences (Intra/inter-organisational and health system)
SOC: Considers issues related to the new technology relevant to patients, carers, and social groups
LEG: Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

The frameworks' coverage of HTA domains, DHT-specific content, and HTA content recommendations are summarised below by HTA domain.

Domain 1: Health problem and current use of the technology (CUR)

More than one-third of frameworks covered CUR but only three frameworks (seven percent) recommended DHT-specific content, the least out of all domains (See Table 2.2). The topics and issues raised by the frameworks for CUR were the same as the HTA Core Model. DHT-specific content was confined to issues of the new technology's current and expected utilisation (See Table 2.3).

Domain 2: Description and technical characteristics of the technology (TEC)

TEC was covered by nineteen frameworks (forty-three percent), with seventeen discussing DHT-specific content (See Table 2.2). The topics raised by the frameworks for TEC were the same as the HTA Core Model. However, thirteen frameworks suggested a new issue addressing how well the features of the DHT and its comparator(s) overcome technical barriers. DHT-specific content was recommended for HTA Core Model issues of material investments, training, and information required to use the technology (See Table 2.3).

Domain 3: Safety (SAF)

SAF had the most DHT-specific content, with all twenty-three frameworks covering this domain recommending DHT-specific content (See Table 2.2). The frameworks recommended three DHT topics (covering a total of ten issues) not in the HTA Core Model for SAF: Quality and safeguarding (data security and privacy, interoperability, usability and accessibility, transparency, and adequate disclosures for algorithms); technical safety (technical reliability and stability, continuity and updates); and communicating for safety (See Table 2.3).

Table 2.3: Digital specific content to be considered when undertaking a Health Technology Assessment (HTA) of DHTs

HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content**	**Issue ID[a c] (Reference)**
CUR	Utilisation (*EUN*)	Describe inputs, algorithms, and outputs of the DHT	F0001 (63)
		Do/will health workers/patients invest in the personal digital technologies required to use the DHT? Costly/difficult to support?	A0011/2 (2, 32)
		Is the DHT limited in terms of platforms, languages, network connectivity, or users' digital literacy?	
		Is(will) data on DHT usage (be)collected and accessible ongoing?	
TEC	Features of Technology (*EUN*)	How well do the DHT and comparator(s) perform in overcoming technical barriers: Interoperability, data extraction, visualisation, etc.?	DHT01 (20, 21, 23, 32, 36, 41, 48, 49, 51, 54, 55, 57, 63)
	Investments/tools required (*EUN*)	Consider device size, battery life/charging method, operating system, connectivity, data access & storage, data security, technical support	B0007 (20, 35, 41, 49, 54, 57, 63)
	Training/ information needed (*EUN*)	Personnel/caregivers/patient/family: Training required/provided on personal data handling, digital skills, and digital health literacy? Also consider these requirements in ORG, Topic: Health delivery process, G0002/3	B0013/4 (32, 48, 49, 63)
SAF	Quality & safeguarding (*NEW*)	How well are data security and privacy managed? Does it comply with GDPR principles of data minimisation/protection by default/design? Also consider laws/binding rules in LEG, Topic: Privacy of the Patient, I0007/9	DHT02 (2, 20, 21, 31, 35, 36, 41, 43, 48, 49, 51, 52, 54, 55, 57, 60, 63)
		How well is interoperability designed and data quality managed?	DHT03 (21, 41, 48, 55, 57)
		How transparent are the DHT risks (e.g., data sharing, conflicts of interest) to the user?	DHT04 (21, 35, 36, 41, 48, 55, 57, 63)
		How well is the DHT designed for usability and accessibility? Also consider ensuring access in ORG, Topic: Structure of the health system, G0101	DHT05 (21, 36, 57)
		Is adequate information disclosed on DHT algorithms to evaluate their risk?	DHT06 (55, 56)
	Technical safety (Reliability & stability) (*NEW*)	How technically reliable and stable are the DHT and comparator(s)?	DHT07 (2, 20, 21, 38, 41, 51, 56, 57, 60, 63)
		How well are updates/continuity of the DHT managed?	DHT08 (21, 63)
	Communicating for safety (*NEW*)	Can the user send critical risk information to the DHT provider?	DHT09 (21, 36)
		Processes for correct identification of users in DHT?	DHT10 (21)
		Processes to communicate changes to or transfer of a patient's care?	DHT11 (21)

HTA Domain[a]	Topic *(EUN)*[a]/*(NEW)*[b]	Issue content	Issue ID[a c] (Reference)
EFF	Demonstrating effectiveness (*NEW*)	Are accepted methods used to overcome common methodological problems in RCTs for DHTs, e.g., achieving blinding, biases from informed consent?	DHT12 (22, 23, 35, 39)
		Is it clear whether the DHT was changed (bug fixes, content) during the trial?	
		Was digital literacy an implicit eligibility criterion?	
		Was the comparator group restricted in the DHT to which they had access?	DHT13 (44, 47)
		Have DHT-specific and validated outcome measures been collected: i.e., the intensity of use (dose, exposure), online adherence, engagement	DHT14 (2, 35, 50, 53)
		Has data collection embedded in the DHT created systematic bias?	
		Is reporting of the RCT in accordance with CONSORT E-HEALTH?	DHT15 (46, 50)
	Reliable information content (*NEW*)	Is the health information provided by DHT accurate, valid, up to date, comprehensive, clear, and tailored to the users' diversity?	DHT16 (2, 20, 21, 35, 36, 41, 51, 60, 63)
	Use of appropriate behaviour change techniques (*NEW*)	Does the DHT use appropriate and best-practice behaviour change techniques? Is the mechanism credible?	DHT17 (2, 35, 39, 41, 43, 44, 47, 51)
		Is the targeted behaviour change apparent to the user, and are the appropriate supports in place? Is it relevant for the target population?	
	External validity/ generalisability (*NEW*)	Has patient identity validation and obtaining offline contact details to improve follow-up rates jeopardised external validity?	DHT18 (44, 47)
		Are results generalisable to settings where telecommunication infrastructure is poor or there is low network connectivity?	DHT19 (20, 59)
	Patient satisfaction (*EUN*)	Is there evidence that the DHT is usable and accessible for a diverse range of users, including those with disabilities or limited technical ability? Are there obvious design issues hindering usability, e.g., washable, durable, cause skin allergies?	D0017 (20, 41, 44, 49, 51, 57, 59)
ECO	Resource utilisation (*EUN*)	Consider the costs of supporting health care providers in using DHT and costs to use the DHT in the health system (licensing, platforms, hardware, etc.)	E0001/2/9
	Validity of the model(s) (*EUN*)	Are changes in fixed costs for scaling up the DHT known? Is the cost function per patient smooth or stepped?	DHT20 (20)
	Measurement & estimation of outcomes (*EUN*)	Have DHT-specific outcomes been considered and measured where possible, e.g., self-management benefits, better-connected healthcare professionals?	E0005 (29, 32, 48)
		Given that all the functionalities of DHTs may not be used, and many people may not use the DHT from the outset, are the estimated benefits of the DHT realistic?	

HTA Domain[a]	Topic *(EUN)*[a]/*(NEW)*[b]	Issue content	Issue ID[a c] (Reference)
ETH	Benefit-harm balance (*EUN*)	Is the DHT designed and used for clearly defined purposes that uphold the health system's social values or society's?	F0011 (52)
		Is the value of patient data realised but protected from commercial use?	
		Does the DHT preserve and enhance direct contact between patients and healthcare professionals while supporting them to manage their health?	
		Where are alerts about a patient's health reported? Is real-time data securely transmitted? How does the DHT affect the participant's safety and welfare?	F0003 (35, 45)
		Can the DHT promote a false sense of security or create harm from patients having access to their data without someone to interpret it?	
	Autonomy (*EUN*)	Does the DHT use simple and understandable language?	F0005 (41)
		For DHTs targeting behaviour change, what controls limit the DHT influencing a person's behaviour for purposes other than those stated?	F0004 (30)
		Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT?	
		Are any potential conflicts of interest (funding, promotion) clearly disclosed?	F0006 (41, 45, 63)
		Is there concise information on how DHT's contents were selected?	
		Is the data collected by the DHT, its use, and availability clearly disclosed?	
	Respect for persons (*EUN*)	Does the DHT clearly identify who holds any personal data?	F0101 (21, 31, 41, 48)
		Is the DHT regularly audited for transmissions with third parties that include linkable identifiers? Is the user informed of this risk?	
	Justice & Equity (*EUN*)	How does the DHT overcome access barriers, e.g., patients/ with a lack of economic resources, poor IT skills/digital health literacy?	H0012 (21, 55, 63)
		Is the DHT compatible with common assistive technologies and available in a wide number of languages?	
ORG	Health delivery process (*EUN*)	How does removing the constraints of distance and sharing patient data impact staff work methods and the interactions between medical staff, patients, and their carers?	G0100 (23)
		Consider changes to electronic communication, information/reporting systems, face-to-face consultations, and staff communication	G0004 (20)
	Contextual issues (*NEW*)	Consider all contextual barriers and enablers to DHT uptake: Infrastructure, clinical endorsement, champions of DHT, supplementary payments, etc	DHT21 (32-34)

HTA Domain[a]	Topic *(EUN)*[a]/*(NEW)*[b]	Issue content	Issue ID[a c] (Reference)
SOC	Social group aspects (*EUN*)	How much does the DHT improve the connectivity between the healthcare team and the patient? Is access improved for remote patients?	H0201 (49)
	Communication aspects (*EUN*)	Are expected direct and data usage costs made clear to the user to improve adherence rates?	H0203 (21, 32-34)
LEG	Ownership & liability (*EUN*)	Professional liability: Clarify responsible parties, litigation risks, and insurance implications of DHT recommendation or use	DHT22 (63)

[a]From EUNetHTA HTA Core Model version 3.0(19)
[b]New topic
[c]DHT prefixes denote new issues (i.e., DHTXX)

Domain 4: Clinical effectiveness (EFF)

EFF was the most commonly covered domain, with thirty frameworks (sixty-eight percent) making recommendations in this domain. The frameworks suggested four additional topics (and eight issues) for EFF: Demonstrating effectiveness (DHT appropriate study design, comparators, outcome measures, and transparent reporting of effectiveness studies); ensuring reliable information content; the use of appropriate and best practice behaviour change; and the measures for assessing the external validity/generalisability of DHT effectiveness studies. DHT-specific content was also recommended for the HTA Core Model issue of patient satisfaction.

Domain 5: Costs and Economic Evaluation (ECO)

Nineteen frameworks covered ECO, with twelve making DHT-specific recommendations. Cost-effectiveness and budget impact frameworks comprise this domain. The topics raised by the frameworks for ECO were the same as the HTA Core Model. However, a new issue within the validity of the model(s) topic was recommended to ensure that the changes in fixed costs for scaling up DHTs from the trial to the health-system level have been investigated. DHT-specific content was recommended for estimating resource utilisation, costs, and health outcomes.

Domain 6: Ethical analysis (ETH)

Fourteen frameworks covered ETH, with ten making DHT-specific recommendations. The topics and issues raised by the frameworks for ETH were the same as the HTA Core Model. However, DHT-specific content was recommended for four HTA Core Model topics (seven issues): Benefit-harm balance (benefits and harms for stakeholders other than the patient, and hidden unintended consequences of the technology), autonomy (vulnerable persons, threats to autonomy, and supports required); respect for persons (privacy); and justice and equity (accessibility).

Domain 7: Organisational aspects (ORG)

Fourteen frameworks covered ORG, with nine making DHT-specific recommendations. A new topic not in the HTA Core Model for ORG, namely contextual issues for barriers and enablers to DHT implementation, was recommended. DHT-specific content was also recommended for two HTA Core Model topics (five issues): Health delivery process (changes to current work processes, resources, training, co-operation, and communication) and the structure of the health system (processes to ensure access to the new technology).

Domain 8: Patients and social aspects (SOC)

SOC was the least covered with only eight frameworks making recommendations, and only four making DHT-specific recommendations. The topics and issues raised by the frameworks for SOC were the same as HTA Core Model. DHT-specific content was limited to two issues: Improving access to healthcare and upfront communication of direct and data usage costs of the DHT to improve treatment adherence.

Domain 9: Legal aspects (LEG)

Fourteen frameworks covered LEG, with almost all, thirteen, making DHT-specific recommendations. A new issue of professional liability was recommended for the HTA Core

Model topic of ownership and liability. DHT-specific content was also recommended for the HTA Core Model topic of patient privacy, i.e., designing the DHT to comply with laws/binding rules for data security and privacy.

Table 2.4: Existing health technology assessment (HTA) content that is common across DHTs and non DHTs

HTA Domain[a]	**Topic[a]**	**Issue content**	**Issue ID[a] (Reference)**
CUR	Current management of the condition	What DHT do those with the condition already have available to them?	A0018 (55)
TEC	Features of the technology	Is there evidence the DHT is relevant to the health system and can perform to the expected number of users (e.g., is the server size adequate)?	B0003 (2, 20)
		As DHTs often develop rapidly, is the DHT in a steady-state to enable a robust economic analysis to be performed?	
SAF	Risk management	Are there defined parameters to identify and respond to a patient's acute deterioration?	C0062 (21)
EFF	Patient satisfaction	Is there evidence to show relevant stakeholders were involved in the design and satisfied with the DHT?	D0017 (2, 20, 21, 35, 36, 41, 43, 44, 49, 51, 54, 57, 59, 62)
		Is ongoing data collected on user satisfaction that will be acted upon and available to decision-makers?	
		Has qualitative data been collected and analysed to evaluate the mode of action, differences between recipients and sites, and identify barriers to uptake or implementation?	
		Does the DHT create additional burdens on the patient or caregiver that may affect uptake or adherence?	
ECO	None noted		
ETH	Benefit-harm balance	What will be done with any incidental findings?	F0003 (45)
	Autonomy	Does the DHT provider: Identify the diversity of service users/groups of users at higher risk of harm and adapt the DHT accordingly? Have systems to minimise the risk for children and young people to be harmed?	F0005 (21)
	Justice & Equity	Show evidence of the DHT being used in hard-to-reach populations	H0012 (2)
ORG	Health delivery process	Describe the steps in the proposed new care pathway or pathways incorporating the DHT intervention for the relevant population and setting	G0100 (2, 62)
		Detail any infrastructure and service-level changes needed to existing pathways and associated systems to implement, operate, and maintain the new pathway	

HTA Domain[a]	Topic[a]	Issue content	Issue ID[a] (Reference)
	Culture	Does the DHT have credibility with healthcare professionals?	G0010 (2, 21, 60)
		Is there published or publicly available evidence documenting the relevant health care experts' role in the design, development, testing, or sign-off of the DHT?	
SOC	None noted		
LEG	None noted		

[a]From EUNetHTA HTA Core Model version 3.0(19)

2.5. Discussion

To our knowledge, we have conducted the most extensive systematic search of international peer-reviewed and grey literature for HTA and evaluation frameworks for DHTs designed to actively monitor or treat a diagnosed chronic non-communicable disease at home. These DHTs, such as remote monitoring via digital devices or web-based treatment programs, are classified into the highest risk evidence tier under the NICE Evidence Standards (2) and are strictly regulated under medical device regulation (3). Deliberately focusing on a high-risk DHT class has allowed us to identify a fuller range of DHT-specific content, with the expectation that not all this content will apply to lower-risk DHT classes.

The findings from this systematic review demonstrate there is no single framework that is used uniformly across jurisdictions to assess the comparative safety, effectiveness, and cost-effectiveness of DHTs. NICE's Evidence Standards for DHTs (2), whilst DHT-specific, focus primarily on the EFF and ECO domains. Our review highlights the need for more comprehensive technology-specific questions for undertaking HTA of DHTs across all HTA domains.

Our analysis shows HTA Core Model topics are relevant for funding assessment of DHTs, covering all topics raised by the frameworks in six domains. However, the included frameworks recommend adding DHT-specific content in 28 of 145 issues (18 of the 51 topics) and all nine domains of the HTA Core Model (see Table 2.3). They also recommend

another twenty-two issues (eight topics) that are not currently included in the HTA Core Model (see Table 2.3). Collectively, this suggests the HTA Core Model is not sufficiently comprehensive for undertaking an HTA of DHTs that manage chronic non-communicable disease at home.

We also highlight existing HTA content common to digital and non-digital technologies but essential for DHTs in Table 2.4. Given the rapid growth in DHTs over recent years, identifying current alternative DHTs available for patients with the targeted condition (25) assists in estimating the expected utilisation of the DHT and understanding the DHTs available to comparator groups. Rapid growth in DHT development also makes identifying the DHT's stage in the product lifecycle crucial. NICE (2) requires evidence that the DHT is relevant and has been piloted successfully in the health care system and evidence the DHT can perform for the expected number of users, e.g., adequate server size. Kidholm et al. (20) also require that the technology is in a steady-state to enable a robust economic analysis to be performed. The lack of face-to-face contact in remote monitoring/self-management interventions may also require heightened risk management controls. For example, defined parameters to identify and respond to a patient's acute deterioration and controls for vulnerable users (21) may reduce patient risk. Remote monitoring DHTs require consideration of the management of incidental findings. All DHTs require evidence of improved access to health care.

Because the DHTs of interest to this study are used directly by the patient for self-management, existing HTA content examining patient satisfaction is crucial. Identifying changes to infrastructure, services, and systems for existing and new care pathways associated with the DHT is also critical when changing health care delivery from in-person consultations to remote. An organisational enabler to successful implementations of DHTs is

its credibility with healthcare professionals; NICE (2) requires published or publicly available evidence documenting the relevant healthcare experts' role in the development of the DHT.

There was much discussion in the included frameworks about innovative trial designs for assessing the clinical effectiveness of DHTs in EFF and the complexity of economic evaluation in ECO. However, no evidence was provided that these alternate trial designs are appropriate when the DHT has reached a steady-state. The framework authors concluded that a high-quality randomised controlled trial (RCT) conducted in people with the target condition in a setting relevant to the health system (2) remains the most unbiased evidence of clinical effectiveness for DHTs (2, 22-26). Advice for overcoming common methodological problems for RCTs of DHTs, such as blinding and informed consent, was given by the Haute Autorité de Santé (22). Little justification was provided for using a pre-test/post-test design for DHTs that are an adjunct to standard care (relevant to many DHTs that manage chronic non-communicable disease at home) because the ideal comparator group, people having standard care (2), should not generally create ethical issues (22). For economic evaluation methods in ECO, frameworks state that DHTs are complex interventions implemented in a complex health system (17, 27-29). This complexity presents challenges for economic evaluation, such as instability in preference values (29). However, McNamee et al. (27) consider it is valid to use standard economic methods for DHTs, and where there are interactions, non-linearity in changes, or multiplier effects, these can be dealt with by sensitivity analyses (27, 29) and data from cluster trials (29).

Twenty of the twenty-eight existing HTA Core Model issues recommended for DHT-specific content are concentrated in four domains. The identification of DHT-specific content for the technical characteristics in TEC, the estimation of DHT-specific resource utilisation and costs in ECO, and the DHT-specific changes to work processes in ORG were expected. The large amount of DHT-specific content identified in ETH is warranted when we consider the

description by Sax et al. (30) of the unique risks of DHTs that collect a large amount of personal data to develop predictive algorithms of behaviour. Consequently, there are ethical issues in terms of the potential for DHTs to influence the behaviour of a susceptible person at critical times for commercial purposes.

A weakness of the included frameworks is the lack of discussion and recommendations on patients' perspectives in the domain of SOC. We acknowledge the ability of a DHT to engage and motivate a patient is implicit in any demonstration of DHT effectiveness, and we are not suggesting that effectiveness from a patient perspective should be re-evaluated during an HTA. Rather, we suggest information regarding patient preferences and experience with a DHT will be informative to judgments regarding the transferability of effectiveness from one population and setting to another.

The eight new topics (and nineteen of the twenty-two new issues) are concentrated in the three domains of SAF, EFF, and ORG. The new SAF topics address issues of technical reliability and stability, data security and privacy, accessibility, and communications that promote the safety of the user and the autonomy of stakeholders. Although examples of data privacy breaches/threats (e.g., Australia's HealthEngine, UK NHS ransomware attacks) are plentiful, it is the less overt data privacy breaches that occur when the DHT operates on personal devices that patients use for social media and the internet (i.e., not purpose-built medical devices) that are a unique threat for DHTs. Huckvale et al. (31), show evidence of the prevalence of data transmissions with linkable identifiers from depression and smoking cessation apps to technology companies for marketing and analytics purposes without disclosures in privacy policies. The authors recommend regular audits of data transmissions rather than reliance on privacy disclosures.

The new EFF topics focus on high-quality evidence generation, transparent and standardised reporting of effectiveness studies, ensuring the reliability of health information content, and

the use of appropriate and best practice behaviour change techniques. Contextual issues for barriers and enablers to DHT implementation in ORG are comprehensively addressed by Drury et al. (32), Lennon et al. (33), and Rojahn et al. (34).

A strength of our analysis is the use of many sources, including grey literature. Additionally, focusing on a particular class of DHT with its specific risk/benefit profile has allowed us to identify and extend DHT-specific content to all HTA Core Model domains. Identifying content specific to the chronic non-communicable disease target population and the active monitoring/treatment MDSW DHT class may limit the applicability of our analysis to other clinical circumstances, but many of the issues are sufficiently generic to be broadly applicable across other health areas and DHT classes. We also aimed to identify content broadly applicable across jurisdictions. However, some tailoring to meet local HTA needs may be required. While a focus on the most recent five years in our search strategy was appropriate given the rapid development of DHTs, we have managed the risk of missing DHT-specific content in earlier evaluation frameworks by pearling included frameworks.

As DHT development continues apace, greater clarity is required regarding the evidence needed to inform policymakers and payers of the value of DHTs. By specifying additional DHT-specific content, we hope researchers can better plan to gather standardised and robust evidence that meets decision-makers' needs.

Future research is recommended on the applicability of the new topics and issues to lower-risk DHT classes and their relative importance to specific chronic diseases.

2.6. Conclusion

Development of DHT-specific content for HTA frameworks is hampered by DHTs having varied benefit and risk profiles. By focusing on a particular DHT class, we demonstrate that relevant evaluation frameworks from peer-reviewed and grey literature can be used to extend

DHT-specific content to all HTA Core Model domains. We plan to develop companion resources for designing research studies and undertaking HTAs of DHTs that manage chronic non-communicable disease at home.

2.7. References

1. Australian Institute of Health and Welfare. Chronic disease overview. [Internet] 2020; Available from: https://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/chronic-disease/overview. Accessed 10 February 2021.
2. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies [Pdf]. 2018 [updated March 2019]; Available from: https://www.nice.org.uk. Accessed 15 August 2020.
3. Medical Device Coordination Group (MDCG). Guidance on qualification and classification of software in regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR. European Commission; 2019.
4. O'Rourke B, Oortwijn W, Schuller T. International Joint Task Group. The new definition of health technology assessment: A milestone in international collaboration. *Int J Technol Assess Health Care*. 2020;36(3):187-90.
5. Australian Government Department of Health and Ageing. Review of health technology assessment in Australia. Canberra (AU): Commonwealth of Australia; 2009.
6. Regulation (EU) 2017/745 of the European Parliament and of the Council, *Official Journal.* 2017;L117:1-175.
7. Regulation (EU) 2016/679 of the European Parliament and of the Council, *Official Journal;* 2016;L119:1-88.
8. Moshi MR, Tooher R, Merlin T. Suitability of current evaluation frameworks for use in the health technology assessment of mobile medical applications: A systematic review. *Int J Technol Assess Health Care*. 2018;34(5):464-75.

9. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mhealth? A systematic review of economic evaluations of mhealth solutions. *PLoS One*. 2017;12(2):e0170581.

10. Kidholm K, Kristensen MBD. A scoping review of economic evaluations alongside randomized controlled trials of home monitoring in chronic disease management. *Appl Health Econ Health Policy*. 2018;16(2):167-76.

11. Vukovic V, Favaretti C, Ricciardi W, de Waure C. Health technology assessment evidence on e-health/m-health technologies: Evaluating the transparency and thoroughness. *Int J Technol Assess Health Care*. 2018;34(1):87-96.

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.

13. Grey matters: A practical tool for searching health-related grey literature. [Internet] Ottawa (CA): CADTH; 2018 [updated April 2019]; Available from: https://www.cadth.ca/resources/finding-evidence. Accessed 4 April 2020

14. Hailey D, Ohinmaa A, Roine R. *Study quality and evidence of benefit in recent assessments of telemedicine*. London (UK): SAGE Publications; 2004. p. 318-24.

15. Gagnon M-P, Scott R. Striving for evidence in e-health evaluation: Lessons from health technology assessment. *J Telemed Telecare*. 2005;11:S34-6.

16. Reardon T. Research findings and strategies for assessing telemedicine costs. *Telemed e-Health*. 2005;11(3):348-69.

17. Shiell A, Hawe P, Gold L. Complex interventions or complex systems? Implications for health economic evaluation. *BMJ*. 2008;336:1281-3.

18. Dávalos ME, French MT, Burdick AE, Simmons SC. Economic evaluation of telemedicine: Review of the literature and research guidelines for benefit-cost analysis. *Telemed e-Health*. 2009;15(10):933-48.

19. EUnetHTA Joint Action 2, Work Package 8. HTA Core Model® version 3.0. [Pdf]; 2016. Available from: https://www.htacoremodel.info/BrowseModel.aspx. Accessed 29 February 2020.

20. Kidholm K, Ekeland AG, Jensen LK, Rasmussen J, Pedersen CD, Bowes A, et al. A model for assessment of telemedicine applications: MAST. *Int J Technol Assess Health Care*. 2012;28(1):44.

21. Australian Commission on Safety and Quality in Health Care. National safety and quality digital mental health standards - consultation draft. [Pdf]; 2020. Available from: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-safety-and-quality-digital-mental-health-standards-consultation-draft. Accessed 5 September 2020.

22. Haute Autorité de Santé [French National Authority for Health]. Methodological choices for the clinical development of medical devices. Paris (FR): HAS; 2013.

23. Haute Autorité de Santé (HAS) [French National Authority for Health]. Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement. Paris (FR): HAS; 2019.

24. Mookherji S, Mehl G, Kaonga N, Mechael P. Unmet need: Improving mHealth evaluation rigor to build the evidence base. *J Health Commun*. 2015;20(10):1224-9.

25. Philpott D, Guergachi A, Keshavjee K. Design and validation of a platform to evaluate mhealth apps. *Stud Health Technol Inform*. 2017; 235:3-7.

26. Wyatt JC. How can clinicians, specialty societies and others evaluate and improve the quality of apps for patient use? *BMC Med*. 2018;16(1):225.

27. McNamee P, Murray E, Kelly MP, Bojke L, Chilcott J, Fischer A, et al. Designing and undertaking a health economics study of digital health interventions. *Am J Prev Med*. 2016;51(5):852-60.

28. Rickles D, Hawe P, Shiell A. A simple guide to chaos and complexity. *J Epidemiol Community Health*. 2007;61(11):933-7.

29. Bergmo TS. How to measure costs and benefits of eHealth interventions: An overview of methods and frameworks. *J Med Internet Res*. 2015;17(11):e254.

30. Sax M, Helberger N, Bol N. Health as a means towards profitable ends: Mhealth apps, user autonomy, and unfair commercial practices. *J Consumer Policy*. 2018;41(2):103-34.

31. Huckvale K, Torous J, Larsen ME. Assessment of the data sharing and privacy practices of smartphone apps for depression and smoking cessation. *JAMA Network Open*. 2019;2(4):e192542.

32. Drury P, Roth S, Jones T, Stahl M, Medeiros D. Guidance for investing in digital health. Manila (PH): Asian Development Bank (ADB); 2018.

33. Lennon MR, Bouamrane MM, Devlin AM, O'Connor S, O'Donnell C, Chetty U, et al. Readiness for delivering digital health at scale: Lessons from a longitudinal qualitative evaluation of a national digital health innovation program in the United Kingdom. *J Med Internet Res*. 2017;19(2):e42.

34. Rojahn K, Laplante S, Sloand J, Main C, Ibrahim A, Wild J, et al. Remote monitoring of chronic diseases: A landscape assessment of policies in four European countries. *PLoS One.* 2016;11(5):e0155738.

35. Eysenbach G. Consort-ehealth: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res.* 2011;13(4):e126.

36. Andalusian Health Quality Agency (ES). Complete list of recommendations on design, use and assessment of health apps. [Internet] 2012 [accessed 16 Aug 2020]; Available from: http://www.calidadappsalud.com/en/listado-completo-recomendaciones-app-salud/. Accessed 16 August 2020.

37. Khoja S, Durrani H, Scott RE, Sajwani A, Piryani U. Conceptual framework for development of comprehensive e-health evaluation tool. *Telemed e-Health.* 2013;19(1):48-53.

38. Lewis TL, Wyatt JC. Mhealth and mobile medical apps: A framework to assess risk and promote safer use. *J Med Internet Res.* 2014;16(9):e210.

39. Mohr DC, Schueller SM, Riley WT, Brown CH, Cuijpers P, Duan N, et al. Trials of intervention principles: Evaluation methods for evolving behavioral intervention technologies. *J Med Internet Res.* 2015;17(7):e166.

40. Steventon A, Grieve R, Bardsley M. An approach to assess generalizability in comparative effectiveness research: A case study of the whole systems demonstrator cluster randomized trial comparing telehealth with usual care for patients with chronic health conditions. *Med Decis Making.* 2015;35(8):1023-36.

41. Ruck A, Wagner Bondorf S, Lowe C (Consard Limited). Second draft of guidelines, EU guidelines on assessment of the reliability of mobile health applications. European Commission, Directorate-General of Communications Networks, Content & Technology; 2016.

42. Gorski I, Bram JT, Sutermaster S, Eckman M, Mehta K. Value propositions of mhealth projects. *J Med Eng Technol.* 2016;40(7-8):400-21.

43. McMillan B, Hickey E, Patel MG, Mitchell C. Quality assessment of a sample of mobile app-based health behavior change interventions using a tool based on the national institute of health and care excellence behavior change guidance. *Patient Educ Couns.* 2016;99(3):429-35.

44. Murray E, Hekler EB, Andersson G, Collins LM, Doherty A, Hollis C, et al. Evaluating digital health interventions: Key questions and approaches. *Am J Prev Med.* 2016;51(5):843-51.

45. IRBs could address ethical issues related to tracking devices: Mobile devices raise new concerns. *IRB Advisor.* 2017;17(11):8-9.

46. Maar MA, Yeates K, Perkins N, Boesch L, Hua-Stewart D, Liu P, et al. A framework for the study of complex mhealth interventions in diverse cultural settings. *JMIR MHealth and UHealth*. 2017;5(4):e47.

47. Michie S, Yardley L, West R, Patrick K, Greaves F. Developing and evaluating digital interventions to promote behavior change in health and health care: Recommendations resulting from an international workshop. *J Med Internet Res.* 2017;19(6):e232.

48. European Commission. Synopsis report, Consultation: Transformation health and care in the digital single market. Luxembourg City (LU): European Commission; 2018.

49. Hogaboam LS. Assessment of technology adoption potential of medical devices: Case of wearable sensor products for pervasive care in neurosurgery and orthopedics [PhD]. Ann Arbor: Portland State University; 2018.

50. Jurkeviciute M. Planning of a holistic summative eHealth evaluation: The interplay between standards and reality [Licentiate]. Ann Arbor: Chalmers Tekniska Hogskola (Sweden); 2018.

51. Nielsen S, Rimpiläinen S. Report on international practice on digital apps. Glasgow (UK): Digital Health and Care Institute; 2018.

52. Academy of Medical Sciences (UK). Our data-driven future in healthcare: People and partnerships at the heart of health related technologies. London (UK): Academy of Medical Sciences, 2018.

53. Beintner I, Vollert B, Zarski AC, Bolinski F, Musiat P, Gorlich D, et al. Adherence reporting in randomized controlled trials examining manualized multisession online interventions: Systematic review of practices and proposal for reporting standards. *J Med Internet Res.* 2019;21(8):e14181.

54. Caulfield B, Reginatto B, Slevin P. Not all sensors are created equal: A framework for evaluating human performance measurement technologies. *NPJ Digit.* 2019;2(1).

55. Department of Health & Social Care (UK). Code of conduct for data-driven health and care technology. [Internet] 2019 [updated 18 Jul 2019; accessed 18 Aug 2020]; Available from: https://www.gov.uk/government/publications/code-of-conduct-for-data-driven-health-and-care-technology/initial-code-of-conduct-for-data-driven-health-and-care-technology.

56. Haute Autorité de Santé (HAS) [French National Authority for Health]. Public consultation on the draft analysis grid intended for use by CNEDiMTS to contribute to its evaluation of medical devices embedding decision systems based on automatic learning processes ("artificial intelligence"). Paris (FR): HAS, 2019.

57. NHS Digital (UK). How we assess health apps and digital tools. [Internet] 2019 [updated 17 May 2019; accessed 13 Apr 2020]; Available from: https://digital.nhs.uk/services/nhs-apps-library/guidance-for-health-app-

developers-commissioners-and-assessors/how-we-assess-health-apps-and-digital-tools.

58. Rajan B, Tezcan T, Seidmann A. Service systems with heterogeneous customers: Investigating the effect of telemedicine on chronic care. *Manag Sci.* 2019;65(3):1236-67.

59. Dick S, O'Connor Y, Thompson MJ, O'Donoghue J, Hardy V, Wu TJ, et al. Considerations for improved mobile health evaluation: Retrospective qualitative investigation. *JMIR MHealth UHealth*. 2020;8(1):e12424.

60. Federal Ministry of Health (DE), Regulation on the procedure and requirements for testing the eligibility for reimbursement of digital health applications in the statutory public health insurance (Digital Health Applications Ordinance - DiGAV) (Draft bill), Bonn (DE): 2020.

61. Health Information and Quality Authority (IE). International review of consent models for the collection, use and sharing of health information. Cork (IE): 2020.

62. Medical Services Advisory Committee (AU). Draft guidelines for preparing assessment reports for the medical services advisory committee. Canberra (AU): 2020.

63. Moshi MR, Tooher R, Merlin T. Development of a health technology assessment module for evaluating mobile medical applications. *Int J Technol Assess Health Care.* 2020;36(3):252-61.

64. World Health Organisation (WHO). WHO guideline: Recommendations on digital interventions for health system strengthening. Geneva (CH): WHO; 2019.

Chapter 3 Application of a health technology assessment framework to digital health technologies that manage chronic disease: A systematic review

The material in this chapter has been published as:

Von Huben A, Howell M, Carrello J, Norris S, Wortley S, Ritchie A, Howard K. Application of a health technology assessment framework to digital health technologies that manage chronic disease: A systematic review, *Int. J. Technol. Assess. Health Care.* 2022;38(1):e9. doi: 10.1017/S0266462321001665.

A statement of the specific contribution of the co-authors can be found in Appendix B.

Purpose of chapter

To understand current research trends and examine how much of the identified HTA content was being covered in primary research, a systematic review of DHT primary research over the period 1 January 2015 to 20 March 2020 was undertaken.

3.1. Abstract

Background: As health services increasingly make investment decisions in digital health technologies (DHTs), a DHT-specific and comprehensive health technology assessment (HTA) process is crucial in assessing value-for-money. Research in DHTs is ever-increasing, but whether it covers the content required for HTA is unknown.

Objectives: To summarise current trends in primary research on DHTs that manage chronic disease at home, particularly the coverage of content recommended for DHT-specific and comprehensive HTA.

Methods: Medline, Embase, Econlit, CINAHL, and The Cochrane Library (1 January 2015 to 20 March 2020) were searched for primary research studies using keywords related to DHT and HTA domains. Studies were assessed for coverage of the most frequently recommended content to be considered in a nine domain DHT-specific HTA previously developed.

Results: 178 DHT interventions were identified, predominantly randomised controlled trials targeting cardiovascular disease/diabetes in high to middle-income countries. A coverage assessment of 112 cardiovascular and diabetes DHT studies revealed less than half covered DHT-specific content in all but the health problem domain. Content common to all technologies but essential for DHTs was covered by more than half the studies in all domains except for the effectiveness and ethical analysis domains.

Conclusions: Although DHT research is increasing, it is not covering all the content recommended for a DHT-specific and comprehensive HTA. The inability to conduct such an HTA may lead to health services making suboptimal investment decisions. Measures to increase the quality of trial design and reporting are required in DHT primary research.

3.2. Introduction

The recent pandemic has accelerated awareness of the beneficial role of digital health technology (DHT) in providing continuity of healthcare at home balanced against the substantial investment required for its optimal and ongoing use. As health services increasingly make investment decisions on DHTs for managing the health needs of people with chronic disease, performing a DHT-specific comprehensive Health Technology Assessments (HTA) is crucial in ensuring a systematic and multidisciplinary approach (1) to assessing value-for-money.

Growth in development and demand for DHT interventions that manage chronic disease at home has led to a steady increase in peer-reviewed primary research studies. However, it is unknown whether this research covers the content required for a DHT-specific comprehensive HTA. Systematic reviews on the adequacy of evidence generation (published up to 2015) for HTAs found that less than half of electronic/mobile health HTA reports considered organisational or social domains. Very few considered the technology, safety, ethical and legal domains (2). Mobile health economic evaluations varied significantly in reporting quality, costing strategies, and length of follow-up periods (3). For home monitoring DHTs, economic evaluations varied greatly in the types of equipment and the types of tasks for health care staff that were included in the costs (4). More recently, Forsyth et al. (5) found over half the peer-reviewed studies on DHTs for self-management of Type 2 diabetes failed the NICE framework effectiveness standards due to poor trial design or reporting: absence of comparator group; no justification of sample size; no measurable improvement in condition-related outcomes; lack of statistical analysis.

DHT-specific evaluation frameworks used in HTA, such as the NICE Evidence Standards Framework for DHTs (6), are maturing. In a prior systematic review (7) (Figure 3.1), we

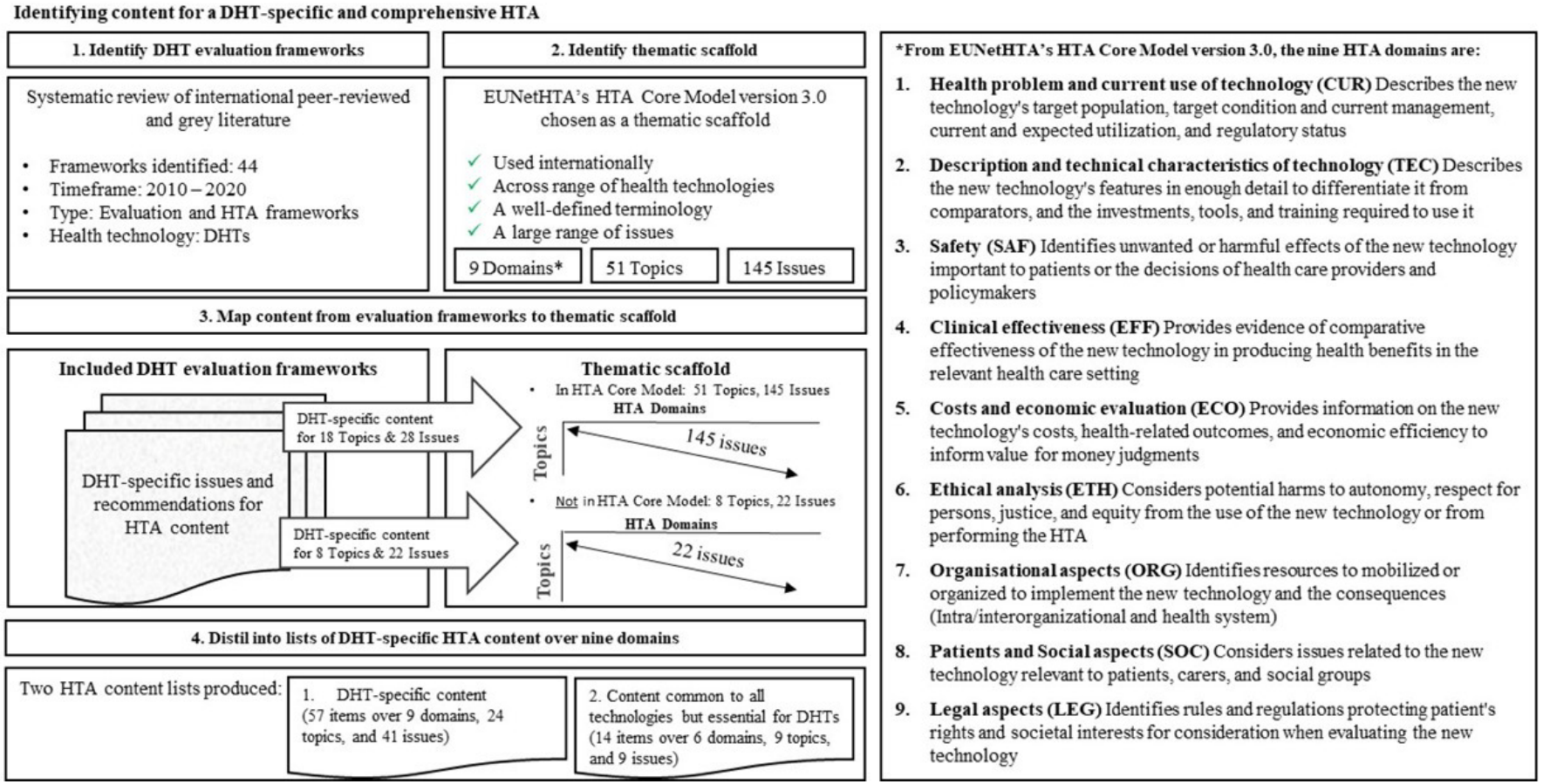

Figure 3.1: Process diagram for identifying content for a DHT-specific and comprehensive HTA

conducted an extensive search of international peer-reviewed and grey literature to identify evaluation frameworks specific to DHTs that manage chronic disease at home. We compiled a comprehensive list of the most frequently recommended content across a nine domain HTA framework based on the EUNetHTA Core Model (8). The nine domains to be covered in an HTA report cover the current health problem, the technology, safety, clinical effectiveness, costs and economic evaluation, ethical, social, organisational, and legal aspects. We identified fifty-seven DHT-specific content items, e.g., cyber safety/security, and fourteen content items common to all technologies but essential for a comprehensive DHT HTA.

This systematic review aims to summarise the current trends in primary research on DHTs that manage chronic disease at home, particularly the coverage of previously identified (7) (Figure 3.1) content recommended for a DHT-specific comprehensive HTA.

DHT interventions can include multiple DHT components, and functions can vary from communication (telehealth) to continuous remote patient monitoring. This variation gives rise to heterogeneity in the level and types of evidence required for an HTA. To minimise this heterogeneity and set a consistent evidence generation threshold for the current review, we have limited study inclusion to DHT interventions that manage chronic disease at home and have a primary intervention function of "active monitoring" or "treat" as defined by the NICE framework (6). NICE classifies DHTs providing these functions into the highest evidence tier (Tier C) as they present the highest potential risk to the user. They are also strictly regulated as Medical Device Software (MDSW) under the new European Union (EU) Medical Devices Regulation (MDR)(9).

3.3. Methods

This systematic review was registered with PROSPERO (#CRD42021224833) and is reported in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (10).

3.3.1. Information sources and search strategy

Given the focus of this review is current trends in DHT primary research, Medline, Embase, Econlit, CINAHL, and the Cochrane Library were searched from 1 January 2015 to 20 March 2020 using keywords related to HTA domains (safety, effectiveness, and economic evaluation) and DHT. The full search strategy is presented in Table A 5.

3.3.2. Inclusion criteria

Eligible for inclusion were peer-reviewed journal articles examining the comparative safety, effectiveness, cost, or cost-effectiveness of a DHT intervention used by a patient at home to "actively monitor" or "treat" the risk factors, symptoms, or common comorbidities (e.g., depression) of a diagnosed non-communicable chronic disease. Chronic disease is defined as any long-lasting disease with persistent effects (11), e.g., diabetes, cardiovascular disease. NICE defines "active monitoring" as the automatic recording and transmission of patient data to health services to inform clinical management decisions, and "treat" as providing treatment for a diagnosed condition.

3.3.3. Exclusion criteria

DHTs solely targeting populations diagnosed with a chronic mental or behavioural disorder were excluded given the more heterogeneous nature of these diseases and populations. Studies for DHTs that were not MDSW or that did not "actively monitor" or "treat" a diagnosed chronic non-communicable disease population at home were excluded. Studies not published in English were also excluded.

3.3.4. Study selection

All authors participated in title and abstract screening. Full-text screening was undertaken by AvH, with ten percent of full texts reviewed independently by JC and conflicts resolved by MH.

3.3.5. Data extraction

Data extraction elements included year of publication, country/region, chronic disease population targeted, technology function (active monitoring/treatment), technology type (e.g., mobile or website applications “Apps”, SMS “text messages”), study objectives (clinical effectiveness/non-clinical impacts/cost analysis/economic evaluation), study type, age group (child/adult), sample size, characteristics (of intervention, comparator, and patients), duration (of intervention and follow up), primary/key secondary outcomes, declared or apparent conflicts of interest, the inclusion of disabled and rural/remote participants, use of a DHT-specific framework such as CONSORT E-HEALTH or MAST, number of languages provided, and information on exclusions based on digital literacy.

Data extraction was conducted by AvH and checked by JC.

3.3.6. Coverage assessment

DHT studies were assessed for coverage of the most frequently recommended content across a nine domain DHT-specific HTA. The assessment also included all relevant papers referenced in the included studies to ensure the review covered DHT design, feasibility, efficacy/accuracy, effectiveness, economic evaluation, or implementation testing.

As discussed, the recommended HTA content items were identified in a prior systematic review (see Figure 3.1). The content items are structured in two lists: 1. DHT-specific content, 2. Content common to all technologies but essential for DHTs. The content lists were tested and refined over multiple samples of DHT studies, with AvH assessing coverage and

MH, SN, and KH providing feedback. This process resulted in modifications of content items (provided in Table A 6) for greater clarity and applicability to primary research.

A coverage rating scale was also developed and refined over multiple samples of DHT studies. We extended the ratings of "Yes", "Partly" and "No" of Vukovic et al. (2) at the HTA domain level, into more granular ratings at the content item level such as "Not covered" (item is relevant to the study scope, but was not mentioned), "Poor" (item mentioned in limitations of current study/for future research), "Fair" (defined for each content item), and "Good" (defined for each content item). "NA" (not applicable to intervention) and "Not reported" (not relevant to the scope of the study) were provided for specific content items. Defining ratings at the content item level (Table A 6) assisted with rating consistency over the larger sample.

The final coverage assessment was conducted by AvH on DHT intervention studies targeting a population with cardiovascular disease, diabetes, or both. Ten percent of these studies were independently rated by JC. Discordance in ratings before discussion resulted from differing interpretations of words in the content items rather than differing use of the rating scale. All discordance was resolved by clarifying keywords.

3.3.7. Synthesis of results

For current research trends, the included studies were summarised over the data extraction elements to identify the most/least common study characteristics. For the coverage assessment, the proportion of studies in each rating category for each content item was calculated.

As the focus of this review was a coverage assessment of previously defined content items, risk of bias assessment was not relevant.

3.4. Results

3.4.1. Study characteristics

The search identified 11,824 records (Figure A 3). Removing duplicates, protocols, and reference types that were not published papers produced 6,676 records for title and abstract screening, of which 6,454 did not meet the inclusion criteria. Full-text reviews of 222 papers identified 201 reports (see Table A 7 for paper references) of 178 DHT intervention studies published between 1 January 2015 and 20 March 2020.

Table 3.1 summarises the included study characteristics. The studies are predominantly in high/middle-income countries in Europe/North America. Thirty-eight percent of DHT interventions targeted cardiovascular disease populations, sixteen percent diabetes, and nine percent two or more chronic diseases. Seven percent of DHTs were designed for children or adolescents.

Ninety-four percent of studies included an effectiveness trial within the search period, but fifty-nine percent had yet to conduct a cost analysis or economic evaluation. Eleven percent had examined changes in health service utilisation without costing. Seventy-eight percent of studies conducted randomised controlled trials (RCTs) for effectiveness, and a further sixteen percent conducted a comparative trial with concurrent controls. Median sample sizes were 170 (IQR: 90-350) participants, median duration six (IQR: three-twelve) months, and follow-up six (IQR: four-twelve) months.

Fifty-seven percent of DHTs provided an active monitoring component, mostly via standalone telemonitoring devices. The remaining DHT interventions provided treatment without active monitoring, primarily via mobile or web-based applications.

Table 3.1: Characteristics of included papers and studies

Characteristics of papers		**N=201**	
		n	**%**
Year published	2015	30	15
	2016	29	15
	2017	42	21
	2018	39	19
	2019	45	22
	2020 (to 20 March 2020)	16	8

Characteristics of studies		**N=178**	
		n	**%**
Region	Europe	74	42
	North America	63	35
	Asia-Pacific	33	19
	Middle East	3	2
	South America	2	1
	Africa	2	1
	International	1	1
Chronic disease population targeted	Cardiovascular	68	38
	Diabetes	29	16
	General chronic – 2+ diseases (e.g., Cardiovascular & Diabetes)	16	8
	Nervous system (e.g., Parkinson's disease)	14	8
	Respiratory system (e.g., COPD, Asthma)	13	7
	Musculoskeletal system (e.g., Arthritis, back pain)	9	5
	Cancer	8	4
	Chronic kidney disease	6	3
	Obesity	5	3
	Pain	4	2
	Digestive system (e.g., Crohn's, Celiac disease)	4	2
	Ear diseases (Tinnitus)	2	1
Technology function	**Active monitoring[a]**	**101**	**57**
Technology type	"Apps" Mobile phone & web-based applications	8	5
	"Chatbot" Avatars, IVR, and chatbots	8	5
	"Text" Mobile phone short messaging service (SMS)	2	1
	"VR" Virtual reality & computer games	1	1
	Implantable (e.g., RM transmitter for CIED)	15	8
	Standalone telemonitoring device	47	26
	Wearables and sensors	13	7
	Web-based portal	7	3
	Treatment[b]	**78**	**43**
	"Apps" Mobile phone & web-based applications	43	24
	"Chatbot" Avatars, IVR, and chatbots	2	1
	"Text" Mobile phone short messaging service (SMS)	17	10
	"VR" Virtual reality & computer games	3	2
	Implantable (e.g., RM transmitter for CIED)	1	1
	Standalone telemonitoring device	2	1
	Wearables and sensors	6	3
	Web-based portal	2	1
Age groups targeted	Adult	166	93
	Children and adolescents	11	6
	Both	1	1
Study objectives	Clinical effectiveness	168	94
	Non-clinical impacts without costing	19	11
	Cost analysis	27	15
	Economic evaluation	46	26

Characteristics of studies		**N=178**	
		n	**%**
Study type[c]	II: Randomised Controlled Trial RCT	139	78
	III-1: A pseudorandomised controlled trial	1	1
	III-2: A comparative study with concurrent controls	27	15
	III-3: A comparative study without concurrent controls	1	1
	IV: Case series with either post-test or pre-test/post-test outcomes	10	5
Declared or apparent conflicts	Yes	60	34
	No	115	64
	Not covered	3	2
Disability exclusions	Yes	89	50
	No	89	50
Enough information to determine the extent of digital literacy exclusions	Yes	62	35
	No	116	65
Number of languages provided	One	54	30
	Two	8	4
	Three	1	1
	Four	1	1
	No language exclusions	114	64
Includes rural/remote participants	Yes	14	8
	No	164	92
Use digital specific framework CONSORT E-HEALTH/MAST	Yes	8	5
	No	170	95
Sample size and duration		**Mean (SD)**	**Median (IQR)**
Sample size	Number of participants	2,503 (13,401)	170 (90-350)
Duration of intervention	Maximum intervention in months	8 (6)	6 (3-12)
Duration of follow up	Maximum follow up in months	9 (8)	6 (4 -12)

[a]Includes active monitoring as a component of the intervention, but the intervention may also include treatment components
[b]Includes no active monitoring component in the intervention
[c]Study type: II: Randomised Controlled Trial RCT, III-1: A pseudorandomised controlled trial (i.e., alternate allocation or some other method), III-2: A comparative study with concurrent controls: Non-randomised, experimental trial, Cohort study, Case-control study, Interrupted time series with a control group, III-3: A comparative study without concurrent controls: Historical control study, Two or more single-arm study, Interrupted time series without a parallel control group, IV: Case series with either post-test or pre-test/post-test outcomes

Thirty-four percent of studies were funded by pharma/biotechnology/health insurance companies. Half the studies did not explicitly exclude people with mental or physical disabilities. In thirty-five percent of studies, there was enough information to understand the level to which participants were excluded based on their digital literacy. Only six percent stated they provided an intervention with two or more languages, and only eight percent reported involving rural/remote participants in testing. A digital-specific framework such as CONSORT E-HEALTH (12) or MAST(13) was referenced in only five percent of studies.

3.4.2. Coverage assessment

The coverage assessment was undertaken for DHT interventions targeting cardiovascular disease, diabetes, or both (112 studies, sixty-three percent of all included studies). DHTs for chronic disease management have been pioneered in these disease populations, so this sample is most likely representative of DHT research practice in other chronic disease populations.

Less than half of studies covered DHT-specific content in all but the health problem domain (Figure 3.2 and Table A 8).

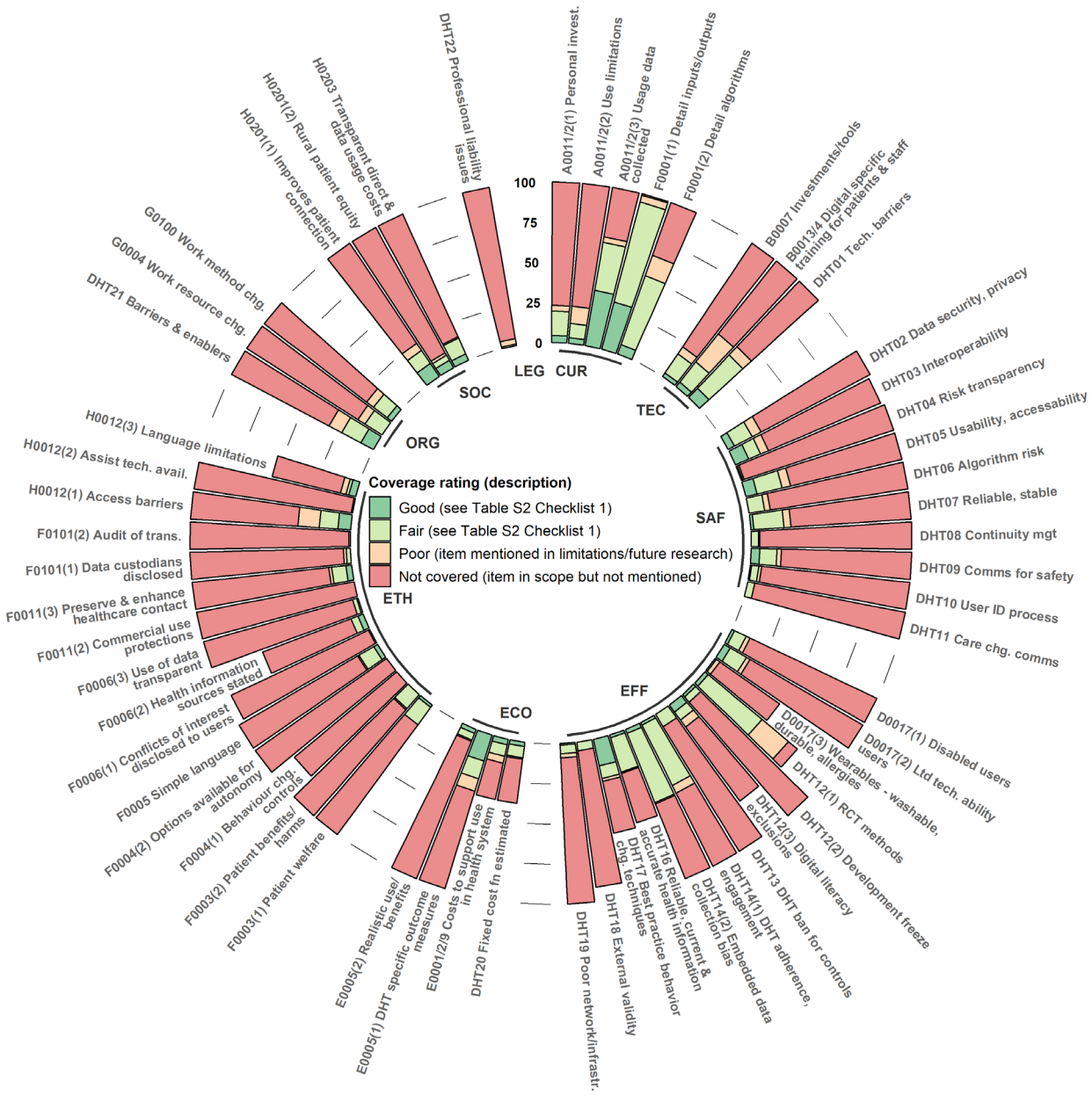

Figure 3.2: Digital health technology (DHT) specific content items for a health technology assessment (HTA). Percentage of included studies attaining each coverage rating

Coverage of content common to all technologies but essential for DHTs was greater than fifty percent in all but effectiveness and ethical domains (Figure 3.3 and Table A 9).

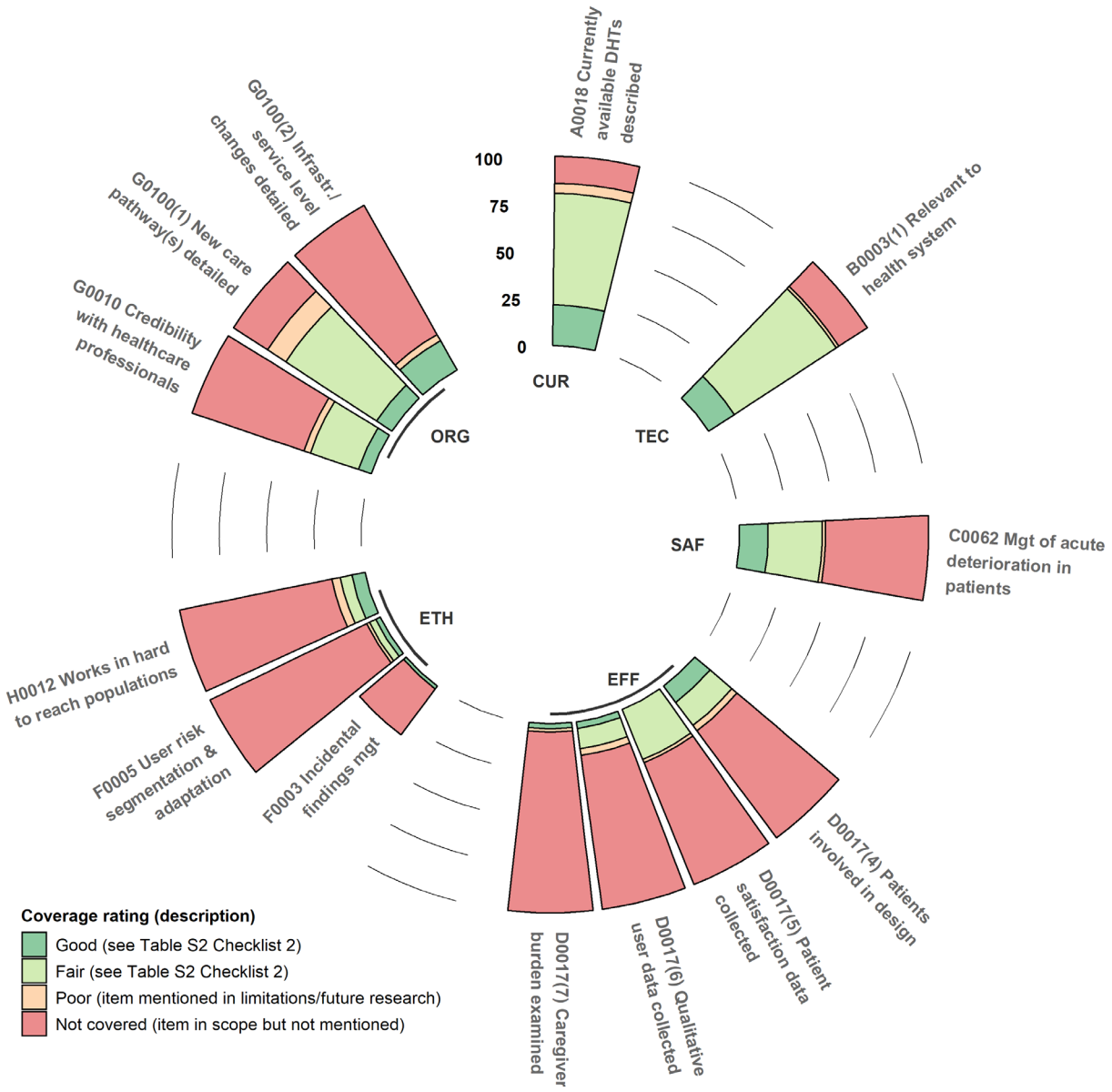

Figure 3.3: Content items common to all technologies but essential for a digital health technology (DHT) health technology assessment (HTA). Percentage of included studies attaining each coverage rating.

Coverage assessment is summarised by HTA domain below.

Domain 1: Health problem and current use of the technology (CUR)

Because this was the best-covered category (Figure 3.2 and Figure 3.3), we describe the percentage of studies attaining the "good" category to highlight emerging good practices. Almost all DHT studies rely on the participant to pay for data usage costs, and many require a personal mobile phone or computer. Only four percent of studies examined whether patients would pay, or estimated costs, for data usage fees and the cost of personal technology required to use the DHT. None addressed whether the health service or patient should pay for data usage fees or provide the personal technology. Three percent of studies discussed how the DHT was designed to overcome utilisation limitations such as available platforms, languages, connectivity, and digital literacy. The NICE requirement to collect ongoing DHT usage data was found for one-third of interventions. Almost one-third explained the comparative advantage of inputs and outputs of the DHT, but only six percent detailed the algorithms/engine logic well enough to understand its limitations/advantages over other DHTs. Twenty-one percent explained the DHTs people with the condition already had available to them (Figure 3.3).

Domain 2: Description and technical characteristics of technology (TEC)

As this domain was moderately well covered, we focus on "good" category studies. Discussion of how the DHT was designed to minimise investments in technology required to run the DHT in the health service was detailed in three percent. Four percent discussed privacy/cyber safety/digital literacy training for patients and staff. Mention of more than one DHT feature for overcoming technical barriers such as interoperability, data extraction, or visualisation was found in eight percent (Figure 3.2). Although most DHTs were tested within the health system (Figure 3.3), small sample sizes in all but sixteen percent limit the

evidence that the DHT could cater to the expected patient population. Over forty percent of DHT studies indicated the technology was mature with no significant future development anticipated.

Domain 3: Safety (SAF)

This DHT-specific domain was poorly covered, so we focus on studies attaining a "fair" rating. Controls for cybersafety and cybersecurity, such as compliance with privacy and data security legislation, were covered in less than one-fifth of studies. Only one study reported that users were given the DHT owner's contact information and information on how their data was collected and protected. Without screenshots/archived DHTs, as recommended in CONSORT E-HEALTH, we could not investigate this further. Only six studies mentioned processes for correctly identifying users within the DHT (a cybersafety control).

In terms of interoperability, less than one-fifth could demonstrate a process to support the creation and maintenance of accurate healthcare records that could be integrated with health system databases. In terms of algorithm risk, only ten percent disclosed enough detail to understand the limitations of the data used, algorithms deployed, output validation, or how the algorithms control the clinical decision-making process (an essential control for learning or complex algorithms).

One-fifth of studies discussed the technical reliability and stability of the DHT. There were few references to prior technical reliability trials, and only four percent addressed updates or continuity management. However, over forty percent discussed the process of identifying and responding to a patient's acute deterioration (Figure 3.3).

Domain 4: Clinical effectiveness (EFF)

As effectiveness was not well covered, we focus on "fair" studies. Three-quarters of DHT studies employed RCTs for effectiveness. Methods to achieve at least single blinding were mentioned in sixty percent of these. Online adherence or use was reported in over forty percent of studies. Whether changes were made in the DHT during the trial, control groups were restricted in DHT use, or biases arose from implicit exclusions based on digital literacy or embedded data collection were more difficult to determine given that there was little use of CONSORT E-HEALTH.

Reliable information content and use of appropriate behaviour change techniques

For these NICE framework requirements, less than half the DHTs providing health information referenced a reliable source or development of content by health professionals at the DHT development stage. Only two studies evidenced a process to keep this information up to date. Of the sixty percent of DHTs that aimed to promote behaviour change, less than half referenced a peer-reviewed behaviour change theory relevant to the purpose of the DHT.

External validity/ generalisability

Six percent of studies reported including participants in rural or remote areas; ten percent reported disabled participants, and sixteen percent reported participants with limited prior use of digital technology. However, very little subgroup analysis was provided.

Patient satisfaction

There was no evidence of patient involvement (patient surveys/focus groups/useability and feasibility testing) in the design of almost three-quarters of DHTs. Although twenty-seven percent had evidence of patient satisfaction data being collected and analysed in the effectiveness trial, no studies demonstrated ongoing collection/extraction of this data.

Domain 5: Costs and economic evaluation (ECO)

We discuss “fair” and “good” rating results for this domain for better practice discrimination. Of the forty-three studies that produced a cost analysis/economic evaluation, twelve studies estimated the costs to support the running of the DHT service (fair), and four estimated the costs to provide it at a scale for health system use (good). Eleven acknowledged a change in fixed costs for scaling up the DHT (fair), but only three estimated this cost function (good).

For all rated studies, DHT-specific outcomes such as self-management benefits or better-connected healthcare professionals were reported in almost one-third (fair), with seventeen percent using validated measures (good). Seven percent considered start-up times and the realistic use of DHT functions (fair), but only three percent incorporated this into an economic evaluation (good).

Domain 6: Ethical analysis (ETH)

Similar to safety, the ethics domain contains many DHT-specific controls to promote cybersafety and provide safeguards when the patient is remote from the clinician. As this domain was not covered well, we focus on “fair” rated studies. A description of a secure process for data transmissions, especially alerts about a patient's health, was reported in only fifteen percent of studies. No study discussed protecting patient data from commercial use. The user was informed of the data collected by the DHT and its intended use in four percent of studies. Only three percent named all parties that hold personal data collected by the DHT. Only one study indicated that users would be informed of the potential risks of data sharing when using the DHT. No study stated that the DHT is regularly audited for transmissions with third parties.

Twelve percent of studies noted patient feedback on the DHT promoting a false sense of security or creating harm from accessing data without someone to interpret it. Managing

incidental findings from testing done by the DHT was discussed in only two of thirty-two applicable studies. Discussion of the DHT design using simple, understandable language, or collection of patient feedback on this, was found in twelve percent of studies.

Autonomy

For DHTs targeting behaviour change, controls to limit the DHT's influence on a person's behaviour for purposes other than those stated or how the range of options was chosen so the user could make independent decisions were not discussed. Only one study stated that potential conflicts of interest (e.g., funding, promotion) were disclosed to DHT users. For DHTs providing health information, eight percent provided concise information for the user on how the DHT content was selected or who was responsible for the content.

Justice & equity

Descriptions of how the DHT overcame access barriers for patients with a lack of economic resources, poor IT skills, disabilities, or low digital health literacy were found in one-fifth of studies. Seven studies justified the choice of languages provided, discussed language as a limitation on use, or provided many languages. Unless the DHT was explicitly targeted towards hard-to-reach patients (thirteen percent), e.g., patients in low-socioeconomic areas or low-income countries, there was no evidence of how effective the DHT would be for these populations.

Domain 7: Organisational aspects (ORG)

"Good" studies provided qualitative or quantitative evidence on how staff work methods and interactions with patients changed (four percent). A "fair" discussion of changes to electronic communication, information reporting systems, face-to-face consultations, and staff communication required for the DHT to operate was found in thirteen percent of studies. Implementation studies are rare but provided better coverage of required changes and

recommendations for enablers of DHT uptake (nine percent). Evidence of a relevant healthcare expert's involvement in the design, development, testing, or sign-off of the DHT (fair) was only found in one-third of studies.

Domain 8: Patients and social aspects (SOC)

Twenty percent of studies gave qualitative or quantitative feedback on increases in connectivity between patients and healthcare providers (fair). Five percent reported qualitative or quantitative analysis on rural and remote participants (good). Only four percent stated that users were provided with expected direct and data usage costs, an important enabler of treatment adherence (good).

Domain 9: Legal aspects (LEG)

This was the least covered domain, with only one study clarifying the parties responsible for medical advice, monitoring, or reviewing patient data, and who owned the DHT-related data. No study discussed potential litigation risks, insurance, or professional registration consequences to healthcare practitioners using or recommending the DHT.

3.5. Discussion

Current research trends

The growth in effectiveness studies of chronic disease DHTs over the last five years is encouraging, particularly with the majority being RCTs employing practices to overcome methodological problems associated with DHTs, e.g., single-blinding and choice of a comparator reflecting standard care. However, small sample sizes, short trial durations, and short follow-up periods limit the ability to detect treatment effects, determine the optimal treatment dose, and estimate the persistence of effects. Lack of inclusion of populations from low-income countries, settings where telecommunication infrastructure/connectivity is poor (e.g., rural, and remote communities), and exclusion of people who do not speak the primary

language or own the required personal technology, limits the generalisability of these studies. As most studies had yet to conduct a cost or economic analysis, cost-effectiveness compared to alternate interventions remains largely unknown.

Coverage assessment

Close examination of the included CVD/diabetes DHT studies revealed that content coverage in technical, safety, ethical and legal domains remain low, as was found by Vukovic et al. (2) in HTA reports to 2016. Although DHT-specific controls for cybersecurity, cybersafety, technical reliability and stability exist across multiple domains, they are mainly concentrated in safety and ethical analysis domains. These domains were not well-covered despite being significant areas of risk to the user.

In terms of effectiveness, the NICE framework standards of ensuring reliable and accurate health information and best practice behaviour change techniques were only evidenced in a minority of studies providing these services. The lack of evidence for ongoing controls to keep health information up to date is concerning. Three-quarters of studies could not provide evidence of patient involvement in the DHT design, which is a critical failure for technologies designed for patients to use at home. In the organisational aspects domain, two-thirds could not evidence a relevant healthcare expert's role in the design, development, testing, or sign-off of the DHT, a key enabler for DHT uptake.

In terms of economic evaluations, similar to Kidholm (4), we found that the inclusion of costs was variable. Most studies only included the cost of the equipment for the patient, not the costs for the equipment required to run the DHT service or downstream costs of changes in health outcomes resulting from the DHT. The fixed costs of providing the DHT in the health system and at scale (licensing, platforms, hardware, security) can escalate rapidly from costs involved in a clinical trial. These costs should be estimated and included. Even though most

DHT trials assume the patient will pay data usage fees and bring their own device, at a minimum, a sensitivity analysis including these costs should be reported.

Existing DHT-specific frameworks and a phased research approach with improved referencing to prior work could be employed immediately to improve the quality of trial design and reporting to meet the needs of HTA. Coverage of at least six of the thirteen DHT-specific effectiveness items plus four additional items over technical, safety, and ethics domains, could be achieved by designing and reporting effectiveness studies in compliance with CONSORT E-HEALTH (12), a reporting standard available since 2011. This reporting standard should not be limited to RCTs as many items are relevant to other comparative study designs. A phased research approach should, at a minimum, include a review of existing DHTs available to the target population, design and initial testing with target patients and relevant health professionals, efficacy/accuracy testing, and safety testing for technical reliability, stability, cybersecurity, and cybersafety, before clinical effectiveness trials. This prior work should be referenced or reported in clinical effectiveness publications. Finally, economic evaluations should be performed considering increases in costs for operating the DHT service in the health system at the expected scale.

Limitations

Our findings are limited to the information reported in the included peer-reviewed journal papers, referenced papers, and supplementary materials. No attempt was made to contact the authors for additional information. While using the seventy-one content items recommended for a DHT-specific comprehensive HTA promotes a thorough investigation, we recognise that these items' number and equal weighting are not efficient for regular use. Refining these lists into more practical companion materials for performing or assessing HTAs is warranted.

3.6. Conclusion

Although primary research in DHTs that manage chronic disease at home is steadily increasing, it is not covering the content required for a DHT-specific comprehensive HTA, particularly in the critical areas of cybersafety, cybersecurity, technical reliability, stability, and patient satisfaction. The inability to conduct such an HTA will likely result in suboptimal decisions in the investment of health service budgets. Measures to increase the quality of trial design and reporting using existing tools and DHT-specific frameworks are required.

3.7. References

1. O'Rourke B, Oortwijn W, Schuller T. International Joint Task Group. The new definition of health technology assessment: A milestone in international collaboration. *Int J Technol Assess Health Care. 2020*;36(3):187-90.
2. Vukovic V, Favaretti C, Ricciardi W, de Waure C. Health technology assessment evidence on e-health/m-health technologies: Evaluating the transparency and thoroughness. *Int J Technol Assess Health Care*. 2018;34(1):87-96.
3. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mhealth? A systematic review of economic evaluations of mhealth solutions. *PLoS One*. 2017;12(2):e0170581.
4. Kidholm K, Kristensen MBD. A scoping review of economic evaluations alongside randomised controlled trials of home monitoring in chronic disease management. *Appl. Health Econ. Health Policy*. 2018;16(2):167-76.
5. Forsyth JR, Chase H, Roberts NW, Armitage LC, Farmer AJ. Application of the national institute for health and care excellence evidence standards framework for digital health technologies in assessing mobile-delivered technologies for the self-management of type 2 diabetes mellitus: Scoping review. *JMIR Diabetes*. 2021;6(1):e23687.
6. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Pdf], 2018 [updated 23 April 2021]. Available from: https://www.nice.org.uk Accessed 19 July 2021.
7. Von Huben A, Howell M, Howard K, Carrello J, Norris S. Health technology assessment for digital technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2021;37(1).

8. EUnetHTA Joint Action 2, Work Package 8. HTA core model® version 3.0. [Pdf] 2016; Available from: www.htacoremodel.info/BrowseModel.aspx. Accessed 29 February 2020.

9. Medical Device Coordination Group. Guidance on qualification and classification of software in regulation (EU) 2017/745 – MDR and regulation (EU) 2017/746 – IVDR. European Commission; 2019.

10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.

11. Australian Institute of Health and Welfare. Chronic disease overview. [Internet] 2020; Available from: https://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/chronic-disease/overview. Accessed 10 February 2021.

12. Eysenbach G. Consort-ehealth: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J. Med. Internet Res*. 2011;13(4):e126.

13. Kidholm K, Ekeland AG, Jensen LK, Rasmussen J, Pedersen CD, Bowes A, et al. A model for assessment of telemedicine applications: MAST. *Int J Technol Assess Health Care*. 2012;28(1):44.

Chapter 4 Stakeholder preferences for attributes of digital health technologies to consider in health service funding

The material in this chapter has been published as:

Von Huben A, Howell M, Norris S, Wong KC, Tang J, Kazi S, Laranjo L, Chow KC, Howard K. Stakeholder preferences for attributes of digital health technologies to consider in health service purchasing. *Int. J. Technol. Assess. Health Care.* 2023;39(1):e12. doi:10.1017/S0266462323000089.

A statement of the specific contributions of the co-authors can be found in Appendix B.

Purpose of chapter

To prioritise the content for a DHT-specific and comprehensive HTA into a practical checklist, a best-worst scaling survey was undertaken with patients, carers, health professionals and the general community.

4.1. Abstract

Objectives: Health service providers are currently making decisions on the public funding of digital health technologies (DHTs) for managing chronic diseases with limited understanding of stakeholder preferences for DHT attributes. This study aims to understand the community, patient/carer, and health professionals' preferences to help inform a prioritised list of evaluation criteria.

Methods: An online best-worst scaling survey was conducted in Australia, New Zealand, Canada, and the United Kingdom to ascertain the relative importance of twenty-four DHT attributes among stakeholder groups using an efficient incomplete block design. The attributes were identified from a systematic review of DHT evaluation frameworks for consideration in a health technology assessment (HTA). Results were analysed with multinomial models by stakeholder group and latent class.

Results: A total of 1,251 participants completed the survey: 576 community members, 543 patients/carers, and 132 health professionals. Twelve attributes achieved a preference score above 50 percent in the stakeholder group model, predominantly related to safety but also covering technical features, effectiveness, ethics, and economics. Results from the latent class model supported this prioritisation. Overall, connectedness with the patient's healthcare team seemed the most important; with *"Helps health professionals respond quickly when changes in patient care are needed"* as the most highly prioritised of all attributes.

Conclusions: It is proposed these prioritised twelve attributes be considered in all evaluations of chronic disease self-management DHTs, supplemented with a limited number of attributes that reflect the specific perspective of funders, such as equity of access, cost, and system-level implementation considerations.

4.2. Introduction

The COVID-19 pandemic has highlighted the potentially beneficial role of digital health technologies (DHTs) in helping patients with chronic disease self-manage their illness at home. The two most common technologies are 1. Telemonitoring at home, and 2. Web or mobile phone management programs. These technologies can differ widely in technical function, reliability, stability, connectedness with clinicians and health system data, safety, ease of use, access, clinical effectiveness, and the cost of implementation and usage. For health service providers in countries where a Health Technology Assessment (HTA) approach is used to inform decisions on the public funding of new healthcare technologies, a question arises over the most important issues to consider when evaluating DHTs.

HTA models such as EUNetHTA's HTA Core Model (1) provide checklists of questions to be specifically considered for non-digital health technologies (e.g., pharmaceuticals, diagnostics, and screening) over nine domains, from the current use of the technology to legal aspects. Our systematic review of DHT evaluation frameworks (2) identified recommendations for DHT-specific issues in all nine domains, particularly safety and ethical analysis. Recently, specific HTA frameworks for DHTs have been developed and used for funding decisions (e.g., UK's ESF (2) and DTAC (3), Germany's DiGAV, and Finland's Digi-HTA (4, 5)), but none cover issues in all nine domains. In addition, to our knowledge, there have been no studies over a broad cross-section of the general community, patients, carers, and health professionals, to understand the relative importance of the issues included in these DHT frameworks and recommended in the DHT evaluation literature. A vital enabler of the effectiveness of these technologies is stakeholder buy-in (6-8); hence understanding stakeholder preferences is critical to the DHT evaluation process. The quantitative discrete choice analysis methodology employed in this study allows for estimating the relative preference of many issues over a large sample of stakeholders.

This best-worst survey aims to understand stakeholder preferences for attributes of the technology relevant to the public funding of DHTs by health service providers. Identifying areas of agreement on the priority of the issues to be considered, and any areas of divergence by specific population groups, will enable us to develop a prioritised and specific DHT checklist to accompany standard HTA evaluation checklists and assist publicly funded health service providers in their evaluations.

4.3. Methods

4.3.1. Study population

Adult survey respondents were recruited from Australia, New Zealand, Canada, and the United Kingdom, given they have government-funded healthcare systems and use an HTA approach to inform public funding decisions. Respondents were recruited by an online research panel administered by an external organisation (Dynata LLC, Shelton, CT, USA). Quota sampling by country and the absence or presence of chronic disease was used to obtain a representative sample of chronic disease patients and the general community in these four countries. Respondents could indicate they were all/any of chronic disease patients, carers of chronic disease patients, and health professionals, or if none of these, a general community member. Health professionals were recruited by advertising in Australian and international health professional network newsletters and member email lists. Networks covered general practice, specialists, nurses and nurse practitioners, health service researchers, and guidelines international network (GIN) members. Links to the survey website were provided for online survey completion in English. The study was approved by the University of Sydney Human Research Ethics Committee (Project Number: 2021/847). Data were collected from January to April 2022.

4.3.2. Best-worst scaling

Case 1 "object" best-worst scaling (BWS) is a type of discrete choice experiment that allows for the measurement of relative preferences for various attributes on the same scale, providing better discrimination than the use of rating scales (9, 10). In our survey, respondents repeatedly chose two objects in varying sets of three (where the "objects" are the DHT attributes) that represent the most perceptual difference, e.g., the "most" and "least important," on the continuum of attributes (10). The probabilities of the respondents' choices were modelled using the multinomial logit (MNL) model, where the model coefficients (β) can be interpreted as the relative preferences for the attributes (10). Robust standard errors were used in estimation to allow for the correlation from individuals completing more than one choice set (11).

4.3.3. Development of the issues and DHT attributes

To identify issues to be considered when evaluating DHTs for funding, we conducted an extensive systematic review of international peer-reviewed and grey literature to identify evaluation frameworks specific to DHTs that manage chronic disease at home (12). We compiled comprehensive lists of the most frequently recommended content across a nine-domain HTA and refined this into a more practical set of questions for each issue by applying them to a systematic review of recent primary research studies (13).

Because the list of issues and associated questions can be repetitive over HTA domains, they were grouped and translated into a set of non-overlapping DHT attributes that most represented the grouped issues. Several iterations were undertaken to form these attributes, with AvH drafting, MH, SN, and CC reviewing, and KH resolving conflicts. A pilot of the BWS was also undertaken with a mix of fifteen patients, carers, health professionals, and general community members, who commented on whether they thought the attributes

represented multiple issues, duplicated issues, or omitted essential issues. In response, attributes were modified. See Table A 10 for the final list of twenty-four DHT attributes. References to the DHT evaluation framework literature and the EUnetHTA Core Model domains and issue identifiers (1) that suggested the content are given for each attribute/grouped issue for traceability with our prior work (12, 13) and integration with the EUnetHTA model.

4.3.4. Survey design

SAS V9.4 (SAS Institute Inc., Cary, NC, USA) was used to find a statistically D-efficient nearly balanced incomplete block design, minimum sample size n = 288, resulting in 96 choice sets with three objects, blocked into eight versions of twelve questions to minimise survey fatigue and improve response efficiency (14). The surveys were programmed into Qualtrics (Qualtrics Software, Provo, UT, USA). Minor changes to the survey questions to minimise respondent completion time were made after piloting. The final survey was structured as follows: Participant information, consent, socio-demographics, patient/health professional experience with DHTs, explanation of the choice task with definitions of key terms, the scenario, and an example of a completed choice task (Figure A 4). Participants completed twelve choice questions and were asked to list any other important issues not included in the choice task. The survey concluded with questions on access to the internet, the level of help required when using personal digital technology, and one eHealth literacy question (15).

4.4. Analysis

Participant characteristics were summarised. The number of participants who responded to "list any other important issues not included in the choice task" was counted, and responses examined.

The sequential best-worst (16) multinomial logit (SBWMNL) model and panel latent class sequential best-worst MNL were estimated in R Statistical Software (v4.1.2; R Core Team 2021) (17) using the Apollo R package (v0.2.4) (11, 18). In sequential best-worst, the participant is assumed in each choice question to pick the "best" choice first and then the "worst" out of the remaining choices. A reverse of this assumption was also tested with little change in the relative preferences.

Because we were interested in the extent of consensus and divergence in preferences over these stakeholder groups, models were constructed and tested for model fit by adding interaction terms to capture stakeholder groups in various combinations, i.e., two stakeholder groups (1. health professionals, 2. all others), three groups (1. health professionals, 2. patients and carers, 3. community members), four groups (with the fourth group being respondents that were carers but not patients, previously in group 2). Health professionals who are also carers or patients will have additional knowledge and experiences of the healthcare system compared to non-health professionals. To reduce any potential risk of bias from this additional knowledge and experience in the patient and carer groups, these small number of health professionals were classified into the health professional group. Model fit was assessed by likelihood ratio tests and Akaike and Information Criterion (AIC). The regression coefficients of the MNL model provide the relative importance of each attribute on the same scale and were scaled to 0-100 (least to most important) for ease of interpretation. The scaled coefficients are denoted as "preference scores" in tables and figures. To identify the most important issues for inclusion in a practical HTA checklist, we set an arbitrary preference score cut-off of fifty (fifty percent) in at least one stakeholder group to determine the "prioritised" attributes.

A panel latent class SBWMNL model is a common technique used in choice modelling to investigate the heterogeneity of preferences that may not be captured in the base SBWMNL

model. In this model, additional classes were added until the model with the best fit was found, with model fit assessed by the Bayesian Information Criterion (BIC) and the proportion of participants classified in each latent class with a posterior probability above seventy-five percent; the higher the proportions at these levels the lower the number of participants not ambiguously classified in each latent class (19, 20). Although participants belong in a class to a certain probability in a latent class model, the model allows for examining associations between covariates (e.g., age and gender) and class membership probability. To identify these associations, all variables collected on all participants (i.e., not patient, carer, and health professional-specific) were entered into the class membership model, and variables with the highest p-value were removed sequentially until the best model fit was found based on the AIC. Before fitting the model, covariates with low numbers of respondents in specific categories were grouped with the most relevant neighbouring response category for model stability; i.e., the twenty-three students in employment status were grouped with part-time and casual workers, the eleven participants residing in "Other" countries were grouped with the United Kingdom, given they were residing in European countries, and responses to how often help was required when using technology were collapsed into never/rarely and sometimes/often/always. R packages Gmisc for plot and table output (21) and knitr (22) for reproducible research were also used in the analysis.

4.5. Results

4.5.1. Participants

1,317 participants consented, 27 completed fewer than three choice questions, and 39 surveys were excluded due to survey completion occurring in one-third of the median time (identified as "speeders" or possible bots), leaving 1,251 (95 percent) surveys for analysis. Respondent characteristics are reported in Table 4.1. Respondent types were 576 (46 percent) community members, 543 (43 percent) patient/carers (397 patients, 146 carers), and 132 (11 percent)

health professionals. Participants were aged eighteen to eighty-plus years and fifty-four percent of the sample was female. While community members and patients/carers were evenly spread across the four countries, nearly half the health professionals were Australian, reflecting the health professional networks available to us. Twenty-one percent of participants lived in rural or remote areas. Although over ninety percent of participants spoke mainly English, eighteen percent spoke a second language at home.

Table 4.1: Demographics of survey respondents by stakeholder group (N = 1,251)

	Stakeholder group		
	Community Member N = 576	**Patient/Carer N = 543**	**Health Professional N = 132**
Age group			
18-39	143 (24.8%)	134 (24.7%)	58 (43.9%)
40-69	298 (51.7%)	301 (55.4%)	72 (54.5%)
70 and over	135 (23.4%)	108 (19.9%)	2 (1.5%)
Gender			
Male	285 (49.8%)	243 (44.8%)	38 (29.0%)
Female	287 (50.2%)	299 (55.2%)	93 (71.0%)
Country of residence			
Australia	145 (25.2%)	129 (23.8%)	64 (48.5%)
Canada	150 (26.0%)	138 (25.4%)	15 (11.4%)
New Zealand	143 (24.8%)	124 (22.8%)	23 (17.4%)
United Kingdom	135 (23.4%)	150 (27.6%)	23 (17.4%)
Other	3 (0.5%)	2 (0.4%)	7 (5.3%)
Location			
Rural or Remote	127 (22.0%)	119 (21.9%)	19 (14.4%)
Urban	449 (78.0%)	424 (78.1%)	113 (85.6%)
Main language spoken at home			
English	529 / 576 (91.8%)	514 / 543 (94.7%)	112 / 130 (86.2%)
Speak a second language at home			
Yes	92 / 576 (16.0%)	87 / 543 (16.0%)	43 / 130 (33.1%)
Employment status			
Full time	223 / 576 (38.7%)	212 / 543 (39.0%)	84 / 130 (64.6%)
Part time/casual	70 / 576 (12.2%)	63 / 543 (11.6%)	40 / 130 (30.8%)
Not employed/Unable to work	68 / 576 (11.8%)	95 / 543 (17.5%)	2 / 130 (1.5%)
Retired	204 / 576 (35.4%)	165 / 543 (30.4%)	0 / 130 (0.0%)
Student	11 / 576 (1.9%)	8 / 543 (1.5%)	4 / 130 (3.1%)
Highest level of education			
Primary school	9 / 576 (1.6%)	6 / 543 (1.1%)	0 / 130 (0.0%)
Secondary/high school	208 / 576 (36.1%)	162 / 543 (29.8%)	9 / 130 (6.9%)
Professional certificate	131 / 576 (22.7%)	141 / 543 (26.0%)	16 / 130 (12.3%)
Undergraduate/Bachelor's Degree	155 / 576 (26.9%)	170 / 543 (31.3%)	39 / 130 (30.0%)
Postgraduate Degree (Master/Doctoral)	73 / 576 (12.7%)	64 / 543 (11.8%)	66 / 130 (50.8%)
Internet access			
Have mobile internet access	473 / 576 (82.1%)	453 / 543 (83.4%)	121 / 130 (93.1%)
Have home internet access	545 / 576 (94.6%)	511 / 543 (94.1%)	123 / 130 (94.6%)
On a typical day, for how many hours do you have internet access?			
Median (IQR)	24.0 (8.0 - 24.0)	24.0 (10.0 - 24.0)	24.0 (20.2 - 24.0)
Missing	*0 (0%)*	*0 (0%)*	*2 (1.5%)*
How often do you need someone to help you when using your computer, mobile phone, tablet, or smartwatch?			
Never	265 / 575 (46.1%)	225 / 542 (41.5%)	49 / 130 (37.7%)
Rarely	193 / 575 (33.6%)	190 / 542 (35.1%)	49 / 130 (37.7%)
Sometimes	79 / 575 (13.7%)	88 / 542 (16.2%)	19 / 130 (14.6%)
Often	21 / 575 (3.7%)	23 / 542 (4.2%)	7 / 130 (5.4%)
Always	17 / 575 (3.0%)	16 / 542 (3.0%)	6 / 130 (4.6%)

		Stakeholder group	
How often do you use the internet to find health information?			
Not at all	63 / 575 (11.0%)	33 / 543 (6.1%)	3 / 130 (2.3%)
A few times a year	296 / 575 (51.5%)	209 / 543 (38.5%)	13 / 130 (10.0%)
A few times a month	145 / 575 (25.2%)	180 / 543 (33.1%)	26 / 130 (20.0%)
A few times a week	53 / 575 (9.2%)	84 / 543 (15.5%)	35 / 130 (26.9%)
Daily	18 / 575 (3.1%)	37 / 543 (6.8%)	53 / 130 (40.8%)
Patient and Carer survey			
Patient		397 / 543 (73.1%)	
Carer		146 / 543 (26.9%)	
Patient (or patient cared for) chronic conditions			
Cardiovascular/heart conditions		134 / 543 (24.7%)	
Diabetes		170 / 543 (31.3%)	
Digestive system conditions (e.g., Crohn's, Celiac disease)		70 / 543 (12.9%)	
Nervous system conditions (e.g., Parkinson's disease)		53 / 543 (9.8%)	
Chronic pain of unknown cause		89 / 543 (16.4%)	
Cancer		56 / 543 (10.3%)	
Kidney disease		33 / 543 (6.1%)	
Musculoskeletal system conditions (e.g., Arthritis, back problems)		165 / 543 (30.4%)	
Obesity		95 / 543 (17.5%)	
Respiratory conditions (e.g., COPD, asthma)		146 / 543 (26.9%)	
Other/s chronic disease		37 / 543 (6.8%)	
Patient (or patient cared for) use of DHT			
Currently use a digital health technology to manage my/their chronic disease		117 / 543 (21.5%)	
Do not use one currently, but want to use a digital health technology		167 / 543 (30.8%)	
Have used a digital health technology in the past, but not currently		36 / 543 (6.6%)	
None of the above		223 / 543 (41.1%)	
Health professional survey			
I manage/treat patients with chronic disease			86 / 132 (65.2%)
I have purchased digital health technologies for my health service to manage/treat patients with chronic disease			22 / 132 (16.7%)
I am looking to purchase digital health technologies for my health service to manage/treat patients with chronic disease			19 / 132 (14.4%)
None of above			31 / 132 (23.5%)

*Non-binary: Community Member 4(0.7%), Patient or Carer 1(0.2%); Prefer not to say: Health Professional 1(0.8%)

In terms of internet access (Table 4.1), over eighty/ninety-five percent had mobile/home internet access. However, areas of inequity in access were observed, with a quarter of community members and patients/carers having ten or fewer hours of available internet access per day. Regarding perceived competency with personal-use digital technologies, only seven percent stated they often or always needed someone to help them when using these technologies. Concerning e-Health literacy, a substantially higher proportion of health professionals reported using the internet daily to find health information than other groups.

For the patient and carer survey (Table 4.1), there was a broad representation of common chronic diseases. Twenty-two percent of patients, or the person they cared for, were currently using a DHT to manage their condition, nearly one-third wanted to use a DHT but did not currently, and only seven percent had used one in the past but not currently. For the health professional survey (Table 4.1), nearly two-thirds managed or treated patients with chronic disease, seventeen percent had purchased a DHT for their health service to manage or treat patients with chronic disease, and fourteen percent were looking to purchase such a DHT for their health service.

Thirty-one percent (394) of participants responded to "list any other important issues not included in the choice task". Noting that the choice task was designed so participants would not see all attributes, most issues raised were already included issues (e.g., easy to use) or sub-issues (e.g., consider user age). Only one issue outside of those included, cultural safety, was raised by more than one participant (three health professionals).

4.5.2. Preferences for attributes

For the SBWMNL model, the best fit based on the likelihood ratio test and AIC included interactions for three stakeholder groups; indicating sufficient preference differences between community members, patient/carers, and health professionals, but insufficient difference

between patients and carers to warrant a separate carer group. Model results with scaled preference scores (0 to 100; least to most important) are displayed in Table 4.2. Mean and 95% confidence interval preference scores are plotted by stakeholder group in Figure 4.1. Even though statistical differences exist, the preferences indicate a similar ranking between community members and patients/carers. While health professionals had some differing priorities, all stakeholder groups agreed on the eleven most important DHT attributes, six being in the Safety HTA domain. The most important attribute for all stakeholder groups was "*It helps health professionals respond quickly when changes in patient care are needed"* (Table 4.2 and Figure 4.1).

Table 4.2: Relative preferences of attributes from sequential best-worst multinomial model (SBWMNL) with three stakeholder groups: Community Member, Patient/Carer, Health Professional

HTA Domain*	Attributes	Community Member (N = 576)				Patient/Carer (N = 543)				Health Professional (N = 132)			
		β	(95% CI)	Preference Score	*p*	*β*	(95% CI)	Preference Score	*p*	*β*	(95% CI)	Preference Score	*p*
SAF	Helps health professionals respond quickly when changes in patient care are needed	2.03	(1.84, 2.23)	100.0	<0.001	1.84	(1.63, 2.04)	92.0	<0.001	1.47	(1.05, 1.88)	76.9	<0.001
TEC/SAF	Always records the correct information about patients	1.95	(1.76, 2.14)	96.7	<0.001	1.73	(1.53, 1.93)	87.6	<0.001	1.23	(0.85, 1.60)	67.1	<0.001
SAF	It is highly reliable and stable	1.68	(1.50, 1.86)	85.7	<0.001	1.73	(1.54, 1.91)	87.5	<0.001	1.01	(0.62, 1.40)	58.1	<0.001
EFF	The health advice it provides is always up-to-date and correct	1.59	(1.41, 1.77)	82.0	<0.001	1.51	(1.32, 1.70)	78.7	<0.001	1.15	(0.77, 1.53)	63.9	<0.001
SAF/ETH	Ensures patient information is always kept private and safe from hacking	1.57	(1.38, 1.76)	81.2	<0.001	1.52	(1.32, 1.71)	78.9	<0.001	1.45	(1.07, 1.83)	76.1	<0.001
EFF/ECO	Has additional benefits - patients more confident in their managing condition, less travel and waiting, more connected health team	1.23	(1.05, 1.41)	67.3	<0.001	1.29	(1.11, 1.47)	69.8	<0.001	1.12	(0.71, 1.52)	62.6	<0.001
TEC	Shows patient information clearly and explains it	1.15	(0.99, 1.31)	63.9	<0.001	1.17	(1.00, 1.34)	64.7	<0.001	0.74	(0.41, 1.07)	47.2	<0.001
ETH	Prevents patients misinterpreting test results or having a false sense of security	1.13	(0.95, 1.30)	63.1	<0.001	0.91	(0.73, 1.10)	54.4	<0.001	0.81	(0.45, 1.18)	50.3	<0.001
TEC	Good training and technical support to keep users safe	1.12	(0.96, 1.29)	62.9	<0.001	1.08	(0.91, 1.25)	61.1	<0.001	0.76	(0.42, 1.11)	48.2	<0.001
TEC/SAF	With patient consent, their data can be easily linked to existing medical records for clinician review	1.05	(0.87, 1.24)	60.0	<0.001	0.97	(0.79, 1.15)	56.6	<0.001	0.76	(0.40, 1.13)	48.2	<0.001
CUR/SAF/ EFF/ETH	Easy to access and use for everyone	0.93	(0.76, 1.09)	54.9	<0.001	0.90	(0.73, 1.08)	53.9	<0.001	0.64	(0.26, 1.03)	43.3	0.001
ORG	The new care pathway is mapped out, staff can adapt to it easily, and they have the resources they need	0.78	(0.61, 0.96)	49.0	<0.001	0.63	(0.46, 0.81)	42.9	<0.001	0.33	(-0.04, 0.70)	30.6	0.078
ETH	Does not limit the user in their treatment options	0.73	(0.55, 0.91)	46.9	<0.001	0.84	(0.66, 1.02)	51.5	<0.001	0.11	(-0.26, 0.48)	21.6	0.564
EFF	It is at least as effective as usual (face-to-face) care	0.68	(0.51, 0.86)	44.8	<0.001	0.75	(0.57, 0.93)	47.8	<0.001	0.25	(-0.15, 0.64)	27.2	0.223
SAF	There is enough information for users to know how it works and what could go wrong	0.59	(0.42, 0.76)	41.2	<0.001	0.67	(0.49, 0.84)	44.3	<0.001	0.20	(-0.15, 0.55)	25.1	0.270
ORG	Relevant health professionals have been involved in the design and they support its use	0.57	(0.42, 0.73)	40.4	<0.001	0.57	(0.40, 0.74)	40.3	<0.001	0.54	(0.20, 0.89)	39.2	0.002

HTA Domain*	Attributes	Community Member (N = 576)				Patient/Carer (N = 543)				Health Professional (N = 132)			
		β	(95% CI)	Preference Score	*p*	*β*	(95% CI)	Preference Score	*p*	*β*	(95% CI)	Preference Score	*p*
EFF	When trying to change patient habits, it uses best practice and respected methods	0.52	(0.36, 0.68)	38.2	<0.001	0.45	(0.29, 0.61)	35.5	<0.001	0.50	(0.17, 0.83)	37.6	0.003
CUR	Low extra costs (data usage & personal technology) for users and carers	0.40	(0.23, 0.58)	33.4	<0.001	0.60	(0.42, 0.77)	41.5	<0.001	0.31	(-0.04, 0.66)	29.7	0.084
TEC	The patient can download all their data in a useable format	0.36	(0.19, 0.52)	31.7	<0.001	0.36	(0.19, 0.54)	31.9	<0.001	-0.21	(-0.55, 0.14)	8.7	0.240
TEC/ECO	Low extra costs (equipment, IT, services) for the health service to support it	0.26	(0.10, 0.43)	27.8	0.002	0.36	(0.18, 0.53)	31.6	<0.001	-0.18	(-0.56, 0.19)	9.6	0.335
LEG	It is clear who is legally responsible for what and who owns the data	0.26	(0.10, 0.42)	27.7	0.002	0.16	(-0.01, 0.33)	23.6	0.073	-0.12	(-0.46, 0.22)	12.2	0.483
EFF/ETH/ SOC	Can be used anywhere	0.18	(0.01, 0.35)	24.5	0.039	0.39	(0.21, 0.56)	32.9	<0.001	-0.20	(-0.56, 0.16)	9.0	0.283
CUR	Lets the health service know how many patients are using it, so any improvements can be made	0.13	(-0.04, 0.29)	22.3	0.137	0.22	(0.04, 0.40)	26.2	0.015	-0.42	(-0.79, -0.05)	0.0	0.027
EFF	Patients and caregivers helped design it and were happy with it	Reference				Reference				Reference			

Model Fit: Likelihood Ratio Test (LRT) p-value = 0.003 (3 stakeholder groups versus 2 stakeholder groups model; where 2 stakeholder groups versus constant only model LRT p-value <0.001, and 4 stakeholder groups versus 3 stakeholder groups model LRT p-value=0.99), Pseudo r2 0.074, Akaike Information Criterion (AIC) 49322.09 (lowest out of constant only model: 49341.94, 2 groups model: 49322.42, 4 groups model: 49369.64), Bayesian Information Criterion (BIC) = 49895.46 (second lowest out of constant only model: 49533.06, 2 groups model: 49704.67, 4 groups model: 50134.14), Respondents n = 1,251 (576, 543, 132 observations), β = Regression model coefficient estimates.

*HTA Domain = Health Technology Assessment (HTA) Domains of the EUNetHTA HTA Core Model version 3.0(1):

CUR: Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status
TEC: Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it
SAF: Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers
EFF: Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting
ECO: Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value for money judgments
ETH: Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA
ORG: Identifies resources mobilised or organised to implement the new technology and the consequences (Intra/inter-organisational and health system)
SOC: Considers issues related to the new technology relevant to patients, carers, and social groups
LEG: Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

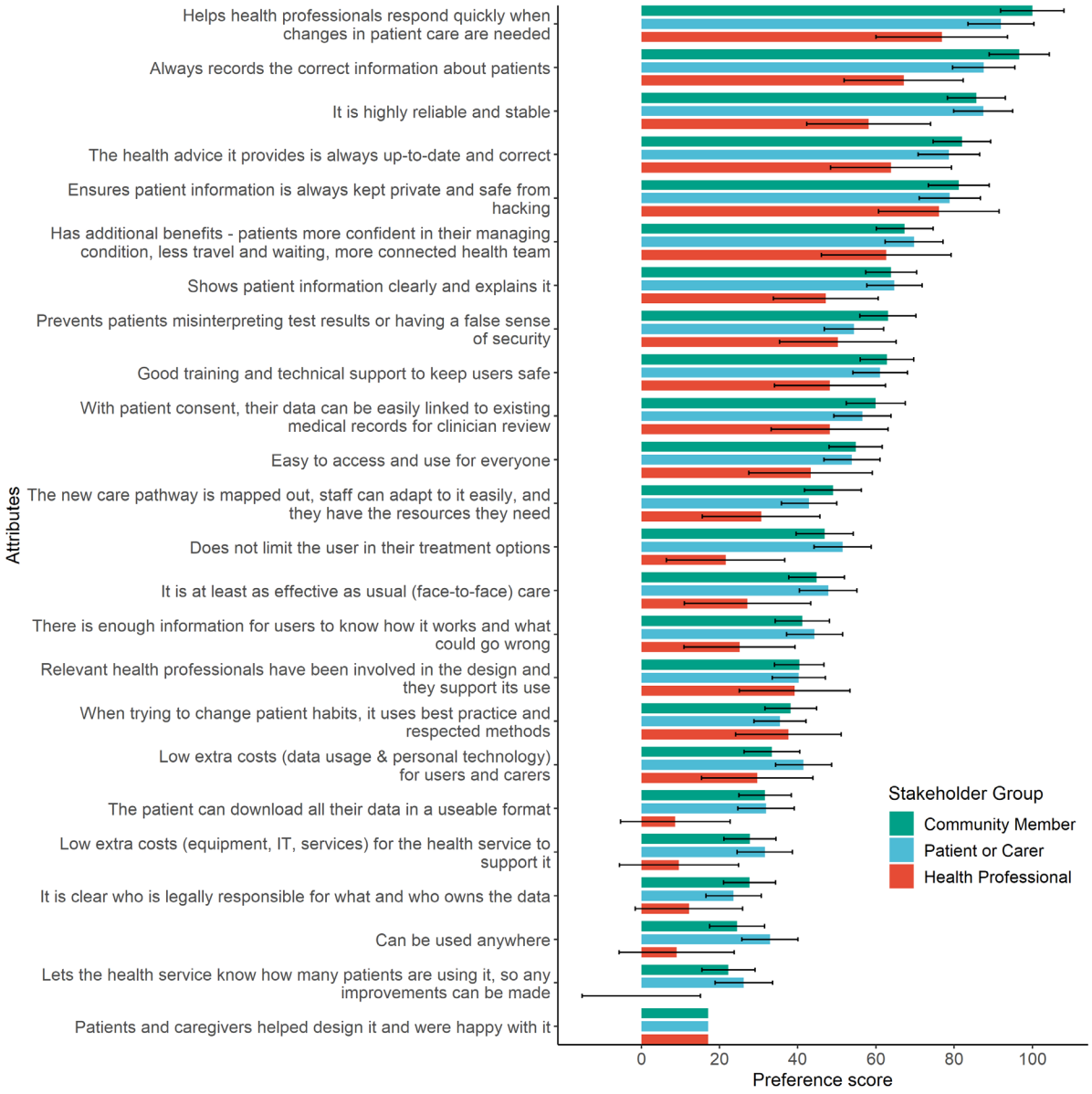

Figure 4.1: Mean preference scores and 95% confidence intervals for DHT attributes from the sequential best-worst multinomial model (SBWMNL) with three stakeholder groups. Preference scores are coefficients scaled from 0 to 100 (least important to most important)

Using our criteria for prioritised attributes, twelve attributes achieved a preference score above fifty in at least one stakeholder group (Table 4.3). The only statistically significant differences in these twelve prioritised attributes (Figure 4.1) are between health professionals and the other stakeholder groups, where health professionals have lower preference scores for the attributes *"It is highly reliable and stable"* and *"Does not limit the user in their treatment options"* than patients/carers and community members.

Table 4.3: Prioritised attributes for consideration in an evaluation of a digital health technology (DHT)

#	Attribute	HTA domain	Highest Preference Score
1	Helps health professionals respond quickly when changes in patient care are needed	SAF	100.0
2	Always records the correct information about patients	TEC/SAF	96.7
3	It is highly reliable and stable	SAF	87.5
4	The health advice it provides is always up-to-date and correct	EFF	82.0
5	Ensures patient information is always kept private and safe from hacking	SAF/ETH	81.2
6	Has additional benefits – patients more confident in their managing condition, less travel and waiting, more connected health team	EFF/ECO	69.8
7	Shows patient information clearly and explains it	TEC	64.7
8	Prevents patients misinterpreting test results or having false sense of security	ETH	63.1
9	Good training and technical support to keep users safe	TEC	62.9
10	With patient consent, their data can be easily linked to existing medical records for clinician review	TEC/SAF	60.0
11	Easy to access and use for everyone	CUR/SAF/ EFF/ETH	54.9
12	Does not limit the user in their treatment options	ETH	51.5

Outside of the twelve prioritised attributes, there were more differences in relative priorities between stakeholder groups. Health professionals prioritised having *"Relevant health professionals involved in design and support its use"* (organisational aspects) and *"When trying to change patient habits, it uses best practice and respected methods"* (clinical effectiveness). In contrast, community members prioritised *"The new care pathway is mapped out, staff can adapt to it easily, and they have the resources they need"* (organisational aspects). Patients /carers preferred *"It is at least as effective as usual (face-to-face) care"* (clinical effectiveness).

The least important attributes of all stakeholder groups were: Reporting actual use to the health service to prompt improvements (current use), having patients and caregivers involved in the design and satisfied with the DHT (clinical effectiveness), being able to use the DHT anywhere (clinical effectiveness, ethical analysis, and social aspects), clarity on who is legally responsible and who owns the data (legal aspects), low additional costs for the health system to support it and patients and carers to use it (current use and costs), and the ability for the patient to download and use their data (technical characteristics).

4.5.3. Latent class analysis

Latent class SBWMNL models with between one to four classes were examined; the model with three classes provided the lowest BIC, with at least sixty-two percent of participants classified in each latent class with a posterior class-membership probability above seventy-five percent. The covariates predictive of class membership were stakeholder group, gender, age, country of residence, speaking a second language at home, employment status, and how often a participant needed to ask for someone's help using personal digital technologies. Rural versus urban location, the highest level of education, access to home or mobile internet, and the frequency of internet use to find health information were not predictive of class membership. Model results for the final model are displayed in Table A 11 and Figure A 5.

Class 1 had similar preference scores across all attributes, showing no clear preferences. Class 2 were characterised by their top concern being the privacy of patient information and were the only group to show a preference for considering legal responsibility and who owns the data. Class 3 most preferred the ability of the DHT to "*help health professionals to respond quickly when changes to patient care are needed*" and preferred a similar top eleven attributes as in the base case MNL model, except for preferring "*It is at least as effective as usual (face-to-face) care*" over patient information privacy and ease of access and use.

Statistically significant differences in socio-demographics between classes existed by gender, age group, how often you needed someone's help when using personal digital technologies, and employment status (Table A 11). Moderate evidence of differences existed by stakeholder group, speaking a second language at home, and country of residence. Class 2 were less likely to be patients or carers than Class 3, OR 0.63 (95% CI 0.41, 0.98). Class 1 were less likely to be female, OR 0.53 (0.33,0.85), and less likely to be in the older age categories (forty to sixty-nine years old OR 0.44 (0.25,0.75); seventy years or older OR 0.16 (0.05,0.46)) than Class 3. Likely related to their younger age, Class 1 were also less likely to

be in part-time/casual employment or retired. Class 1 were also more likely to state they needed someone's help more frequently to use their personal digital technologies OR 5.30 (2.98,9.42) than Class 3 and were more likely to speak a second language at home.

4.6. Discussion

Our results indicate a broad level of agreement amongst stakeholder groups and little heterogeneity from the latent classes regarding the twelve most important attributes (preference score above fifty in at least one stakeholder group) for health services to consider when funding DHTs for patients with chronic disease to use at home (Table 4.3). Six of these attributes were in the safety HTA domain. Above all, the theme of connectedness with a patient's healthcare team seems the most important with "*Helps health professionals respond quickly when changes in patient care are needed"* the most preferred of all attributes, along with *"Has additional benefits – patients more confident in their managing condition, less travel and waiting, more connected health team"* and "*With patient consent, their data can be easily linked to existing medical records for clinician review*" having preference scores above sixty. Our findings are important because attributes such as "*Helps health professionals respond quickly when changes in patient care are needed"* and "*Does not limit the user in their treatment options"* are not a focus of existing HTA frameworks for DHTs. Outside of the top twelve, some attributes were preferred by only one stakeholder group, which may be important to consider if prioritising issues for a particular stakeholder. Relative to other stakeholder groups, community members preferred the health care pathway being mapped out and well-resourced; patients/carers preferred the DHT being at least as effective as face-to-face care, and health professionals preferred relevant health professionals being involved in designing and supporting the use of the DHT, and that behaviour change techniques used by the DHT should represent best practice.

The strength of the survey was the large sample and broad cross-section of stakeholders. Nonetheless, there are limitations to be noted. The smaller sample size for health professionals resulted in larger confidence intervals which lowered our ability to prioritise the least important attributes. Our sample countries may limit the generalisability of our results to some countries, such as low and middle-income countries, but are likely to be generalisable to countries where a HTA approach is used to inform public funding decisions on healthcare. How we framed the scenario with the DHTs approved by the government for efficacy and safety (Figure A 4) may have made participants less concerned about safety. However, six of the twelve prioritised attributes were from the safety HTA domain. Stating that the DHTs had the same price may have made participants not consider additional cost attributes as important, but this was necessary for participants to consider what attributes maximised value for the same price. Stating that studies had found the DHTs to be equally effective may also have made participants deprioritise being equally effective as usual (face-to-face) care. However, this attribute was still rated quite highly in latent class groups. The phrasing of the attributes may have biased responses or misrepresented the issues; however, piloting the survey with feedback and subsequent changes and the large sample sizes should have lessened these risks.

Our objective was to identify the most important attributes to stakeholders to make it practical to consider all the underlying issues for these prioritised attributes, as listed in Table S1, when evaluating a DHT for public funding. Not all issues in this list will always be relevant, but they should be considered. We aimed to develop a practical and focused list of DHT-specific considerations over the nine domains of the EUnetHTA model. We found evidence that this list should prioritise safety domain DHT issues, especially connectedness with clinician and health care records with appropriate privacy controls, along with clinical effectiveness domain issues such as keeping health advice up to date and correct, and the

additional benefits that DHTs can bring for patient self-confidence, less travel and waiting, and a more connected health team. Technical features, such as displaying and explaining patient information clearly, and ethical issues, such as preventing patients from misunderstanding test results or having a false sense of security, were also highly rated.

In prioritising these issues, we may omit consideration of other issues recommended when evaluating DHTs (12), and it must be noted that our cutoff for prioritised attributes at fifty percent is somewhat arbitrary. However, preference score results for all attributes are shown so users can set their own cut-off if needed. Some of these lower priority issues most affect the health services directly, such as additional costs to support DHTs, legal responsibilities, ownership of data, and monitoring patient usage to prompt improvement or replacement of ineffective DHTs. If health service providers had been included as respondents, we may have observed higher preferences for these attributes. However, the survey context was to specifically identify community, patient/carer, and health professional preferences.

As to issues that directly impact the surveyed stakeholders, such as having enough information for users to know how it works and what could go wrong, and patients being able to download and use their own data, we conclude these are not as important and have not been included in the focused list. Surprisingly, being able to use the DHT anywhere, which may affect people in areas of low connectivity, was given a low preference across all groups with no evidence of a higher preference from rural/remote participants. This attribute may be seen as being captured by "Easy to access and use for everyone," which rated higher in all groups.

Given the mounting evidence of the benefits of consumer involvement in health research (23-25), in recent years, we have seen the establishment of consumer councils in healthcare organisations, HTA consumer consultative committees, and research funding agencies requiring evidence of consumer involvement. Therefore, it was unexpected that the attribute

"Patients and caregivers helped design it and were happy with it" was rated so low by community members and patients/carers. This result may reflect the late and slow cultural shift towards involving consumers in healthcare compared to other areas of the economy, particularly digital health (26, 27). Our results should not be taken to suggest that consumer involvement in codesign and HTA is unimportant. On the contrary, our results show that consumers prioritise other attributes over having their say or their needs met. They bring different perspectives on priorities for digital health attributes, enhancing the design and HTA process.

4.7. Conclusion

We observed broad consensus among community members, patients/carers, and health professionals on the most important attributes to be considered by health service providers when funding DHTs for patients with chronic disease to use at home. Twelve primary attributes, mainly in the safety HTA domain and with a priority for connectedness with a patient's healthcare team, were identified as most important by the stakeholder groups. As existing HTA frameworks for DHT currently do not cover all these prioritised issues, we aim to develop a practical list of DHT-specific considerations over the nine domains of the EUnetHTA model.

4.8. References

1. EUnetHTA Joint Action 2 Work Package 8. HTA core model® version 3.0. [Pdf] 2016; Available from: www.htacoremodel.info/BrowseModel.aspx.
2. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Pdf] 2018 [updated 09 August 2022]; Available from: https://www.nice.org.uk/corporate/ecd7. Accessed 15 August 2022.
3. NHS Digital (UK). The digital technology assessment criteria for health and social care (DTAC). [Internet] 2019 [updated 16 April 2021]; Available from: https://transform.england.nhs.uk/key-tools-and-info/digital-technology-assessment-criteria-dtac/. Accessed 18 August 2022.
4. Haverinen J, Keränen N, Falkenbach P, Maijala A, Kolehmainen T, Reponen J. Digi-HTA: Health technology assessment framework for digital healthcare services. *FinJeHeW*. 2019;11(4).
5. Haverinen J, Turpeinen M, Falkenbach P, Reponen J. Implementation of a new Digi-HTA process for digital health technologies in Finland. *Int J Technol Assess Health Care*. 2022;38(1).
6. Drury P, Roth S, Jones T, Stahl M, Medeiros D. Guidance for investing in digital health. Manila (PH): Asian Development Bank (ADB), 2018.
7. Lennon MR, Bouamrane MM, Devlin AM, O'Connor S, O'Donnell C, Chetty U, et al. Readiness for delivering digital health at scale: Lessons from a longitudinal qualitative evaluation of a national digital health innovation program in the United Kingdom. *J Med Internet Res.* 2017;19(2):e42.

8. Rojahn K, Laplante S, Sloand J, Main C, Ibrahim A, Wild J, et al. Remote monitoring of chronic diseases: A landscape assessment of policies in four European countries. *PLoS One.* 2016;11(5):e0155738.

9. Chrzan K, Peitz M. Best-worst scaling with many items. *J Choice Model*. 2019;30:61-72.

10. Finn A, Louviere JJ. Determining the appropriate response to evidence of public concern: The case of food safety. *J Public Policy Mark*. 1992;11(2):12-25.

11. Hess S, Palma D. Apollo version 0.2.4 user manual [Pdf] 2020; Available from: http://www.apollochoicemodelling.com/. Access 27 July 2021.

12. Von Huben A, Howell M, Howard K, Carrello J, Norris S. Health technology assessment for digital technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2021;37(1):e66.

13. Von Huben A, Howell M, Carrello J, Norris S, Wortley S, Ritchie A, et al. Application of a health technology assessment framework to digital health technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2022;38(1):e9.

14. Reed Johnson F, Lancsar E, Marshall D, Kilambi V, Mühlbacher A, Regier DA, et al. Constructing experimental designs for discrete-choice experiments: Report of the ISPOR conjoint analysis experimental design good research practices task force. *Value Health*. 2013;16(1):3-13.

15. Norman CD, Skinner HA. eHEALS: The eHealth literacy scale. *J Med Internet Res*. 2006;8(4):e27.

16. Lancsar E, Louviere J, Donaldson C, Currie G, Burgess L. Best worst discrete choice experiments in health: Methods and an application. *Soc Sci Med*. 2013;76:74-82.

17. R Core Team. R: A language and environment for statistical computing. 4.1.2 ed. Vienna, Austria: R Foundation for Statistical Computing; 2021.

18. Hess S, Palma D. Apollo: A flexible, powerful and customisable freeware package for choice model estimation and application. *J Choice Model*. 2019;32:100170.

19. Proust-Lima C, Séne M, Taylor JMG, Jacqmin-Gadda H. Joint latent class models for longitudinal and time-to-event data: A review. *Stat Methods Med Res*. 2014;23(1):74-90.

20. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: The R package lcmm. *J Stat Softw*. 2017;78(2):1 - 56.

21. Gordon M. Gmisc: Descriptive statistics, transition plots, and more 2022.

22. Xie Y. Knitr: A general-purpose package for dynamic report generation in r. 2021.

23. Bombard Y, Baker GR, Orlando E, Fancott C, Bhatia P, Casalino S, et al. Engaging patients to improve quality of care: A systematic review. *Implement Sci*. 2018;13(1):98.

24. Greenhalgh T, Jackson C, Shaw S, Janamian T. Achieving research impact through co-creation in community-based health services: Literature review and case study. *Milbank Q*. 2016;94(2):392-429.

25. Halvorsrud K, Kucharska J, Adlington K, Rüdell K, Brown Hajdukova E, Nazroo J, et al. Identifying evidence of effectiveness in the co-creation of research: A systematic review and meta-analysis of the international healthcare literature. *J Public Health (Oxf)*. 2021;43(1):197-208.

26. Noorbergen TJ, Adam MTP, Roxburgh M, Teubner T. Co-design in mHealth systems development: Insights from a systematic literature review. *AIS Transactions on Computer-Human Interaction*. 2021;13(2):175-205.

27. Sumner J, Chong Lin S, Bundele A, Wei Lim Y. Co-designing technology for aging in place: A systematic review. *Gerontologist*. 2021;61(7):e395-e409.

Chapter 5 An extended EUnetHTA Core Model checklist for digital health technologies that manage chronic disease

Purpose of this chapter

To develop a DHT-specific checklist for DHTs that manage chronic disease based on the literature and stakeholder priorities to extend an internationally accepted model for HTA, the EUnetHTA Core Model ("the Core Model").

5.1. Abstract

Background: Digital Health Technologies (DHTs) for remote monitoring or self-management of patients with chronic disease are becoming ubiquitous in health service delivery. As for more established health technologies (e.g., pharmaceuticals), these DHTs have a common set of specific issues informed by nearly twenty years of evaluation literature for consideration in a nine-domain Health Technology Assessment (HTA).

Objectives: To develop a DHT-specific checklist for DHTs that manage chronic disease that is based on both the literature and stakeholder priorities to extend an internationally accepted model for HTA, the EUnetHTA Core Model ("the Core Model").

Methods: Identification of DHT-specific content relevant for HTA was performed via systematic review of DHT evaluation frameworks to March 2020, using the Core Model as a scaffold. Content was further refined for duplication, redundancy, and terminology during a systematic review of DHT primary research studies that manage chronic disease between 1 January 2015 to 20 March 2020. Stakeholder prioritisation of the content was performed via a best-worst scaling preference study in 2022 with a large sample of patients, carers, health professionals, and general community stakeholders in Australia, Canada, the United Kingdom, and New Zealand. Prior to the preference study, content items were grouped by issue similarity into non-overlapping attributes of a DHT over several iterations of feedback and a pilot best-worst scaling survey. An arbitrary threshold of a preference score over 50% in at least one stakeholder group was set to identify "prioritised" attributes for a more practical list of content for a DHT-specific HTA. The content relating to the prioritised DHT attributes was grouped by Core Model (or new DHT-specific) issue ID into a checklist of DHT-specific "clarifications" to extend the Core Model.

Results: The DHT framework authors recommended 71 DHT evaluation content items covering 50 issues (28 Core Model issues and 22 DHT-specific issues). Content items could be grouped into twenty-four attributes of a DHT that represented issues to be considered for the public funding of a DHT that manages chronic disease. Twelve attributes met the predefined threshold for "prioritisation" in the stakeholder preference study. The twelve prioritised attributes mapped to content items in 16 Core Model issues and 6 DHT-specific issues. The "extended checklist" thus comprised 22 DHT-specific clarifications reported by Core Model or new DHT-specific issue ID and issue, along with literature references and the issue IDs with similar themes in other HTA domains. To assist with the standardisation of assessment and reporting, recommendations on *evidence data sources* (from peer-reviewed and grey literature*), suggested methods, tools and measures*, and *evidence types* (i.e., narrative, or comparative) were provided by checklist item.

Conclusions: Evaluators and authors of HTA reports can use this "extended checklist" for DHTs that manage chronic disease in conjunction with the Core Model to perform a comprehensive and DHT-specific HTA that is informed by DHT evaluation literature and stakeholder priorities.

5.2. Introduction

Digital Health Technologies (DHTs) for remote (e.g., home) active monitoring or self-management of chronic disease are becoming a ubiquitous component of the delivery of healthcare services. Nearly twenty years of peer-reviewed literature on DHT evaluation frameworks have identified common considerations for evaluating these technologies (1-5). As for more established health technologies (e.g., pharmaceuticals), DHTs that manage chronic disease have a common set of specific issues to be considered in a nine-domain Health Technology Assessment (HTA).

EUnetHTA's HTA Core Model version 3.0 ("the Core Model") (6) is used across many countries to assess a wide range of health technologies. Technology-specific content in this model is available for *medical and surgical interventions*, *diagnostics*, *pharmaceuticals*, and *screening technologies* but not for DHTs. Although issues common to all technologies in the Core Model are quite comprehensive, three stages of research (detailed in Section 5.3) have identified a literature-informed and stakeholder-prioritised set of content for DHTs which, when combined with the Core Model, enables a comprehensive and DHT-specific HTA for DHTs that manage chronic disease. The purpose of this Chapter is to present this DHT-specific HTA content in one practical checklist (the "extended checklist") that extends the Core Model.

The extended checklist is designed to be used with the Core Model when the subject of the HTA is a DHT for the remote active monitoring or self-management of chronic disease. Envisaged users are evaluators and authors of HTA reports when performing HTA for public funding decisions. In addition, it is designed to be used by developers and researchers of such DHTs in the design of the DHT and the planning and reporting of primary research. It is further envisaged that HTA agencies could incorporate the content of the extended checklist

when updating technical guidelines, noting incorporation of DHT-specific content in HTA guidelines has been limited to date (7-10).

5.3. Approach

Methods for the three stages of research are reported elsewhere (11-13). Briefly, the first stage involved identifying content for a DHT-specific HTA via a systematic review of international peer-reviewed and grey literature on DHT evaluation frameworks to March 2020 (12). The most frequently recommended DHT evaluation content from the included frameworks was mapped to the Core Model by domain, topic, and issue ID to produce content lists for a DHT-specific HTA ("the content lists") (12). The framework authors recommended DHT evaluation content in 28 of the 145 Core Model issues. However, they also recommended a further 22 DHT-specific issues not covered in the Core Model; ten in safety and nine in clinical effectiveness. Seventy-one content items covering the fifty issues were identified and split into two content lists: 1. DHT-specific content (covering forty-one issues), and 2. Content common to all technologies but essential for DHTs (covering nine issues).

In the second stage, the question sets of the seventy-one content items were tested for duplication, redundancy, and appropriate terminology via a systematic review and coverage analysis of 112 peer-reviewed primary research studies on DHTs for managing cardiovascular disease and diabetes from 1 January 2015 to 20 March 2020 (11). Refinements were made to the question sets of the content items for duplication and terminology, but the number of content items and equal weighting of issues were not efficient for regular use. A prioritisation of the content items was required.

In the third stage, prioritisation of the content items was performed via a best-worst scaling (BWS) preference study with stakeholders (patients, carers, health professionals and the

general community) in Australia, Canada, the United Kingdom, and New Zealand in early 2022 (13). Prior to the preference study, the content items were grouped by issue similarity into 24 non-overlapping attributes of a DHT over several iterations of feedback and a pilot best-worst scaling survey. Stakeholders were asked which DHT attributes were the most and least important to consider in the public funding of DHTs that manage chronic disease. Each stakeholder was randomised to one of eight 12-question choice sets of three attributes. An arbitrary threshold of a preference score over 50% in at least one stakeholder group was set to identify "prioritised" attributes for a practical list of DHT content for HTA. Final study results were analysed with multinomial models by stakeholder group and by latent class to investigate the heterogeneity of preferences that may not be captured in the stakeholder model.

In the final best-worst scaling survey of 1,251 stakeholders (576 community members, 543 patients/carers, and 132 health professionals), twelve DHT attributes achieved the predefined threshold for a "prioritised" attribute. These attributes predominantly related to safety but also technical features, effectiveness, ethics, and economics. Results from the latent class model supported this prioritisation. Overall, connectedness with the patient's healthcare team seemed the most important, with *"Helps health professionals respond quickly when changes in patient care are needed"* as the most highly prioritised of all attributes.

The twelve "prioritised" DHT attributes were mapped back to their constituent content items. The content items were then grouped by Core Model (or new DHT-specific) issue ID. The mapping of the prioritised attributes, in order of priority, to issue IDs is shown in Table 5.1. The prioritised content items related to sixteen Core Model issues and six new DHT-specific issues (shaded in grey). This resulted in a set of 22 issues containing the prioritised content items and their corresponding questions., i.e., an extended checklist of 22 DHT-specific clarifications.

Table 5.1: Prioritised attributes for consideration in an evaluation of digital health technologies (DHTs) that manage chronic disease

No.	Prioritised DHT attribute	Domain[a]	Topic *(EUN)*[a]/*(NEW)*[b]	Issue ID[a c]
1	Helps health professionals respond quickly when changes in patient care are needed	SAF	Risk Management *(EUN)*	C0062
		ETH	Benefit-harm balance *(EUN)*	F0011
2	Always records the correct information about patients	TEC	Features of Technology (*EUN*)	DHT01
		SAF	Quality & safeguarding (*NEW*)	DHT03
3	It is highly reliable and stable	SAF	Technical safety (Reliability & stability) (*NEW*)	DHT08
4	The health advice it provides is always up-to-date and correct	EFF	Reliable information content *(NEW)*	DHT16
5	Ensures patient information is always kept private and safe from hacking	SAF	Quality & safeguarding (*NEW*)	DHT02
		ETH	Benefit-harm balance (*EUN*), Respect for persons (*EUN*)	F0003, F0101
		LEG	Privacy of the patient (EUN)	I0007, I0009
6	Has additional benefits – patients more confident in their managing condition, less travel and waiting, more connected health team	ECO	Measurement & estimation of outcomes (*EUN*)	E0005
		ETH	Benefit-harm balance (*EUN*)	F0011
7	Shows patient information clearly and explains it	TEC	Features of Technology (*EUN*)	DHT01
8	Prevents patients misinterpreting test results or having false sense of security	ETH	Benefit-harm balance (*EUN*)	F0003
9	Good training and technical support to keep users safe	TEC	Training & information needed to use the technology (*EUN*)	B0013, B0014
10	With patient consent, their data can be easily linked to existing medical records for clinician review	TEC	Features of Technology (*EUN*)	DHT01
11	Easy to access and use for everyone	CUR	How much are the technologies utilised? (EUN), What kind of variations in use are there across countries/regions/ settings? (EUN)	A0011, A0012
		SAF	Quality & safeguarding (*NEW*)	DHT05
		EFF	Patient satisfaction (*EUN)*	D0017
		ETH	Justice & Equity (*EUN*)	H0012
		SOC	Social group aspects (*EUN*)	H0201
12	Does not limit the user in their treatment options	ETH	Autonomy (*EUN*)	F0004, F0005

[a]HTA Domain = Health Technology Assessment (HTA) Domains of the EUNetHTA HTA Core Model version 3.0 (6):

CUR: Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status
TEC: Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it
SAF: Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers
EFF: Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting
ECO: Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value for money judgments
ETH: Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA
ORG: Identifies resources to be mobilised or organised to implement the new technology and the consequences (Intra/inter-organisational and health system)
SOC: Considers issues related to the new technology relevant to patients, carers, and social groups
LEG: Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

[b]New topic

[c]DHT prefixes denote new issues (i.e., *DHTXX*)

Key

New topic or issue

Note that the six new DHT-specific issues relate to three new topics not in the Core Model (shaded in grey in Table 5.1). For practicality, we reviewed these new topics and, wherever possible, included them in existing Core Model topics with similar themes. As a result, the new topic of communicating for safety was moved into the risk management topic in the safety domain. However, three new topics had themes additional to the existing topics in the appropriate domain and were retained as separate topics. For example, *quality and safeguarding* (privacy/security, data quality, ease of use/accessibility) is critical to the safe operation of DHTs but is not captured by any existing safety topics. Although *privacy of the patient* is partially covered in the ethical analysis and legal aspects domains, it is not covered in any safety issues.

5.4. Scope and use

We have designed the DHT-specific content to extend the Core Model. This model promotes and supports consideration of technology-specific questions over a nine-domain HTA in three ways. The first way is by providing an explicit definition of the technology and any limitations in scope when using the content of the Core Model for an HTA. This definition is critical to guide the user in identifying whether the content in the model is relevant and comprehensive enough to use for a particular HTA. Suggested wording for the definition and limitation of content provided for DHTs that manage chronic disease is:

Digital Health Technologies (DHTs) for which the content of this model is suitable are those which, when used alone or in conjunction with other medical technologies or human interventions, have the intention to provide measurable health benefits for patients with diagnosed non-communicable chronic disease through remote (e.g., home) active monitoring and/or self-management.

The second way is in the introductory description for each HTA domain, where, if applicable, a brief description of the specific technology's differences compared to other technologies in the context of the domain is provided. The most critical issues in the domain for the specific technology are highlighted. Suggested wording for chronic disease management digital health technology (DHT)-specific content by HTA domain to extend the HTA domain introduction sections of the Core Model is listed in Table A 12.

The third and most detailed way is in the technology-specific "clarification" within each issue of a domain, when applicable. The extended checklist is a list of the 22 issues with DHT-specific clarifications for use with the Core Model (Table 5.2). The checklist consists of an item number, the Core Model or DHT-specific issue ID and issue, the DHT-specific clarification for the issue, the reference papers from which the clarifications came ("Refs"), and issue IDs with similar themes in other HTA domains ("Content relations"). To assist with standardisation of assessment and reporting, recommendations on *evidence data sources* (from peer-reviewed and grey literature*), suggested methods, tools and measures*, and *evidence types* (i.e., narrative or comparative), are provided by checklist item.

All but three topics in the extended checklist are existing Core Model topics. The three new topics are 1) *Quality & Safeguarding* and 2) *Technical safety (reliability & stability)* in the Safety (SAF) domain, and 3) *Reliable information content* in the Clinical Effectiveness (EFF) domain. These three new topics introduce five new issues denoted by issue identifiers with the prefix "DHT". In addition, one new issue sits within the existing topic of *features of the technology*.

Table 5.2: Extended EUnetHTA Core Model version 3.0a checklist for digital health technologies (DHTs) that manage chronic disease

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Domain 1: Health problem and current use of technology (CUR)[a]								
Topic: Utilisation (EUN)								
1	A0011: How much are the technologies utilised?	***Is it available for everyone?*** When estimating future utilisation rates for the technology, consider what may limit or improve usage over comparators in terms of DHT-specific design aspects: e.g., requirements for platforms and operating systems, network connectivity, technical skills, cost of personal digital technologies and data usage, and available languages.	(8, 14)	DHT05, D0017	CONSORT-EHEALTH 1b) 4a),5vii), viii),6aii), 15i),16i) Functional description of technology, Trial data usage by digital divide issues (e.g., age, socioeconomic status, eHealth literary measured by eHEALS (15))	National statistics, surveys, utilisation studies, manufacturer sales data, Market prices (6)	From effectiveness trials: • DHT functional description • Implicit eligibility criteria (computer/internet literacy, have mobile phone) • DHT usage by digital divide issues Part 2c, Functional suitability assessment, WHO, M&E DHT practical guide (16) Other suggested measures: % monthly income for rental of personal digital technology and data usage fees % population owning the required technology % population with internet access	Narrative
2	A0012: What kind of variations in use are there across countries/regions / settings?	***Is it available for everyone?*** Is the technology being used in settings where telecommunication infrastructure is poor or there is low network connectivity?	(3, 17, 18)	DHT19, H0012, H0201	CONSORT-EHEALTH: 21i), ii) Generalisability	National statistics, surveys, utilisation studies, manufacturer sales data (6)	From effectiveness trials: • Testing of DHT in these settings • Actual use/adherence to DHT in these areas Part 2c, Functional suitability assessment Technology adaptation to the local context, WHO, M&E DHT practical guide (16) Other suggested measures: • Number of hours population in these areas has access to internet	Narrative
Domain 2: Description and technical characteristics of technology (TEC)[a]								
Topic: Training & information needed to use the technology (EUN)								
3	B0013: What kinds of skills and training characteristics and information are needed for the personnel/ caregivers using this technology?	***Is there training and technical support to keep personnel/caregivers safe?*** Do personnel/caregivers need training for digital skills, personal data handling, and cyber-safety along with 24-hour technical support to ensure efficacy and safety of the technology. Describe what training and support is provided and estimate whether it meets identified requirements.	(4, 14, 19, 20)	C0020, C0062, C0063	CONSORT-EHEALTH: 5x) Clarify the level of human involvement (care providers or health professionals, also technical assistance)	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions	Safety by design principles (21) Guide to Data Protection (22)	Narrative

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
4	B0014: What kind of training resources and information should be provided to the patient who uses the technology, or for his family?	***Is there training and technical support to keep patient and family safe?*** Do patients and their family need training for digital skills, digital health literacy, and cyber-safety along with 24-hour technical support to ensure efficacy and safety of the technology? Describe what training and support is provided and estimate whether it meets identified requirements.	(4, 14, 19, 20)	C0062	CONSORT-EHEALTH 5xii) Describe any co-interventions (incl. training/support) Distinguish trial from routine application X29) Describe any education or training to reduce likelihood of harm	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions	Safety by design principles (21) Guide to Data Protection (22)	Narrative
Topic: Features of Technology (EUN)								
5	DHT01: How well is the technology designed to overcome technical barriers in relation to comparator(s); e.g., interoperability, visualisation, feedback	***With patient consent, can their data be easily linked to existing medical records for clinician review?*** Provide information on the technology's level of interoperability in relation to comparators, i.e., can the DHT be easily integrated with multiple information systems using the relevant patient/provider identifiers and standard terminologies, and does it use standardised access and extraction mechanisms?	(19, 23-27)	DHT03	Design studies	• Requirements, software, and data specification documents. • Data dictionary. • Data flow diagrams. • Report on compliance with interoperability standards in jurisdiction.	ISO 11073 for personal health data Interoperability standards for jurisdiction, e.g., NHS England Digital Technology Assessment Criteria (DTAC) – interoperability (26)	Narrative or comparative to other DHTs being considered
		Does the technology show patient information clearly and explain it well to: • ***Personnel/caregivers?*** • ***Patient/family?*** Provide information on the technology's presentation of patient information. Is it easy to access and understand? Comment on DHT-specific features such as data visualisations and feedback mechanisms and how they may affect the efficacy and safety of the technology.			CONSORT-EHEALTH 5ii) Describe the history/ development process of the application and previous formative evaluations (e.g., focus groups, usability testing)	Surveys of patient, family, and healthcare professionals	Part 2c, Useability assessment, WHO, M&E DHT practical guide (16) System Usability Scale (SUS) (28) IEC 62366-1:2015, Medical devices — Part 1: Application of usability engineering to medical devices MHRA Guidance: Medical device stand-alone software including apps, Medical device essential requirements– general item 1 (29)	Narrative or comparative to other DHTs being considered

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Domain 3: Safety (SAF)[a]								
Topic: Quality & safeguarding (*NEW*)								
6	DHT02: How well does the technology manage data security and privacy?	***Is patient information always kept private and safe from hacking?*** Does it comply with General Data Protection Regulation (GDPR) principles of data minimisation/protection by default/design, and data protection legislation/binding rules? Does it allow users to manage access to their data? Does it employ authentication, encryption, and threat analysis to avoid unauthorised access to personal data? Is there safeguarding around peer-to-peer and other communications within the DHT?	(8, 19, 23, 25-27, 30, 31)	I0009, F0003, F0101,	NA	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions • Compliance reports • Data audit reports • Privacy policy	Digi-HTA: information security and data protection requirements (32) NHS England Digital Technology Assessment Criteria (DTAC) – data protection (26) Guide to Data Protection (22)	Narrative
7	DHT03: How well does the technology manage data quality?	***Does the technology always record the correct information about a patient?*** Identify whether the DHT has processes to support the creation and maintenance of accurate healthcare records. Can it identify users correctly without human intervention? Is there evidence that uploading or downloading of patient information is correct on a consistent basis?	(19, 23, 25-27, 33)	DHT01	NA	• Requirements, software, data specification documents • Data flow diagram with controls • Data control testing reports	Part 3b, Tools for monitoring, WHO, M&E DHT practical guide (16) UK NICE Evidence Standards Framework for DHTs Standard 6 (8) MHRA guiding principles on good machine learning practice for medical device development (34)	Narrative
8	DHT05: Is the technology designed for usability and accessibility for safety?	***Is it designed to be easy to access and use for everyone?*** Is the DHT designed to minimise the barriers associated with hardware, software, data requirements, and platform services, or the language/location, age, culture, and ability of users?	(23, 26, 33)	A0011, D0017	CONSORT-EHEALTH 5ii) Describe the history/ development process of the application and previous formative evaluations (e.g., focus groups, usability testing),	Reports on compliance with useability and accessibility standards	Part 2c, Useability assessment, WHO, M&E DHT practical guide (16) NHS England Digital Technology Assessment Criteria (DTAC) – useability and accessibility (26) (e.g., Web Content Accessibility Guidelines, ISO 9241-210:2010 Ergonomics of human-system interaction — Part 210: Human-centred design for interactive systems, accessibility features) Human-centred design (HCD) (35)	Narrative

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Topic: Technical safety (Reliability & stability) (*NEW*)								
9	DHT08: Is the technology reliable and stable?	***Is the technology reliable and stable?*** Is there evidence of accurate and reliable transmission of unbiased data? Does the DHT alert the user when working suboptimally or experiencing interference, e.g., low or no network connectivity? Does it perform well outside the laboratory? Is it validated for use on multiple platforms? Is it resilient to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions? Is there evidence that operating system updates and patches, service continuity, backup, and recovery mechanisms are well managed?	(3, 4, 8, 9, 23, 26, 27, 31, 36, 37)	None	Design and feasibility studies	• Design documentation • Stability and reliability testing reports	Part 3c: Digital health process monitoring components, WHO, M&E DHT practical guide (16), Functionality, Stability, Fidelity, Quality IEC 62366-1:2015, Medical devices — Part 1: Application of usability engineering to medical devices NHS England Digital Technology Assessment Criteria (DTAC) – Technical Stability (26) MHRA Guidance: Medical device stand-alone software including apps - Medical device essential requirements – General & Design and construction (29)	Narrative
Topic: Risk Management (EUN)								
10	C0062: How can one reduce safety risks for patients (including technology, user-, and patient-dependent aspects)?	***Does the technology help health professionals respond quickly when changes in patient care are needed?*** Provide information on the defined parameters programmed within the technology to identify and respond to a patient's acute deterioration. How are they set, maintained, and changed? Does the DHT allow the user to communicate to their healthcare team critical information about changes in their condition or information on risks of using the DHT? Is there a contact mechanism for technical support with a fixed response time? Are there processes within the DHT to communicate changes to or transfer of a patient's care?	(23, 33)	None	CONSORT- EHEALTH viii) Describe mode of delivery, features/ functionalities/ components of the intervention and comparator This also includes a description of communication delivery channels and – if computer-mediated communication is a component – whether communication was synchronous or asynchronous	• Design specification • Technical manual • User instruction manual • Procedures manuals for technical support • Compliant registers • Adverse events reporting	ISO 14971 application of risk management to medical devices MHRA Guidance: Medical device stand-alone software including apps - Medical device essential requirements – General & Design and construction (29) National Safety and Quality Digital Mental Health Standards (NSQDMH) by the Australian Commission on Safety and Quality in Health Care (ACSQHC) (23)	Comparative to usual care

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Domain 4: Clinical Effectiveness (EFF)[a]								
Topic: Patient Satisfaction (EUN)								
11	D0017: Were patients satisfied with the technology?	***Is it easy to use for everyone?*** Is there evidence that the DHT is usable for a diverse range of users, including those with disabilities or limited ability with digital technology or digital health literacy? Are there obvious design issues hindering usability, e.g., washable, durable, cause skin allergies?	(3, 17, 20, 24, 26, 27, 31, 38)	A0011, DHT05	CONSORT-EHEALTH Eligibility 4a)i), Use metrics 1b)iv), 6aii) 5ii) Useability testing studies Qualitative feedback on use 6a)iii), 19ii)	Compliant registers	Part 2c, Useability assessment, WHO, M&E DHT practical guide (16) System Usability Scale (SUS) (28) IEC 62366-1:2015 + A1:2020, Medical devices — Part 1: Application of usability engineering to medical devices IEC 62366-2:2016 Guidance on the application of usability to engineering to medical devices	Comparative to usual care
Topic: Reliable information content (*NEW*)								
12	DHT16: Does the technology always provide up-to-date and correct health advice?	***Is the health advice it provides always up-to-date, and correct?*** Evaluate whether the health advice provided by DHT is accurate, valid, up to date, comprehensive, clear, and tailored to the users' diversity. Provide evidence of an ongoing quality assurance process to maintain this accurate and up-to-date health advice.	(3, 4, 8, 9, 18, 23, 27, 31, 33)	None	CONSORT-EHEALTH 5iv) Provide information on quality assurance methods to ensure accuracy and quality of information provided	Quality assurance procedures Quality assurance monitoring reports	ISO 13485:2016 Medical devices — Quality management systems — Requirements for regulatory purposes IEC 82304-1 for safety and security for health software	Narrative
Domain 5: Costs and economic evaluation (ECO)[a]								
Topic: Measurement & estimation of outcomes (*EUN*)								
13	E0005: What is (are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s)?	***Have DHT-specific benefits been considered?*** Provide information on DHT-specific outcomes such as improved access to health information and services, reduced waiting time, less burdensome travels, a feeling of security, transfer of skills, better-managed care through self-management and digitally connected healthcare professionals.	(3, 19, 39)	F0011, H0201	User acceptability testing Qualitative analysis RCT measurement of self-efficacy for managing chronic disease outcomes	Time observation studies, surveys, travel logs, google maps	Part 2c, Process improvement, WHO, M&E DHT practical guide (16), client/provider/health system level indicators of efficiency, quality, utilisation, costs Societal perspective economic evaluation methods (e.g., Impact inventory) (5) Patient-Reported Inventory of Self-Management of Chronic Conditions (PRISM-CC) measurement tool(40) Measuring connections to healthcare professionals, Working alliance inventory (41)	Comparative to usual care

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Domain 6: Ethical analysis (ETH)[a]								
Topic: Benefit-harm balance (EUN)								
14	F0003: Are there any other hidden or unintended consequences of the technology and its applications for patients/users, relatives, other patients, organisations, commercial entities, society etc.?	***Is patient information always kept private and safe from hacking and tracking?*** Describe how the technology's data collection and communications may affect the patient's safety and welfare. Where are alerts about a patient's health reported? Is real-time data securely transmitted? Have there been any perceived or real privacy breaches, technical problems, unexpected/unintended incidents created by the technology? Consider tracking from other software on the platform/device, or operating system and malicious software (e.g., ransom ware, viruses, malware, etc.)	(18, 42)	DHT02, I0009	CONSORT-EHEALTH 19i) Report incidents such as perceived or real privacy breaches as harms	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions	eSafety resources for investors(21): (https://www.esafety.gov.au/industry/safety-by-design/investors) • Safety by Design principles • Investment checklist • Safety by Design Model clauses for due diligence • Assessment tool: Start-ups/enterprise NHS England Digital Technology Assessment Criteria (DTAC) – data protection (26)	Narrative or comparative to usual care
		What prevents patients misinterpreting test results or having a false sense of security? Estimate the likelihood and severity of harm from patients having access to the data from the technology without assistance to help them interpret what it means, or a false sense of security that the data collected by the DHT is being monitored by a clinician. Describe the controls in place to minimise these risks.			User acceptability testing	Literature search. Expert opinion. Stakeholder hearing (6)	Risk and controls assessment	
15	F0011: What are the benefits and harms of the technology for relatives, other patients, society, etc.?	***Does the technology help health professionals respond quickly when changes in patient care are needed?*** Explain how the DHT preserves and enhances direct contact between patients and healthcare professionals while supporting them to manage their health.	(43)	E0005	CONSORT-EHEALTH 19ii) Include qualitative feedback from participants or observations from staff/researchers, if available, on strengths and shortcomings of the application	Surveys of patient, family, and healthcare professional	Qualitative research with patients and health care professionals	Narrative or comparative to usual care

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Topic: Autonomy (EUN)								
16	F0004: Does the implementation or use of the technology affect the patient´s capability and possibility to exercise autonomy?	***Does the technology limit the user in their treatment options?*** Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT? For DHTs targeting behaviour change, what controls limit the DHT influencing behaviour for purposes other than those stated, e.g., commercial?	(44)	None	CONSORT-EHEALTH 4bii) Report how institutional affiliations are displayed 5i) Mention names, credential, affiliations of the developers, sponsors, and owners. X27 state if the authors/evaluators are distinct from or identical with the developers/ sponsors of the intervention 5viii) Describe theoretical framework for design in accepted terminologies (45, 46)	Any documentation relating to the DHT Information displayed with DHT Treatment guidelines for condition	Assess treatments available in DHT against treatment guidelines For behaviour change DHTs, check theoretical framework is best practice (8) Assessment of autonomy – independence, authenticity, and options (44)	Narrative or comparative to usual care
17	F0005: Is the technology used for individuals that are especially vulnerable?	***Does the technology limit the user in their treatment options?*** Estimate the likelihood that the technology may influence a person's behaviour for commercial purposes when they are most vulnerable, i.e., consider the degree to which the DHT has access to a large amount of personal data, behavioural-economic insights, algorithmic predictive analyses, and can communicate with the patient continuously. Describe the controls in place to minimise this risk. For example, does the DHT use simple and understandable language? Does it provide concise information on how health information was chosen, who is responsible for the content, and information on potential conflicts of interest (funding, promotion)?	(27, 44)	None	CONSORT-EHEALTH 5viii) Detail the content including where it is coming from and who developed it and whether and how it is tailored to individuals	Any documentation relating to the DHT and information displayed with DHT	Risk assessment and assessment of adequacy of controls	Narrative

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Topic: Respect for persons (EUN)								
18	F0101: Does the technology invade the sphere of privacy of the patient/user?	***Is patient information always kept private and safe from hacking and tracking?*** Does the DHT clearly identify who holds any personal data? Is the supplier's cookie policy stated and clear? Is only data necessary for a particular treatment shared with the doctor, and then only after explicit consent that the patient can revoke? Can patients opt-out if they are not able or unwilling to manage their data? Does the DHT provider have privacy policies that are easy to understand, uphold users' rights and choices, and are readily available to users before and while using the DHT, compliant with privacy laws, privacy principles, and best practices? Are changes to privacy policies communicated to users in a timely way? Is the DHT regularly audited for transmissions with third parties that include linkable identifiers and is the user informed of this risk?	(19, 23, 27, 30)	DHT02, I0007	CONSORT-EHEALTH X26 iii) Safety and security procedures, incl. privacy considerations, and "any steps taken to reduce the likelihood or detection of harm (e.g., education and training, availability of a hotline)"	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions	The data ethics canvas (47) Audit of actual data transmissions to third parties	Narrative
Topic: Justice & Equity (*EUN*)								
19	H0012: Are there factors that could prevent a group or person from gaining access to the technology?	***Is it easy to access for everyone?*** Is there evidence that the DHT is accessible for a diverse range of users, including those with a lack of economic resources, disability, limited ability with digital technology, or limited digital health literacy? Is the DHT compatible with common assistive technologies, meet relevant web page or web application standards, and available in a wide number of languages and platforms?	(4, 8, 23, 25)	A0011, DHT05, D0017	CONSORT-EHEALTH 15i) report digital divide issues, such as age, education, gender, social-economic status, computer/Internet/ehealth literacy of the participants, if known.	User surveys Reports on compliance with accessibility standards/guidelines	NHS Digital's guide on digital inclusion for health and social care (48) Web Content Accessibility Guidelines (49)	Narrative or comparative to usual care
Domain 8: Patient and social aspects (SOC)[a]								
Topic: Social group aspects (*EUN*)								
20	H0201: Are there groups of patients who currently do not have good access to available therapies?	***Is it easy to access for everyone?*** Does the technology improve access for those on lower incomes, disabled, elderly, neurodiverse, indigenous populations, ethnic minorities,or rural and remote patients? Is there evidence of the DHT being used, or being designed to be used in hard-to-reach populations?	(8, 20, 23)	A0012, DHT19	NA	Surveys on patient groups, national statistics, Manufacturer sales	NHS Digital's guide on digital inclusion for health and social care (48)	Narrative or comparative to usual care

Item No	Issue ID[a] [c]: Issue	Clarification[*] for Digital Health Technologies	Refs	Content relations[**]	Evidence data sources		Suggested methods, tools, and measures	Evidence types
					Peer reviewed literature	Grey literature		
Domain 9: Legal aspects (LEG)								
Topic: Privacy of the patient (EUN)								
21	I0007: Is there a possibility that the use of the technology produces additional information that is not directly related to the current care of the patient and may violate their right to respect for privacy?	***Is patient information always kept private and safe from hacking and tracking?*** This possibility exists with almost all DHTs – refer to the content listed in F0101, DHT02, and F0003 for consideration. Consider General Data Protection Regulation (GDPR) principles (e.g., data minimisation and purpose limitation). Has a data protection by design and default approach been used? Has a data protection impact assessment been completed?	(27, 31)	F0101, DHT02, F0003	Design study	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions Data impact assessment report	Data protection self-assessment toolkit (22)	Narrative
22	I0009: What do laws/binding rules require with regards to appropriate measures for securing patient data and how should this be addressed when implementing the technology?	***Is patient information always kept private and safe from hacking and tracking?*** Review General Data Protection Regulation (GDPR) principles and data protection legislation/standards and provide evidence of compliance. Does the manufacturers cyber-insurance policy cover privacy breaches and privacy law violations?	(27, 31)	DHT02	NA	Websites of: • online safety regulator • information commissioners/data protection regulator in the relevant jurisdictions Reports on compliance with data protection legislation/standards of jurisdiction Cyber-insurance policy terms and conditions	Compliance with GDPR principles (22) data protection legislation/standards of jurisdiction Check manufacturer's insurance covers privacy breaches and privacy law violations	Narrative

[a]From EUnetHTA HTA Core Model version 3.0 (6).
[b]New topic
[c]DHT prefixes denote new issues (i.e., *DHTXX*)
[*]Clarification = A more detailed description of what the issue addresses (6)
[**]Content relations = A list of Issue IDs that deal with similar themes as this Issue ID (6)
GDPR = General Data Protection Regulation (22)

5.5. Discussion

We anticipate this checklist will be useful to all who need to plan, author, or evaluate HTA reports on DHTs, authors of HTA guidelines, health service providers evaluating DHTs, and developers and researchers of DHTs.

The strengths of this checklist are that it has been objectively informed by a systematic review of international peer-reviewed and grey literature covering nearly twenty years of DHT evaluation frameworks, it has been tested and refined through a content coverage assessment of a 112 DHT primary research studies, and the issues have been prioritised by a robust best-worst scaling survey conducted in a large sample (1,251) of patients, carers, health professionals and general community stakeholders from four countries. An additional strength is its practicality, having been designed as an extension to the Core Model. It uses the existing model ontology, making it easy to use for those familiar with the Core Model. Even for those less familiar, the use of internationally accepted HTA terminology as defined by the Core Model makes for simple application. References for all peer-reviewed and grey literature that suggested elements of the content are provided for traceability. In addition, the three development papers (11-13) and their supplementary materials provide transparency of the development process.

To identify the largest number of DHT-specific issues, our systematic reviews focused on DHTs that require the highest level of evidence under the UK NICE functional classification (Tier C) (8) and are classified as Medical Device Software (MDSW) under the European Union (EU) Medical Devices Regulation (MDR) (50). There was potential for overidentifying issues by concentrating on DHTs with a higher risk profile. However, prioritisation via a best-worst scaling preference survey with stakeholders reduced the DHT-specific content to a manageable number of considerations.

Whilst priorities and preferences are based on a large and diverse stakeholder sample, as discussed in the preference study (13), one limitation of the current extended checklist is that further work is needed to incorporate the preferences of policy and decision-makers. This could be achieved by undertaking a similar preference study involving these stakeholders, who may have different priorities around issues such as equity of access, cost, and system-level implementation considerations, e.g., additional cost to support DHTs, legal responsibilities, ownership of data, monitoring patient usage to prompt improvement or replacement of ineffective DHTs. This additional work would enable a wider range of stakeholders' views to be incorporated into the extended checklist.

In addition, some further testing and streamlining of the extended checklist over the many DHTs that manage chronic disease in different jurisdictions and HTA settings would be valuable. The checklist items are designed to be sufficiently generic to be relevant for all DHTs that manage chronic disease and all jurisdictions that use HTA to inform public funding decisions, but this needs to be tested across different case studies. Ideally, the checklist could be extended to other classes of DHTs representative of those most likely to undergo HTA for public funding. For example, DHTs that assist health professionals in diagnosis and decision-making, e.g., clinical decision support systems.

Once the extended checklist is published, uptake will be monitored through prospective review of citations in peer-reviewed and grey literature. Regular review of checklist content would be required to capture identified changes in practice and ways in which it could be improved.

5.6. Conclusion

This chapter has presented an extended EUnetHTA Core Model checklist for DHTs that manage chronic disease. The extended checklist comprises 22 DHT-specific clarifications

that extend the Core Model ontology. Use of the extended checklist with the Core Model allows for a DHT-specific comprehensive and HTA on DHTs that manage chronic disease that is informed by almost twenty years of DHT evaluation literature and underpinned by the preferences and priorities of key stakeholders.

5.7. References

1. Hailey D, Ohinmaa A, Roine R. Study quality and evidence of benefit in recent assessments of telemedicine. *J Telemed Telecare*. 2004;10(6):318-24.
2. Gagnon M-P, Scott RE. Striving for evidence in e-health evaluation: Lessons from health technology assessment. *J Telemed Telecare*. 2005;11(2_suppl):34-6.
3. Kidholm K, Ekeland AG, Jensen LK, Rasmussen J, Pedersen CD, Bowes A, et al. A model for assessment of telemedicine applications: MAST. *Int J Technol Assess Health Care*. 2012;28(1):44.
4. Moshi MR, Tooher R, Merlin T. Development of a health technology assessment module for evaluating mobile medical applications. *Int J Technol Assess Health Care*. 2020;36(3):252-61.
5. Gomes M, Murray E, Raftery J. Economic evaluation of digital health interventions: Methodological issues and recommendations for practice. *Pharmacoeconomics*. 2022;40(4):367-78.
6. EUnetHTA Joint Action 2 Work Package 8. HTA core model® version 3.0. [Pdf] 2016; Available from: www.htacoremodel.info/BrowseModel.aspx.; Accessed 14 August 2022.
7. Haute Autorité de Santé (HAS) [French National Authority for Health]. Functional classification, according to their intended use, of digital solutions used in the context of medical and paramedical care. Paris (FR): HAS, 2021.
8. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Pdf] 2018 [updated 09 August 2022]; Available from: https://www.nice.org.uk/corporate/ecd7; Accessed 15 August 2022.

9. Regulation on the procedure and requirements for testing the eligibility for reimbursement of digital health applications in the statutory public health insurance, S. Digital Health Applications Ordinance (DiGAV), Federal Ministry of Health (DE) (2019).
10. Haverinen J, Keränen N, Falkenbach P, Maijala A, Kolehmainen T, Reponen J. Digi-HTA: Health technology assessment framework for digital healthcare services. *FinJeHeW*. 2019;11(4).
11. Von Huben A, Howell M, Carrello J, Norris S, Wortley S, Ritchie A, et al. Application of a health technology assessment framework to digital health technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2022;38(1):e9.
12. Von Huben A, Howell M, Howard K, Carrello J, Norris S. Health technology assessment for digital technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2021;37(1):e66.
13. von Huben A, Howell M, Norris S, Wong KC, Tang J, Kazi S, et al. Stakeholder preferences for attributes of digital health technologies to consider in health service funding. *Int J Technol Assess Health Care*. 2023;39(1):e12.
14. Drury P, Roth S, Jones T, Stahl M, Medeiros D. Guidance for investing in digital health. Manila (PH): Asian Development Bank (ADB), 2018.
15. Norman CD, Skinner HA. eHEALS: The eHealth literacy scale. *J Med Internet Res*. 2006;8(4):e27.
16. World Health Organisation (WHO). Monitoring and evaluating digital health interventions: A practical guide to conducting research and assessment. Geneva (CH): WHO, 2016.

17. Dick S, O'Connor Y, Thompson MJ, O'Donoghue J, Hardy V, Wu TJ, et al. Considerations for improved mobile health evaluation: Retrospective qualitative investigation. *JMIR MHealth and UHealth*. 2020;8(1):e12424.

18. Eysenbach G. Consort-ehealth: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res*. 2011;13(4):e126.

19. European Commission. Synopsis report, consultation: Transformation health and care in the digital single market. Luxembourg City (LU): European Commission, 2018.

20. Hogaboam LS. Assessment of technology adoption potential of medical devices: Case of wearable sensor products for pervasive care in neurosurgery and orthopedics [Ph.D.]. Ann Arbor: Portland State University; 2018.

21. Australian Government eSafety Commissioner. Industry - safety by design. [Internet] 2023; Available from: https://www.esafety.gov.au/industry/safety-by-design/investors; Accessed 19 February 2023.

22. Information Commissioner's Office (ICO) (UK). Guide to Data Protection. [Internet] 2019 [Updated April 2021]. Available from: Accessed 19 February 2023.

23. Australian Commission on Safety and Quality in Health Care (ACSQHC). National safety and quality digital mental health standards. Sydney (AU): ACSQHC; 2020.

24. Caulfield B, Reginatto B, Slevin P. Not all sensors are created equal: A framework for evaluating human performance measurement technologies. *NPJ Digit*. 2019;2(1).

25. Department of Health & Social Care (UK). A guide to good practice for digital and data-driven health technologies. [Internet] London (UK): Department of

Health & Social Care (UK); 2019 [Updated 19 January 2021]; Available from: https://www.gov.uk/government/publications/code-of-conduct-for-data-driven-health-and-care-technology/initial-code-of-conduct-for-data-driven-health-and-care-technology; Accessed 18 August 2022.

26. NHS Digital (UK). The digital technology assessment criteria for health and social care (DTAC). [Internet] 2019 [updated 16 April 2021]; Available from: https://transform.england.nhs.uk/key-tools-and-info/digital-technology-assessment-criteria-dtac/; Accessed 18 August 2022.

27. Ruck A, Wagner Bondorf S, Lowe C, Consard Limited. Second draft of guidelines, EU guidelines on assessment of the reliability of mobile health applications European Commission, Directorate-General of Communications Networks, Content & Technology, 2016.

28. Lewis JR. The system usability scale: Past, present, and future. *Int J Hum Comput Interact*. 2018;34(7):577-90.

29. Medicines and Healthcare Regulatory Authority. Guidance: Medical device stand-alone software including apps (including IVDMDs) v1.10. [Pdf] 2014 [updated 8 September 2022]; Available from: https://www.gov.uk/government/publications/medical-devices-software-applications-apps; Accessed 20 February 2023.

30. Huckvale K, Torous J, Larsen ME. Assessment of the data sharing and privacy practices of smartphone apps for depression and smoking cessation. JAMA Network Open. 2019;2(4):e192542.

31. Nielsen S, Rimpiläinen S. Report on international practice on digital apps. Glasgow (UK): Digital Health and Care Institute, 2018.

32. Jääskelä J, Haverinen J, Kaksonen R, Reponen J, Halunen K, Tokola T, et al. Digi-HTA, assessment framework for digital healthcare services: Information security and data protection in health technology – initial experiences. Finnish *FinJeHeW*. 2022;14(1):19-30.

33. Andalusian Health Quality Agency (ES). Complete list of recommendations on design, use and assessment of health apps. [Internet] 2012; Available from: http://www.calidadappsalud.com/en/listado-completo-recomendaciones-app-salud/; Accessed 16 August 2020.

34. Medicines and Healthcare products Regulatory Agency (MHRA). Good machine learning practice for medical device development: Guiding principles. [Internet] 2021; Available from: https://www.gov.uk/government/publications/good-machine-learning-practice-for-medical-device-development-guiding-principles/good-machine-learning-practice-for-medical-device-development-guiding-principles; Accessed 19 Feb 2023.

35. IDEO.org. The field guide to human centered design. [Pdf] 2015; Available from: https://www.designkit.org/resources/1; Accessed 19 February 2023.

36. Haute Autorité de Santé (HAS) [French National Authority for Health]. Public consultation on the draft analysis grid intended for use by CNEDiMTS to contribute to its evaluation of medical devices embedding decision systems based on automatic learning processes ("artificial intelligence"). Paris (FR): HAS; 2019.

37. Lewis TL, Wyatt JC. Mhealth and mobile medical apps: A framework to assess risk and promote safer use. *J Med Internet Res*. 2014;16(9):e210.

38. Murray E, Hekler EB, Andersson G, Collins LM, Doherty A, Hollis C, et al. Evaluating digital health interventions: Key questions and approaches. *Am J Prev Med*. 2016;51(5):843-51.

39. Bergmo TS. How to measure costs and benefits of eHealth interventions: An overview of methods and frameworks. *J Med Internet Res*. 2015;17(11):e254-e.

40. Kephart G, Packer T, Audulv Å, Chen Y-T, Robinson A, Olsson I, et al. Item selection, scaling and construct validation of the patient-reported inventory of self-management of chronic conditions (PRISM-CC) measurement tool in adults. *Qual Life Res*. 2022;31(9):2867-80.

41. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working alliance inventory-short revised (WAI-SR): Psychometric properties in outpatients and inpatients. *Clin Psychol Psychother*. 2010;17(3):231-9.

42. IRBs could address ethical issues related to tracking devices: Mobile devices raise new concerns. *IRB Advisor*. 2017;17(11):8-9.

43. Academy of Medical Sciences (UK). Our data-driven future in healthcare: People and partnerships at the heart of health related technologies. London (UK): Academy of Medical Sciences; 2018.

44. Sax M, Helberger N, Bol N. Health as a means towards profitable ends: Mhealth apps, user autonomy, and unfair commercial practices. *J Consumer Policy*. 2018;41(2):103-34.

45. Cugelman B, Thelwall M, Dawes P. Online interventions for social marketing health behaviour change campaigns: A meta-analysis of psychological architectures and adherence factors. *J Med Internet Res*. 2011;13(1):e17.

46. Proudfoot J, Klein B, Barak A, Carlbring P, Cuijpers P, Lange A, et al. Establishing guidelines for executing and reporting internet intervention research. *Cogn Behav Ther*. 2011;40(2):82-97.

47. Open Data Institute. The data ethics canvas. [Internet] 2021; Available from: https://theodi2022.wpengine.com/article/the-data-ethics-canvas-2021/. Accessed 20 February 2023.

48. NHS Digital (UK). Digital inclusion guide for health and social care. [Pdf] 2019; Available from: https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/digital-inclusion#document-content; Accessed 19 February 2023.

49. W3C Web Accessibility Initiative (WAI). Web content accessibility guidelines (WCAG) international standard. [Internet] 2005 [updated 25 January 2023]; Available from: https://www.w3.org/WAI/standards-guidelines/wcag/; Accessed 20 February 2023.

50. Medical Device Coordination Group. Guidance on qualification and classification of software in regulation (EU) 2017/745 – MDR and regulation (EU) 2017/746 – IVDR. European Commission; 2019.

51. Loke YK, Price D, Herxheimer A. Systematic reviews of adverse effects: Framework for a structured approach. *BMC Med Res Methodol*. 2007;7(1):32-.

52. Haute Autorité de Santé (HAS) [French National Authority for Health]. Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement. Paris (FR): HAS; 2019.

53. Lennon MR, Bouamrane MM, Devlin AM, O'Connor S, O'Donnell C, Chetty U, et al. Readiness for delivering digital health at scale: Lessons from a longitudinal qualitative evaluation of a national digital health innovation program in the United Kingdom. *J Med Internet Res*. 2017 02 16;19(2):e42.

54. Medical Services Advisory Committee (AU). Guidelines for preparing assessment reports for the medical services advisory committee. [Pdf] 2021 [updated 18 May 2021]; Available from:

http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Documents-for-Applicants-and-Assessment-Groups; Accessed 12 August 2022.

55. Rojahn K, Laplante S, Sloand J, Main C, Ibrahim A, Wild J, et al. Remote monitoring of chronic diseases: A landscape assessment of policies in four European countries. *PLoS One*. 2016;11(5):e0155738.

Chapter 6 eADVICE: an economic evaluation of a web-based program for children with incontinence

The material in this chapter has been submitted to *Pediatrics* and is under review as follows:

Von Huben A, Howell M, Richards D, Hamilton S, Howard K, Teixeira-Pinto A, Craig JC, Seton C, Waters K, Deshpande A, Scott K, Caldwell PHY. eADVICE: an economic evaluation of a web-based program for children with incontinence. 2023, *[Manuscript submitted for publication]*.

A statement of the specific contributions of the co-authors can be found in Appendix B.

Purpose of this chapter

To perform an economic evaluation of a self-management DHT for chronic disease (eADVICE) considering the extended checklist items (Chapter 5). As this publication is aimed at a clinical audience, the assessment of the recommended content of the checklist for relevance and practicality in evaluating eADVICE is summarised in Chapter 7.

6.1. Abstract

Objectives: Children who require specialist outpatient care typically wait substantial periods during which their condition may progress, making treatment more difficult and costly. Timely and effective therapy during this period may reduce the need for lengthy specialist care. This study evaluates the cost-effectiveness of an individualised, evidence-informed, web-based program for children with urinary incontinence awaiting a specialist appointment (eADVICE) compared to usual care. eADVICE is primary physician-supervised and delivered by avatar.

Methods: Using the results of the ADVICE multicentre waitlist-controlled randomised trial, a cost-effectiveness analysis was performed from the perspective of the healthcare funder. Preplanned outcome measures were the incremental cost per incremental change in continence status and quality of life on an intention-to-treat basis. Uncertainty was examined using cost-effectiveness planes, scenario, and one-way sensitivity analyses. Costs were valued in 2021 Australian dollars (AUD) and a government-stipulated 7% discount rate was used.

Results: The use of eADVICE was found to be cost-effective (dominant) over usual care with a higher proportion of patients dry over 14 days at six months (risk difference 0.13; 95% CI 0.02 to 0.23) and mean healthcare costs reduced by AUD188 (95% CI 61 to 315) per patient.
Conclusions: An individualised evidence-informed web-based program delivered by avatar is likely to provide timely, effective, and cost-saving therapy for children with urinary incontinence awaiting a specialist appointment. The potential economic impact of such a program is substantial and may be transferable to outpatient clinic settings for other chronic health conditions.

6.2. Introduction

Children who require specialist outpatient care typically wait for substantial periods. During this time their underlying condition may progress, making treatment more difficult. This waiting period is underutilised. Timely and effective therapy during this period may reduce the need for specialist outpatient care.

Approximately 10% of school-aged children have problems with urinary continence (1). Incontinence can be either diurnal or nocturnal or both, and one-third seek medical help (2). First-line treatments used in primary care such as an enuresis alarm or desmopressin have success rates of 50% to 70%.(3-5) If these treatments fail, children can have a substantial wait for a specialist appointment; on average six to twelve months in Australia.(6, 7)

A primary care physician-supervised web-based evidence-informed management support system for patients awaiting their specialist appointment has the potential to provide treatment earlier and conveniently during the waiting period. This may reduce the need for specialist care and reduce waiting times.

The eADVICE (electronic Advice and Diagnosis Via the Internet following Computerized Evaluation) continence program is a web-based program delivered by an avatar. It was developed and piloted by pediatric continence specialists with parents, children, clinicians, and information technology specialists (8). A cohort study over three years suggested an absolute risk reduction of 13% in the proportion of children wetting from eADVICE versus usual care and a reduction in the mean number of clinic visits from 3.6 to 3.0 per patient (7).

The aim of this economic evaluation is to establish the cost-effectiveness of eADVICE for children with urinary incontinence versus usual care using information from the eADVICE waitlist controlled randomised trial (eADVICE trial) (9).

6.3. Methods

6.3.1. Study design

The detailed study design for the eADVICE trial is reported in the clinical effectiveness paper (9). Briefly, the trial was a waitlist randomised controlled trial to determine the comparative effectiveness of eADVICE against usual care for patients referred to three metropolitan specialist continence clinics in New South Wales (NSW), Australia. Patients aged 5 to 18 years who had daytime incontinence (at least twice per week) or enuresis (at least three times per week) and who could self-initiate toileting were eligible; children with an organic cause for urinary incontinence were excluded. Families required internet access, and only one child per family could participate to minimise contamination. There were no exclusions based on other disabilities, eHealth literacy, or computer/internet experience. The study was approved by the human research ethics committee of the Children's Hospital at Westmead (Ref: HREC/18/SCHN/360) and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12618001484235).

Randomisation was performed centrally by the National Health and Medical Research Centre (NHMRC) Clinical Trials Centre, ensuring appropriate sequence generation and adequate allocation concealment. Balance over treatment groups by age (<10, ⩾10 years), gender, type of incontinence (daytime, nocturnal, or both), and referral clinic was achieved via minimisation. Participants randomised to the intervention were given access to the eADVICE website for six months while controls continued waiting for their outpatient appointment. Data analysts were blinded but blinding parents and children was not possible. Data was collected online at baseline and six months by surveys programmed into Qualtrics (Qualtrics Software, Provo, UT, USA).

6.3.2. Intervention

The development and operation of eADVICE are detailed in the design paper (8). Briefly, eADVICE is a web-based program that uses a relational agent (or "avatar") to interact with the child and family while they are waiting for a specialist clinic appointment. Individualised treatment advice, assessment, and diagnosis are facilitated by using the child's own data to determine the best treatment protocol (10-12). eADVICE was developed, and pilot-tested, with parents, children, clinicians, and information technology specialists, using evidence-informed guidelines and user-centred design principles (13, 14).

Families could access the password-protected program online or download it, revisiting the program for further assessment and treatment advice. Participants nominated a supervising primary care physician to whom data was sent from the program to aid in decision-making and provide education.

Patients in the intervention and control groups could attend primary care appointments and use any incontinence treatments but attending specialist appointments in the six-month trial was very unlikely given average waiting periods exceeding one year.

6.3.3. Economic evaluation design

Because this within-trial cost-effectiveness analysis is conducted from a healthcare funder perspective, incremental health outcomes and healthcare costs of eADVICE compared to usual care are estimated. Scenarios for implementation in the health system and for improving equity of access to the intervention were also performed. A pre-defined economic analysis plan was followed, and the analysis is reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist (15).

6.3.4. Health outcomes

Health outcomes were patient or parent-reported and collected at baseline and six months via online survey. Predefined outcomes for economic analysis were patients dry both day and night for fourteen consecutive days at six months, patients no longer meeting the International Children's Continence Society's (ICCS) criteria for a "significant" condition (enuresis or daytime urinary incontinence at least once a month measured over three months or more) (i.e., "insignificant" wetting), patients no longer meeting the criteria for "frequent" enuresis (more than four nights per week)(16) (i.e., "infrequent" bedwetting), and patient quality of life (QoL).

QoL was measured using the disease-specific, validated Paediatric Incontinence Questionnaire (PinQ) (17, 18) using the "modified" PinQ score of Deshpande et al., 2011 (19). The PinQ is designed for child self-administration measuring psychometric attributes of importance to children with bladder problems. The higher the "modified" PinQ score, the lower the QoL, with a maximum score of seven (minimum 1.75). There are no published studies that report utility values for the PinQ, so calculation of quality-adjusted life years (QALYs) for the trial participants, and hence a cost utility analysis, was not possible.

6.3.5. Costs and discounting

All costs were valued in 2021 Australian dollars (AUD). Only estimated future specialist clinic visit costs were discounted as incurred in the second-year post randomisation, given average waiting times exceed one year. All other costs and benefits occurred in the first six months (i.e., within the trial period), so did not require discounting. A discount rate of 7% per annum was used as per government guidelines (20).

6.3.6. Intervention costs

Resource quantities, unit costs, and data sources for the intervention are provided in Table 6.1.

Table 6.1: Resources and unit costs for intervention – (a) within trial and (b) implementation in the New South Wales (NSW) health system

Intervention costs	Unit	# Units	Rate (AUD)	Average cost per year (AUD)	
				(a) Within trial	(b) Implementation
Technology costs				**3,576**	**6,876**
Database	Year	1	2700	-	2,700‡
Web server hardware	Annualised*	1	2000	488	488
Web server software	Months	12	50	-	600 VC
Hardware for maintenance	Annualised*	1	2000	488	488
Software for maintenance	Year	1	2000	2,000	2,000
Data fees for maintenance	Months	12	50	600	600
Staff costs				**14,880**	**23,342**
IT programmers Software program maintenance	Hours per week	3 hours x 48 weeks	56‖	8,736	8,736
Clinical advisor Advice on clinical problems with intervention	Hours per month	2 hours x 12 months	131¶	3,144	3,144
Patient enrolment Onboarding, helping with access to program	Hours per proportion of patients requiring help	1 hour x 0.25 patients x 240 patients	50‖	3,000	3,000 VC
Ongoing implementation costs					
Ongoing compliance security control costs	Hours per month	2 hours x 12 months	56‖	-	4,488
Ongoing review of clinical content	Hours per month	2 hours x 12 months	131¶		
One-off implementation costs§					
One-off development of compliance with state-wide standards and cybersecurity controls	Annualised†			-	3,974
	Programming fees	1	20,000**		
	Hours	70	113††		
Total cost per year				**18,456**	**30,217**
Total cost per six-month intervention period				**9,228**	**15,109**
Cost per user (based on 120 participants per six months)				*77*	*126*

VC Variable cost - Cost depends on number of participants
*Useful life 5 years, NSW treasury discount rate 7% per annum
†Useful life 10 years, NSW treasury discount rate 7% per annum
‡NSW health might already have a licence
§Additional cost for building compatibility with eMR may also be required, but this has not been designed or built
‖Rates of IT developers and a research assistant from research grant financial reporting, the annual cost divided by 1800 working hours per year
¶Staff specialist rates (State Award 2021) INDUSTRIAL RELATIONS COMMISSION OF NEW SOUTH WALES
**Cost of previous compliance work with NSW eHealth
††Academic rates starting 25 March 202: MQ-ACADEMIC-STAFF-ENTERPRISE-AGREEMENT-2018

Development costs were excluded as not relevant to the running cost of eADVICE. The primary analysis considered "within-trial" costs to run and maintain the intervention. Expected costs to run and maintain the intervention in the NSW health system were considered in an "implementation" scenario.

Within-trial costs consisted of technology and staff costs. Utilisation and unit costs of hardware and software were estimated via interviews with software developers. Hardware purchase costs were annualised, assuming an estimated useful life of five years. Staff activity hours were estimated via interviews with the project team. Unit costs for staff activity were derived from research grant financial reporting, State Awards, and University Enterprise Agreements.

As the intervention was delivered and measured over six months, half of the yearly intervention costs were allocated to the intervention group in the trial.

6.3.7. Healthcare costs

Costs for two of the three referral clinics were obtained over the most recent six-month period of the trial, July to December 2021. Costs for the third clinic were not requested because they contributed only 3% of patients in the trial. Encounters were filtered for patients in the trial age range of 5 to 18 years. The average cost per encounter was calculated for both clinics to provide a range of cost estimates for a clinic visit, which was then averaged again to provide the visit cost estimate for the primary analysis. To be conservative, fixed costs that would occur regardless of whether a patient visited the clinic were excluded using a rule of thumb of thirty percent, as advised by hospital finance staff.

All visits of trial participants to the three specialist clinics were recorded over the trial period, with no missing data. Given estimated waiting times of over one year (7), few participants were expected to secure a clinic appointment over the trial period. A prior cohort study over

three years found the average number of clinic visits for patients without eADVICE was 3.6 per patient, compared to 3.0 per patient for those with access to eADVICE prior to their first clinic appointment (7). Healthcare costs were estimated as the cost of visits over the six-month trial plus the cost of expected future visits if the participant indicated they still required a clinic visit at six months. Future clinic visits were assumed to be 3.6 for the control group and 3.0 for the intervention group minus the clinic visits already attended at six months.

6.4. Analysis

6.4.1. Primary analysis

A complete case analysis was used in the primary analysis. A predefined analysis plan was followed to analyse the incremental effectiveness of the specified binary health outcomes via log-binomial regression and continuous health outcomes via normal linear regression. Health outcomes at six months were adjusted by baseline measurements for imbalances at baseline. Incremental costs were estimated by normal linear regression. Bootstrapping was used to estimate uncertainty and calculate incremental cost-effectiveness ratio (ICER) point estimates and 95% confidence intervals. Point estimates were plotted on a cost-effectiveness plane.

6.4.2. Multiple imputation for missing data

To validate the inferences from the complete case analysis, missing data were imputed using Fully Conditional Specification (FCS) with the **mice** package (version 3.14.0) (21) for R. Bootstrapping of the incremental cost-effectiveness ratio with multiple imputation was performed with the **bootImpute** package (version 1.2.0) for R using the von Hippel and Barlett approach (22).

6.4.3. Scenario analyses

Two scenarios were considered: 1. Additional costs to implement the intervention in the healthcare system (see Table 6.1: (b)), 2. Additional costs to implement and increase access to the intervention to address equity (i.e., subsidise tablet rental, data plan, enuresis alarm, and translate the program for non-English speakers). Details on the cost estimates for scenarios are presented in Figure A 6.

6.4.4. One-way sensitivity analyses

One-way sensitivity analyses were undertaken on clinic visit costs, the estimated average number of future visits for the eADVICE group, and the discount rate. Sensitivity analyses were applied to the primary analysis and the scenarios.

All analyses were undertaken using R (version 4.1.2) (23).

6.5. Results

6.5.1. Participants

662 participants were recruited and screened for eligibility between 18 December 2018 to 15 December 2020. 239 participants met the inclusion criteria and provided informed consent. Baseline participant characteristics are reported in Table 6.2. Missing data was found to be less likely in patients with frequent wetting, who had tried past treatments, and in referral sites with higher waitlist times. Therefore, data missing at random was likely to be a valid assumption, and 34 data sets were imputed based on 34% missing data.

Table 6.2: Baseline characteristics by treatment group

	Treatment group		
	eADVICE N = 120 (%)	**Control N = 119 (%)**	**Total N = 239 (%)**
Age group (yrs), n (%)			
< 8	39 (32.5)	34 (28.6)	73 (30.5)
8 to 11	67 (55.8)	70 (58.8)	137 (57.3)
≥ 12	14 (11.7)	15 (12.6)	29 (12.1)
Gender, n (%)			
Male	73 (60.8)	75 (63.0)	148 (61.9)
Referral Site, n (%)			
Site 1	105 (87.5)	102 (85.7	207 (86.6)
Site 2	11 (9.2)	13 (10.9)	24 (10.0)
Site 3	4 (3.3)	4 (3.4)	8 (3.3)
[†]SEIFA Quintiles – IRSD, n (%)			
1 - Most disadvantaged	12 (10.0)	11 (9.2)	23 (9.6)
2	10 (8.3)	4 (3.4)	14 (5.9)
3	13 (10.8)	24 (20.2)	37 (15.5)
4	42 (35.0)	39 (32.8)	81 (33.9)
5 - Least disadvantaged	43 (35.8)	41 (34.5)	84 (35.1)
Urinary incontinence history, n (%)			
Daytime urinary incontinence	45 (37.5)	41 (34.5)	86 (36.0)
Nocturnal urinary incontinence	116 (96.7)	115 (96.6)	231 (96.7)
[‡]ICCS Significant wetting	120 / 120 (100.0)	116 / 118 (98.3)	236 / 238 (99.2)
[¶]ICCS Frequent bedwetting	98 / 116 (84.5)	93 / 113 (82.3)	191 / 229 (83.4)
Incontinence treatment history, n (%)			
Tried treatments before	68 (56.7)	62 (52.1)	130 (54.4)
Alarm training	45 (37.5)	43 (36.1)	88 (36.8)
Desmopression	19 (15.8)	19 (16.0)	38 (15.9)
[§]Quality of Life (QoL)			
Mean [#]Modified PinQ score (SD)	5.37 (±2.18)	5.32 (±2.20)	5.34 (±2.18)

[†]Socio-economic indices Australia, 2016, quintiles derived from NSW deciles by child's postal area, IRSD - Index of Relative Socio-economic Disadvantage
[‡]ICCS Significant wetting = Wetting day or night at least once a month measured over 3 months or more
[¶]ICCS Frequent bedwetting = Wetting of bed at least four times per week
[§]PinQ, Paediatric Incontinence Questionnaire, the higher the score, the lower the Quality of Life (QoL)
[#]The Modified PinQ score is an equally weighted score of the seven domain scores

6.5.2. Incremental costs

Within the trial, the intervention cost was estimated at AUD77 per participant (Table 6.1). Regarding health care costs, the variable cost of a specialist clinic visit ranged from AUD322 to AUD397 over the clinics. The average of these two estimates, AUD360 per visit, was used in the primary analysis.

A summary of actual and estimated future clinic visits with mean cost estimates is presented in Table 6.3. The mean total costs were AUD864 for the intervention group and AUD1,052 for the control group; an incremental cost saving of AUD188 (95% CI 61 to 315) from eADVICE.

Table 6.3: Incremental costs, benefits, and incremental cost-effectiveness ratios (ICERs) – (a) complete case and (b) imputed data

Incremental Costs

(a) Complete case	Treatment group: eADVICE N = 88	Treatment group: Control N = 98	Increment	
	Mean (SD)	**Mean (SD)**	**Mean difference (95% CI)**	**p-value**
Clinic visits 0-6 months	0.01 (±0.11)	0.08 (±0.37)	-0.07 (-0.15, 0.01)	0.088
Cost visits 0-6 months (AUD)	4 (±38)	29 (±134)	-25 (-54, 4)	0.088
Estimated future clinic visits	0.78 (±0.42)	0.84 (±0.36)	-0.07 (-0.19, 0.05)	0.247
Cost future clinic visits (AUD)	782 (±424)	1,022 (±442)	-240 (-369, -110)	<0.001
Intervention cost (AUD)	77 (±0)	0 (±0)	77 (0,0)	
Total costs (AUD)	**864 (±428)**	**1,052 (±423)**	**-188 (-315, -61)**	**0.004**
(b) Imputed data	**eADVICE N = 120**	**Control N = 119**	**Increment**	
	Mean (SE)	**Mean (SE)**	**Mean difference (95% CI)**	**p-value**
Clinic visits 0-6 months	0.07 (±0.05)	0.09 (±0.03)	-0.03 (-0.11, 0.06)	0.559
Cost visits 0-6 months (AUD)	24 (±19)	33 (±11)	-9 (-40, 22)	0.559
Estimated future clinic visits	0.70 (±0.07)	0.81 (±0.04)	-0.12 (-0.22, -0.01)	0.097
Cost future clinic visits (AUD)	705 (±74)	987 (±43)	-282 (-400, -163)	<0.001
Intervention cost (AUD)	77 (±0)	0 (±0)	77 (0,0)	
Total costs (AUD)	**806 (±73)**	**1,020 (±42)**	**-214 (-331, -97)**	**0.005**

Incremental Benefits and Incremental Cost-Effectiveness Ratios (ICERs)

(a) Complete case	Treatment group: eADVICE N = 88	Treatment group: Control N = 98	Increment: *Risk/ Mean difference (95% CI)	ICER	Bootstrapped Cost-Effectiveness plane estimates (% outcomes): NE	SE	SW	NW
Dry patients	20 (22.7%)	10 (10.2%)	**0.13 (0.02, 0.23)**	**Dominant**	-	98.80	1.20	-
†Insignificant wetting	22 (25.6%)	10 (10.3%)	**0.15 (0.04, 0.26)**	**Dominant**	0.40	99.20	0.40	-
‡Infrequent bedwetting	39 (45.3%)	31 (32.0%)	**0.15 (0.02, 0.28)**	**Dominant**	0.00	98.20	1.70	0.10
§QoL	3.5 (3.3, 3.8)	3.9 (3.6, 4.1)	**0.37 (0.03, 0.71)**	**Dominant**	-	97.80	2.20	-
(b) Imputed data	**eADVICE N = 120**	**Control N = 119**	***Risk/ Mean difference (95% CI)**	**ICER**	**NE**	**SE**	**SW**	**NW**
Dry patients	28 (22.9%)	14 (11.9%)	**0.11 (0.01, 0.20)**	**Dominant**	0.45	97.60	1.90	0.05
†Insignificant wetting	27 (22.6%)	12 (10%)	**0.12 (0.03, 0.22)**	**Dominant**	0.50	99.15	0.35	-
‡Infrequent bedwetting	62 (52%)	45 (37.6%)	**0.17 (0.05, 0.29)**	**Dominant**	0.50	97.85	1.65	-
§QoL	3.4 (2.7, 4.1)	3.8 (3.3, 4.2)	**0.34 (0.05, 0.63)**	**Dominant**	0.50	95.35	4.15	-

*Adjusted for imbalances at baseline for infrequent bedwetting and QoL

†ICCS insignificant wetting = Less than once a month measured over 3 months or more day and night

‡ICCS infrequent bedwetting = Less than four nights per week
§QoL, Quality of Life as measured by the reduction in modified Paediatric Incontinence Questionnaire (PinQ) score

6.5.3. Incremental effectiveness

Proportions of dry children, "insignificant" wetters, and "infrequent" bedwetters at six months adjusted by baseline were all higher (13% to 15% absolute risk difference) in the intervention group than in the control group (Table 6.3). Quality of life (QoL) as measured by mean modified PinQ score was better (lower PinQ score) in the intervention group than control; a mean improvement in the QoL of 0.37 (95% CI 0.03 to 0.71) (Table 6.3).

6.5.4. Incremental cost-effectiveness analysis

Because the intervention resulted in improved health outcomes on all health measures at a lower cost, eADVICE dominated usual care on all health outcomes (Table 6.3). Ninety-eight to ninety-nine percent of bootstrapped replicates fell in the southeast quadrant of the cost-effectiveness plane; that is, where eADVICE was more effective and less costly compared to usual care (Table 6.3 and Figure 6.1). Analysis of datasets with multiple imputation for missing data confirmed the findings from the primary analysis (Table 6.3 and Figure A 7).

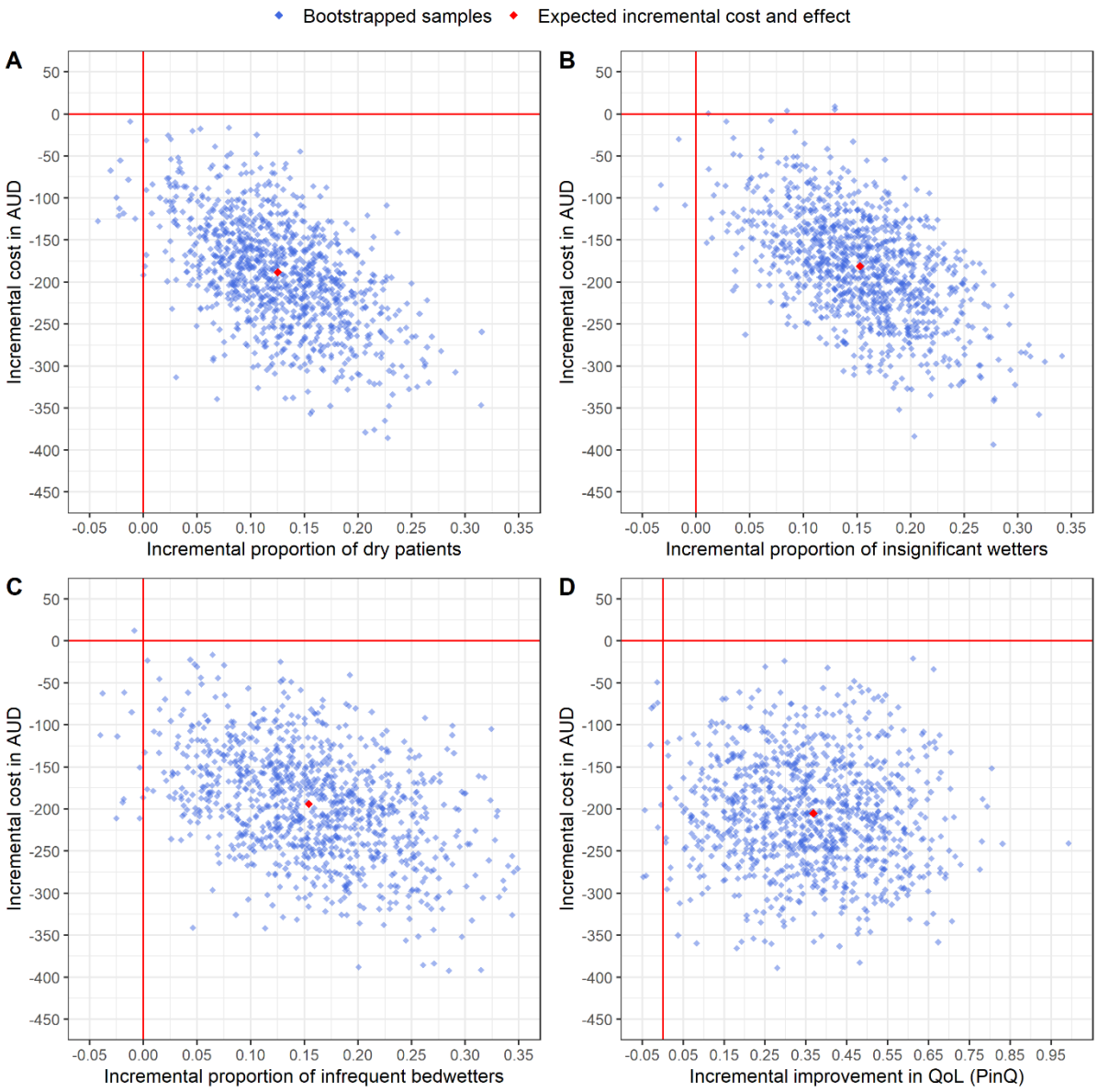

Figure 6.1: Incremental cost-effectiveness planes for improvement in proportion (A) dry patients, (B) patients with insignificant* daytime urinary incontinence and enuresis, and (C) patients with infrequent* enuresis. Incremental cost-effectiveness planes for improvement in mean (D) Quality of Life (QoL) as measured by the Paediatric Incontinence Questionnaire (PinQ)
*Terms defined by the International Children's Continence Society (ICCS)

6.5.5. Scenario analyses

For scenario 1, the cost of the intervention when implemented in the NSW health system was estimated at AUD126 per participant (Table 6.1: (b)). Estimated incremental cost savings from eADVICE under Scenario 1 were AUD139 (95% CI 12 to 266) (Figure 6.2). As

incremental effectiveness is assumed unchanged under Scenario 1, eADVICE still dominated usual care; that is, eADVICE is cost-saving and beneficial.

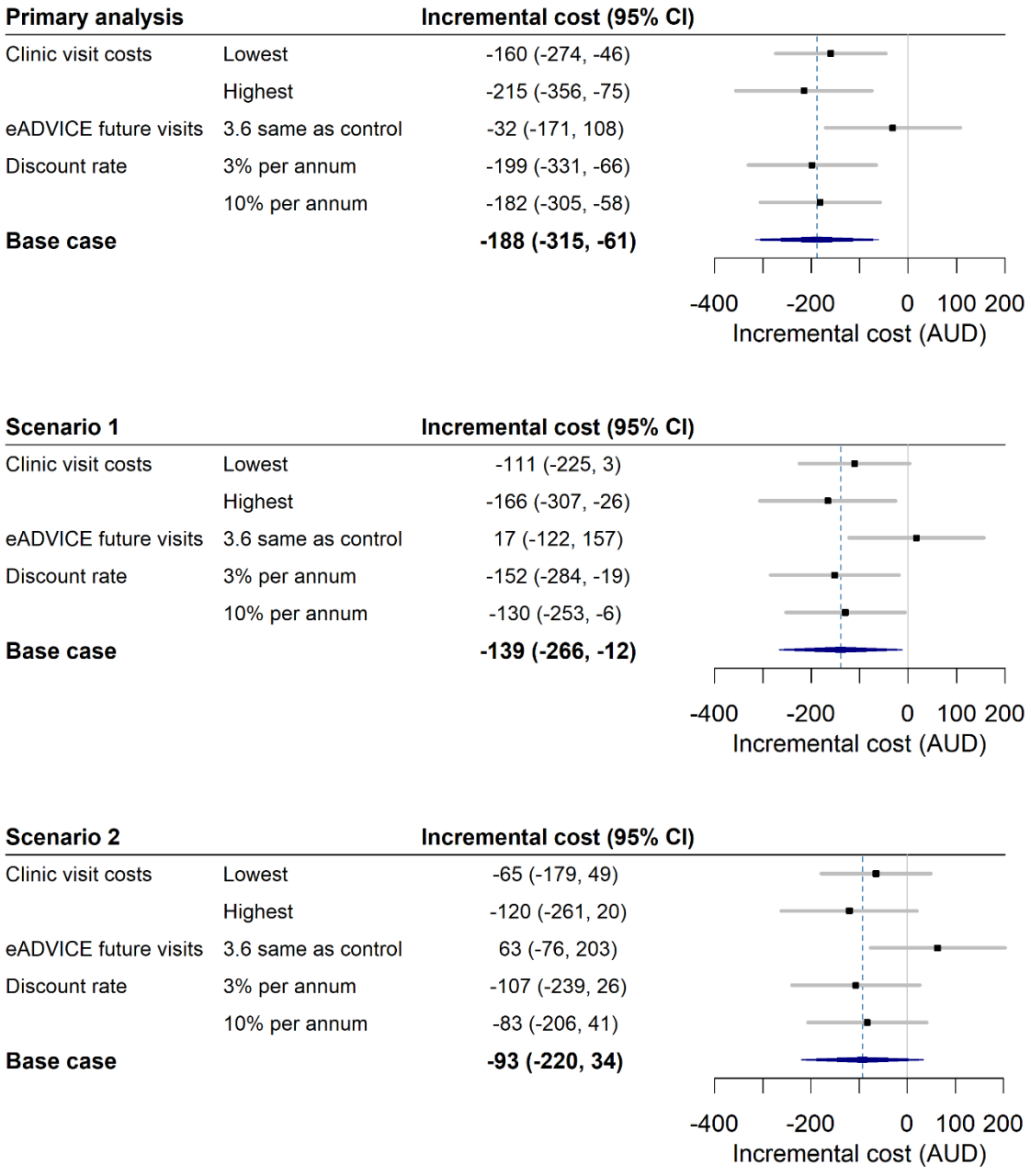

Figure 6.2: Incremental costs of one-way sensitivity analyses on primary analysis and scenarios

For scenario 2, the cost to improve equity in access to the intervention was estimated at AUD46 per participant, and with implementation costs, the total cost of the intervention was estimated at AUD172. Again, eADVICE dominated usual care with incremental cost savings

of AUD93 (95% CI 34 to 220) (Figure 6.2) and 94% of bootstrapped replicates in the southeast quadrant.

6.5.6. One-way sensitivity and threshold analyses

Figure 6.2 also presents the incremental costs of the primary analysis and the two scenarios with one-way sensitivities for low (AUD322) / high (AUD397) clinic visit costs; the number of future clinic visits for the eADVICE group increased to be the same as the control group (i.e., 3.6 instead of 3.0); and a low (3%) / high (10%) discount rate. Incremental costs from the sensitivity analyses vary little, except where the expected future clinic visits for eADVICE were assumed to be equal to the control group. Under this worst-case assumption, the probability of eADVICE being cost-saving was 63% for within-trial evaluation, 45% for implementation (Scenario 1), and 20% for implementation with improved equity in access to the intervention (Scenario 2). For the threshold analysis, the intervention cost would have to increase to over AUD265 per participant for the intervention to have a less than 50% chance of being cost-saving.

6.6. Discussion

This within-trial cost-effectiveness analysis found eADVICE to be cost-saving and more effective (i.e., dominant) compared to usual care. In scenarios where implementation costs and costs to improve access to the intervention were considered, eADVICE remained lower cost with improved outcomes. The intervention also remained cost-saving and more effective under one-way sensitivity analyses for high and low-cost estimates of specialist clinic visits and high and low-discount rates. Threshold analysis found intervention costs would have to be more than AUD265 per participant, compared to a baseline estimate of AUD77, for eADVICE to have less than a 50% chance of being cost-saving.

The primary driver for cost-effectiveness was the difference in the number of clinic visits required by each treatment group. If usual care and eADVICE patients required the same number of clinic visits, the probability of eADVICE being cost-saving would be 63% for within-trial evaluation, 45% for Scenario 1, and 20% for Scenario 2. However, this is a worst-case assumption, as at least some patient data collection, assessment, diagnosis, and education of families will be completed through eADVICE before the first specialist appointment, reducing the time needed with the specialist. Further, eADVICE has been observed in practice to lower the number of required clinic visits (7). This assumption would only be likely to true for the estimated 15% of patients (7) who chose not to use the eADVICE program when given access. As the demand for these services far exceeds the supply there is strong evidence to support the implementation of eADVICE for children with urinary incontinence waiting for specialist appointments.

Data collection on costs and health outcomes through the randomised controlled trial provides robust evidence that eADVICE is cost-effective compared to usual care in the trial settings. However, in this trial, waiting periods for a specialist appointment did vary by clinic and subgroup analysis found more loss to follow-up in clinics with shorter waiting times, and hence our power to detect significant effects in sites with shorter waiting times was limited. Generalisability to other clinic situations should be considered in terms of estimated waiting times. Another limitation was the short trial duration of six-months which did not allow for observation of the durability of intervention effectiveness. Participants in the control group were assessed at 12 months, and there was evidence on a pre-post basis that the intervention group continued to improve over six to twelve months on all health outcomes except for their quality of life. However, because the control group was offered the intervention at six months, we were unable to separate the effect of the intervention post-treatment from natural improvements given the absence of a suitable control group.

Not being able to collect costs from an implemented version of eADVICE in the NSW healthcare system is another limitation for which we have relied on estimates. We have assumed the number of users to be around 240 per year, which is around half of the current yearly capacity of the clinics. The current hardware and software capacity is sufficient for a doubling of users to the capacity of the clinics, i.e., 500 per year, but if the program is to be scaled up to the potential number of school-aged children in NSW requiring specialist paediatric continence clinics, estimated in the order of 13,000 children, server hardware and software fees would be higher than assumed in this analysis.

We have conducted the cost-effectiveness analysis from the perspective of NSW Health, so appropriately we have only included NSW hospital healthcare costs. Healthcare costs funded by the Australian government such as services performed outside of hospital under the Medicare Benefits Scheme (MBS) and prescription medications under the Pharmaceutical Benefits Scheme (PBS) were excluded from our analysis.

We have conducted the cost-effectiveness analysis from the perspective of NSW Health, so appropriately we have only included NSW hospital healthcare costs. Healthcare costs funded by the Australian government such as services performed outside of hospital under the Medicare Benefits Scheme (MBS) and prescription medications under the Pharmaceutical Benefits Scheme (PBS) were excluded from our analysis.

6.7. Conclusion

eADVICE is a cost-effective program that has the potential to improve the health of children currently waiting for specialist pediatric continence clinic appointments, reduce waiting times, minimise harder-to-treat conditions in older patients, and increase the capacity to treat patients. This type of program also has the potential to provide cost-effective solutions for other specialist clinics with long waitlists.

6.8. References

1. Forsythe WI, Redmond A. Enuresis and spontaneous cure rate: Study of 1129 enuretics. *Arch Dis Child*. 1974;49(4):259-63.
2. Bower WF, Moore KH, Shepherd RB, Adams RD. The epidemiology of childhood enuresis in Australia. *Br J Urol*. 1996;78(4):602-6.
3. Glazener CM, Evans JH, Peto RE. Alarm interventions for nocturnal enuresis in children. *Cochrane Database Syst Rev*. 2005 (2).
4. Glazener CMA, Evans JHC. Desmopressin for nocturnal enuresis in children. *Cochrane Database Syst Rev*. 2002 (3).
5. Nevéus T, Fonseca E, Franco I, Kawauchi A, Kovacevic L, Nieuwhof-Leppink A, et al. Management and treatment of nocturnal enuresis—an updated standardization document from the international children's continence society. *J Pediatr Urol*. 2020;16(1):10-9.
6. Eiselen C, Trajanovska M, Griffith A, Phan T, Goldfeld S, Gibb S, et al. Audit of enuresis referrals on the waiting list for a tertiary hospital outpatient clinic. *J Paediatr Child Health*. 2021;57(10):1645-50.
7. NSW Government. Young people with urinary incontinence: Data evaluation report. Agency for Clinical Innovation; 2018.
8. Richards D, Caldwell P. Improving health outcomes sooner rather than later via an interactive website and virtual specialist. *IEEE Journal of Biomedical and Health Informatics*. 2018;22(5):1699-706.
9. Caldwell PHY, Richards D, Hamilton S, Von Huben A, Teixeira-Pinto A, Howell M, et al. Eadvice: A randomized controlled trial of a web-based program for children with incontinence. 2023, *[Manuscript submitted for publication]*.

10. Caldwell PHY, Hodson E, Craig JC, Edgar D. 4. Bedwetting and toileting problems in children. *Med J Aust*. 2005;182(4):190-5.

11. Chase J, Austin P, Hoebeke P, McKenna P. The management of dysfunctional voiding in children: A report from the standardisation committee of the international children's continence society. *J Urol*. 2010;183(4):1296-302.

12. Hoebeke P, Bower W, Combs A, De Jong T, Yang S. Diagnostic evaluation of children with daytime incontinence. *J Urol*. 2010;183(2):699-703.

13. Nielsen J. *Usability engineering*. [Updated edition]. ed. San Francisco: Elsevier Science & Technology; 1994.

14. Norman DA. User-centred system design: New perspectives on human-computer interaction. In: Norman DA, Draper, S.W., editor. *Cognitive engineering*. Hillsdale: Lawrence Erlbaum Associates; 1986. p. 31-61.

15. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards 2022 (cheers 2022) statement: Updated reporting guidance for health economic evaluations. *Int J Technol Assess Health Care*. 2022;38(1):e13.

16. Austin PF, Bauer SB, Bower W, Chase J, Franco I, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the international children's continence society. *Neurourol Urodyn*. 2016;35(4):471-81.

17. Bower WF, Sit FKY, Bluyssen N, Wong EMC, Yeung CK. Pinq: A valid, reliable and reproducible quality-of-life measure in children with bladder dysfunction. *J Pediatr Urol*. 2006;2(3):185-9.

18. Bower WF, Wong EMC, Yeung CK. Development of a validated quality of life tool specific to children with bladder dysfunction. *Neurourol Urodyn*. 2006;25(3):221-7.

19. Deshpande AV, Craig JC, Smith GHH, Caldwell PHY. Factors influencing quality of life in children with urinary incontinence. *J Urol*. 2011;186(3):1048-52.

20. NSW Treasury. NSW government guide to cost-benefit analysis. Sydney (AU), 2017.

21. Van Buuren S, Groothuis-Oudshoorn K. Mice: Multivariate imputation by chained equations in r. *J Stat Softw*. 2011;45(3):1 - 67.

22. Bartlett JW, Hughes RA. Bootstrap inference for multiple imputation under uncongeniality and misspecification. *Stat Methods Med Res*. 2020;29(12):3533-46.

23. R Core Team. R: A language and environment for statistical computing Vienna, Austria: R Foundation for Statistical Computing; 2021.

Chapter 7 Discussion and conclusions

7.1. Summary of findings on research questions

In Chapter 1, the research questions that stimulated the thesis were introduced, namely:

1. The sufficiency of existing HTA frameworks for non-digital technologies to consider the unique risks and benefits of DHTs that manage chronic disease
2. If existing HTA frameworks are found insufficient, then the existence of a single DHT evaluation framework that incorporates all, or at least the majority, of issues raised in the DHT evaluation framework literature to be used in HTA
3. The extent to which primary research on DHTs that manage chronic disease is generating appropriate evidence for a DHT-specific and comprehensive HTA
4. The views of a broad cross-section of community stakeholders as to the most important issues to consider when evaluating DHTs that manage chronic disease for public funding

The following sections discuss the findings of studies performed in Chapters 2 to 4 to address the research questions.

7.1.1. The systematic review of DHT evaluation frameworks (Chapter 2)

The systematic review of peer-reviewed and grey literature on DHT evaluation frameworks aimed to address research questions 1 and 2.

The sufficiency of existing HTA frameworks (Research question 1)

The systematic review identified 44 DHT evaluation frameworks suitable for medical device software (MDSW), mainly covering issues of clinical effectiveness (n = 30) and safety (n = 23). As discussed in Chapter 1, the EUnetHTA Core Model ("the Core Model") (1) was chosen as a representative existing HTA framework for non-digital technologies to assess

whether existing HTA frameworks are sufficient to perform HTAs for DHTs. This is because the Core Model is the only framework developed for international use over a range of technologies, is commonly used in many countries, includes a wide range of issues for content mapping, and uses internationally accepted HTA terminology. By using the Core Model as a scaffold for issue identification from the 44 DHT evaluation frameworks, the sufficiency of content in the Core Model in terms of evaluating DHT-specific risks and benefits could be assessed.

The Core Model topics were relevant for public funding assessment of DHTs, covering all topics raised by the DHT frameworks in six domains. However, the DHT framework authors recommended DHT evaluation content in 28 of the 145 Core Model issues and a further 22 DHT-specific issues not covered in the model, mainly in safety (n =10) and clinical effectiveness (n = 9). This suggested that the Core Model was not sufficiently comprehensive for undertaking a DHT-specific and comprehensive HTA. The review highlighted the need for more technology-specific questions for undertaking the HTA of DHTs across all HTA domains.

The existence of a single DHT evaluation framework that could be used in performing a DHT-specific and comprehensive HTA (Research question 2)

Almost the reverse of research question 1, the 44 DHT evaluation frameworks were examined for whether they were sufficient for performing a DHT-specific and comprehensive HTA. All frameworks had to be used with an existing HTA framework to cover the issues common to all technologies but essential for DHTs. Although the MAST (2) framework was the most complete in this regard because it leverages the Core Model, only some of the issues were addressed in four of the nine HTA domains.

No single framework covered all the forty-one DHT-specific issues raised by the DHT evaluation frameworks. A mobile medical applications (MMA) module (3) was the only framework to propose DHT-specific content in all nine HTA domains but covered only twelve of the forty one issues.

In addition, the review confirmed that most frameworks concentrated on issues in two to three domains. The DHT-specific issues for the current health problem, patients and social aspects, organisational aspects, and ethical analysis domains had the least coverage in the DHT evaluation frameworks. In contrast, DHT-specific issues in safety and clinical effectiveness domains were raised in the majority of frameworks. Furthermore, the UK NICE's ESF (4) was the only DHT evaluation framework to specifically state it was only designed to cover two domains: clinical effectiveness and economic evaluation.

The review concluded none of the 44 DHT evaluation frameworks were sufficient for performing a DHT-specific and comprehensive HTA that included all the recommendations from the DHT evaluation literature.

Conclusions from the systematic review of DHT evaluation frameworks

By focusing on the class of DHTs designed for remote (e.g., home) monitoring or self-management of diagnosed non-communicable chronic disease that have a similar risk and benefit profile, the review demonstrated it was feasible to extend DHT-specific content from DHT evaluation frameworks into all domains of the Core Model. Furthermore, as discussed in Chapter 1, this class of DHTs was chosen to be representative of the most likely technologies to undergo HTA to inform public funding decisions and focusing on this higher-risk DHT class should identify a fuller range of DHT-specific content, with the expectation that not all this content will apply to lower-risk DHT class. As a result, this review adds to the

literature the identification of a large set of issues for HTA relevant to the DHTs most likely to undergo HTA for public funding decisions.

7.1.2. The systematic review of primary research on DHTs that manage chronic disease (Chapter 3)

This systematic review aimed to describe the current trends in primary research for DHTs that manage chronic disease and specifically address research question 3; the extent to which primary research on DHTs that manage chronic disease generates appropriate evidence for a DHT-specific and comprehensive HTA.

Current trends in primary research for DHTs that manage chronic disease

The review identified 178 DHT interventions published between 1 January 2015 and 20 March 2020, increasing year on year, predominantly targeting cardiovascular disease and diabetes in high to middle-income countries. The review confirmed that DHTs that aimed to manage chronic disease predominantly fell into two types: 1. Patient remote monitoring via digital devices, or 2. Web-based or app self-management programs, and that the potential benefits and risks within these two types of DHTs were relatively homogenous.

Encouragingly, the review found most effectiveness studies were randomised controlled trials (RCTs) where the comparator reflected standard care. In addition, they employed practices to overcome methodological problems associated with DHTs, e.g., blinding of research staff where patients could not be blinded. However, small sample sizes, short trial durations, and short follow-up periods limited the ability to detect treatment effects, determine the optimal treatment dose, and estimate the persistence of effects. Lack of inclusion of populations from low-income countries, settings where telecommunication infrastructure/connectivity may be poor (e.g., rural and remote communities), and exclusion of people who did not speak the primary language or own the required personal technology limited the generalisability of

many studies. Most studies have yet to conduct an economic evaluation, so cost-effectiveness compared to alternate interventions remains largely unknown.

The extent to which identified content for HTA is covered in DHT primary research (Research question 3)

An assessment of 112 cardiovascular and diabetes DHT studies revealed that less than half covered DHT-specific content for HTA in all but the health problem domain. In contrast, content common to all technologies but essential for performing HTA on DHTs was covered by more than half the studies in all domains except for the clinical effectiveness and ethical analysis domains.

Content coverage in technical, safety, ethical and legal domains was low, despite being significant areas of risk to the user. In terms of effectiveness, the UK NICE ESF (4) standards of ensuring reliable and accurate health information and best practice behaviour change techniques were only evidenced in a minority of studies providing these services. The lack of evidence for ongoing controls to keep health information up-to-date was concerning. Three-quarters of the studies could not provide evidence of patient involvement in the DHT design, which is a critical failure for technologies designed for patients to use at home. In the organisational aspects domain, two-thirds could not evidence a relevant healthcare expert's role in the design, development, testing, or sign-off of the DHT, despite the observation that this is a key enabler of DHT uptake.

In terms of economic evaluations, similar to Kidholm (5), it was found that there was variability in the types of costs included. Most studies only included the cost of the equipment for the patient, not the costs for the equipment required to run the DHT service or downstream costs associated with changes in health outcomes resulting from the DHT. The fixed costs of providing the DHT in the health system and at scale (licensing, platforms,

hardware, security) can escalate rapidly from costs involved in a clinical trial, and there were few attempts to estimate and include these additional costs. Many studies assumed the patient would pay data usage fees and use their own personal digital devices such as mobiles and laptops.

Although primary research in DHTs that manage chronic disease is steadily increasing, it does not currently address the content required for a DHT-specific comprehensive HTA, particularly in the critical areas of cybersafety, cybersecurity, technical reliability, stability, and patient satisfaction. This will likely lead to suboptimal decisions in the investment of health service budgets. Measures are required to increase the quality of trial design and reporting using existing tools and DHT-specific frameworks.

7.1.3. Stakeholder preferences for DHT attributes to consider in health service funding (Chapter 4)

This study aimed to elicit stakeholder (patients, carers, health professionals and the general community) preferences to address research question 4; the views of a broad cross-section of community stakeholders as to the most important issues to consider when evaluating DHTs that manage chronic disease for public funding.

Community preferences for the most important issues to consider for the public funding of DHTs that manage chronic disease (Research question 4)

To elicit stakeholder preferences for the "most" and "least" important evaluation issues, a best-worst scaling study was conducted. The 71 content items identified and refined in the preceding systematic reviews (Chapters 2 and 3) were grouped by issue similarity into twenty-four non-overlapping attributes of a DHT over several iterations of feedback and a pilot best-worst scaling survey.

In the final survey of 1,251 stakeholders, the important DHT attributes were predominantly related to safety but also related to technical features, effectiveness, ethics, and economics. Broad agreement on attribute priorities was seen across all stakeholder groups, and this finding was supported by latent class analysis. Overall, connectedness with the patient's healthcare team was the highest priority, with *"Helps health professionals respond quickly when changes in patient care are needed,"* the most important of all attributes for all stakeholders. Although patient privacy was important, it was not the most important consideration for all stakeholders. Unique benefits of DHTs such as less waiting, less burdensome travels, a digitally connected health care team, and increased confidence in self-managing conditions were prioritised over whether the DHT was as effective as face-to-face care. Provided the patient feels connected to a responsive healthcare team, the mode of delivery of this care seems to be less important.

DHT-specific HTA frameworks are now being used for funding decisions (e.g., UK's ESF (4) with DTAC (6), Germany's DiGAV (7), and Finland's Digi-HTA (8, 9)). However, to date, there have been few or no studies that include a broad cross-section of the general community, patients, carers, and health professionals, to understand the relative importance of the issues included in these DHT-specific HTA frameworks. Although most of the priority issues were covered in these frameworks, such as data privacy, useability, accessibility, and technical reliability, the issues found in this review to be most important to community stakeholders such as "Helps health professionals respond quickly when changes in patient care are needed" and "Does not limit the user in their treatment options" are not included. These issues should be considered for inclusion in DHT-specific HTA frameworks to reflect community stakeholder preferences.

7.1.4. Conclusions on research questions

The research studies included in Chapters 2 to 4 confirmed that existing HTA frameworks do not consider all the DHT-specific issues required for comprehensive HTA of DHTs, and that current DHT evaluation frameworks are not sufficient for performing a comprehensive HTA. In addition, no current DHT evaluation frameworks cover all issues recommended by the DHT evaluation literature or can demonstrate that the included issues are those that are most important to community stakeholders. Furthermore, DHT primary research on DHTs that manage chronic disease is not generating all the required evidence for DHT-specific and comprehensive HTA.

There is a clear need for developing a literature-informed and stakeholder-prioritised checklist of DHT-specific considerations that extends internationally established frameworks for HTA: to enable users to perform a DHT-specific and comprehensive HTA and encourage primary researchers to collect appropriate data to inform this HTA.

7.2. Findings from developing and testing an extended checklist for DHTs that manage chronic disease

Given the identified need for a literature-informed and stakeholder-prioritised checklist of DHT-specific considerations to extend internationally established frameworks for HTA, Chapters 5 and 6 are concerned with developing and testing such a checklist for DHTs that manage chronic disease ("the extended checklist").

Chapter 5 presents the identified content from DHT evaluation frameworks prioritised by community stakeholder preferences as a possible extension checklist to the EUnetHTA HTA Core Model.

Chapter 6 includes a case study with a cost-effectiveness analysis of a self-management DHT for chronic disease (eADVICE). This case study is an RCT of the eADVICE intervention

designed with children, parents, and health professionals to manage chronic daytime urinary incontinence and enuresis at home. The evaluation of eADVICE presented an opportunity to test the extended checklist, as eADVICE is in the class of DHTs for which the extended checklist has been designed. In addition, public funding is being sought for eADVICE through a state government HTA pathway.

The following sections present the learnings from Chapters 5 and 6.

7.2.1. An extended EUnetHTA Core Model checklist for DHTs that manage chronic disease (Chapter 5)

Chapter 5 demonstrates that it is feasible to use the results from the stakeholder preference study to prioritise the issues identified for HTA from the DHT evaluation frameworks and develop a practical set of 22 DHT-specific clarifications that extends an internationally established framework, i.e., the EUnetHTA Core Model ("the Core Model").

The "extended checklist" comprises the 22 DHT-specific clarifications The checklist consists of an item number, the Core Model or DHT-specific issue ID and issue, the DHT-specific clarification for the issue, the reference papers from which the clarifications came ("Refs"), and issue IDs with similar themes in other HTA domains ("Content relations"). In addition, to assist with standardisation of assessment and reporting, recommendations on *evidence data sources* (from peer-reviewed and grey literature*), suggested methods, tools and measures*, and *evidence types* (i.e., narrative or comparative), are provided by checklist item.

The extended checklist can be used in conjunction with the Core Model to allow a DHT-specific and comprehensive HTA. Although DHT-specific topics and issues not previously incorporated in the Core Model were identified, only three new topics were required: 1) *Quality & Safeguarding,* 2) *Technical safety (reliability & stability)* in the Safety (SAF) domain, and 3) *Reliable information content* in the Clinical Effectiveness (EFF) domain.

Only six new issues were required, five within the new topics and one within the existing topic of *features of the technology*. It is therefore feasible to keep the majority of the extended checklist as clarifications within the current ontology of the Core Model.

The extended checklist would benefit from further testing in different DHTs that manage chronic disease, and in different HTA settings and jurisdictions. It should also be noted that although the current approach produces a practical list of 22 DHT-specific clarifications, preferences and priorities of policy and decision-makers have not yet been assessed or incorporated. These stakeholders may have differing priorities around issues such as equity of access, cost, and system-level implementation considerations. Therefore, it is important to ensure the preferences of all relevant stakeholders are incorporated in determining the final set of issues for inclusion in the extended checklist. A similar preference study to that reported in Chapter 4 could be conducted with these stakeholders. where the pooling of the results from both preference studies will indicate the relative preferences between all stakeholders on the same scale.

7.2.2. Case study testing of the extended checklist (Chapter 6)

As noted, eADVICE is a relevant DHT on which to evaluate the feasibility and practicality of the extended checklist. However, this was an economic evaluation of a randomised controlled trial (RCT) of the technology, which was not specifically designed to address all the final requirements for HTA in consideration of public funding. For example, it was envisaged that the DHT would require more development to be implemented in the state health system, e.g., integration with electronic medical records and work to comply with statewide cybersecurity and privacy requirements. Support by statewide information and communication technology (ICT) teams would also be required. Therefore, not all checklist items were directly relevant to the stage of the evaluation. Nonetheless, each item of the extended checklist was relevant

for consideration to inform the public funding decision, and consideration of the practicality of providing the necessary information required to address the item could be made.

The findings on whether each extended checklist item could be assessed (Y=Yes, N=No, P=Partial), whether the information required for the assessment was published or forthcoming in peer-reviewed literature, and how the item was assessed or the reason for not being assessed has been undertaken separate to the evaluation present in Chapter 6 and is presented in Table A 13.

In summary, eleven items of the extended checklist could be completely assessed, seven partially, and four not at all. Items that could not be assessed were where the researchers did not prioritise and include them in the study protocol. This included testing of the technology in low network connectivity areas for technology availability; testing in hard-to-reach populations (e.g., indigenous, ethnic minorities, culturally and linguistically diverse, disabled, neurodiverse) for technology accessibility; and collecting DHT-specific outcomes (e.g., reduced waiting time, less burdensome travels, a feeling of security, transfer of skills, better-managed care through self-management and digitally connected healthcare professionals) for the cost-effectiveness analysis. In addition, it was not possible to completely assess checklist items where the implementation of the DHT in the health system would require additional assessment not directly relevant to the RCT. For example, identifying the areas where the technology would invade the privacy of the patient/user was not addressed in the trial because it was conducted under specific ethics requirements of data privacy and security. Outside of the trial, the implemented solution in the production environment of the health system may differ in how it impacts patient privacy, being subject to the privacy and security standards of the state health system. In addition, partial assessment could only be made in technical features and data quality management, where the integration with the eMR had yet to be

built, and in training and technical support, where this responsibility would transfer to the state health service.

Whether the information to make an assessment on a checklist item would, under current practices, be routinely published in peer-reviewed literature is also shown in Table A 13. It was true for four checklist items, partially true for nine, and for the remaining nine, it would be unlikely an assessment could be made relying solely on peer-reviewed literature. This finding confirms the challenge of reporting and relying on the information required for HTA in peer-reviewed literature. In preparing the effectiveness and cost-effectiveness studies for eADVICE, the CONSORT-EHEALTH checklist (10), an extension to the CONSORT checklist, was employed. Use of the CONSORT-EHEALTH assisted in deciding which terminology to use in describing the DHT and what details of the trial to specify for consistency of reporting with other DHT trials. This reporting checklist improves coverage of the DHT-specific items in the technical, safety, effectiveness, and ethics domains and is useful as a supplementary table for detail that cannot be included in the main manuscript. However, many journals require the original CONSORT checklist, and the CONSORT-EHEALTH checklist was not submitted with the clinical effectiveness paper. This is not optimal as it reduces the evidence available for HTA that is reported in a consistent format.

Another issue regarding the practicality of the checklist was some duplication in questions over different HTA domains on useability, accessibility, and compliance with data protection legislation. The extended checklist could be streamlined and requires testing over different DHTs and HTA settings.

7.3. Strengths and limitations

The overall strength of the research program is the robustness of the methods, which included systematic reviews of the literature and a large best-worst scaling survey for eliciting

stakeholder preferences. The output is built on the peer-reviewed literature, tested on 112 primary research studies, and 1,251 stakeholders have provided their preferences on the priority of issues. Furthermore, capturing and cataloguing of all the issues and any changes through each study by EUnetHTA Core Model identifiers provides complete traceability of our work and enables reproducibility. Finally, the case study provided a basis for assessing the practical application of the extended checklist and limitations associated with publication.

One limitation of the research program is that further work is required to undertake a similar preference study as reported in Chapter 4, involving policy and decision-makers as respondents. This would ensure that all stakeholders' views have been incorporated into the extended checklist. In addition, further testing and streamlining of the extended checklist are required, i.e., testing over the many DHTs that manage chronic disease in different jurisdictions and HTA settings. The checklist items are designed to be sufficiently generic to be relevant for all DHTs that manage chronic disease and all jurisdictions that use HTA to inform public funding decisions. However, this need to be assessed across different case studies. Furthermore, it would be optimal to extend the checklist to other classes of DHTs representative of those most likely to undergo HTA for public funding. For example, DHTs that assist health professionals in diagnosis and decision-making, e.g., clinical decision support systems.

7.4. What this research adds

The research program for this thesis has added to the literature on HTA frameworks for DHTs that manage chronic disease through:

- An extensive systematic review of international peer-reviewed and grey literature on DHT evaluation frameworks

- A distillation of review findings into the EUnetHTA Core Model by domain, topic, and issue
- An examination of primary research on DHTs that manage chronic disease for coverage of DHT-specific content over a nine-domain HTA on 112 DHT intervention studies
- Performance of a large international best-worst scaling study to elicit the preferences of patients, carers, health professionals and the general community as to the most important attributes of DHTs that manage chronic disease for health service funding
- Development of a checklist comprised of 22 literature-informed and stakeholder-prioritised DHT-specific clarifications that extends the EUnetHTA Core Model
- Testing of the extended checklist for relevance and practicality on a case study of a DHT that manages chronic disease currently seeking public funding in the state health system

7.5. Implications for evaluators, developers, and researchers

The overall objective of the thesis was to assist authors of HTA reports and HTA evaluators to perform a DHT-specific and comprehensive HTA by developing an extension checklist for an internationally established HTA framework. In addition, the identified content of the extended checklist was designed to assist authors of HTA agency guidance in clarifying the evidence required for an assessment of a DHT that manages chronic disease for public funding.

Clarifying the evidence required will assist developers to produce DHTs that meet the criteria, and researchers to plan, collect and report the evidence required. A finding of this thesis was the deficiencies in the coverage of DHT-specific issues in primary research with

less than half covering DHT-specific content in all but the current health problem domain. Coverage of DHT-specific issues in technical, safety, effectiveness, and ethical domains could be achieved by designing and reporting effectiveness studies in compliance with CONSORT E-HEALTH (10), a reporting standard that has been available since 2011. DHT extensions to reporting standards for non RCT trials, e.g., STROBE, could be developed. Use of reporting standards such as CONSORT E-HEALTH not only helps researchers report consistently and transparently, but HTA authors and evaluators to find the required evidence more easily.

In addition, a phased research approach with improved referencing to prior work could be employed immediately to improve the quality of trial design and reporting. A phased research approach should, at a minimum, include a review of existing DHTs available to the target population, design and initial testing with target patients and relevant health professionals, efficacy/accuracy testing, and safety testing for technical reliability, stability, cybersecurity, and cybersafety, before clinical effectiveness trials. This prior work should be referenced or reported in clinical effectiveness publications. Finally, economic evaluations should be performed, considering increases in costs for operating the DHT service in the health system at the expected scale and considering equity of access to the DHT for a diverse range of patients to prevent any worsening of health inequalities.

7.6. Future research

An immediate research priority is to assess and incorporate the preferences of policy and decision-makers in the extended checklist and to test the extended checklist over different types of DHTs that manage chronic disease, jurisdictions, and HTA settings. One objective is to work towards an internationally accepted set of DHT clarifications for DHT that manage chronic disease. Medium-term future research should aim to extend the checklist to all DHTs likely to undergo HTA and an internationally accepted set of DHT clarifications for all

DHTs, which could be used with the EUnetHTA Core Model. In addition, further research is required on tools for researchers to ensure consistent and transparent evidence generation and reporting for DHTs and how to increase the use of these tools with researchers, peer reviewers, and journal editors.

In Australia, much could be done to provide clearer guidance on the evidence required for the HTA of DHTs at national, state/territory and local health district levels. An evaluation of whether the standard HTA pathways are appropriate for DHTs should be undertaken. Explicit clarification and communication of the HTA pathways for DHTs, the responsible entities(s), and assessment criteria would reduce uncertainty for DHT developers and researchers and help to support innovation in DHTs in Australia. Clearly defining the assessment evidence required for DHTs should enable health services to make more optimal funding decisions.

7.7. Conclusions

DHTs that manage chronic disease are increasingly becoming an integral part of healthcare service delivery. There has been a wealth of research on the unique potential benefits and risks and nearly twenty years of research on DHT-specific evaluation content to inform considerations in a nine-domain HTA. Much of the content and methodologies of HTA for more established technologies apply to DHTs, but the quality of HTA for DHTs can be improved by including DHT-specific considerations. There is currently a critical need to communicate these considerations and the evidence required for HTA to improve the quality of research so health services can make optimal funding decisions. This thesis has compiled literature-informed and stakeholder-prioritised DHT-specific considerations for undertaking HTAs of DHTs that manage chronic disease, using internationally accepted HTA terminology and frameworks for ease of adoption in many countries.

7.8. References

1. EUnetHTA Joint Action 2 Work Package 8. HTA core model® version 3.0. [Pdf] 2016; Available from: www.htacoremodel.info/BrowseModel.aspx.; Accessed 14 August 2022.
2. Kidholm K, Ekeland AG, Jensen LK, Rasmussen J, Pedersen CD, Bowes A, et al. A model for assessment of telemedicine applications: Mast. *Int J Technol Assess Health Care*. 2012;28(1):44.
3. Moshi MR, Tooher R, Merlin T. Development of a health technology assessment module for evaluating mobile medical applications. *Int J Technol Assess Health Care*. 2020;36(3):252-61.
4. National Institute for Health and Care Excellence (UK). Evidence standards framework for digital health technologies. [Internet] 2018 [updated 09 August 2022]; Available from: https://www.nice.org.uk/corporate/ecd7; Accessed 15 August 2022.
5. Kidholm K, Clemensen J, Caffery LJ, Smith AC. The model for assessment of telemedicine (mast): A scoping review of empirical studies. *J Telemed Telecare*. 2017;23(9):808-13.
6. NHS Digital (UK). The digital technology assessment criteria for health and social care (DTAC). [Internet] 2019 [updated 16 April 2021]; Available from: https://transform.england.nhs.uk/key-tools-and-info/digital-technology-assessment-criteria-dtac/; Accessed 18 August 2022.
7. Regulation on the procedure and requirements for testing the eligibility for reimbursement of digital health applications in the statutory public health insurance, S. Digital Health Applications Ordinance (DiGAV), Federal Ministry of Health (DE) (2019).

8. Haverinen J, Keränen N, Falkenbach P, Maijala A, Kolehmainen T, Reponen J. Digi-HTA: Health technology assessment framework for digital healthcare services. *FinJeHeW*. 2019;11(4).

9. Haverinen J, Turpeinen M, Falkenbach P, Reponen J. Implementation of a new Digi-HTA process for digital health technologies in Finland. *Int J Technol Assess Health Care*. 2022;38(1).

10. Eysenbach G. Consort-ehealth: Improving and standardizing evaluation reports of web-based and mobile health interventions. *J Med Internet Res*. 2011;13(4):e126.

11. Nielsen J. Usability engineering. [Updated edition]. ed. San Francisco: Elsevier Science & Technology; 1994.

12. Norman DA. User-centered system design: New perspectives on human-computer interaction. In: Norman DA, Draper, S.W., editor. Cognitive engineering. Hillsdale: Lawrence Erlbaum Associates; 1986. p. 31-61.

13. Hatcher RL, Gillaspy JA. Development and validation of a revised short version of the working alliance inventory. *Psychother Res*. 2006;16(1):12-25.

Appendix A: Supplementary materials

This chapter contains supplemental tables and figures referenced in Chapters 2-7.

Chapter 2 supplementary materials

Figure A 1: Peer-reviewed literature search strategy

Database[1] (Ovid)	Search terms[2]
MEDLINE, Embase, CINAHL, Econolit, Cochrane	(1)[3] exp Telemedicine/ or (telehealth or telemedicine) or exp Medical Records Systems, Computerized/ or (ehealth or (electronic adj2 health)) or (digital adj2 health) or (digital adj1 health adj1 intervention) or exp Mobile Applications/ or ((mobile adj1 health) or mhealth) or ((mobile adj1 health adj1 app) or (mobile adj1 health adj1 application)) or (((mobile adj1 medical adj1 app) or (mobile adj1 medical adj1 application))) or exp Text Messaging/ or (sms or text messag$) or (chat room$ or chatroom$ or chatbot$ or avatar) or (wearable$) or ((artificial adj1 intelligence) or (machine adj1 learning))
	(2)[4] (health adj evaluation*) or (project adj evaluation*) or (program* adj evaluation) or (evidence adj1 standards) or (health adj service adj evaluation) or (health adj promotion adj evaluation*) or (systematic adj1 review) or (technology adj2 evaluation) or (implementation adj evaluation*) or (impact adj evaluation*) or (outcome* adj evaluation*) or (decision adj2 making adj2 framework) or (decision adj2 making adj2 standard*) or (decision adj2 making adj2 guideline*) or (technology adj2 appraisal*) or (technology adj validation) or (evaluation adj1 framework*) or ((implementation or translation*) adj2 (study or research)) or (subsid* or rebat* or reimburs*) or Comparative Effectiveness Research/ or exp patient harm/ or exp patient safety/or exp Insurance, Health, Reimbursement/ or exp Legislation, Medical/ or exp Financing, Government/
	(3)[4] Economics/ or exp "Costs and Cost Analysis"/ or (cost benefit analysis) or (economic* adj evaluation*) or (cost adj effect*) or (cost adj benefit) or (cost adj utility) or (cost adj effic*) or (economic* adj analysis) or quality-adjusted life years/ or (quality adjusted life years) or (QALY*)
	(4) randomized controlled trial.pt. or controlled clinical trial.pt. or randomized.ab. or placebo.ab. or Clinical Trials as Topic/ or randomly.ab. or (crossover or cross-over).tw or trial.ti.
	(5)[4] exp epidemiologic studies/ or (Case control) or (cohort adj (study or studies)) or (Cohort analy$) or (Follow up adj (study or studies)) or (observational adj (study or studies)) or (Longitudinal) or (Retrospective) or (Cross sectional)
	(6) ((Health adj2 technology adj2 assessment) or HTA or (technology adj2 assessment)).tw.
	(7) Animals/ not (animals/ and Humans/)

1 Searches modified for Embase, Econolit, CINAHL, Cochrane

2 (1) Search terms used to identify e-Health, m-Health and digital health modes of health delivery (2) Terms used to identify decision making, funding and health evaluation studies (3) Terms to identify economic evaluation studies (4) Terms used to identify Randomised Controlled Trials (5) Terms used to identify observational studies (6) Terms used to identify Health Technology Assessments (7) Terms used to search for animal not human studies

3 All terms were searched using multipurpose (.mp)

4 All terms were searched using text words (.tw)

Search string: Limit yr="2015 - Current" ((1) AND ((2) OR (3)) AND ((4) OR ((5) NOT (4)) OR (6) NOT ((4) OR ((5) NOT (4)))) NOT (7)); Medline/Embase search conducted on 20 March 2020; CINAHL/Econolit search conducted on 22 March 2020.

Table A 1: Grey literature search strategy

The following databases were searched with the terms: “electronic health" or eHealth or “mobile health” or mHealth or telehealth or telemedicine or “digital health” or “digital medicine” over the period January 2015 to August 2020.	
Database and website	**Country/region**
Health Technology Assessment (HTA) Agencies[a]	
Canadian Agency for Drugs and Technologies in Health (CADTH) https://www.cadth.ca/search?keywords	Canada
Health Quality Council of Alberta (HQCA). Completed Reviews http://hqca.ca/studies-and-reviews/completed-reviews/	
Health Quality Ontario (HQO). http://www.hqontario.ca/Evidence-to-Improve-Care/Health-Technology-Assessment	
The Hospital for Sick Children (SickKids). (TASK) http://lab.research.sickkids.ca/task/reports-theses/	
Institut national d’excellence en santé et en services sociaux (INESSS) http://www.inesss.qc.ca/en/publications/publications.html	
Institute of Health Economics (IHE). Publications http://www.ihe.ca/index.php?/publications	
Manitoba Centre for Health Policy (MCHP). Deliverables http://mchp-appserv.cpe.umanitoba.ca/deliverablesList.html	
McGill University Health Centre (MUHC). Technology Assessment Unit Reports https://muhc.ca/tau/page/tau-reports	
NLCAHR: Newfoundland and Labrador Centre for Applied Health Research. Contextualized Health Research Synthesis Program (CHRSP) Completed CHRSP projects http://www.nlcahr.mun.ca/CHRSP/CompletedCHRSP.php	
Programs for Assessment of Technology in Health (Canada). Reports (PATH): https://www.path-hta.ca/research	
University of British Columbia. Centre for Health Services and Policy Research http://chspr.ubc.ca/publications/	
INAHTA Secretariat. International Network of Agencies for Health Technology Assessment http://www.inahta.org/publications/	International
World Health Organization Regional Office for Europe. Health Evidence Network (WHO HEN) http://www.euro.who.int/en/what-we-do/data-and-evidence/health-evidence-network-hen/publications/by-keyword	
Australian Government. Department of Health and Ageing. Australia and New Zealand Horizon Scanning Network (ANZHSN) http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/technologies-assessed-lp-2	Australia
Australian Government Department of Health and Ageing. Medical Services Advisory Committee (MSAC). MSAC Applications http://www.msac.gov.au/internet/msac/publishing.nsf/Content/completed-assessments	
Joanna Briggs Institute (JBI). The Joanna Briggs Institute EBP Database http://connect.jbiconnectplus.org/Search.aspx	
Monash Health. Centre for Clinical Effectiveness (CCE) http://monashhealth.org/health-professionals/cce/cce-publications/	
Queensland Government (Australia). Health Technology Reference Group. Health Technologies Evaluated-Reports and Briefs (COAG Health Council) https://www.coaghealthcouncil.gov.au/Health-Technology-Reference-Group/Reports-and-Briefs	
Institute of Technology Assessment (ITA). Projects http://www.oeaw.ac.at/ita/en/projects	Austria
Ludwig Boltzmann Institute of Health Technology Assessment http://eprints.hta.lbg.ac.at/	
Belgian Health Care Knowledge Centre (KCE) https://kce.fgov.be/en/all-reports	Belgium
French National Authority for Health/Haute Autorité de santé (HAS). http://www.has-sante.fr/portail/jcms/c_946986/en/english-toutes-nos-publications-ligne-principale?portal=r_1457306	France
German Institute of Medical Documentation and Information (DMDI) https://www.dimdi.de/dynamic/en/further-services/health-technology-assessment/hta-reports/	Germany
Health Information and Quality Authority. https://www.hiqa.ie/reports-and-publications/health-technology-assessments	Ireland
Health Service Executive. Irish Health Repository (Lenus) http://www.lenus.ie/hse/	

The following databases were searched with the terms: “electronic health" or eHealth or “mobile health” or mHealth or telehealth or telemedicine or “digital health” or “digital medicine” over the period January 2015 to August 2020.	
Database and website	**Country/region**
De Gezondheidsraad (GR). Health Council of the Netherlands http://www.gezondheidsraad.nl/en/publications	The Netherlands
Zorginstituut Nederland. National Health Care Institute Netherlands https://english.zorginstituutnederland.nl/publications	
Folkehelseinstituttet. Norwegian Institute of Public Health. Publications https://www.fhi.no/en/publ/	Norway
Institute of Health Carlos III http://publicaciones.isciii.es/	Spain
Agency for Health Quality and Assessment of Catalonia http://aquas.gencat.cat/ca/publicacions/	
Swedish Council on Health Technology Assessment (SBU): https://www.sbu.se/en/publications/	Sweden
Healthcare Improvement, Scotland. Published Resources. http://www.healthcareimprovementscotland.org	United Kingdom
National Institute for Health and Care Excellence (NICE) http://www.nice.org.uk/	
National Institute for Health Research. (NIHR). Innovation Observatory http://www.io.nihr.ac.uk/	
NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC). https://www.journalslibrary.nihr.ac.uk/programmes/	
Agency for Healthcare Research and Quality (AHRQ). Technology Assessments: http://www.ahrq.gov/research/findings/ta/ Evidence-Based Practice: http://www.ahrq.gov/research/findings/evidence-based-reports/search.html Effective Health Care Reports: https://effectivehealthcare.ahrq.gov/products-tools/	United States
Centers for Medicare & Medicaid Services (CMS). Technology Assessments: http://www.cms.gov/medicare-coverage-database/indexes/technology-assessments-index.aspx?TAId=85&bc=AAAQAAAAAAAA&	
ECRI Institute: http://www.ecri.org/	
Institute for Clinical and Economic Review (ICER): https://icer-review.org/materials/	
Washington State Health Care Authority (HCA). Health Technology Review: https://www.hca.wa.gov/about-hca/health-technology-assessment/health-technology-reviews	
Health Economics[a]	
Hospital for Sick Children [Toronto]. Paediatric Economic Database Evaluation (PEDE): http://pede.ccb.sickkids.ca/pede/search.jsp	Canada
McMaster University. Centre for Health Economics and Policy Analysis (CHEPA) http://www.chepa.org/research-products	
Toronto Health Economics and Technology Assessment Collaborative (THETA) http://theta.utoronto.ca/content.php?pid=411861&sid=3372336	
Federal Reserve Bank of St. Louis. Economic Research Division. Ideas database (IDEAS): http://ideas.repec.org/	International
NHS Economic Evaluation Database (EED), economic evaluations of health care interventions. Searchable as part of the University of York NHS CRD databases.	
University of Aberdeen. Health Economics Research Unit (HERU) http://www.abdn.ac.uk/heru/outputs/publications/	
ProQuest Dissertations and Theses Global (PQDT)	
ProQuest Dissertations and Theses Global (PQDT)	International

[a]Source: Canadian Agency for Drugs and Technologies in Health (CADTH)’s, “Grey Matters: a practical tool for searching health-related grey literature,” updated April 2019

Table A 2: EUnetHTA Core Model 3.0[a] description of domains and list of domain topics

HTA Domain Number and Name (Three letter acronym)	**Description of the HTA domain**	**HTA domain topics (example topic issues; to clarify topic if required)**
1. Health problem and current use of technology (CUR)	CUR provides background information on target groups, target conditions, and their epidemiology; the individual and societal burden of the health problem; the availability, patterns of use, alternatives, and the technology's regulatory status; and the requirements for the technology's use.	(1) Target population, (2) Target condition, (3) Current management of the condition, (4) Utilisation (current and future use), (5) Regulatory status (market authorization, reimbursement status)
2. Description and technical characteristics of technology (TEC)	TEC describes the technology (or sequence of technologies) in sufficient detail to differentiate it from comparators. Details should cover: When it was developed, first used, and for what purpose(s); claimed benefits over its comparator and current phase of development; who will use it and in what manner, for what conditions and for what level of health care; material requirements for the premises, equipment and staff; and any specific training and information requirements for staff/patients/family/general public. Although this domain covers the technology's regulatory status as a topic, the questions are identical to CUR, so for our assessment purposes, we remove "Regulatory Status" from TEC to prevent duplication.	(1) Training and information needed to use the technology, (2) Features of the technology, (3) Investments and tools required to use the technology, (5) Other (Who manufactures the technology?) Excluded due to duplication with CUR: (4) Regulatory status
3. Safety (SAF)	Safety is an umbrella term for any unwanted or harmful effects caused by using a health technology. Safety issues to be covered are those important to patients, or otherwise likely to be important in guiding healthcare providers and policymakers' decisions. This domain aims to identify any unwanted or harmful effects, estimate each probability and severity, and then identify controls to mitigate or reduce these risks.	(1) Patient safety, (2) Occupational safety, (3) Environmental safety, and (4) Safety risk management
4. Clinical effectiveness (EFF)	EFF focuses on health benefits and the benefit harm balance, using the harms identified in SAF. To provide evidence of a causal relationship between the technology and health outcomes, the generally accepted standard is an appropriately designed and conducted randomised controlled trial (RCT). This RCT should directly compare the new technology with a well-justified comparator in patients who are typical in day-to-day health care settings. The assessment of health benefits should primarily consider patient-relevant outcomes such as mortality, morbidity, and quality of life.	(1) Mortality, (2) Morbidity, (3) Function (Impact on body functions, workability, return to previous living conditions, activities of daily living), (4) Health-related quality of life, (5) Quality of life (Does the knowledge of the test result affect the patient's non-health-related quality of life?), (6) Patient satisfaction, (7) Test-treatment chain (If relevant, is there an effective treatment for the condition the test is detecting?), (8) Test accuracy (If relevant), (9) Patient safety (Consequences of false positive, false negative and incidental findings), (10) Change in management, (11) Benefit harm balance
5. Costs and economic evaluation (ECO)	ECO aims to inform value-for-money judgements about health technologies with information about costs, health-related outcomes, and economic efficiency. The topics and issues are limited to important items for all healthcare settings and are required for other jurisdictions in assessing the transferability of ECO information into their own setting.	(1) Resource utilisations (Resource identification, measurement, valuation, and budget impact of technology and comparator), (2) Measurement and estimation of outcomes (Outcome identification, measurement, and valuation of technology and comparator), (3) Examination of costs and outcome (incremental cost and outcome of technology over comparator), (4) Characterising uncertainty, (5) Characterising heterogeneity (Subgroup analysis), (6) Validity of the models (Methodological assumptions, the validity of estimates of costs, outcomes, and economic evaluations)

HTA Domain Number and Name (Three letter acronym)	Description of the HTA domain	HTA domain topics (example topic issues; to clarify topic if required)
6. Ethical analysis (ETH)	ETH considers prevalent social and moral norms and values relevant to the new technology. It involves an understanding of the consequences of implementing or not implementing a healthcare technology in two respects: The prevailing societal values and the norms and values that the technology itself constructs when it is put into use. ETH also covers moral and ethical issues related to the consequences of performing the health technology assessment (HTA), e.g., choice of specific endpoints and ethical problems related to economic evaluation. ETH includes six topics and 19 issues that stem from the general values of the population, aims of the healthcare system, and values arising from using a technology.	(1) Benefit harm balance, (2) Autonomy, (3) Respect for persons, (4) Justice and Equity, (5) Legislation, (6) Ethical consequences of the HTA
7. Organisational aspects (ORG)	ORG considers how different kinds of resources (e.g., material artifacts, human skills, and knowledge, money, attitudes, work culture) need to be mobilised and organised when implementing technology and the consequences they may produce in the organisation and the healthcare system as a whole. Organisational issues include, e.g., work processes and patient/participant flow, quality and sustainability assurance, centralisation communication and co-operation, managerial structure, and acceptance of technology. Organisational aspects should be considered on three levels: (1) intra-organisational; (2) inter-organisational; and (3) health care system level; to ensure the different aims and expectations of various stakeholders, e.g., payers, providers, and suppliers, are taken into account.	(1) Health process delivery, (2) Structure of health care system, (3) Process-related costs, (4) Management, (5) Culture
8. Patients and Social aspects (SOC)	Patient aspects relate to issues relevant to patients, individuals, and caregivers. Patient refers to a person who receives (or has received) and uses (or used) health technologies and health services in the healthcare sector. The term individual is sometimes used synonymously with 'patient.' Still, it can also refer to a healthy individual who receives health technologies, e.g., a person taking part in a screening program. The term caregivers (sometimes referred to as carers) refers to family, friends, and other persons from the patient's/individual's social network who provide care to the patient and are in other ways involved during the disease. It excludes those paid to give care, such as healthcare professionals. Social aspects are related to social groups, specific groupings of patients, or individuals of specific interest in an HTA, such as older people, people living in remote communities, people with learning disabilities, ethnic minorities, immigrants, etc.	(1) Patients' perspectives, (2) Social group aspects, (3) Communication aspects
9. Legal aspects (LEG)	The objective of LEG is to detect rules and regulations which need to be considered when evaluating the implications and consequences of implementing a health technology. Rules and regulations have been established to protect the patient's rights and societal interests. The rules and regulations may be a part of patient rights legislation, data protection legislation, or health care personnel's provisions, rights, and duties in general.	(1) Autonomy of patients, (2) Privacy of the patients, (3) Equality in health care, (4) Ethical aspects, (5) Authorisation and safety, (6) Ownership and liability, (7) Regulation of market

[a]EUnetHTA Joint Action 2, Work Package 8. HTA Core Model® version 3.0. [Pdf]; 2016. Available from: www.htacoremodel.info/BrowseModel.aspx.

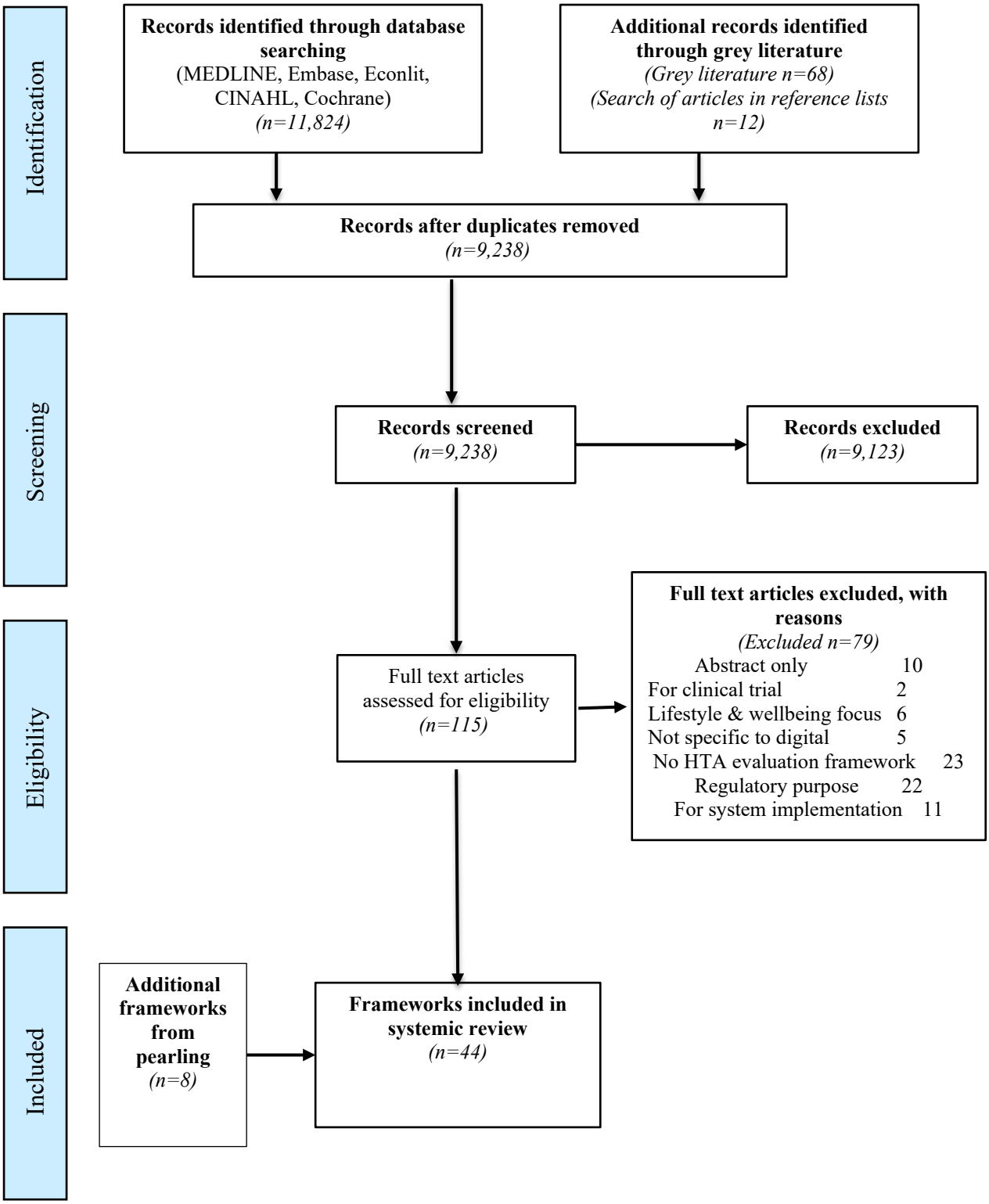

Figure A 2: Preferred reporting items for systematic reviews and meta-analysis (PRISMA) flow diagram for framework study selection

Table A 3: Characteristics of included framework papers

Framework	Year	Country/ Region[a]	Journal citation/ website	Author affiliation	Intended audience	Purpose (name of framework)
Eysenbach 2011 (35)	2011	International	Journal citation	Hospital/ university	Not stated, but assume writers of eHealth trial reports and evaluators of eHealth trials	Information to include when reporting eHealth/mHealth trials (CONSORT-EHEALTH checklist)
Andalusian Health Quality Agency (AHQA) 2012 (36)	2012	Spain	Website/	HTA agency	Citizens, Health Professionals, Health Services Suppliers, and Developers	(Recommendations on design, use, and assessment of mobile health apps)
Kidholm et al. 2012 (20)	2012	Europe	Journal citation	Hospital/ university	Not stated, but assume telemedicine users and stakeholders in decision making	To present the Model for ASsessment of Telemedicine applications (MAST)
Haute Autorité de Santé (HAS) 2013 (22)	2013	France	Website/ Guideline	HTA agency	For manufacturers, research organisations, and project developers	To identify a set of methods and conditions that will allow high-quality clinical assessment, mainly when conventional randomised controlled trials cannot be performed
Khoja 2013 (37)	2013	International	Journal citation	University	Managers, healthcare providers, and clients	eHealth evaluation tool (Khoja–Durrani–Scott Framework for e-Health Evaluation)
Lewis and Wyatt 2014 (38)	2014	International	Journal citation	University	App commissioners, developers, and users	A framework to assess the likely risks posed by a specific app in a specific context
Bergmo 2015 (29)	2015	International	Journal citation	University	Researchers interested in conducting future economic evaluations in eHealth	How to apply economic evaluation to eHealth
Mohr et al. 2015 (39)	2015	International	Journal citation	University	Not stated, but assume researchers in behavioural intervention technologies	Propose adaptations of traditional randomised controlled trial methodology that can support the evaluation of behavioural intervention technologies
Mookherji et al. 2015 (24)	2015	International	Journal citation	University/ NGO	Decision-makers such as ministries of health, technical agencies, donors, and implementing partners	Results of a survey on monitoring, evaluation, and impact assessment of mHealth projects using a (6-point scale of evaluation rigour)
Steventon et al. 2015 (40)	2015	International	Journal citation	University	Not stated, but assume comparative effectiveness researchers and policymakers	Methods to test the generalisability of an RCT of digital health intervention effectiveness

Framework	Year	Country/ Region[a]	Journal citation/ website	Author affiliation	Intended audience	Purpose (name of framework)
EU Draft Consard Ltd 2016 (41)	2016	Europe	Website/ Report	Consultant	Specifies an initial list of target groups: Citizens, mHealth developers, App aggregators, health professionals, and decision-makers in the healthcare system	To propose a set of common quality criteria and assessment methodologies to help stakeholders assess the validity and reliability of mHealth apps (EU guidelines on assessment of the reliability of mobile health applications - 2nd draft)
Gorski 2016 (42)	2016	International	Journal citation	University	mhealth project developers	Identification of nine distinct value propositions for mHealth projects Identification of best practices for financial sustainability in mHealth projects
McMillan et al. 2016 (43)	2016	UK	Journal citation	University	App developers, standards organisations, researchers	Rating tool for health-behaviour change apps, based on the 2014 NICE behaviour change guidance
McNamee et al. 2016 (27)	2016	UK	Journal citation	University	Developers of refined economic tools and methods	To stimulate debate so that existing economic techniques may be refined, or new methods developed
Murray et al. 2016 (44)	2016	International	Journal citation	University	Those charged with appraising evidence for using specific digital health interventions within a publicly funded, resource-limited health system	To outline an evaluation strategy in terms of the research questions needed for digital health interventions
Rojahn et al. 2016 (34)	2016	Europe	Journal citation	Corporate (health care company)	Developers/ manufacturers	Identify public policies concerning remote monitoring in four European countries
IRB Advisor 2017 (45)	2017	International	Journal citation	Consultant	Not stated, but publication is for health professionals	To raise ethical issues in mHealth
Lennon et al. 2017 (33)	2017	International	Journal citation	University	Stakeholders in creating the right market and environment	To examine barriers and facilitators to implementation of digital health at scale
Maar et al. 2017 (46)	2017	International	Journal citation	University	mhealth project developers and managers	a framework for the process evaluations for mHealth interventions in multiple cultural settings
Michie et al. 2017 (47)	2017	UK	Journal citation	University/ Government agency	eHealth researchers and developers, government decision-makers	Considerations for development of guidelines to create, evaluate and implement effective digital healthcare interventions
Philpott et al. 2017 (25)	2017	International	Journal citation	University	Not stated, but assume researchers in digital health technologies	Design and validation of response-adaptive randomised (RAR) trial design to testing mHealth apps

Framework	Year	Country/ Region[a]	Journal citation/ website	Author affiliation	Intended audience	Purpose (name of framework)
Drury et al. 2018 (32)	2018	Asia	Website/ Report	Consultant	Those who need to brief decision-makers (e.g., senior government officials, health manager, donors) about the issues to be considered when making small or large investments in digital health	A digital health impact framework (DHIF)
European Commission (EC) 2018 (48)	2018	Europe	Website/ Report	Government agency	Not stated	Presents the main results of a European Commission consultation focussed on barriers and enablers of health data sharing with a wide range of stakeholders. European focussed, but with a majority of German respondents (individuals 52 percent and organisations 17 percent).
Hogaboam 2018 (49)	2018	International	Thesis	University	Assessors in neurosurgery and orthopaedics	Assessment framework for wearable medical devices in neurosurgery
Jurkeviciute 2018 (50)	2018	International	Thesis	University	eHealth evaluators	Report on the use of standards in eHealth evaluation planning practice
Nielsen and Rimpiläinen/ The Digital Health & Care Institute 2018 (51)	2018	Ireland, Northern Ireland, and Scotland	Website/ Report	Government agency	For the decision-makers in the mPower project - evaluating mHealth Apps for use	Overview and examination of current international initiatives and practices to develop, assess and evaluate the use of mobile health and wellbeing apps and services
Sax et al. 2018 (30)	2018	International	Journal citation	University	Not stated	A framework to evaluate mHealth apps to ensure user autonomy is protected; free from influences on economic behaviour
UK Academy of Medical Sciences 2018 (52)	2018	United Kingdom	Website/ Report	Charity	Those who may use or be responsible for developing, evaluating, regulating, or commissioning data-driven technologies in different contexts and settings	A framework of actionable principles to guide their development, evaluation, and use.
Wyatt 2018 (26)	2018	International	Journal citation	University	mHealth app users, developers, health professionals, and app distributors	Provides checklists and evaluation methods that can be applied to apps and suggestions for how clinical specialty organisations can develop a low-cost curated app repository with explicit risk and quality criteria.

Framework	Year	Country/ Region[a]	Journal citation/ website	Author affiliation	Intended audience	Purpose (name of framework)
Beintner et al. 2019 (53)	2019	International	Journal citation	University	Not stated, but assume those developing reporting standards for trials of online interventions	To propose standards for measuring and reporting adherence to online interventions (Standards for reporting adherence)
Caulfield et al. 2019 (54)	2019	International	Journal citation	University	Researcher/clinicians interested in wearable devices	Evaluation framework for wearable devices for specific applications
UK Dept Health & Social Care 2019 (55)	2019	United Kingdom	Website	Government agency	Developers, deployers, and users of data-driven technologies	Principles for data-driven technologies (Code of conduct for data-driven health and care technology)
HAS 2019 (23)	2019	France	Website	HTA agency	Manufacturers or operators of CMDs applying for individual funding by the French health insurance scheme	(Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement)
Draft HAS 2019 (56)	2019	France	Website	HTA agency	Industrialists, patient associations, national professional colleges, but also developers of IT solutions, researchers, Interdisciplinary Artificial Intelligence Institutes, etc	Consult on complementary analysis grid for the evaluation of AI-based medical devices for health insurance reimbursement
Huckvale et al. 2019[c] (31)	2019	International	Journal citation	University	Health care professionals	Provides a contemporary assessment of the privacy practices of popular apps for depression and smoking cessation by critically evaluating privacy policy content and, specifically, comparing disclosures regarding third-party data transmission to actual behaviour.
UK NICE 2019 (2)	2019	United Kingdom	Website/ Standard	HTA agency	Technology developers and evaluators	Standards for the evidence of effectiveness and economic impact relative to the financial risk (Evidence standards framework for digital health technologies)
NHS Digital 2019 (57)	2019	United Kingdom	Website	HTA agency	Guidance for health app developers, commissioners, and assessors	To make sure that only safe and secure apps and digital tools are published on the NHS Apps Library (Digital assessment questions (DAQ))
Rajan et al. 2019 (58)	2019	International	Journal citation	University	Policymakers	Policy implications for facilitating the further deployment of telemedicine in the care of chronically ill patients

Framework	Year	Country/ Region[a]	Journal citation/ website	Author affiliation	Intended audience	Purpose (name of framework)
Draft Australian commission on safety and quality in health care (CSQHC) 2020 (21)	2020	Australia	Website/ Draft standard	Government agency	Consumers and carers, clinicians, service providers, developers, and any other interested stakeholders	To improve the quality of digital mental health service provision and to protect service users from harm
Dick et al. 2020 (59)	2020	International	Journal citation	University	System developers	A qualitative review of system developers' experiences of evaluating mHealth interventions in the context of a developing country
Draft Federal Ministry of Health Germany 2020 (60)	2020	Germany	Website/ Draft bill	Government agency	Manufacturers	(Requirements for testing the eligibility for reimbursement of digital health applications)
Health Information and Quality Authority (HIQA) Ireland 2020 (61)	2020	Ireland	Website/ Report	Government agency	Not stated but assume Government decision-makers	To review national and international evidence and best practice in relation to models for the collection, use, and sharing of personal health information for the development of recommendation for Ireland
Draft Aust. Medical Services Advisory Committee MSAC 2020[c] (62)	2020	Australia	Website/ Draft guideline	HTA agency	Applicants and assessment groups requesting public funding through MSAC	Guidelines providing advice on the HTA methods used throughout the MSAC assessment pathway for requests for public funding (Draft Guidelines for Preparing Assessment Reports for the Medical Services Advisory Committee)
Moshi et al. 2020 (63)	2020	Australia	Journal citation	University	HTA evaluation framework developers	To propose a module which could be used to facilitate the assessment of mobile medical applications (MMA) for regulatory and reimbursement purposes

HTA, Health Technology Assessment; NGO, Non-government organisation

[a]Country/region for which the framework is intended

[b]While this paper does not strictly meet the evaluation framework inclusion criteria, it provides DHT-specific content on data privacy relevant to the Safety and Ethical Analysis domains

[c]Note this is a draft version of the technical guidelines for MSAC applications that includes DHT specific content. There exist two in-force technical guidelines: One for investigative and one for therapeutic technologies that do not include digital-specific content

See Section 2.7 for references.

Table A 4: Digital health technology (DHT) specific content by HTA Core Model[a] domains from frameworks in review

<table>
<tr><th colspan="2">Digital health technology (DHT) specific content from frameworks in review
Issues of Topic
<u>Issue (Assessment element ID from HTA Core Model or DHT prefix if new)</u></th></tr>
<tr><td colspan="2">Domain 1: Health problem and current use of technology (CUR)
Topics not in HTA Core Model: None</td></tr>
<tr><td>Issues of Utilisation
<u>Is the technology a new, innovative mode of care, an add-on to, or modification of a standard mode of care, or a replacement of a standard mode of care? (F0001)</u>
Describe inputs (i.e., image, physiological status, symptoms, etc.), algorithms (i.e., equations, analysis engine model logic, algorithm, etc.), and outputs (i.e., inform, treat, diagnose) of the DHT (63)</td><td><u>How much are the technologies utilised? (A0011) & What kind of variations in use are there across countries/regions/settings? (A0012)</u>
- Do health workers/patients invest in personal digital technologies (e.g., hardware, operating systems, platforms) required to use the DHT? (32) Are these personal devices costly or difficult to support? (32)
- Is the DHT limited in terms of platforms and languages? (32)
- Is network connectivity or digital literacy a problem? (32)
- Is data on DHT usage collected ongoing to share with decision-makers? (2)</td></tr>
<tr><td colspan="2">Domain 2: Health problem and current use of technology (TEC)
Topics not in HTA Core Model: None</td></tr>
<tr><td>Issues of Features of the technology
<u>How well do the technology and its comparators perform in overcoming technical barriers? (DHT01)</u>
- How well do the technology and its comparators perform in interoperability (20, 21, 23, 32, 41, 48, 49, 51, 55, 57, 63), data quality and technical reliability (21, 48, 51, 55), standardisation of access and extraction mechanisms, including the ability to extract raw data (48, 54), data visualisation and feedback (54)
Issues of Investments and tools required to use the technology
<u>What material investments are needed to use the technology? (B0007)</u>
- Consider device dimensions, battery life and charging methods, calibration requirements, operational system compatibility, connectivity requirements (e.g., wired, Wi-Fi, Bluetooth), data access and storage, data security, technical and data support (20, 35, 41, 49, 54, 57, 63)</td><td>Issues of Training and information needed to use the technology
<u>What kinds of skills and training characteristics and information are needed for the personnel/caregivers using this technology? (B0013)</u>
- Is training required/provided for personal data handling and digital skills? (32, 48, 63)
<u>What kind of training resources and information should be provided to the patient who uses the technology, or for his family? (B0014)</u>
- Is training required/provided for digital health literacy and digital skills? (32, 48, 63)
- Is there provision of technical support? (49)</td></tr>
</table>

Digital health technology (DHT) specific content from frameworks in review
Issues of *Topic*
Issue (Assessment element ID from HTA Core Model or DHT prefix if new)

Domain 3: Safety (SAF)
Topics not in HTA Core Model: *Quality and safeguarding (2, 21, 31, 35, 36, 41, 43, 48, 51, 55-57, 63), Technical safety (technical reliability & stability) (2, 20, 21, 41, 56, 57, 60, 63), Communicating for safety* (21, 36)

Issues of *Quality and safeguarding(New)*

How are data security and privacy managed? (DHT02)

- Does the DHT comply with data protection legislation/standards and allow users to manage access to their data?(21, 41, 48, 51, 55, 57)
- Has the DHT been regularly audited for actual data transmissions to third parties? (31)
- Does the DHT employ authentication, encryption, and threat analysis to avoid unauthorised access to personal data?(21, 41, 48, 51, 55, 57)
- Is there safeguarding around peer-to-peer and other communications within DHT platforms? (2)

How well is the interoperability of the technology designed and data quality managed? (DHT03)

- Does the DHT have processes to support the creation and maintenance of accurate healthcare records that can be integrated with multiple information systems using the relevant patient/ provider identifiers and standard terminologies?(21, 41, 48, 55, 57)

How transparent are the risks of the technology to the user? (DHT04)

- Does the DHT provide users with accurate information on how their data is collected, used, protected, and shared?(21, 41, 48, 55)
- Is there clear identification of the DHT's owners, contact information, funding sources, promotion and sponsorship, and any other conflicts of interest? (35, 36, 41, 63)

How well is the technology and comparator(s) designed for usability and accessibility? (DHT05)

- Is the DHT designed to minimise the barriers associated with hardware, software, data requirements, and platform services, or the language/location, age, culture, and ability of users"?(21)
- Are services compatible with commonly used assistive technologies and do they meet relevant web page or web application standards? (21, 36, 57)
- Are there processes to collect and act on user feedback? (21)

Is there adequate information on algorithms employed in the technology to evaluate their risk? (DHT06)

- Has data quality been validated prior to building and employing algorithms? (23) Are data quality checks built programmatically into artificial intelligence algorithms to avoid harm? (55)
- Does the developer/manufacturer clearly state the limitations of the data used, algorithms deployed, especially any learning algorithms, and how outcomes are validated to users? (56) For learning algorithms, is there adequate disclosure of the characteristics of the training, test, and validation data, the model, and the algorithms to understand how the algorithm controls the clinical decision-making process? (57)

Issues of *Technical safety (technical reliability & stability) (New)*

How technically reliable and stable is the technology and comparator(s)? (DHT07)

- Is there evidence of accurate and reliable transmission of unbiased data? (2, 20, 63) Does the DHT alert the user when working suboptimally or experiencing interference, e.g., low or no network connectivity? (21, 41) Does it perform well outside the laboratory(41), and is it validated for use on multiple platforms? (41)
- Is it resilient to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions? (21, 41, 56, 57, 60, 63)

How well are continuity and updates of the technology managed? (DHT08)

- Is there evidence that platform and operating system updates and patches, service continuity, backup, and recovery mechanisms are well managed? (21, 63) Is there effective communication to users about service changes or interruptions? (21, 63)

Issues of *Communicating for safety (New)*

Are there processes for the user to communicate critical risk information to the provider? (DHT09)

- Does the DHT allow the user to communicate to the provider critical information about changes in their condition or information on risks(21) of the DHT? Is there a contact mechanism for technical support with a fixed response time? (36)

Does the technology have processes for the correct identification of users? (DHT10)

- Are there processes for correctly identifying users to match them with appropriate care and provide accurate health records, protecting anonymity where necessary? (21)

Does the technology have processes to communicate changes to or transfer of a patient's care? (DHT11)

- Are there processes for the service provider to communicate when a user's care emerges or changes, or when all or part of a user's care is transferred? (21)

Digital health technology (DHT) specific content from frameworks in review
Issues of *Topic*
Issue (Assessment element ID from HTA Core Model or DHT prefix if new)

Domain 4: Clinical Effectiveness (EFF)

Topics not in HTA Core Model: *Demonstrating effectiveness(2, 22, 23, 35, 39, 43, 44, 46, 47, 50, 53), Reliable information content(2, 20, 21, 35, 36, 41, 51, 60, 63), Use of appropriate behaviour change techniques(2, 35, 39, 41, 43, 44, 47, 51), External validity/generalisability(20, 35, 44, 47, 59), Patient satisfaction(20, 41, 46, 49, 51, 54, 57, 59)*

Issues of *Demonstrating effectiveness (New)*

Is the study design appropriate for demonstrating effectiveness for these technologies? (DHT12)

- Is it clear whether any changes were made to the DHT during the trial (e.g., major bug fixes or changes in the functionality or content)? (35, 39)
- Was digital literacy an implicit eligibility criterion? (35)
- Have accepted methods been used to overcome common methodological problems for DHT in performing RCTs, e.g., achieving blinding, biases from informed consent procedures? (22, 23, 35)

Is the choice of comparator appropriate for these technologies? (DHT13)

- Was the comparator group restricted in the DHT to which they had access? (44, 47)

Do the outcome measures capture the unique benefits of the technology and are the methods for their collection robust? (DHT14)

- Have DHT specific outcome measures been collected, i.e., metrics of use, the intensity of use (dose, exposure), adherence, attrition (35, 53), user satisfaction, and engagement? (2)
- Are these metrics and their methods of collection described in adequate detail? (35, 53)
- If surveys of health outcomes are completed online, are they validated for online use? (35, 50)
- If data collection is embedded within the DHT, may it have created systematic bias or confounding? (44, 47)

*Is the reporting of effectiveness studies transparent and tailored for the technology? (*DHT15)

Is the reporting of the RCT in accordance with CONSORT E-HEALTH or a similar effectiveness reporting standard designed for DHT interventions? (46, 50)

Issues of *Reliable information content (New)*

Is the health information provided by the technology accurate, valid, up to date, and sufficiently comprehensive? (DHT16)

Is there evidence that the health information provided by the DHT is accurate, valid, up to date, sufficiently comprehensive, clear, tailored to the users' diversity, and that there are quality assurance processes in place?(2, 20, 21, 35, 36, 41, 51, 60, 63)

Issues of *Use of appropriate behaviour change techniques (New)*

(If applicable) Does the technology use appropriate and best practice behaviour change techniques? (DHT17)

- Are appropriate and best practice behaviour change techniques used in the technology? (2, 35, 39, 41, 43, 44, 47, 51) Is the targeted behaviour change apparent to the user, is the mechanism is credible, are the appropriate supports in place, and is it relevant for the target population? (2, 35, 39, 41, 43, 44, 47, 51)

Issues of *External validity/generalisability (New)*

Are the conditions during the trial realistic in practice? (DHT18)

- Have the actions taken to enhance the trial's internal validity, such as participant identity validation and obtaining offline contact details to promote good follow-up rates, skewed participant populations, and jeopardised external validity? (44, 47)

Can the results be transferred to other patient groups/settings/regions? (DHT19)

- Are the results generalisable to the general internet population, to the general patient population, or other organisations? (35) Will it work in regions where telecommunication infrastructure is poor, or there is low network connectivity? (20, 59)

Issues of *Patient satisfaction*

Were patients satisfied with the technology? (D0017)

- Is it usable and accessible for a diverse range of users, including those with disabilities or limited technical ability? (20, 41, 46, 49, 51, 57, 59). Are there obvious design issues hindering usability, e.g., washable, durable, causes skin allergies? (54)

Digital health technology (DHT) specific content from frameworks in review **Issues of *Topic*** *Issue (Assessment element ID from HTA Core Model or DHT prefix if new)*	
Domain 5: Costs and economic evaluation (ECO) ***Topics not in HTA Core Model:*** *None*	
Issues of *Resource utilisation* *What types and amounts of resources are used when delivering the assessed technology and its comparators (resource-use identification)? (E0001& E0002)* *What were the measured and/or estimated costs of the assessed technology and its comparator(s) (resource-use valuation)? (E0009)* - Have the costs of supporting health care providers in using the DHT, such as costs of training, help desks, and change management, been included? (20, 29) - Have costs of the system, platform, licensing, attachable hardware, and versions of DHT that would be used in the health system been included? (63) - Have the costs of the DHT, including the need for additional or recurrent purchases, shipping fees, or technical support subscription charges, as well as relevant supply information, such as availability in the target country and minimum order requirements, been considered? (54)	**Issues of *Validity of the model(s)*** *Are within-trial collected costs and outcomes externally valid? (DHT20)* - Are changes in fixed costs for scaling up the DHT known? Is the cost function per patient smooth or stepped? (20) **Issues of *Measurement and estimation of outcomes*** *What is (are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s) (outcome identification, measurement, and valuation)? (E0005)* - Have DHT specific outcomes been considered and measured where possible, e.g., improved access to health information and services (20), reduced waiting time, less burdensome travels, a feeling of security, transfer of skills (29), better-managed care through self-management and digitally connected healthcare professionals? (48) - Given all the functionalities of DHTs may not be used, and many people may not use the DHT from the outset, are the estimated benefits of the DHT realistic? (32)
Domain 6: Ethical analysis (ETH) ***Topics not in HTA Core Model:*** *None*	
Issues of Benefit-harm balance *What are the benefits and harms of the technology for relatives, other patients, organisations, commercial entities, society, etc.? (F0011)* - Is the DHT designed and used for clearly defined purposes that uphold the health system's social values or society's values? Does it enable fair access to its benefits by all social groups, realise the value of patient data created by the DHT (not to be used for commercial activities), and depending on its purpose, preserve and enhance direct contact between healthcare professionals and patients, enable safe and effective health care, support people to manage their own health, and enable research and innovation? (52) *Are there any other hidden or unintended consequences of the technology and its applications for patients/users, relatives, other patients, organisations, commercial entities, society, etc.? (F0003)* - Where are alerts about a patient's health reported? Is real-time data securely transmitted? How does the DHT affect the participant's safety and welfare? Could patients have a false sense of security if their DHT is collecting real-time data and not being contacted by physicians? Are there harms from the patient having access to the data without someone's assistance to help them interpret what it means? (45)	- Have there been any perceived or real privacy breaches, technical problems, unexpected/unintended incidents created by the DHT? (35) **Issues of *Autonomy*** *Is the technology used for individuals that are especially vulnerable? (F0005)* - Does the DHT use understandable and straightforward language, with clear and short messages, adapted to the target user profile for style and comprehension level? (41) *Does the implementation or use of the technology affect the patient´s capability and possibility to exercise autonomy? (F0004)* - Is there potential for the DHT to influence a person's behaviour for commercial purposes when they are most susceptible? E.g., The DHT has access to a large amount of personal data, behavioural-economic insights, algorithmic predictive analyses, and can communicate with the patient continuously? (30) What controls are in place to limit this risk? - Does the DHT enable the user to make independent and authentic decisions and give an adequate range of options for that decision making? (30)

Digital health technology (DHT) specific content from frameworks in review **Issues of *Topic*** *Issue (Assessment element ID from HTA Core Model or DHT prefix if new)*	
Is there a need for any specific interventions or supportive actions concerning information in order to respect patient autonomy when the technology is used? (F0006) - Does the DHT clearly identify all collaborators in the development of the DHT? Is there sufficient information on funding sources, promotion, and sponsorship of the DHT?(41, 63) - Is there concise information on the procedures used to select the DHT's contents, and does it clearly identify who is responsible for the content? (41) - Is informed consent language clear about what type of data is collected by the DHT, how the data is used, and which data is available to subjects? (45) **Issues of *Respect for persons*** *Does the technology invade the sphere of privacy of the patient/user? (F0101)* - Does the DHT clearly identify who holds any personal data? Is the supplier's cookie policy stated and clear? (41) - Only data necessary for a particular treatment is shared with the doctor and only after explicit consent, which the patient can revoke. Can patients opt-out if they are not able or unwilling to manage their data? (48)	- Data sharing with third parties that includes linkable identifiers is prevalent and difficult to detect in DHTs.(31). Are users informed of this risk by the DHT? - Does the DHT provider have privacy policies that are easy to understand, uphold users' rights and choices, and are readily available to users before and while using the DHT, compliant with privacy laws, privacy principles, and best practices? Are changes to privacy policies communicated to users in a timely way? (21) ***Issues of Justice and Equity*** *Are there factors that could prevent a group or person from gaining access to the technology? (H0012)* - Patients with a lack of economic resources to have a proper infrastructure to access DHTs, or patients and practitioners with low IT skills or digital health literacy can be prevented from using DHTs? How does the DHT overcome these barriers? (48, 63) - Is the DHT compatible with common assistive technologies and available in a wide number of languages and platforms? (21, 63)
Domain 7: Organisational aspects (ORG) ***Topics not in HTA Core Model:*** *Contextual issues for barriers and enablers to implementation (32-34)*	
Issues in Health delivery process *How does the technology affect the current work processes? (G0100)* - What are the impacts on work methods and interactions between medical staff, patients, and their carers from removing distance constraints and offering shared access to the patient's data to medical staff? (23) *What kind of involvement has to be mobilised for patients/participants and important others and/or caregivers? (G0002)* - Consider digital health literacy training and educating patients and caregivers in using the DHT(63) *What kind of process ensures proper education and training of staff? (G0003)* - Digital health literacy training and continual professional development (CPD) courses for using and recommending the DHT in clinical practice(48, 63) *What kinds of co-operation and communication of activities have to be mobilised? (G0004)* - Consider changes to the amount of electronic communication, information and reporting systems, the number of face-to-face patient consultations, the way medical staff communicate and work together(20)	***Issues in Structure of the health system*** *What are the processes ensuring access to the new technology for patients/participants? (G0101)* - Refer to *How well is the technology and comparator(s) designed for usability and accessibility? (*)* under ***Quality and safeguarding*** in SAF ***Issues in Contextual issues for barriers and enablers to implementation*** *What are the contextual issues that are barriers and enablers to implementation? (DHT21)* - Consider barriers: Lack of information technology infrastructure, uncertainty around information governance, lack of incentives to prioritise interoperability, lack of accountability within the commercial sector, and a market perceived as challenging to navigate, a lack of capital for start-up costs, a lack of experience and knowledge in operational details, a lack of high-quality training, need for better algorithms to identify patients with the greatest need for reducing expenditures (32-34) - Consider enablers: clinical endorsement, champions who promote digital health, and public and professional willingness, supplemental payments to help with start-up costs, close collaboration between all providers caring for patients (32-34)

Digital health technology (DHT) specific content from frameworks in review **Issues of *Topic*** *Issue (Assessment element ID from HTA Core Model or DHT prefix if new)*	
Domain 8: Patient and social aspects (SOC) ***Topics not in HTA Core Model:*** *None*	
Issues of social group aspects *Are there groups of patients who currently do not have good access to available therapies? (H0201)* - Consider the ability of the wearable solution to improve interpersonal connectivity (among healthcare team members and the patient) and access to patients as part of the remote healthcare model (49)	***Issues of Communication aspects*** *What specific issues may need to be communicated to patients to improve adherence? (H0203)* - The DHT provider provides service users with clear and transparent information on the: a. Direct costs to access the service, b. Estimated data usage requirements for using the service (21, 32-34)
Domain 9: Legal aspects (LEG) ***Topics not in HTA Core Model:*** *None*	
Issues of *Privacy of the patient* *Is there a possibility that the use of the technology produces additional information that is not directly related to the current care of the patient and may violate their right to respect for privacy? (I0007) What do laws/binding rules require with regard to appropriate measures for securing patient data and how should this be addressed when implementing the technology? (I0009)* - Does the DHT comply with the GDPR principles of data minimisation, data protection by default, and data protection by design? Does the service provider need a data protection officer?(41, 51) - Other aspects to consider are data accountability, governance, transparency, and consent requirements(41) - Also, refer to *How are data security and privacy managed? (*)* under ***Quality and safeguarding*** in SAF	**Issues of *Ownership and liability*** *Professional liability (DHT22)* - Clarifying the party(s): Responsible for medical advice; responsible for monitoring and reviewing patient data; and that own the data related to the DHT(63) - Clarify litigation risks to the healthcare practitioners using or recommending the DHT, how insurance(s) (i.e., professional indemnity, life, health, income) and professional registrations could be affected through use or recommendation of the DHT(63)

Existing health technology assessment (HTA) content common to DHT and non DHTs from frameworks in review **Issues of *Topic*** *Issue (Assessment element ID from HTA Core Model)*
Domain 1: Health problem and current use of technology (CUR) ***Issues of Current management of the condition*** *What are the other typical or common alternatives to the current technology? (A0018)* - What DHT do those with the condition already have available them? (55)
Domain 2: Health problem and current use of technology (CUR) **Issues of *Features of the technology*** *What is the phase of development and implementation of the technology and the comparator(s)? (B0003)* - Is there evidence that the DHT is relevant to the health care system and can perform successfully to the expected number of users (e.g., server size adequate)? (2) - As DHT often develop rapidly, is the DHT is in a steady-state to enable a robust economic analysis to be performed? (20)
Domain 3: Safety (SAF) **Issues of *Safety risk management*** *Are there processes for recognising and responding to the patient's acute deterioration? (C0062)* Does the DHT have defined parameters to identify a patient's acute deterioration that requires care to be escalated(21), criteria for calling for emergency assistance(21), and systems to respond to users showing signs of acute deterioration? (21)
Domain 4: Clinical Effectiveness (EFF) **Issues of *Patient satisfaction*** *Were patients satisfied with the technology? (D0017)* - Is there evidence to show relevant stakeholders were involved in the design and satisfied with the DHT? (2, 21, 35, 36, 43, 59, 62) - Is there ongoing data collected on user satisfaction that will be acted upon and available to decision-makers? (2,21) - Has qualitative data been collected and analysed to evaluate the mode of action, differences between recipients and sites (44,59), and identify barriers to uptake or implementation? (20, 21, 41, 44, 48, 51, 57) - Does the DHT create additional burdens on the patient or caregiver, which may affect uptake or adherence? (44, 59)
Domain 5: Costs and economic evaluation (ECO) None noted

Existing health technology assessment (HTA) content common to DHT and non DHTs from frameworks in review **Issues of *Topic*** *Issue (Assessment element ID from HTA Core Model)*
Domain 6: Ethical analysis (ETH) ***Issues of Benefit-harm balance*** *Are there any other hidden or unintended consequences of the technology and its applications for patients/users, relatives, other patients, organisations, commercial entities, society, etc.? (F0003)* - What will be done with any incidental findings? (45) **Issues of *Autonomy*** *Is the technology used for individuals that are especially vulnerable? (F0005)* - Does the DHT provider identify the diversity of service users and groups of users at higher risk of harm and incorporate this information into the planning and delivery of the service? Does the DHT provider have systems to minimise the risk for children and young people to be harmed? (21) ***Issues of Justice and Equity*** *Are there factors that could prevent a group or person from gaining access to the technology? (H0012)* - Show evidence of the DHT being used in hard-to-reach populations (2)
Domain 7: Organisational aspects (ORG) ***Issues in Health delivery process*** *How does the technology affect the current work processes? (G0100)* - Describe the steps in the proposed new care pathway or pathways incorporating the DHT intervention for the relevant population and setting. Detail any infrastructure and service-level changes needed to existing pathways and associated systems to implement, operate, and maintain the new pathway (2, 62) ***Issues in Culture*** *How is the technology accepted? (G0010)* - Does the DHT have credibility with health care professionals? Is there published or publicly available evidence documenting the relevant health care experts' role in the design, development, testing, or sign-off of the DHT? (2, 21, 60)
Domain 8: Patient and social aspects (SOC) None noted
Domain 9: Legal aspects (LEG) None noted

[a]From EUnetHTA's HTA Core Model version 3.0 (19)
See Section 2.7 for references

Chapter 3 supplementary materials

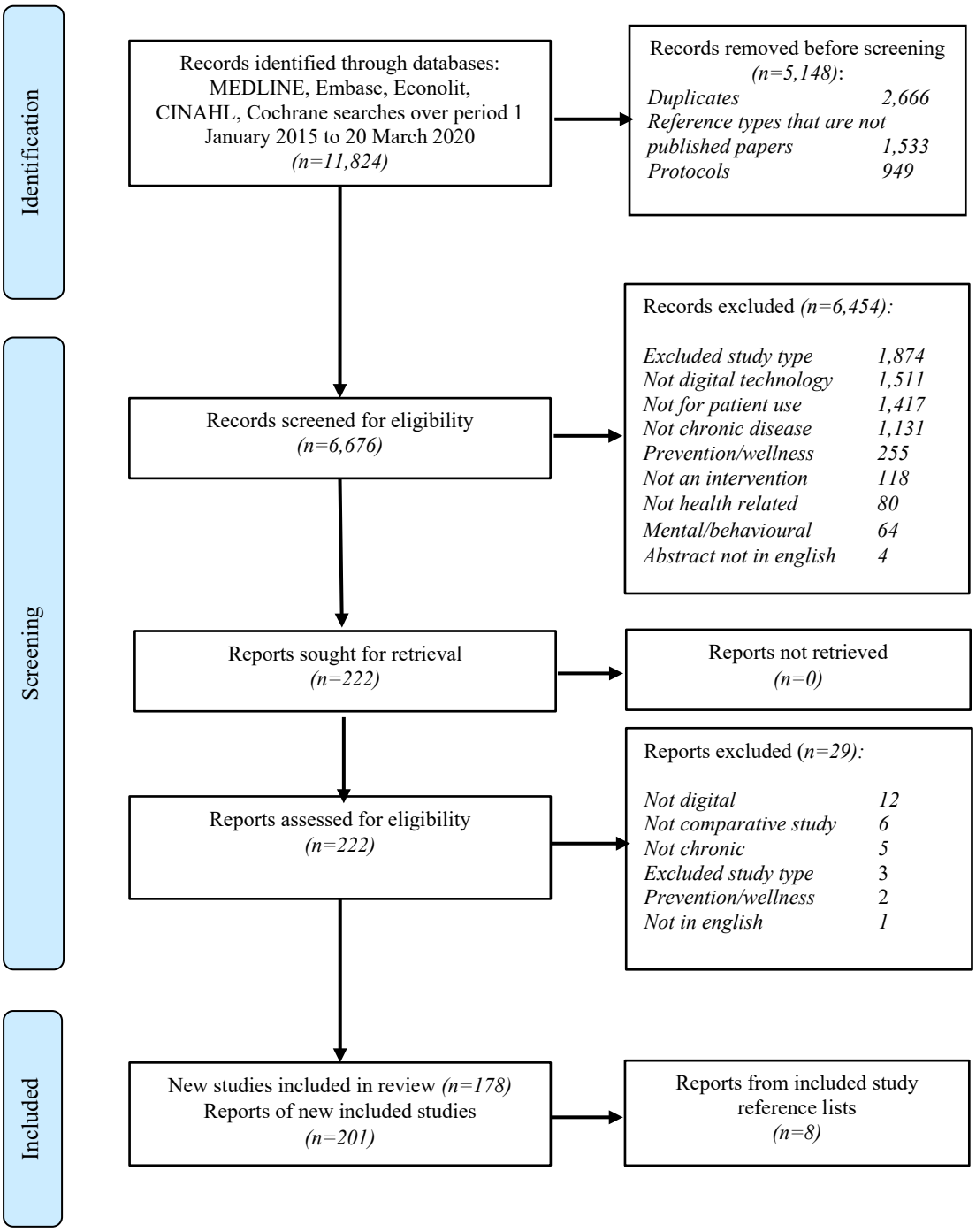

Figure A 3: Preferred reporting items for systematic reviews and meta-analysis (PRISMA) flow diagram for framework study selection

Table A 5: Peer-reviewed literature search strategy

Database[5] **(Ovid)**	**Search terms**[6]
MEDLINE, Embase, CINAHL, Econolit, Cochrane	(1)[7] exp Telemedicine/ or (telehealth or telemedicine) or exp Medical Records Systems, Computerized/ or (ehealth or (electronic adj2 health)) or (digital adj2 health) or (digital adj1 health adj1 intervention) or exp Mobile Applications/ or ((mobile adj1 health) or mhealth) or ((mobile adj1 health adj1 app) or (mobile adj1 health adj1 application)) or (((mobile adj1 medical adj1 app) or (mobile adj1 medical adj1 application))) or exp Text Messaging/ or (sms or text messag$) or (chat room$ or chatroom$ or chatbot$ or avatar) or (wearable$) or ((artificial adj1 intelligence) or (machine adj1 learning))
	(2)[8] (health adj evaluation*) or (project adj evaluation*) or (program* adj evaluation) or (evidence adj1 standards) or (health adj service adj evaluation) or (health adj promotion adj evaluation*) or (systematic adj1 review) or (technology adj2 evaluation) or (implementation adj evaluation*) or (impact adj evaluation*) or (outcome* adj evaluation*) or (decision adj2 making adj2 framework) or (decision adj2 making adj2 standard*) or (decision adj2 making adj2 guideline*) or (technology adj2 appraisal*) or (technology adj validation) or (evaluation adj1 framework*) or ((implementation or translation*) adj2 (study or research)) or (subsid* or rebat* or reimburs*) or Comparative Effectiveness Research/ or exp patient harm/ or exp patient safety/or exp Insurance, Health, Reimbursement/ or exp Legislation, Medical/ or exp Financing, Government/
	(3)[4] Economics/ or exp "Costs and Cost Analysis"/ or (cost benefit analysis) or (economic* adj evaluation*) or (cost adj effect*) or (cost adj benefit) or (cost adj utility) or (cost adj effic*) or (economic* adj analysis) or quality-adjusted life years/ or (quality adjusted life years) or (QALY*)
	(4) randomized controlled trial.pt. or controlled clinical trial.pt. or randomized.ab. or placebo.ab. or Clinical Trials as Topic/ or randomly.ab. or (crossover or cross-over).tw or trial.ti.
	(5)[4] exp epidemiologic studies/ or (Case control) or (cohort adj (study or studies)) or (Cohort analy$) or (Follow up adj (study or studies)) or (observational adj (study or studies)) or (Longitudinal) or (Retrospective) or (Cross sectional)
	(6) ((Health adj2 technology adj2 assessment) or HTA or (technology adj2 assessment)).tw.
	(7) Animals/ not (animals/ and Humans/)

[5] Searches modified for Embase, Econolit, CINAHL, Cochrane

[6] (1) Search terms used to identify e-Health, m-Health, and digital health modes of health delivery (2) Terms used to identify decision making, funding and health evaluation studies (3) Terms to identify economic evaluation studies (4) Terms used to identify Randomised Controlled Trials (5) Terms used to identify observational studies (6) Terms used to identify Health Technology Assessments (7) Terms used to search for animal not human studies

[7] All terms were searched using multipurpose (.mp)

[8] All terms were searched using text words (.tw)

Search string: Limit yr="2015 - Current" ((1) AND ((2) OR (3)) AND ((4) OR ((5) NOT (4)) OR (6) NOT ((4) OR ((5) NOT (4))))NOT (7)); Medline/Embase search conducted on 20 March 2020; CINAHL/Econolit search conducted on 22 March 2020.

Table A 6: Content items for use in primary studies and criteria for "fair" and "good" coverage

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
CUR	Utilisation *(EUN)*	Do/will health workers/patients invest in the personal digital technologies required to use the DHT? Costly/difficult to support? *Provide evidence of whether health workers/patients do or will invest in the personal digital technologies required to use the DHT? Estimate current investment by workers/patients, detail direct and add-on costs, and user willingness to pay.*	Some estimation of how many people have the personal technology required to use the DHT to justify a reasonable user base	Estimate the willingness of users to pay for personal technologies and internet data usage costs to use the DHT or Estimate all personal costs that would have to be reimbursed to the user to use DHT	**A0011/2(1)**
		Is the DHT limited in platforms, languages, network connectivity, or users' digital literacy? *Discuss whether the DHT usage will be affected (or why not) by limitations in terms of platforms, languages, network connectivity, or users' digital literacy?*	Enough information on limitations and how they affect utilisation: • Collect data on users • Analyse utilisation problems, e.g., issues for the less technical, etc.	Describe how the DHT is designed to overcome some or all limitation problems	**A0011/2(2)**
		Is(will) data on DHT usage (be)collected and accessible ongoing? *Has granular data on DHT usage been collected? For example, can this usage data be collected every time the DHT is used or was it difficult to capture, so they only did it in the trial?*	Granular data was presented and analysed on DHT usage collected in the trial. However, no further evidence was provided on how/if usage data will be collected on an ongoing basis.	Evidence DHT can collect this granular usage data on an ongoing basis, e.g., data collection is embedded in the DHT and transmitted to a central database ongoing	**A0011/2(3)**
		Describe inputs (i.e., image, physiological status, symptoms, etc.), algorithms (i.e., equations, analysis engine model logic, algorithm, etc.), and outputs (i.e., inform, treat, diagnose) of the DHT *Split into two separate items:*	See below	See below	**F0001**
		1. Describe inputs (i.e., image, physiological status, symptoms, etc.) and outputs (i.e., inform, treat, diagnose) of the DHT?	1. Details the inputs and outputs of the trialed DHT	1. Explains why the trialed DHT is better/different from DHT comparators in terms of inputs and outputs	**F0001(1)**
		2. Describe the algorithms (i.e., equations, analysis engine model logic, algorithm, etc.) of the DHT	2. Details the rules and parameters used by the DHT in patient clinical management decisions	2. Details the engine model logic and algorithms enough to understand limitations and in what circumstances the DHT will and will not work	**F0001(2)**

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HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
TEC	Investments/ tools required (*EUN*)	Consider device size, battery life/charging method, operating system, connectivity, data access & storage, data security, technical support	Discuss the material investments required to operate in the health system	Discuss how the DHT was designed to minimise these material investments	**B0007**
	Training/ information needed (*EUN*)	Personnel/caregivers/patient/family: Training required/provided on personal data handling, digital skills, and digital health literacy? *(Note: One-off training only on using the DHT is rated as "Poor")*	Provision of continuous technical support for DHT users	Provision of digital literacy and general digital skills for patients or data handling skills for health care professionals	**B0013/4**
	Features of Technology (*EUN*)	How well do the DHT and comparator(s) perform in overcoming technical barriers: Interoperability, data extraction, visualisation, etc.? *(Note: Mention of technical barriers as a limitation of the trial is rated as "Poor")*	Mention at least one technical barrier that the DHT was designed to overcome and its benefits	Mention more than one technical barrier that the DHT was designed to overcome, and its benefits over DHT comparators	**DHT01**
SAF	Quality & safeguarding (*NEW*)	How well are data security and privacy managed? Does it comply with General Data Protection Regulation (GDPR) principles of data minimisation/protection by default/design?	Encrypted data transmissions and secure databases controlled by regulated entities, e.g., government departments of health, listed private hospitals, regulated medical device companies	Evidence of compliance with: • GDPR principles (e.g., data minimisation); or • Privacy and data security legislation of the jurisdiction	**DHT02**
		How well is interoperability designed and data quality managed?	Evidence that DHT has processes to support the creation and maintenance of accurate healthcare records that can be integrated with multiple information systems using the relevant patient/ provider identifiers and standard terminologies	DHT is integrated with relevant health system databases	**DHT03**
		Transparency of risk to the user *How transparent are the DHT risks (e.g., data sharing, conflicts of interest) to the user?*	Evidence that DHT provides users with accurate information on how their data is collected and protected and clear identification of the DHT's owners and contact information	In addition, evidence the DHT provides users with information on data use and sharing along with funding sources, promotion and sponsorship, and any other possible conflicts of interest	**DHT04**
		How well is the DHT designed for usability and accessibility? *Evidence that DHT is designed for usability and accessibility?*	Evidence that the DHT is designed to minimise at least one of the barriers associated with hardware, software, data requirements, and platform services, or the language/location, age, culture, and ability of users, e.g., services are compatible with commonly used assistive technologies, meet relevant web page or web application standards	Evidence that the most relevant/significant barriers have been identified and addressed in the design	**DHT05**
		Is adequate information disclosed on DHT algorithms to evaluate their risk?	There is enough detail to replicate the process or understand the limitations of the data used, algorithms deployed, and how the outputs were validated. For learning algorithms, adequate disclosure of the characteristics of the training, test, and validation data, the model, and the	In addition, data quality is validated before building and employing algorithms For Artificial intelligence algorithms: Data quality checks are built programmatically to avoid harm	**DHT06**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
			algorithms to understand how the algorithm controls the clinical decision-making process		
	Technical safety (Reliability & stability) (*NEW*)	How technically reliable and stable are the DHT and comparator(s)? *Unlikely to evaluate the comparator, so this has been modified to:* *How technically reliable and stable is the DHT?*	There is evidence of accurate and reliable transmission of unbiased data: Minimal complaints from participants or trial staff of dropouts/connectivity problems, data inaccuracies, or failure to work on specific platforms/operating systems	The DHT is designed to: • Alert the user when working suboptimally or experiencing interference, e.g., low or no network connectivity • Resilient to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions • Validated for use on multiple platforms	**DHT07**
		How well are updates/continuity of the DHT managed?	Report how: • Platform and operating system updates and patches, service continuity, backup, and recovery mechanisms are managed • Service changes or interruptions are communicated to users	Evidence of a well-managed update and continuity procedure and controls, e.g., participant/patient feedback on DHT service communications on changes	**DHT08**
	Communicating for safety (*NEW*)	Can the user send critical risk information to the DHT provider?	The DHT provides warning on who should be contacted in an emergency, and there is a contact mechanism for technical support with a fixed response time	The DHT allows the user to communicate critical information to the provider on changes in their condition or risks to the user's health from using the DHT	**DHT09**
		Processes for correct identification of users in DHT?	Use of user logins and passwords reported	There are processes for correctly identifying users to match them with appropriate care and provide accurate health records, protecting anonymity where appropriate	**DHT10**
		Processes to communicate changes to or transfer of a patient's care?	There are processes to communicate changes in the health care team, stopping of care or transfer of a patient's care through the DHT	In addition, there is evidence of these processes working from patients/ health care providers	**DHT11**
EFF	Patient satisfaction (*EUN*)	Is there evidence that the DHT is usable and accessible for a diverse range of users, including those with disabilities or limited technical ability? Are there obvious design issues hindering usability, e.g., washable, durable, cause skin allergies? *Split into three questions:*	See below	See below	**D0017**
		1. Has an analysis been conducted on how effective the DHT is for users with a disability?	1. Report the number of participants with a relevant disability at baseline and discuss any problems/feedback from these users	1. Qualitative or quantitative (subgroup) analysis of participants with disabilities	**D0017(1)**
		2. Has an analysis been conducted on how effective the DHT is for users with limited technical ability?	2. Report the number of users with limited technical ability at baseline/feedback from users with limited technical ability	2. Qualitative or quantitative (subgroup) analysis of participants with limited technical ability	**D0017(2)**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
		3. For wearables, are design issues to increase usability discussed, e.g., washable, durable, cause skin allergies? (*Is NA if no wearables involved in DHT*)		3. Any discussion of wearable issues and designs to overcome them	**D0017(3)**
EFF	Demonstrating effectiveness (*NEW*)	Are accepted methods used to overcome common methodological problems in RCTs for DHTs, e.g., achieving blinding, biases from informed consent, high attrition? *(Note: NA if study not an RCT)*	Single blinding, e.g., blinding of assessor	Double blinding	**DHT12(1)**
		Is it clear whether the DHT was changed (bug fixes, content) during the study?	State that the DHT had changed during the study to fix technical errors	State whether or not DHT development was frozen during the study. If development is not frozen, report what was changed during the trial and how these changes might impact results.	**DHT12(2)**
		Was digital literacy an implicit eligibility criterion? *Did they recognise digital literacy was an implicit eligibility criterion or sample population might be biased towards digitally literate people?* *(Note: This is NA if it is clear that there were no implicit/explicit digital literacy exclusions in the trial)*	Discussion of potential for selection bias with digital literacy/technical ability exclusions and reporting of how those with less digital literacy/technical ability did in the trial or feedback from the participant survey	Made active steps in the design of DHT or trial to ensure those with low digital literacy/technical ability were included	**DHT12(3)**
		Was the comparator group restricted in the DHT to which they had access?	Stated whether or not there were restrictions on DHTs for the comparator group, and if there were, what DHTs were excluded	Explanation of reason for there being no restrictions or where there are restrictions	**DHT13**
		Have DHT specific and validated outcome measures been collected: i.e., the intensity of use (dose, exposure), online adherence, engagement	Use, online adherence, or engagement is measured and reported. These metrics and their methods of collection are described in adequate detail	In addition, validated measures are used. And if surveys of health outcomes are completed online, they are validated for online use	**DHT14**
		Has data collection embedded in the DHT created systematic bias?	Independent process to collect health outcomes outside of DHT or acknowledgment of bias from DHT data collection with some estimation of direction and magnitude of bias	Design of DHT data capture to minimise this bias	
		Is reporting of the RCT in accordance with CONSORT E-HEALTH? *Or similar DHT specific reporting standard, e.g., CONSORT AI or MAST* *(Note that this question is now covered in the overall summary as a Yes/No answer)*	NA	NA	**DHT15**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
	Reliable information content (*NEW*)	Is the health information provided by DHT accurate, valid, up to date, comprehensive, clear, and tailored to the users' diversity? *(Note: This is NA if it is clear that the DHT provides no health information)*	Evidence of a process to ensure this at the time of development of the DHT	In addition, evidence of ongoing process to maintain this standard for the DHT	**DHT16**
	Use of appropriate behaviour change techniques (*NEW*)	Does the DHT use appropriate and best practice behaviour change techniques? Is the mechanism credible? Is the targeted behaviour change apparent to the user, and are the appropriate supports in place?	Reference to a peer-reviewed behaviour change theory with justification why it applies to the DHT's purpose and evidence the apparent behaviour change is evident to the user and the mechanism is credible	In addition, a description of appropriate supports in place to enable the behaviour change and evidence it applies to the target population	**DHT17**
	External validity/ generalisability (*NEW*)	Has patient identity validation and obtaining offline contact details to improve follow-up rates jeopardised external validity? *(Note: This is NA if the study is retrospective data analysis*)		Discussion of how the processes for the trial are different from the intended operation of the DHT and how that may affect the external validity of the trial	**DHT18**
		Are results generalisable to settings where telecommunication infrastructure is poor, or there is low network connectivity?	Report number of participants in areas with poor infrastructure/connectivity at baseline, or as a minimum report the number of participants that experience these problems during the study	Qualitative or quantitative (subgroup) analysis of participants in areas with poor infrastructure/connectivity	**DHT19**
ECO	Validity of the model(s) (*EUN*)	Are changes in fixed costs for scaling up the DHT known? Is the cost function per patient smooth or stepped? *(Note: Rated "Not reported" if no costing analysis done as yet*)	Some discussion/awareness of this problem	The cost function is known	**DHT20**
	Resource utilisation (*EUN*)	Consider costs of supporting healthcare providers in using DHT and costs to use the DHT in the health system (licensing, platforms, hardware, etc.) *(Note: Rated "Not reported" if no costing analysis done as yet*)	Discusses or presents the partial evaluation of costs of supporting health care providers	Detailed evaluation of the additional cost of using in the health system as well	**E0001/2/9**
	Measurement & estimation of outcomes (*EUN*)	Have DHT-specific outcomes been considered and measured where possible, e.g., self-management benefits, better-connected healthcare professionals?	DHT specific outcomes considered with feedback from patients/healthcare professionals	Validated self-management measures collected and analysed	**E0005(1)**
		Given that all the functionalities of DHTs may not be used, and many people may not use the DHT from the outset, are the estimated benefits of the DHT realistic?	Consideration of start-up times and realistic use of DHT functions	Estimates of how long it will take to see full effects and incorporates this into economic evaluation	**E0005(2)**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
ETH	Benefit-harm balance (*EUN*)	Where are alerts about a patient's health reported? Is real-time data securely transmitted? How does the DHT affect the participant's safety and welfare? *How does the DHT affect the participant's safety and welfare:* *- Are alerts about a patient's health held securely?* *- Is real-time data securely transmitted?*	Description of a secure process for data transmissions	Details given about security controls for data transmissions	**F0003(1)**
		Can the DHT promote a false sense of security or harm patients having access to their data without someone to interpret it?	Discussion provided or patient feedback reported	Patient feedback on both issues reported	**F0003(2)**
	Autonomy (*EUN*)	For DHTs targeting behaviour change, what controls limit the DHT influencing a person's behaviour for purposes other than those stated?		Discussion of this risk and controls	**F0004(1)**
		Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT?		Discussion of how the range of options have been chosen so user can make independent and authentic decisions and any limitations on decisions	**F0004(2)**
		Does the DHT use simple and understandable language?	Discussion of how this was addressed in development **or** patient feedback reported	Discussion of how this was addressed in development **and** patient feedback reported	**F0005**
		Are any potential conflicts of interest (funding, promotion) disclosed *to the DHT users?* *(Note: Is NA if it is clear that there are no conflicts of interest or funding to disclose)*		Yes	**F0006(1)**
		For DHTs providing health information, is there concise information for the user on how the DHT's contents were selected *and who is responsible for the content?* *(Note: Is NA if it is clear that the DHT does not provide health information)*		Yes	**F0006(2)**
		Is the data collected by the DHT, its use, and availability disclosed to the user? *Is the user informed of the data collected by the DHT, its use, and availability to users to extract for their own purposes?*	The user is informed of these details	In addition, the patient can easily extract and use their own data	**F0006(3)**
	Benefit-harm balance (*EUN*)	Is the DHT designed and used for clearly defined purposes that uphold the health system's social values or societies? *This is a summary question and is unable to determine from primary studies. Therefore, it is not evaluated further.*	NA	NA	**F0011(1)**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
		Is the value of patient data realised but protected from commercial use?		Discussion of risks and controls	**F0011(2)**
		Does the DHT preserve and enhance direct contact between patients and healthcare professionals while supporting them to manage their health?	Some patient or health professional feedback reported on this issue	DHT was designed with this in mind, and qualitative feedback by both patients and healthcare professionals reported	**F0011(3)**
	Respect for persons (*EUN*)	Does the DHT clearly identify who holds any personal data?	All data custodians identified for each set of personal data	In addition, a detailed description of the extent to which third parties may gain access to this personal data is given	**F0101(1)**
		Is the DHT regularly audited for transmissions with third parties that include linkable identifiers? Is the user informed of this risk?	States that users will be informed of the potential risks of data sharing	Evidence of regular audits of third-party transmissions with linkable identifiers	**F0101(2)**
	Justice & Equity (*EUN*)	1. How does the DHT overcome access barriers, e.g., patients with a lack of economic resources, poor IT skills, digital health literacy?	1. Partial evaluation/description of how DHT overcomes one access barrier	1. Description of how DHT overcomes multiple access barriers	**H0012(1)**
		Is the DHT compatible with common assistive technologies and is available in several languages? *Split into two questions:*	See below	See below	**H0012(2)**
		2. Is the DHT compatible with common assistive technologies *for the hearing or visually impaired*?		2. Yes, the DHT is compatible with common assistive technologies for the hearing or visually impaired	**H0012(2)**
		3. Justification given of the available languages in DHT for the target population or recognition of limitation? *(Note: Is NA if it is clear that the DHT does not have a language restriction)*	3. Recognise provided languages are a limitation and estimate the impact from restriction	3. Justify the choice of languages provided for the target population or provide relevant languages	**H0012(3)**
ORG	Contextual issues (*NEW*)	Consider all contextual barriers and enablers to DHT uptake: Infrastructure, clinical endorsement, champions of DHT, supplementary payments, etc.	Discussion of barriers and why DHT failed or was successful in this regard	Discussion of how to overcome barriers and use enablers in the new care pathway	**DHT21**
	Health delivery process (*EUN*)	Are changes to electronic communication, information/reporting systems, face-to-face consultations, and staff communication considered?	Discussion of the changes required		**G0004**
		How does removing the constraints of distance, and sharing patient data, impact staff work methods and the interactions between medical staff, patients, and their carers?	Detail impacts in examples	Provide qualitative/quantitative? evidence on impacts	**G0100**
SOC	Social group aspects (*EUN*)	How much does the DHT improve the connectivity between the healthcare team and the patient? Is access improved for remote patients? *Split into two questions:*	See below	See below	**H0201**
		1. How much does the DHT improve the connectivity between the healthcare team and the patient?	1. Qualitative/quantitative feedback from patients and healthcare providers	1. In addition, discussion of how the DHT care pathway has been designed to improve connectivity	**H0201(1)**

Checklist 1: Digital-specific content to be considered when undertaking a Health Technology Assessment (HTA) of Digital Health Technology (DHT)					
HTA Domain[a]	**Topic *(EUN)*[a]/*(NEW)*[b]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a c] (Item No.)**
		2. Evidence that access is improved for rural/remote patients?	2. Report the number of rural/remote participants at baseline or feedback from rural/remote users	2. Qualitative or quantitative (subgroup) analysis on rural/remote users	**H0201(2)**
	Communication aspects (*EUN*)	Are expected direct and data usage costs made clear to the user to improve adherence rates?	Direct access costs and data usage costs reimbursed/provided for free	DHT provides service users with clear and transparent information on the: a. Direct costs to access the service, b. Estimated data usage requirements for using the service	**H0203**
LEG	Ownership & liability (*EUN*)	Professional liability: Clarify responsible parties, litigation risks, and insurance implications of DHT recommendation or use	State parties responsible for medical advice; responsible for monitoring and reviewing patient data; and that own the data related to the DHT	Additionally, discuss litigation risks to the healthcare practitioners using or recommending the DHT, how insurance(s) (i.e., professional indemnity, life, health, income) and professional registrations could be affected through use or recommendation of the DHT	**DHT22**

Checklist 2: Content common to digital and non-digital technologies, but essential for Health Technology Assessments (HTAs) of Digital Health Technologies (DHTs)					
HTA Domain[a]	**Topic[a]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a] (Item No.)**
CUR	Current management of the condition	What DHT do those with the condition already have available to them?	Background on other DHT trials and some comparison of the features between DHTs	Discuss current market products and why this DHT is an improvement/different	**A0018**
TEC	Features of the technology	Is there evidence that the DHT is relevant to the health system and can perform to the expected number of users (e.g., is the server size adequate)?	Evidence of being tested in the healthcare system	And that it can handle a large number of patients	**B0003(1)**
		As DHTs often develop rapidly, is the DHT in a steady state to perform a robust economic analysis? *i.e., no more development planned?* *(Yes = No more development planned,* *No = More development planned,* *Not covered = Unable to tell)* *This question is moved to summary table*	NA	NA	**B0003(2)**
SAF	Risk management	Are there defined parameters to identify and respond to a patient's acute deterioration?	Some discussion of the process	Parameters are given, and detailed processes discussed	**C0062**
EFF	Patient satisfaction	Is there evidence to show relevant stakeholders were involved in the design and satisfied with the DHT?	Evidence that patients were consulted in the design stage (focus groups/useability and feasibility testing)	In addition, qualitative survey, or multiple quantitative questions on patient satisfaction in the design stage and changes to the design made if required	**D0017(4)**
		Is ongoing data collected on user satisfaction that will be acted upon and available to decision-makers? *Has/will data be collected on user satisfaction that will be acted upon and available to decision-makers?*	Evidence of patient satisfaction data being collected and analysed in an effectiveness trial	There are processes in place to collect data ongoing that are extractable and available	**D0017(5)**
		Has qualitative data been collected and analysed to evaluate the mode of action, differences between recipients and sites, and identify barriers to uptake or implementation?	Some presentation of qualitative data	Qualitative data was collected and analysed on most of these points	**D0017(6)**

Checklist 2: Content common to digital and non-digital technologies, but essential for Health Technology Assessments (HTAs) of Digital Health Technologies (DHTs)					
HTA Domain[a]	**Topic[a]**	**Issue content (*Modifications*)**	**"Fair" coverage**	**"Good" coverage**	**Issue ID[a] (Item No.)**
		Does the DHT create additional burdens on the patient or caregiver that may affect uptake or adherence?	Feedback from patients or caregivers on caregiver burden	Validated caregiver burden surveys were done and results presented	**D0017(7)**
ECO	None noted				
ETH	Benefit-harm balance	What will be done with any incidental findings? *(Note: Is NA if it is clear that the DHT does not do any testing or only tests for the disease targeted)*		Any ethical discussion of how incidental findings should be managed	**F0003**
	Autonomy	Does the DHT provider: • Identify the diversity of service users, or groups of users, at higher risk of harm and adapt the DHT accordingly? • Have systems to minimise the risk for children and young people to be harmed? • Identify those with suicide ideation in depression treatments?	Risk segmentation of users and adaptation of DHT with regards to targeted disease only	Risk segmentation of users and adaptation of DHT for those users with regards to all potential risks from using the DHT	**F0005**
	Justice & Equity	Show evidence of the DHT being used in hard-to-reach populations	Define hard-to-reach populations and report participants at baseline	And show evidence of use in these populations	**H0012**
ORG	Culture	Does the DHT have credibility with health care professionals? i.e., is there published or publicly available evidence documenting the relevant healthcare experts' role in the design, development, testing, or sign-off of the DHT?	Any evidence of relevant health care experts' role in the design, development, testing, or sign-off of the DHT	And qualitative/quantitative feedback from healthcare professionals	**G0010**
	Health delivery process	Describe the steps in the proposed new care pathway or pathways incorporating the DHT intervention for the relevant population and setting	A detailed description of the intervention care pathway versus the usual care pathway in the trial setting	A detailed description of how the DHT care pathway would work in relevant population and setting	**G0100(1)**
		Detail any infrastructure and service-level changes needed to existing pathways and associated systems to implement, operate, and maintain the new pathway		Any discussion of infrastructure/service-level/systems changes to implement and operate new care pathway	**G0100(2)**
SOC	*None noted*				
LEG	*None noted*				

[a]From EUNetHTA HTA Core Model version 3.0. HTA domains are defined as:

CUR: Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status

TEC: Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it

SAF: Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers

EFF: Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting

ECO: Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value for money judgments

ETH: Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA

ORG: Identifies resources to mobilise or organise to implement the new technology and the consequences (Intra/interorganisational and health system)

SOC: Considers issues related to the new technology relevant to patients, carers, and social groups

LEG: Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

[b]New topic

[c]DHT prefixes denote new issues (i.e., *DHTXX*)

Table A 7: References for included papers

Included papers	References
In coverage assessment (i.e., DHT interventions targeting diabetes, cardiovascular disease, or both)	(1-130)
DHT interventions targeting other chronic diseases	(131-201)

1. Abaza H, Marschollek M. Sms education for the promotion of diabetes self-management in low & middle-income countries: A pilot randomized controlled trial in Egypt. *BMC public health*. 2017;17(1):962.
2. Alonso-Domínguez R, Sánchez-Aguadero N, Patino-Alonso MC, García-Ortiz L, Recio-Rodríguez JI, Gómez-Marcos MA. Effect of a multifactorial intervention on the increase in physical activity in subjects with type 2 diabetes mellitus: A randomized clinical trial (emid study). *European Journal of Cardiovascular Nursing*. 2019;18(5):399-409.
3. Amara W, Montagnier C, Cheggour S, Boursier M, Gully C, Barnay C, et al. Early detection and treatment of atrial arrhythmias alleviates the arrhythmic burden in paced patients: The setam study. *Pacing Clin Electrophysiol*. 2017;40(5):527-36.
4. Augustovski F, Chaparro M, Palacios A, Shi L, Beratarrechea A, Irazola V, et al. Cost-effectiveness of a comprehensive approach for hypertension control in low-income settings in Argentina: Trial-based analysis of the hypertension control program in Argentina. *Value in Health*. 2018;21(12):1357-64.
5. Barnason S, Zimmerman L, Schulz P, Pullen C, Schuelke S. Weight management telehealth intervention for overweight and obese rural cardiac rehabilitation participants: A randomized trial. *Journal of Clinical Nursing (John Wiley & Sons, Inc)*. 2019;28(9/10):1808-18.
6. Battelino T, Liabat S, Veeze HJ, Castaneda J, Arrieta A, Cohen O. Routine use of continuous glucose monitoring in 10 501 people with diabetes mellitus. *Diabetic Medicine*. 2015 Dec;32(12):1568-74.
7. Bekelman DB, Plomondon ME, Carey EP, Sullivan MD, Nelson KM, Hattler B, et al. Primary results of the patient-centered disease management (pcdm) for heart failure study: A randomized clinical trial. *JAMA Internal Medicine*. 2015;175(5):725-32.
8. Beran M, Asche SE, Bergdall AR, Crabtree B, Green BB, Groen SE, et al. Key components of success in a randomized trial of blood pressure telemonitoring with medication therapy management pharmacists. *Journal of the American Pharmacists Association: JAPhA*. 2018;58(6):614-21.
9. Bernocchi P, Vitacca M, La Rovere MT, Volterrani M, Galli T, Baratti D, et al. Home-based telerehabilitation in older patients with chronic obstructive pulmonary disease and heart failure: A randomized controlled trial. *Age & Ageing*. 2018;47(1):82-8.
10. Bobrow K, Farmer AJ, Springer D, Shanyinde M, Ly-Mee Y, Brennan T, et al. Mobile phone text messages to support treatment adherence in adults with high blood pressure (SMS-text adherence support [star]): A single-blind, randomized trial. *Circulation*. 2016;133(6):592-600.
11. Bohingamu Mudiyanselage S, Stevens J, Watts JJ, Toscano J, Kotowicz MA, Steinfort CL, et al. Personalised telehealth intervention for chronic disease management: A pilot randomized controlled trial. *Journal of Telemedicine & Telecare*. 2019;25(6):343-52.
12. Bravo-Escobar R, Gonzalez-Represas A, Gomez-Gonzalez AM, Montiel-Trujillo A, Aguilar-Jimenez R, Carrasco-Ruiz R, et al. Effectiveness and safety of a home-based cardiac rehabilitation programme of mixed surveillance in patients with ischemic heart disease at moderate cardiovascular risk: A randomized, controlled clinical trial. *BMC Cardiovascular Disorders*. 2017;17(1).
13. Burn E, Nghiem S, Jan S, Redfern J, Rodgers A, Thiagalingam A, et al. Cost-effectiveness of a text message programme for the prevention of recurrent cardiovascular events. *Heart*. 2017;103(12):893.1-4.
14. Caceres BA, Hickey KT, Bakken SB, Biviano AB, Garan H, Goldenthal IL, et al. Mobile electrocardiogram monitoring and health-related quality of life in patients with atrial fibrillation: Findings from the iPhone helping evaluate atrial fibrillation rhythm through technology (iHeart) study. *Journal of Cardiovascular Nursing*. 2020;03:03.
15. Celler B, Varnfield M, Jayasena R. What have we learned from the CSIRO national NBN telehealth trial?...5th global telehealth meeting, Adelaide, Australia, November 2017. *Studies in Health Technology & Informatics*. 2018;246:1-17.
16. Chatzakis C, Floros D, Papagianni M, Tsiroukidou K, Kosta K, Vamvakis A, et al. The beneficial effect of the mobile application euglyca in children and adolescents with type 1 diabetes mellitus: A randomized controlled trial. *Diabetes Technology and Therapeutics*. 2019;21(11):627-34.

17. Cho JH, Kim HS, Yoo SH, Jung CH, Lee WJ, Park CY, et al. An internet-based health gateway device for interactive communication and automatic data uploading: Clinical efficacy for type 2 diabetes in a multi-center trial. *Journal of Telemedicine & Telecare*. 2017;23(6):595-604.
18. Choudhary P, Portu S, Arrieta A, Castañeda J, Campbell FM. Use of sensor-integrated pump therapy to reduce hypoglycaemia in people with type 1 diabetes: A real-world study in the UK. *Diabetic Medicine*. 2019;36(9):1100-8.
19. Chow CK, Redfern J, Hillis GS, Thakkar J, Santo K, Hackett ML, et al. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: A randomized clinical trial. *JAMA: Journal of the American Medical Association*. 2015;314(12):1255-63.
20. Cichosz SL, Udsen FW, Hejlesen O. The impact of telehealth care on health-related quality of life of patients with heart failure: Results from the danish telecare north heart failure trial. *Journal of telemedicine and telecare*. 2019.
21. Clark MA, Szymkiewicz SJ, Volosin K. Mortality and costs associated with wearable cardioverter-defibrillators after acute myocardial infarction: A retrospective cohort analysis of medicare claims data. *Journal of Innovations in Cardiac Rhythm Management*. 2019;10(10):3866-73.
22. Comin-Colet J, Enjuanes C, Verdu-Rotellar JM, Linas A, Ruiz-Rodriguez P, Gonzalez-Robledo G, et al. Impact on clinical events and healthcare costs of adding telemedicine to multidisciplinary disease management programmes for heart failure: Results of a randomized controlled trial. *Journal of Telemedicine & Telecare*. 2016;22(5):282-95.
23. Crowley MJ, Edelman D, McAndrew AT, Kistler S, Danus S, Webb JA, et al. Practical telemedicine for veterans with persistently poor diabetes control: A randomized pilot trial. *Telemedicine journal and e-health*. 2016;22(5):376-84.
24. Crowley MJ, Olsen MK, Woolson SL, King HA, Oddone EZ, Bosworth HB. Baseline antihypertensive drug count and patient response to hypertension medication management. *Journal of Clinical Hypertension*. 2016;18(4):322-8.
25. Dario C, Delise P, Gubian L, Saccavini C, Brandolino G, Mancin S. Large controlled observational study on remote monitoring of pacemakers and implantable cardiac defibrillators: A clinical, economic, and organizational evaluation. *Interact J Med Res*. 2016;5(1):e4.
26. Davidson TM, McGillicuddy J, Mueller M, Brunner-Jackson B, Favella A, Anderson A, et al. Evaluation of an mhealth medication regimen self-management program for African American and Hispanic uncontrolled hypertensives. *Journal of personalized medicine*. 2015;5(4):389-405.
27. Del Favero S, Place J, Kropff J, Messori M, Keith-Hynes P, Visentin R, et al. Multicenter outpatient dinner/overnight reduction of hypoglycemia and increased time of glucose in target with a wearable artificial pancreas using modular model predictive control in adults with type 1 diabetes. *Diabetes, Obesity, and Metabolism*. 2015;17(5):468-76.
28. Del Rosario M, Lovell NH, Fildes J, Holgate K, Yu J, Ferry C, et al. Evaluation of an mhealth-based adjunct to outpatient cardiac rehabilitation. *IEEE Journal of biomedical and health informatics*. 2017.
29. Desteghe L, Vijgen J, Koopman P, D DI-B, Schurmans J, Dendale P, et al. Telemonitoring-based feedback improves adherence to non-vitamin k antagonist oral anticoagulants intake in patients with atrial fibrillation. *European Heart Journal*. 2018;39(16):1394-403.
30. Dobson R, Whittaker R, Jiang Y, Maddison R, Shepherd M, McNamara C, et al. Effectiveness of text message based, diabetes self management support programme (sms4bg): Two arm, parallel randomized controlled trial. *BMJ (Clinical research ed)*. 2018;361:k1959.
31. Dobson R, Whittaker R, Jiang Y, McNamara C, Shepherd M, Maddison R, et al. Long-term follow-up of a randomized controlled trial of a text-message diabetes self-management support programme, sms4bg. *Diabetic Medicine*. 2020;37(2):311-8.
32. Doñate-Martínez A, Ródenas F, Garcés J. Impact of a primary-based telemonitoring programme in HRQoL, satisfaction and usefulness in a sample of older adults with chronic diseases in valencia (Spain). *Archives of Gerontology & Geriatrics*. 2016;62:169-75.
33. Dorje T, Zhao G, Tso K, Wang J, Chen Y, Tsokey L, et al. Smartphone and social media-based cardiac rehabilitation and secondary prevention in china (smart-cr/sp): A parallel-group, single-blind, randomized controlled trial. *The Lancet Digital Health*. 2019;1(7):e363-e74.
34. Ebert DD, Nobis S, Lehr D, Baumeister H, Riper H, Auerbach RP, et al. The 6-month effectiveness of internet-based guided self-help for depression in adults with type 1 and 2 diabetes mellitus. *Diabetic Medicine*. 2017;34(1):99-107.
35. Egede LE, Williams JS, Voronca DC, Knapp RG, Fernandes JK. Randomized controlled trial of technology-assisted case management in low income adults with type 2 diabetes. *Diabetes Technology and Therapeutics*. 2017;19(8):476-82.
36. Evers PD, Anderson JB, Ryan TD, Czosek RJ, Knilans TK, Spar DS. Wearable cardioverter-defibrillators in pediatric cardiomyopathy: A cost-utility analysis. *Heart Rhythm*. 2020;17(2):287-93.

37. Fountoulakis S, Papanastasiou L, Gryparis A, Markou A, Piaditis G. Impact and duration effect of telemonitoring on ηba1c, BMI and cost in insulin-treated diabetes mellitus patients with inadequate glycemic control: A randomized controlled study. *Hormones (Athens, Greece)*. 2015;14(4):632-43.
38. Frederix I, Hansen D, Coninx K, Vandervoort P, Vandijck D, Hens N, et al. Medium-term effectiveness of a comprehensive internet-based and patient-specific telerehabilitation program with text messaging support for cardiac patients: Randomized controlled trial. *Journal of Medical Internet Research*. 2015;17(7):e185.
39. Frederix I, Hansen D, Coninx K, Vandervoort P, Vandijck D, Hens N, et al. Effect of comprehensive cardiac telerehabilitation on one-year cardiovascular rehospitalization rate, medical costs and quality of life: A cost-effectiveness analysis. *European Journal of Preventive Cardiology*. 2016;23(7):674-82.
40. Frederix I, Solmi F, Piepoli MF, Dendale P. Cardiac telerehabilitation: A novel cost-efficient care delivery strategy that can induce long-term health benefits. *European Journal of Preventive Cardiology*. 2017;24(16):1708-17.
41. Frederix I, Vanderlinden L, Verboven AS, Welten M, Wouters D, De Keulenaer G, et al. Long-term impact of a six-month telemedical care programme on mortality, heart failure readmissions and healthcare costs in patients with chronic heart failure. *Journal of Telemedicine & Telecare*. 2019;25(5):286-93.
42. Frederix I, Vandijck D, Hens N, De Sutter J, Dendale P. Economic and social impact of increased cardiac rehabilitation uptake and cardiac telerehabilitation in Belgium - a cost-benefit analysis. *Acta Cardiologica*. 2018;73(3):222-9.
43. Fritzen K, Basinska K, Rubio-Almanza M, Nicolucci A, Kennon B, Verges B, et al. Pan-European economic analysis to identify cost savings for the health care systems as a result of integrating glucose monitoring based telemedical approaches into diabetes management. *J Diabetes Sci Technol*. 2019;13(6):1112-22.
44. Gallagher J, Mc Carthy S, Woods N, Ryan F, O' Shea S, Byrne S. Economic evaluation of a randomized controlled trial of pharmacist-supervized patient self-testing of warfarin therapy. *Journal of Clinical Pharmacy & Therapeutics*. 2015;40(1):14-9.
45. Gatwood J, Balkrishnan R, Erickson SR, An LC, Piette JD, Farris KB. The impact of tailored text messages on health beliefs and medication adherence in adults with diabetes: A randomized pilot study. *Research in Social & Administrative Pharmacy*. 2016;12(1):130-40.
46. Grady M, Katz LB, Cameron H, Levy BL. Diabetes app-related text messages from health care professionals in conjunction with a new wireless glucose meter with a color range indicator improves glycemic control in patients with type 1 and type 2 diabetes: Randomized controlled trial. *JMIR Diabetes*. 2017;2(2):e19
47. Graetz I, Huang J, Muelly ER, Fireman B, Hsu J, Reed ME. Association of mobile patient portal access with diabetes medication adherence and glycemic levels among adults with diabetes. *JAMA Network Open*. 2020;3(2):e1921429-e.
48. Grustam AS, Severens JL, De Massari D, Buyukkaramikli N, Koymans R, Vrijhoef HJM. Cost-effectiveness analysis in telehealth: A comparison between home telemonitoring, nurse telephone support, and usual care in chronic heart failure management. *Value in Health*. 2018;21(7):772-82.
49. Guo Y, Chen Y, Lane DA, Liu L, Wang Y, Lip GYH. Mobile health technology for atrial fibrillation management integrating decision support, education, and patient involvement: Maf app trial. *American Journal of Medicine*. 2017;130(12):1388-96.e6.
50. Hawes EM, Lambert E, Reid A, Tong G, Gwynne M. Implementation and evaluation of a pharmacist-led electronic visit program for diabetes and anticoagulation care in a patient-centered medical home. *Am J Health-Syst Pharm*. 2018;75(12):901-10.
51. Hay JW, Lee P-J, Jin H, Guterman JJ, Gross-Schulman S, Ell K, et al. Cost-effectiveness of a technology-facilitated depression care management adoption model in safety-net primary care patients with type 2 diabetes. *Value in health*. 2018;21(5):561-8.
52. He J, Irazola V, Mills KT, Poggio R, Beratarrechea A, Dolan J, et al. Effect of a community health worker–led multicomponent intervention on blood pressure control in low-income patients in Argentina: A randomized clinical trial. *JAMA: the journal of the American Medical Association*. 2017;318(11):1016-25.
53. Heidbuchel H, Hindricks G, Broadhurst P, Van Erven L, Fernandez-Lozano I, Rivero-Ayerza M, et al. Euroeco (European health economic trial on home monitoring in ICD patients): A provider perspective in five European countries on costs and net financial impact of follow-up with or without remote monitoring. *European Heart Journal*. 2015;36(3):158-69.
54. Hummel JP, Leipold RJ, Amorosi SL, Bao H, Deger KA, Jones PW, et al. Outcomes and costs of remote patient monitoring among patients with implanted cardiac defibrillators: An economic model based on the predict rm database. *Journal of Cardiovascular Electrophysiology*. 2019;30(7):1066-77.

55. Islam SMS, Niessen LW, Ferrari U, Ali L, Seissler J, Lechner A. Effects of mobile phone SMS to improve glycemic control among patients with type 2 diabetes in Bangladesh: A prospective, parallel-group, randomized controlled trial. *Diabetes Care*. 2015;38(8):e112-e3.
56. Islam SMS, Peiffer R, Chow CK, Maddison R, Lechner A, Holle R, et al. Cost-effectiveness of a mobile-phone text messaging intervention on type 2 diabetes-a randomized-controlled trial. *Health Policy and Technology*. 2020.
57. Jiang X, Ming WK, You JHS. Potential cost-effectiveness of wearable cardioverter-defibrillator for patients with implantable cardioverter-defibrillator explant in a high-income city of china. *Journal of Cardiovascular Electrophysiology*. 2019;30(11):2387-96.
58. Jing C, Wei J, Wen Shuai D, Cheng Chuan R, Yan J, Feng Lei Q, et al. Effects of home-based telesupervising rehabilitation on physical function for stroke survivors with hemiplegia. A randomized controlled trial. *American Journal of Physical Medicine & Rehabilitation*. 2017;96(3):152-60.
59. Kamran Kamal A, Shaikh Q, Pasha O, Azam I, Islam M, Ali Memon A, et al. A randomized controlled behavioral intervention trial to improve medication adherence in adult stroke patients with prescription tailored short messaging service (SMS) - sms4stroke study. *BMC Neurology*. 2015;15(1):1-11.
60. Kao DP, Lindenfeld J, Macaulay D, Birnbaum HG, Jarvis JL, Desai US, et al. Impact of a telehealth and care management program on all-cause mortality and healthcare utilization in patients with heart failure. *Telemed J E Health*. 2016;22(1):2-11.
61. Katalenich B, Shi L, Liu S, Shao H, McDuffie R, Carpio G, et al. Evaluation of a remote monitoring system for diabetes control. *Clin Ther*. 2015;37(6):1216-25.
62. Kenealy TW, Parsons MJ, Rouse AP, Doughty RN, Sheridan NF, Hindmarsh JK, et al. Telecare for diabetes, CHF or COPD: Effect on quality of life, hospital use and costs. A randomized controlled trial and qualitative evaluation. *PloS one*. 2015;10(3):e0116188.
63. Kidholm K, Rasmussen MK, Andreasen JJ, Hansen J, Nielsen G, Spindler H, et al. Cost-utility analysis of a cardiac telerehabilitation program: The teledialog project. *Telemed J E Health*. 2016;22(7):553-63.
64. Kim EK, Kwak SH, Jung HS, Koo BK, Moon MK, Lim S, et al. The effect of a smartphone-based, patient-centered diabetes care system in patients with type 2 diabetes: A randomized, controlled trial for 24 weeks. *Diabetes Care*. 2019;42(1):3-9.
65. Kim JY, Wineinger NE, Steinhubl SR. The influence of wireless self-monitoring program on the relationship between patient activation and health behaviors, medication adherence, and blood pressure levels in hypertensive patients: A substudy of a randomized controlled trial. *Journal of Medical Internet Research*. 2016;18(6):49-.
66. Koehler F, Koehler K, Deckwart O, Prescher S, Wegscheider K, Kirwan BA, et al. Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): A randomized, controlled, parallel-group, unmasked trial. *Lancet*. 2018;392(10152):1047-57.
67. Kolominsky-Rabas PL, Kriza C, Djanatliev A, Meier F, Uffenorde S, Radeleff J, et al. Health economic impact of a pulmonary artery pressure sensor for heart failure telemonitoring: A dynamic simulation. *Telemedicine journal and e-health: the official journal of the American Telemedicine Association*. 2016;22(10):798-808.
68. Kooiman TJM, de Groot M, Hoogenberg K, Krijnen WP, van der Schans CP, Kooy A. Self-tracking of physical activity in people with type 2 diabetes: A randomized controlled trial. *CIN: Computers, Informatics, Nursing*. 2018;36(7):340-9.
69. Kotooka N, Kitakaze M, Nagashima K, Asaka M, Kinugasa Y, Nochioka K, et al. The first multicenter, randomized, controlled trial of home telemonitoring for Japanese patients with heart failure: Home telemonitoring study for patients with heart failure (homes-hf). *Heart and Vessels*. 2018;33(8):866-76.
70. Kraai I, de Vries A, Vermeulen K, van Deursen V, van der Wal M, de Jong R, et al. The value of telemonitoring and ICT-guided disease management in heart failure: Results from the in touch study. *International Journal of Medical Informatics*. 2016;85(1):53-60.
71. Kraal JJ, Elske Van Den Akker-Van Marle M, Abu-Hanna A, Stut W, Peek N, Kemps HMC. Clinical and cost-effectiveness of home-based cardiac rehabilitation compared to conventional, center-based cardiac rehabilitation: Results of the fit@home study. *European Journal of Preventive Cardiology*. 2017;24(12):1260-73.
72. Kurland J, Anna L, Stokes P. Effects of a tablet-based home practice program with telepractice on treatment outcomes in chronic aphasia. *Journal of Speech, Language & Hearing Research*. 2018;61(5):1140-56.
73. Labovitz DL, Shafner L, Reyes Gil M, Virmani PD, Hanina A, Virmani D. Using artificial intelligence to reduce the risk of nonadherence in patients on anticoagulation therapy. *Stroke (00392499)*. 2017;48(5):1416-9.

74. Ladapo JA, Turakhia MP, Ryan MP, Mollenkopf SA, Reynolds MR. Health care utilization and expenditures associated with remote monitoring in patients with implantable cardiac devices. *Am J Cardiol*. 2016;117(9):1455-62.
75. Lee JY, Lee SWH, Nasir NH, How S, Tan CSS, Wong CP. Diabetes telemonitoring reduces the risk of hypoglycaemia during Ramadan: A pilot randomized controlled study. *Diabetic Medicine*. 2015;32(12):1658-61.
76. Levy N, Moynihan V, Nilo A, Singer K, Bernik LS, Etiebet MA, et al. The mobile insulin titration intervention (miti) for insulin adjustment in an urban, low-income population: Randomized controlled trial. *Journal of medical Internet research*. 2015;17(7):e180.
77. Levy NK, Orzeck-Byrnes NA, Aidasani SR, Moloney DN, Nguyen LH, Park A, et al. Transition of a text-based insulin titration program from a randomized controlled trial into real-world settings: Implementation study. *Journal of Medical Internet Research*. 2018 03 19;20(3):e93.
78. Linder SM, Rosenfeldt AB, Bay RC, Sahu K, Wolf SL, Alberts JL. Improving quality of life and depression after stroke through telerehabilitation. *American Journal of Occupational Therapy*. 2015;69(2):1-11.
79. Liu S, Brooks D, Thomas SG, Eysenbach G, Nolan RP. Effectiveness of user- and expert-driven web-based hypertension programs: An RCT. *American Journal of Preventive Medicine*. 2018;54(4):576-83.
80. Lloréns R, Noé E, Colomer C, Alcañiz M. Effectiveness, usability, and cost-benefit of a virtual reality–based telerehabilitation program for balance recovery after stroke: A randomized controlled trial. *Archives of Physical Medicine & Rehabilitation*. 2015;96(3):418-25.e2.
81. López-Liria R, López-Villegas A, Enebakk T, Thunhaug H, Lappegård KT, Catalán-Matamoros D. Telemonitoring and quality of life in patients after 12 months following a pacemaker implant: The Nordland study, a randomized trial. *International Journal of Environmental Research and Public Health*. 2019;16(11):2001.
82. Lopez-Villegas A, Catalan-Matamoros D, Peiro S, Lappegard KT, Lopez-Liria R. Cost-utility analysis of telemonitoring versus conventional hospital-based follow-up of patients with pacemakers. The Nordland randomized clinical trial. *PLoS ONE*. 2020;15(1).
83. Lopez-Villegas A, Catalan-Matamoros D, Robles-Musso E, Bautista-Mesa R, Peiro S. Cost-utility analysis on telemonitoring of users with pacemakers: The Poniente study. *Journal of Telemedicine & Telecare*. 2019;25(4):204-12.
84. Lopez-Villegas A, Catalan-Matamoros D, Robles-Musso E, Peiro S. Comparative effectiveness of remote monitoring of people with cardiac pacemaker versus conventional: Quality of life at the 6 months. *Rev Esp Salud Publica*. 2015;89(2):149-58.
85. Lopez-Villegas A, Catalan-Matamoros D, Robles-Musso E, Peiro S. Effectiveness of pacemaker tele-monitoring on quality of life, functional capacity, event detection and workload: The Poniente trial. *Geriatr Gerontol Int*. 2016;16(11):1188-95.
86. Lopez-Villegas A, Catalan-Matamoros D, Robles-Musso E, Peiro S. Workload, time and costs of the informal cares in patients with tele-monitoring of pacemakers: The Poniente study. *Clin*. 2016;105(4):307-13.
87. Maddison R, Pfaeffli L, Whittaker R, Stewart R, Kerr A, Jiang Y, et al. A mobile phone intervention increases physical activity in people with cardiovascular disease: Results from the heart randomized controlled trial. *European Journal of Preventive Cardiology*. 2015;22(6):701-9.
88. Maddison R, Rawstorn JC, Stewart RAH, Benatar J, Whittaker R, Rolleston A, et al. Effects and costs of real-time cardiac telerehabilitation: Randomised controlled non-inferiority trial. *Heart*. 2019;105(2):122-9.
89. Margolis K, Asche S, Bergdall A, Dehmer S, Maciosek M, Nyboer R, et al. A successful multifaceted trial to improve hypertension control in primary care: Why did it work? *JGIM: Journal of General Internal Medicine*. 2015;30(11):1665-72.
90. Meng-Yao W, Meng-Jie S, Li-Hong W, Miao-Miao M, Zhen W, Li-Li L, et al. Effects of a comprehensive reminder system based on the health belief model for patients who have had a stroke on health behaviors, blood pressure, disability, and recurrence from baseline to 6 months: A randomized controlled trial. *Journal of Cardiovascular Nursing*. 2020;35(2):156-64.
91. Mierdel S, Owen K. Telehomecare reduces er use and hospitalizations at William Osler health system. *Studies in health technology and informatics*. 2015;209:102-8.
92. Mirro M, Daley C, Wagner S, Rohani Ghahari R, Drouin M, Toscos T. Delivering remote monitoring data to patients with implantable cardioverter-defibrillators: Does medium matter? *Pacing and Clinical Electrophysiology*. 2018;41(11):1526-35.
93. Monahan M, Jowett S, Nickless A, Franssen M, Grant S, Greenfield S, et al. Cost-effectiveness of telemonitoring and self-monitoring of blood pressure for antihypertensive titration in primary care (tasminh4). *Hypertension*. 2019;73(6):1231-9.

94. Moorhead P, Zavala A, Kim Y, Virdi NS. Efficacy and safety of a medication dose reminder feature in a digital health offering with the use of sensor-enabled medicines. *Journal of the American Pharmacists Association*. 2017;57(2):155-61.e1.
95. Morgan JM, Kitt S, Gill J, McComb JM, Ng GA, Raftery J, et al. Remote management of heart failure using implantable electronic devices. *European Heart Journal*. 2017 Aug 07;38(30):2352-60.
96. Murray E, Sweeting M, Dack C, Pal K, Modrow K, Hudda M, et al. Web-based self-management support for people with type 2 diabetes (help-diabetes): Randomised controlled trial in English primary care. *BMJ Open*. 2017;7(9):e016009.
97. Nobis S, Ebert DD, Lehr D, Smit F, Buntrock C, Berking M, et al. Web-based intervention for depressive symptoms in adults with types 1 and 2 diabetes mellitus: A health economic evaluation. *British Journal of Psychiatry*. 2018;212(4):199-206.
98. Nouryan CN, Morahan S, Pecinka K, Akerman M, Lesser M, Chaikin D, et al. Home telemonitoring of community-dwelling heart failure patients after home care discharge. *Telemed J E Health*. 2019;25(6):447-54.
99. Padwal RS, So H, Wood PW, McAlister FA, Siddiqui M, Norris CM, et al. Cost-effectiveness of home blood pressure telemonitoring and case management in the secondary prevention of cerebrovascular disease in Canada. *Journal of Clinical Hypertension*. 2019;21(2):159-68.
100. Parahuleva MS, Soydan N, Divchev D, Lusebrink U, Schieffer B, Erdogan A. Home monitoring after ambulatory implanted primary cardiac implantable electronic devices: The home ambulance pilot study. *Clin Cardiol*. 2017;40(11):1068-75.
101. Pedone C, Rossi FF, Cecere A, Costanzo L, Antonelli Incalzi R. Efficacy of a physician-led multiparametric telemonitoring system in very old adults with heart failure. *J Am Geriatr Soc*. 2015;63(6):1175-80.
102. Peng X, Su Y, Hu Z, Sun X, Li X, Dolansky MA, et al. Home-based telehealth exercise training program in Chinese patients with heart failure a randomized controlled trial. *Medicine (United States)*. 2018;97(35).
103. Persell SD, Peprah YA, Lipiszko D, Lee JY, Li JJ, Ciolino JD, et al. Effect of home blood pressure monitoring via a smartphone hypertension coaching application or tracking application on adults with uncontrolled hypertension: A randomized clinical trial. *JAMA Network Open*. 2020;3(3):e200255-e.
104. Piccini JP, Mittal S, Snell J, Prillinger JB, Dalal N, Varma N. Impact of remote monitoring on clinical events and associated health care utilization: A nationwide assessment. *Heart Rhythm*. 2016;13(12):2279-86.
105. Piotrowicz E, Zielilski T, Bodalski R, Rywik T, Dobraszkiewicz-Wasilewska B, Sobieszczalska-Malek M, et al. Home-based telemonitored nordic walking training is well accepted, safe, effective and has high adherence among heart failure patients, including those with cardiovascular implantable electronic devices: A randomized controlled study. *European Journal of Preventive Cardiology*. 2015;22(11):1368-77.
106. Ploux S, Swerdlow CD, Strik M, Welte N, Klotz N, Ritter P, et al. Towards eradication of inappropriate therapies for ICD lead failure by combining comprehensive remote monitoring and lead noise alerts. *Journal of Cardiovascular Electrophysiology*. 2018;29(8):1125-34.
107. Poduval S, Ahmed S, Marston L, Hamilton F, Murray E. Crossing the digital divide in online self-management support: Analysis of usage data from help-diabetes. *JMIR Diabetes*. 2018;3(4):e10925.
108. Price-Haywood EG, Luo Q, Monlezun D. Dose effect of patient-care team communication via secure portal messaging on glucose and blood pressure control. *Journal of the American Medical Informatics Association*. 2018;25(6):702-8.
109. Queenan C, Cameron K, Snell A, Smalley J, Joglekar N. Patient heal thyself: Reducing hospital readmissions with technology-enabled continuity of care and patient activation. *Production and Operations Management*. 2019;28(11):2841-53.
110. Ramadas A, Chan CKY, Oldenburg B, Hussein Z, Quek KF. Randomized-controlled trial of a web-based dietary intervention for patients with type 2 diabetes: Changes in health cognitions and glycemic control. *BMC public health*. 2018;18(1):716.
111. Ricci RP, Vicentini A, D'Onofrio A, Sagone A, Rovaris G, Padeletti L, et al. Economic analysis of remote monitoring of cardiac implantable electronic devices: Results of the health economics evaluation registry for remote follow-up (tariff) study. *Heart Rhythm*. 2017;14(1):50-7.
112. Smith DH, O'Keeffe-Rosetti M, Owen-Smith AA, Rand C, Tom J, Vupputuri S, et al. Improving adherence to cardiovascular therapies: An economic evaluation of a randomized pragmatic trial. *Value in Health*. 2016;19(2):176-84.
113. Srivastava A, Do J-M, Sales VL, Ly S, Joseph J. Impact of patient-centred home telehealth programme on outcomes in heart failure. *Journal of Telemedicine & Telecare*. 2019;25(7):425-30.

114. Thies K, Anderson D, Cramer B. Lack of adoption of a mobile app to support patient self-management of diabetes and hypertension in a federally qualified health center: Interview analysis of staff and patients in a failed randomized trial. *JMIR Hum Factors*. 2017;4(4):e24.
115. Torrisi M, Maresca G, De Cola MC, Cannavo A, Sciarrone F, Silvestri G, et al. Using telerehabilitation to improve cognitive function in post-stroke survivors: Is this the time for the continuity of care? *International Journal of rehabilitation research*. 2019;42(4):344-51.
116. Varleta P, Acevedo M, Akel C, Salinas C, Navarrete C, García A, et al. Mobile phone text messaging improves antihypertensive drug adherence in the community. *Journal of Clinical Hypertension*. 2017;19(12):1276-84.
117. Vestergaard AS, Hansen L, Sorensen SS, Jensen MB, Ehlers LH. Is telehealthcare for heart failure patients cost-effective? An economic evaluation alongside the danish telecare north heart failure trial. *BMJ Open*. 2020;10(1):e031670.
118. Wagenaar KP, Broekhuizen BDL, Jaarsma T, Kok I, Mosterd A, Willems FF, et al. Effectiveness of the European society of cardiology/heart failure association website 'heartfailurematters.Org' and an e-health adjusted care pathway in patients with stable heart failure: Results of the 'e-vita hf' randomized controlled trial. *European Journal of Heart Failure*. 2019;21(2):238-46.
119. Ware P, Ross HJ, Cafazzo JA, Laporte A, Gordon K, Seto E. Evaluating the implementation of a mobile phone-based telemonitoring program: Longitudinal study guided by the consolidated framework for implementation research. *JMIR Mhealth Uhealth*. 2018;6(7):e10768.
120. Warren R, Carlisle K, Mihala G, Scuffham PA. Effects of telemonitoring on glycaemic control and healthcare costs in type 2 diabetes: A randomized controlled trial. *Journal of Telemedicine & Telecare*. 2018;24(9):586-95.
121. Wayne N, Perez DF, Kaplan DM, Ritvo P. Health coaching reduces hba1c in type 2 diabetic patients from a lower-socioeconomic status community: A randomized controlled trial. *Journal of Medical Internet Research*. 2015;17(10):e224.
122. Whaley CM, Bollyky JB, Lu W, Painter S, Schneider J, Zhao Z, et al. Reduced medical spending associated with increased use of a remote diabetes management program and lower mean blood glucose values. *J Med Econ*. 2019;22(9):869-77.
123. Williams C, Wan TTH. A cost analysis of remote monitoring in a heart failure program. *Home Health Care Services Quarterly*. 2016;35(3/4):112-22.
124. Williams C, Wan TTH. The influence of remote monitoring on clinical decision making. *Home Health Care Management & Practice*. 2016;28(2):86-93.
125. Wilson M, Hewes C, Barbosa-Leiker C, Mason A, Wuestney KA, Shuen JA, et al. Engaging adults with chronic disease in online depressive symptom self-management. *Western Journal of Nursing Research*. 2018;40(6):834-53.
126. Wu S, Ell K, Jin H, Vidyanti I, Chou CP, Lee PJ, et al. Comparative effectiveness of a technology-facilitated depression care management model in safety-net primary care patients with type 2 diabetes: 6-month outcomes of a large clinical trial. *Journal of Medical Internet Research*. 2018;20(4):e147.
127. Yang Y, Lee EY, Kim HS, Lee SH, Yoon KH, Cho JH. Effect of a mobile phone-based glucose-monitoring and feedback system for type 2 diabetes management in multiple primary care clinic settings: Cluster randomized controlled trial. *JMIR Mhealth Uhealth*. 2020;8(2):e16266.
128. Young HM, Miyamoto S, Dharmar M, Tang-Feldman Y. Nurse coaching and mobile health compared with usual care to improve diabetes self-efficacy for persons with type 2 diabetes: Randomized controlled trial. *JMIR Mhealth Uhealth*. 2020;8(3):e16665.
129. Yun YH, Kang E, Cho YM, Park SM, Kim YJ, Lee HY, et al. Efficacy of an electronic health management program for patients with cardiovascular risk: Randomized controlled trial. *Journal of medical Internet research*. 2020;22(1):e15057.
130. Zha P, Qureshi R, Porter S, Chao Y-Y, Pacquiao D, Chase S, et al. Utilizing a mobile health intervention to manage hypertension in an underserved community. *Western Journal of Nursing Research*. 2020;42(3):201-9.
131. Achelrod D, Schreyogg J, Stargardt T. Health-economic evaluation of home telemonitoring for COPD in Germany: Evidence from a large population-based cohort. *European Journal of Health Economics*. 2017;18(7):869-82.
132. Adams AS, Schmittdiel JA, Altschuler A, Bayliss EA, Neugebauer R, Ma L, et al. Automated symptom and treatment side effect monitoring for improved quality of life among adults with diabetic peripheral neuropathy in primary care: A pragmatic, cluster, randomized, controlled trial. *Diabetic Medicine*. 2019;36(1):52-61.
133. Ambeba EJ, Lei Y, Sereika SM, Styn MA, Acharya SD, Sevick MA, et al. The use of mhealth to deliver tailored messages reduces reported energy and fat intake. *Journal of Cardiovascular Nursing*. 2015;30(1):35-43.

134. Ariza-Garcia A, Lozano-Lozano M, Galiano-Castillo N, Postigo-Martin P, Arroyo-Morales M, Cantarero-Villanueva I. A web-based exercise system (e-cuidatechemo) to counter the side effects of chemotherapy in patients with breast cancer: Randomized controlled trial. *Journal of medical Internet research*. 2019 24;21(7):e14418.
135. Beukes EW, Baguley DM, Allen PM, Manchaiah V, Andersson G. Audiologist-guided internet-based cognitive behavior therapy for adults with tinnitus in the united kingdom: A randomized controlled trial. *Ear Hear*. 2018;39(3):423-33.
136. Cao F, Li L, Lin M, Lin Q, Ruan Y, Hong F. Application of instant messaging software in the follow-up of patients using peritoneal dialysis, a randomized controlled trial. *Journal of Clinical Nursing (John Wiley & Sons, Inc)*. 2018;27(15-16):3001-7.
137. Comans T, Mihala G, Sakzewski L, Boyd RN, Scuffham P. The cost-effectiveness of a web-based multimodal therapy for unilateral cerebral palsy: The mitii randomized controlled trial. *Dev Med Child Neurol*. 2017;59(7):756-61.
138. Compen F, Adang E, Bisseling E, van der Lee M, Speckens A. Cost-utility of individual internet-based and face-to-face mindfulness-based cognitive therapy compared with treatment as usual in reducing psychological distress in cancer patients. *Psychooncology*. 2020;29(2):294-303.
139. Connelly M, Ibarra M, Klein-Gitelman MS, Lawson E, Stinson J, Schanberg LE, et al. Multisite randomized clinical trial evaluating an online self-management program for adolescents with juvenile idiopathic arthritis. *Journal of Pediatric Psychology*. 2019;44(3):363-74.
140. Cubo E, Mariscal N, Solano B, Becerra V, Armesto D, Calvo S, et al. Prospective study on cost-effectiveness of home-based motor assessment in Parkinson's disease. *Journal of Telemedicine & Telecare*. 2017;23(2):328-38.
141. Del Hoyo J, Nos P, Bastida G, Faubel R, Munoz D, Garrido-Marin A, et al. Telemonitoring of Crohn's disease and ulcerative colitis (teccu): Cost-effectiveness analysis. *Journal of Medical Internet Research*. 2019;21(9):e15505.
142. Devito Dabbs A, Song MK, Myers BA, Li R, Hawkins RP, Pilewski JM, et al. A randomized controlled trial of a mobile health intervention to promote self-management after lung transplantation. *American Journal of Transplantation*. 2016.
143. Dijkstra A, Heida A, van Rheenen PF. Exploring the challenges of implementing a web-based telemonitoring strategy for teenagers with inflammatory bowel disease: Empirical case study. *Journal of Medical Internet Research*. 2019;21(3):e11761.
144. El Miedany Y, El Gaafary M, El Aroussy N, Bahlas S, Hegazi M, Palmer D, et al. Toward electronic health recording: Evaluation of electronic patient reported outcome measures (e-proms) system for remote monitoring of early systemic lupus patients. *Clinical rheumatology*. 2017;36(11):2461-9.
145. Ellis TD, Cavanaugh JT, DeAngelis T, Hendron K, Thomas CA, Saint-Hilaire M, et al. Comparative effectiveness of mhealth-supported exercise compared with exercise alone for people with Parkinson's disease: Randomized controlled pilot study. *Physical Therapy*. 2019;99(2):203-16.
146. Gandolfi M, Geroin C, Dimitrova E, Boldrini P, Waldner A, Bonadiman S, et al. Virtual reality telerehabilitation for postural instability in Parkinson's disease: A multicenter, single-blind, randomized, controlled trial. *BioMed Research International*. 2017;2017 (no pagination).
147. Gordon R, Bloxham S. Influence of the Fitbit Charge HR on physical activity, aerobic fitness and disability in non-specific back pain participants. *Journal of Sports Medicine & Physical Fitness*. 2017;57(12):1669-75.
148. Haas K, Martin A, Park KT. Text message intervention (teach) improves quality of life and patient activation in celiac disease: A randomized clinical trial. *Journal of Pediatrics*. 2017;185:62-7.e2.
149. Heapy AA, Higgins DM, Goulet JL, LaChappelle KM, Driscoll MA, Czlapinski RA, et al. Interactive voice response-based self-management for chronic back pain: The copes noninferiority randomized trial. *JAMA Internal Medicine*. 2017;177(6):765-73.
150. Heida A, Dijkstra A, Kobold AM, Rossen JW, Kindermann A, Kokke F, et al. Efficacy of home telemonitoring versus conventional follow-up: A randomized controlled trial among teenagers with inflammatory bowel disease. *Journal of Crohn's and Colitis*. 2018;12(4):432-41.
151. Heldman DA, Giuffrida JP, Cubo E. Wearable sensors for advanced therapy referral in Parkinson's disease. *Journal of Parkinson's disease*. 2016;6(3):631-8.
152. Isetta V, Negrin MA, Monasterio C, Masa JF, Feu N, Alvarez A, et al. A bayesian cost-effectiveness analysis of a telemedicine-based strategy for the management of sleep apnoea: A multicentre randomized controlled trial. *Thorax*. 2015 Nov;70(11):1054-61.
153. Janse A, Worm-Smeitink M, Bleijenberg G, Donders R, Knoop H. Efficacy of web-based cognitive-behavioural therapy for chronic fatigue syndrome: Randomised controlled trial. *British Journal of Psychiatry*. 2018;212(2):112-8.

154. Jiang Y, Sereika SM, DeVito Dabbs A, Handler SM, Schlenk EA. Using mobile health technology to deliver decision support for self-monitoring after lung transplantation. *International Journal of Medical Informatics*. 2016 01 Oct;94:164-71.
155. Kadri R, Krein SL, Abdul-Wahab Y, Richardson CR. Adverse events experienced by participants in a back pain walking intervention: A descriptive study. *Chronic Illness*. 2016;12(1):71-80.
156. Kaiser K, Hils S, Fetzer S, Hehn P, Schmid A, Hauschke D, et al. Results of a randomized controlled trial analyzing telemedically supported case management in the first year after living donor kidney transplantation - a budget impact analysis from the healthcare perspective. *Health economics review*. 2017;7(1).
157. Kanera IM, Willems RA, Bolman CAW, Mesters I, Verboon P, Lechner L. Long-term effects of a web-based cancer aftercare intervention on moderate physical activity and vegetable consumption among early cancer survivors: A randomized controlled trial. *International Journal of Behavioral Nutrition & Physical Activity*. 2017;14:1-13.
158. Kessler R, Casan-Clara P, Koehler D, Tognella S, Viejo JL, Dal Negro RW, et al. Comet: A multicomponent home-based disease-management programme versus routine care in severe COPD. *European Respiratory Journal*. 2018;51(1).
159. Kloek CJJ, van Dongen JM, de Bakker DH, Bossen D, Dekker J, Veenhof C. Cost-effectiveness of a blended physiotherapy intervention compared to usual physiotherapy in patients with hip and/or knee osteoarthritis: A cluster randomized controlled trial. *BMC Public Health*. 2018;18(1):1082.
160. Kroenke K, Baye F, Lourens SG, Evans E, Weitlauf S, McCalley S, et al. Automated self-management (asm) vs. Asm-enhanced collaborative care for chronic pain and mood symptoms: The cammps randomized clinical trial. *Journal of General Internal Medicine*. 2019;34(9):1806-14.
161. Lally RM, Kupzyk KA, Bellavia G, Hydeman J, Gallo S, Helgeson VS, et al. Caringguidancetm after breast cancer diagnosis ehealth psychoeducational intervention to reduce early post-diagnosis distress. *Supportive Care in Cancer*. 2019.
162. Landtblom A-M, Guala D, Martin C, Olsson-Hau S, Haghighi S, Jansson L, et al. Rebiqol: A randomized trial of telemedicine patient support program for health-related quality of life and adherence in people with MS treated with Rebif. *PLOS ONE*. 2019;14(7):e0218453.
163. Law EF, Groenewald CB, Zhou C, Palermo TM. Effect on health care costs for adolescents receiving adjunctive internet-delivered cognitive-behavioral therapy: Results of a randomized controlled trial. *J Pain*. 2018;19(8):910-9.
164. Lew SQ, Sikka N, Thompson C, Magnus M. Impact of remote biometric monitoring on cost and hospitalization outcomes in peritoneal dialysis. *Journal of Telemedicine & Telecare*. 2019;25(10):581-6.
165. Lilholt PH, Witt Udsen F, Ehlers L, Hejlesen OK. Telehealthcare for patients suffering from chronic obstructive pulmonary disease: Effects on health-related quality of life: Results from the danish 'telecare north' cluster-randomized trial. *BMJ Open*. 2017;7(5):e014587.
166. Little P, Stuart B, Hobbs FR, Kelly J, Smith ER, Bradbury KJ, et al. An internet-based intervention with brief nurse support to manage obesity in primary care (power+): A pragmatic, parallel-group, randomized controlled trial. *Lancet Diabetes Endocrinol*. 2016 10;4(10):821-8.
167. Lugo VM, Garmendia O, Suarez-Giron M, Torres M, Vazquez-Polo FJ, Negrin MA, et al. Comprehensive management of obstructive sleep apnea by telemedicine: Clinical improvement and cost-effectiveness of a virtual sleep unit. A randomized controlled trial. *PLoS ONE*. 2019;14(10):e0224069.
168. Mauro J, Mathews KB, Sredzinski ES. Effect of a smart pill bottle and pharmacist intervention on medication adherence in patients with multiple myeloma new to lenalidomide therapy. *J Manag Care Spec Pharm*. 2019;25(11):1244-54.
169. Mbada C, Olaoye M, Ayanniyi O, Johnson O, Odole A, Dada O. Comparative efficacy of clinic-based and telerehabilitation application of mckenzie therapy in low-back pain. *Archives of physical medicine and rehabilitation*. 2017; Conference: 94th Annual Conference of the American Congress of Rehabilitation Medicine, ACRM 2017. United States. 98(10):e46-e7.
170. McDowell JE, McClean S, FitzGibbon F, Tate S. A randomized clinical trial of the effectiveness of home-based health care with telemonitoring in patients with COPD. *Journal of Telemedicine & Telecare*. 2015;21(2):80-7.
171. Mercier HW, Ni P, Houlihan BV, Jette AM. Differential impact and use of a telehealth intervention by persons with ms or sci. *American Journal of Physical Medicine & Rehabilitation*. 2015;94(11):987-99.
172. Milan Manani S, Rosner MH, Virzi GM, Giuliani A, Berti S, Crepaldi C, et al. Longitudinal experience with remote monitoring for automated peritoneal dialysis patients. *Nephron*. 2019;142(1):1-9.
173. Munafo D, Hevener W, Crocker M, Willes L, Sridasome S, Muhsin M. A telehealth program for CPAP adherence reduces labor and yields similar adherence and efficacy when compared to standard of care. *Sleep Breath*. 2016;20(2):777-85.

174. Paganini S, Lin J, Kahlke F, Buntrock C, Leiding D, Ebert DD, et al. A guided and unguided internet- and mobile-based intervention for chronic pain: Health economic evaluation alongside a randomized controlled trial. *BMJ Open*. 2019;9(4):e023390.
175. Park OL, Kim SR. Integrated self-management program effects on hemodialysis patients: A quasi-experimental study. *Japan Journal of Nursing Science*. 2019;16(4):396-406.
176. Ren Q, Lian M, Liu Y, Thomas-Hawkins C, Zhu L, Shen Q. Effects of a transtheoretical model-based wechat health education programme on self-management among haemodialysis patients: A longitudinal experimental intervention study. *Journal of Advanced Nursing (John Wiley & Sons, Inc)*. 2019;75(12):3554-65.
177. Rothgangel A, Braun S, Winkens B, Beurskens A, Smeets R. Traditional and augmented reality mirror therapy for patients with chronic phantom limb pain (pact study): Results of a three-group, multicentre single-blind randomized controlled trial. *Clinical Rehabilitation*. 2018;32(12):1591-608.
178. Rutledge T, Skoyen JA, Wiese JA, Ober KM, Woods GN. A comparison of move! Versus telemove programs for weight loss in veterans with obesity. *Obesity Research and Clinical Practice*. 2017;11(3):344-51.
179. Saengryeol P, Kwangnam K, Hyun Kyu A, Jong Won K, Gyurang M, Byung Ha C, et al. Impact of lifestyle intervention for patients with prostate cancer. *American Journal of Health Behavior*. 2020;44(1):90-9.
180. Skolarus TA, Metreger T, Wittmann D, Hwang S, Kim HM, Grubb RL, et al. Self-management in long-term prostate cancer survivors: A randomized, controlled trial. *Journal of Clinical Oncology*. 2019 20;37(15):1326-35.
181. Smith J, Faux SG, Gardner T, Hobbs MJ, James MA, Joubert AE, et al. Reboot online: A randomized controlled trial comparing an online multidisciplinary pain management program with usual care for chronic pain. *Pain Medicine*. 2019;20(12):2385-96.
182. Sniehotta FF, Evans EH, Sainsbury K, Adamson A, Batterham A, Becker F, et al. Behavioural intervention for weight loss maintenance versus standard weight advice in adults with obesity: A randomized controlled trial in the UK (nulevel trial). *PLoS Med*. 2019;16(5):e1002793.
183. Soriano JB, Garcia-Rio F, Vazquez-Espinosa E, Conforto JI, Hernando-Sanz A, Lopez-Yepes L, et al. A multicentre, randomized controlled trial of telehealth for the management of COPD. *Respir Med*. 2018;144:74-81.
184. Steventon A, Bardsley M, Mays N. Effect of a telephonic alert system (healthy outlook) for patients with chronic obstructive pulmonary disease: A cohort study with matched controls. *Journal of Public Health*. 2015;37(2):313-21.
185. Stoddart A, van der Pol M, Pinnock H, Hanley J, McCloughan L, Todd A, et al. Telemonitoring for chronic obstructive pulmonary disease: A cost and cost-utility analysis of a randomized controlled trial. *Journal of Telemedicine & Telecare*. 2015;21(2):108-18.
186. Stukus DR, Farooqui N, Strothman K, Ryan K, Zhao S, Stevens JH, et al. Real-world evaluation of a mobile health application in children with asthma. *Annals of allergy, asthma & immunology*. 2018;120(4):395-400.
187. Suman A, Schaafsma FG, van Dongen JM, Elders PJM, Buchbinder R, van Tulder MW, et al. Effectiveness and cost-utility of a multifaceted ehealth strategy to improve back pain beliefs of patients with non-specific low back pain: A cluster randomized trial. *BMJ Open*. 2019;9(12):e030879.
188. Talboom-Kamp EP, Verdijk NA, Kasteleyn MJ, Harmans LM, Talboom IJ, Looijmans-van den Akker I, et al. The effect of integration of self-management web platforms on health status in chronic obstructive pulmonary disease management in primary care (e-vita study): Interrupted time series design. *Journal of Medical Internet Research*. 2017;19(8):e291.
189. Taveras EM, Marshall R, Sharifi M, Avalon E, Fiechtner L, Horan C, et al. Comparative effectiveness of clinical-community childhood obesity interventions a randomized clinical trial. *JAMA Pediatrics*. 2017;171(8).
190. Theodoros DG, Hill AJ, Russell TG. Clinical and quality of life outcomes of speech treatment for Parkinson's disease delivered to the home via telerehabilitation: A noninferiority randomized controlled trial. *American Journal of Speech-Language Pathology*. 2016;25(2):214-32.
191. Thomsen T, Aadahl M, Beyer N, Hetland ML, Loppenthin K, Midtgaard J, et al. The efficacy of motivational counselling and SMS reminders on daily sitting time in patients with rheumatoid arthritis: A randomized controlled trial. *Annals of the Rheumatic Diseases*. 2017;76(9):1603-6.
192. Turino C, de Batlle J, Woehrle H, Mayoral A, Castro-Grattoni AL, Gomez S, et al. Management of continuous positive airway pressure treatment compliance using telemonitoring in obstructive sleep apnoea. *European Respiratory Journal*. 2017;49(2):02.

193. Vasbinder EC, Goossens LM, Rutten-van Molken MP, de Winter BC, van Dijk L, Vulto AG, et al. E-monitoring of asthma therapy to improve compliance in children (e-matic): A randomized controlled trial. *European Respiratory Journal*. 2016;48(3):758-67.
194. Vriezinga S, Borghorst A, van den Akker-van Marle E, Benninga M, George E, Hendriks D, et al. E-healthcare for Celiac disease-a multicenter randomized controlled trial. *Journal of Pediatrics*. 2018;195:154-60.e7.
195. Walker PP, Pompilio PP, Zanaboni P, Bergmo TS, Prikk K, Malinovschi A, et al. Telemonitoring in chronic obstructive pulmonary disease (chromed). A randomized clinical trial. *Am J Respir Crit Care Med*. 2018;198(5):620-8.
196. Wang P, Yu T, Yang L. Web-based remote psychological intervention improves cancer treatment. *Psychology, Health & Medicine*. 2017;22(7):879-87.
197. Weise C, Kleinstäuber M, Andersson G. Internet-delivered cognitive-behavior therapy for tinnitus: A randomized controlled trial. *Psychosomatic Medicine*. 2016;78(4):501-10.
198. Witt Udsen F, Lilholt PH, Hejlesen O, Ehlers L. Cost-effectiveness of telehealthcare to patients with chronic obstructive pulmonary disease: Results from the danish 'telecare north' cluster-randomized trial. *BMJ Open*. 2017;7(5):e014616.
199. Witt Udsen F, Lilholt PH, Hejlesen OK, Ehlers LH. Subgroup analysis of telehealthcare for patients with chronic obstructive pulmonary disease: The cluster-randomized danish telecare north trial. *ClinicoEcon*. 2017;9:391-401.
200. Xie H, Ji T, Ma J, Liu Q, Jiang Y, Cai L, et al. Remote programming: A convenient and cost-effective measure of vagus nerve stimulation for children with epilepsy. *Epilepsy Research*. 2020;159.
201. Zhou Y, Lu Y, Zhu H, Zhang Y, Li Y, Yu Q. Short-term effect of a smart nebulizing device on adherence to inhaled corticosteroid therapy in asthma predictive index-positive wheezing children. *Patient Preference and Adherence*. 2018;12:861-8.

Table A 8: DHT-specific content to be considered when undertaking a Health Technology Assessment (HTA) of DHTs

HTA Domain	Topic (EUN)/(NEW)	Issue ID (modifier)	Issue content	N=112 n (%)					
				Good	Fair	Poor	Not covered	NR	NA
CUR	Utilisation (EUN)	**A0011/2(1)**	Provide evidence of whether health workers/patients do or will invest in the personal digital technologies required to use the DHT? Estimate current investment by workers/patients, detail direct and add-on costs, and user willingness to pay	5(4)	17(15)	4(4)	86(77)		
		A0011/2(2)	Discuss whether the DHT usage will be affected (or why not) by limitations in terms of platforms, languages, network connectivity, or users' digital literacy?	4(3)	10(9)	12(11)	86(77)		
		A0011/2(3)	Has granular data on DHT usage been collected? Can this usage data be collected every time the DHT is used or was it difficult for them to capture so they only did it in the trial?	39(35)	34(30)	4(4)	35(31)		
		F0001(1)	Describe inputs (i.e., image, physiological status, symptoms, etc.) and outputs (i.e., inform, treat, diagnose) of the DHT?	34(30)	72(64)	5(5)	1(1)		
		F0001(2)	Describe the algorithms (i.e., equations, analysis engine model logic, algorithm, etc.) of the DHT?	7(6)	51(46)	15(13)	39(35)		
TEC	Investments/tools required (EUN)	**B0007**	Considerations of device size, battery life/charging method, operating system, connectivity, data access & storage, data security, technical support	3(3)	16(14)	6(5)	87(78)		
	Training/information needed (EUN)	**B0013/4**	Personnel/caregivers/patient/family: Training required/provided on personal data handling, digital skills, and digital health literacy?	4(4)	18(16)	25(22)	65(58)		
	Features of Technology (EUN)	**DHT01**	Discussion of how well the DHT and comparator(s) perform in overcoming technical barriers: Interoperability, data extraction, visualisation, etc.?	9(8)	32(29)	8(7)	63(56)		
SAF	Quality & safeguarding (NEW)	**DHT02**	How well are data security and privacy managed - Does it comply with GDPR principles of data minimisation/protection by default/design?	5(4)	14(13)	7(6)	86(77)		
		DHT03	How well is interoperability designed and data quality managed?	10(9)	9(8)	6(5)	85(76)		2(2)
		DHT04	How transparent are the DHT risks (e.g., data sharing, conflicts of interest) to the user?		1(1)	1(1)	110(98)		
		DHT05	Evidence that DHT designed for usability and accessibility?	8(7)	18(16)	6(5)	80(72)		
		DHT06	Is adequate information disclosed on DHT algorithms to evaluate their risk?		11(10)	4(3)	97(87)		
	Technical safety (Reliability & stability) (NEW)	**DHT07**	How technically reliable and stable is the DHT?	2(2)	21(19)	5(4)	84(75)		
		DHT08	How well are updates/continuity of the DHT managed?		5(4)	1(1)	101(95)		
	Communicating for safety (NEW)	**DHT09**	Can the user send critical risk information to the DHT provider?	6(5)	12(11)	3(3)	91(81)		
		DHT10	Processes for correct identification of users in DHT?	1(1)	5(4)	2(2)	104(93)		
		DHT11	Processes to communicate changes to or transfer of a patient's care		5(4)		107(96)		

HTA Domain	Topic (EUN)/(NEW)	Issue ID (modifier)	Issue content	N=112 n (%)					
				Good	Fair	Poor	Not covered	NR	NA
EFF	Patient satisfaction (EUN)	**D0017(1)**	Has an analysis been conducted on how effective the DHT is for users with a disability?	2(2)	9(8)	3(3)	98(87)		
		D0017(2)	Has an analysis been conducted on how effective the DHT is for users with limited technical ability?	5(4)	13(12)	3(3)	91(81)		
		D0017(3)	For wearables, are design issues to increase usability discussed, e.g., washable, durable, cause skin allergies?	1(1)		3(3)	51(45)		57(51)
	Demonstrating effectiveness (NEW)	**DHT12(1)**	Are accepted methods used to overcome common methodological problems in RCTs for DHTs, e.g., achieving blinding, biases from informed consent, high attrition	3(3)	49(44)	24(21)	8(7)		28(25)
		DHT12(2)	Is it clear whether the DHT was changed (bug fixes, content) during the trial?	2(2)	5(4)		105(94)		
		DHT12(3)	Did they recognise digital literacy was an implicit eligibility criterion or sample population may be biased towards digitally literate people?	6(5)	7(7)	6(5)	64(57)		29(26)
		DHT13	Was the comparator group restricted in the DHT to which they had access?		10(9)		102(91)		
		DHT14(1)	Have DHT specific and validated outcome measures been collected: i.e., the intensity of use (dose, exposure), online adherence, engagement?	2(2)	47(42)	6(5)	57(51)		
		DHT14(2)	Has data collection embedded in the DHT created systematic bias or confounding?	3(3)	52(46)	1(1)	56(50)		
	Reliable information content (NEW)	**DHT16**	Is the health information provided by DHT accurate, valid, up to date, comprehensive, clear, and tailored to the users' diversity?	2(2)	25(22)	1(1)	36(32)		48(43)
	Use of appropriate behaviour change techniques (NEW)	**DHT17**	Does the DHT use appropriate and best practice behaviour change techniques? Is the mechanism credible? Is the targeted behaviour change apparent to the user, and are the appropriate supports in place? Is it relevant for the target population?	19(17)	9(8)	2(2)	37(33)		45(40)
	External validity/ generalisability (NEW)	**DHT18**	Discuss whether patient identity validation and obtaining off-line contact details to improve follow-up rates has jeopardised external validity?		6(5)		96(86)		10(9)
		DHT19	Are results generalisable to settings where telecommunication infrastructure is poor, or there is low network connectivity?	1(1)	6(5)	3(3)	102(91)		
ECO	Validity of the model(s) (EUN)	**DHT20**	Are changes in fixed costs for scaling up the DHT known? Is the cost function per patient smooth or stepped?	3(3)	8(7)	1(1)	31(27)	69(62)	
	Resource utilisation (EUN)	**E0001/2/9**	Consider costs of supporting health care providers in using DHT and costs to use the DHT in the health system (licensing, platforms, hardware, etc.)	4(4)	8(7)	5(4)	26(23)	69(62)	
	Measurement & estimation of outcomes (EUN)	**E0005(1)**	Have DHT-specific outcomes been considered and measured where possible, e.g., self-management benefits, better-connected healthcare professionals?	19(17)	13(12)	9(8)	71(63)		
		E0005(2)	Given that all the functionalities of DHTs may not be used, and many people may not use the DHT from the outset, are the estimated benefits of the DHT realistic?	3(3)	5(4)	1(1)	103(92)		
ETH	Benefit-harm balance (EUN)	**F0003(1)**	How does the DHT affect the participant's safety and welfare? - Are alerts about a patient's health held securely? - Is real-time data securely transmitted?	2(2)	15(13)		95(85)		

HTA Domain	Topic (EUN)/(NEW)	Issue ID (modifier)	Issue content	N=112					
				n (%)					
				Good	Fair	Poor	Not covered	NR	NA
		F0003(2)	Can the DHT promote a false sense of security or harm patients by having access to their data without someone to interpret it?		13(12)	1(1)	98(87)		
	Autonomy (EUN)	**F0004(1)**	For DHTs targeting behaviour change, what controls limit the DHT influencing a person's behaviour for purposes other than those stated?				93(83)		19(17)
		F0004(2)	Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT?				112(100)		
		F0005	Does the DHT use simple and understandable language?	3(2)	12(11)	1(1)	96(86)		
		F0006(1)	Are any potential conflicts of interest (funding, promotion) clearly disclosed to DHT users?		1(1)		106(95)		5(4)
		F0006(2)	For DHT's providing health information, is there concise information for the user on how the DHT's contents were selected and who is responsible for the content?	4(4)	5(4)		66(59)		37(33)
		F0006(3)	Is the user informed of the data collected by the DHT, its use, and availability to users to extract for their own purposes?	1(1)	3(3)		108(96)		
	Benefit-harm balance (EUN)	**F0011(2)**	Is the value of patient data realised but protected from commercial use?				112(100)		
		F0011(3)	Does the DHT preserve and enhance direct contact between patients and healthcare professionals while supporting them to manage their health?	4(3)	10(9)	2(2)	96(86)		
	Respect for persons (EUN)	**F0101(1)**	Does the DHT clearly identify for the user who holds any personal data?		3(3)	2(2)	107(95)		
		F0101(2)	Is the DHT regularly audited for transmissions with third parties that include linkable identifiers?		1(1)		111(99)		
	Justice & Equity (EUN)	**H0012(1)**	How does the DHT overcome access barriers, e.g., patients with a lack of economic resources, poor IT skills, digital health literacy?	9(8)	13(12)	15(13)	75(67)		
		H0012(2)	Is the DHT compatible with common assistive technologies for hearing and visually impaired?	1(1)			111(99)		
		H0012(3)	Justification is given for the available languages given the target population, or there is recognition of the limitation	5(4)	2(2)	4(4)	49(44)		52(46)
ORG	Contextual issues (NEW)	**DHT21**	Discussion of contextual barriers and enablers to DHT uptake: Infrastructure, clinical endorsement, champions of DHT, supplementary payments, etc.	10(9)	15(13)	10(9)	77(69)		
	Health delivery process (EUN)	**G0004**	Are changes to electronic communication, information/reporting systems, face-to-face consultations, and staff communication considered?		14(13)	6(5)	92(82)		
		G0100	How does removing the constraints of distance, and sharing patient data, impact staff work methods and the interactions between medical staff, patients, and their carers	4(4)	12(11)	6(5)	90(80)		
SOC	Social group aspects (EUN)	**H0201(1)**	How much does the DHT improve the connectivity between the healthcare team and the patient?	11(10)	11(10)	6(5)	81(75)		
		H0201(2)	Evidence that access is improved for rural/remote patients?	6(5)	4(4)	2(2)	100(89)		
	Communication aspects (EUN)	**H0203**	Are expected direct and data usage costs made clear to the user to improve adherence rates?	5(4)	12(11)	1(1)	94(84)		

HTA Domain	Topic (EUN)/(NEW)	Issue ID (modifier)	Issue content	N=112					
				n (%)					
				Good	Fair	Poor	Not covered	NR	NA
LEG	Ownership & liability (EUN)	**DHT22**	Professional liability: Clarify responsible parties, litigation risks, and insurance implications of DHT recommendation or use		1(1)	4(4)	107(95)		

DHT, Digital Health Technology; HTA, Health Technology Assessment; NR, not reported; NA, not applicable

Table A 9: Health technology assessment (HTA) content that is common across DHTs and non-DHTs, but essential for DHT

HTA Domain	Topic	Issue ID (modifier)	Issue content	N=112 n(%)				
				Good	Fair	Poor	Not covered	NA
CUR	Current management of the condition	**A0018**	What DHT do those with the condition already have available to them?	24(21)	66(59)	6(6)	16(14)	
TEC	Features of the technology	**B0003(1)**	Is there evidence that the DHT is relevant to the health system and can perform to the expected number of users (e.g., is the server size adequate)?	18(16)	72(64)	2(2)	20(18)	
		B0003(2)	As DHTs often develop rapidly, is the DHT in a steady-state? i.e., No more development planned? (Yes = No more development planned; No = More development planned; Not covered = unable to tell)	Yes 47(42)	No 53(47)		Unable to tell 12(11)	
SAF	Risk management	**C0062**	Are there defined parameters to identify and respond to a patient's acute deterioration?	17(15)	32(29)	2(2)	61(54)	
EFF	Patient satisfaction	**D0017(4)**	Is there evidence to show that relevant patient stakeholders were involved in the design of the DHT?	12(11)	17(15)	4(4)	79(70)	
		D0017(5)	Has/will data be collected on user satisfaction that will be acted upon and available to decision-makers?		32(28)	2(2)	78(70)	
		D0017(6)	Has qualitative data been collected and analysed to evaluate the mode of action, differences between recipients and sites, and identify barriers to uptake or implementation?	4(4)	12(10)	4(4)	92(82)	
		D0017(7)	Does the DHT create additional burdens on the patient or caregiver that may affect uptake or adherence?	3(3)		2(2)	107(95)	
ETH	Benefit-harm balance	**F0003**	What will be done with any incidental findings?	2(2)			34(30)	76(68)
	Autonomy	**F0005**	Does the DHT provider identify the diversity of service users, or groups of users, at higher risk of harm and adapt the DHT accordingly? E.g., have systems to minimise the risk for children and young people to be harmed, identify those with suicide ideation in depression treatments, and have procedures for monitoring and responding to acute events.	3(3)	4(3)	2(2)	103(92)	
	Justice & Equity	**H0012**	Is there evidence of the DHT being used in hard-to-reach populations?	8(7)	7(6)	5(5)	92(82)	
ORG	Culture	**G0010**	Is there evidence that the DHT has credibility with health care professionals? i.e., Is there published or publicly available evidence documenting the relevant health care experts' role in the design, development, testing, or sign-off of the DHT?	8(7)	30(27)	4(3)	70(63)	
	Health delivery process	**G0100(1)**	Describe the steps in the proposed new care pathway or pathways incorporating the DHT intervention for the relevant population and setting	11(10)	64(57)	13(12)	24(21)	
		G0100(2)	Detail any infrastructure and service-level changes needed to existing pathways and associated systems to implement, operate, and maintain the new pathway	20(18)		4(3)	88(79)	

Chapter 4 supplementary materials

Table A 10: Mapping of DHT attributes to DHT issues

#	Attribute	Grouped issue questions	HTA Domain[a]	Issue ID[a] (Reference)
1	Low extra costs (data usage & personal technology) for users and carers	Do/will health patients/carers invest in the personal digital technologies (mobiles/tablets) and data usage fees required to use the DHT? Is it costly/difficult to support?	CUR	A0011/2 (2, 32)
2	Easy to access and use for everyone	Is the DHT limited in terms of platforms, languages, network connectivity, or users' digital literacy?	CUR	A0011/2 (2, 32)
		Is the DHT designed to minimise the barriers associated with hardware, software, data requirements, and platform services, or the language/location, age, culture, and ability of users?	SAF	DHT05 (21, 36, 57)
		Is there evidence DHT is usable and accessible for a diverse range of users, including those with disabilities or limited technical ability? Are there obvious design issues hindering usability, e.g., washable, durable, cause skin allergies?	EFF	D0017 (20, 41, 44, 49, 51, 54, 57, 59)
		How does the DHT overcome access barriers, e.g., patients/with a lack of economic resources, poor IT skills/digital health literacy? Is the DHT compatible with common assistive technologies, meet relevant web page or web application standards and available in a wide number of languages and platforms?	ETH	H0012 (21, 55, 63)
3	Lets the health service know how many patients are using it, so any improvements can be made	Is(will) data on DHT usage (be)collected and easily accessible ongoing to make future investment decisions?	CUR	A0011/2 (2, 32)
4	Good training and technical support to keep users safe	Is their training on digital skills, personal data handling, digital health literacy, and cyber-safety for all users along with 24-hour technical support?	TEC	B0013/4 (32, 48, 49, 63)
5	Always records the correct information about patients	How well do the DHT and comparator(s) perform in overcoming technical barriers such as interoperability and data extraction?	TEC	DHT01 (21, 41, 48, 55, 57)
		How well is interoperability designed and data quality managed: - Does the DHT have processes to support the creation and maintenance of accurate healthcare records that can be integrated with multiple information systems using the relevant patient/ provider identifiers and standard terminologies?	SAF	DHT03 (21, 41, 48, 55, 57)
6	Shows patient information clearly and explains it	How well do the DHT and comparator(s) perform in overcoming technical barriers such as data visualisation and feedback?	TEC	DHT01 (54)
7	The patient can download all their data in a useable format	Is there standardisation of access and extraction mechanisms, including the ability for users to extract raw data?	TEC	DHT01 (48, 54)
8	Low extra costs (equipment, IT, services) for the health service to support it	What investment/tools are required: - Have device dimensions, battery life and charging methods, calibration requirements, operational system compatibility, connectivity requirements (e.g., wired, Wi-Fi, Bluetooth), data access and storage, data security, technical and data support been considered?	TEC	B0007(20, 35, 41, 49, 54, 57, 63)
		Have costs of supporting health care providers in using DHT and costs to use the DHT in the health system (licensing, platforms, hardware, etc.) been considered, e.g.: - Training, help desks, and change management system - Platform, licensing, attachable hardware, and versions of DHT that would be used in the health system - The need for additional or recurrent purchases, shipping fees, or technical support subscription charges, as well as relevant supply information, such as availability in the target country and minimum order requirements	ECO	E0001/2/9 (20, 29, 54, 63),
		Given all the functionalities of DHTs may not be used, and many people may not use the DHT from the outset, are the estimated benefits of the DHT realistic?	ECO	E0005 (32)
		Are within-trial collected costs and outcomes externally valid? Are changes in fixed costs for scaling up the DHT known? Is the cost function per patient smooth or stepped?	ECO	DHT20 (20)

#	Attribute	Grouped issue questions	HTA Domain[a]	Issue ID[a] (Reference)
9	Ensures patient information is always kept private and safe from hacking	How well are data security and privacy managed? - Does it comply with GDPR principles of data minimisation/protection by default/design? - Does the DHT comply with data protection legislation/standards - Does it allow users to manage access to their data? - Has the DHT been regularly audited for actual data transmissions to third parties and is the user informed of this risk? - Does the DHT employ authentication, encryption, and threat analysis to avoid unauthorised access to personal data? - Is there safeguarding around peer-to-peer and other communications within DHT platforms?	SAF	DHT02 (2, 21, 31, 41, 48, 51, 55, 57)
		- Where are alerts about a patient's health reported? - Is real-time data securely transmitted? - How does the DHT affect the participant's safety and welfare? - Have there been any perceived or real privacy breaches, technical problems, unexpected/unintended incidents created by the DHT?	ETH	F0003 (35, 45)
		- Does the DHT clearly identify who holds any personal data? - Is the supplier's cookie policy stated and clear? Is only data necessary for a particular treatment is shared with the doctor and only after explicit consent, which the patient can revoke? - Can patients opt-out if they are not able or unwilling to manage their data? - Does the DHT provider have privacy policies that are easy to understand, uphold users' rights and choices, and are readily available to users before and while using the DHT, compliant with privacy laws, privacy principles, and best practices? - Are changes to privacy policies communicated to users in a timely way?	ETH	F0101 (21, 31, 41, 48)
10	There is enough information for users to know how it works and what could go wrong	How transparent are the DHT risks (e.g., data sharing, conflicts of interest) to the user? - Does the DHT provide users with accurate information on how their data is collected, used, protected, and shared? - Is there clear identification of the DHT's owners, contact information, funding sources, promotion and sponsorship, and any other possible conflicts of interest?	SAF	DHT04 (21, 35, 36, 41, 48, 55, 57, 63)
		Is adequate information disclosed on DHT algorithms to evaluate their risk? - Has data quality been validated prior to building and employing algorithms? - Are data quality checks built programmatically into artificial intelligence algorithms to avoid harm? - Does the developer/manufacturer clearly state the limitations of the data used, algorithms deployed, especially any learning algorithms, and how outcomes are validated to users? - For learning algorithms, is there adequate disclosure of the characteristics of the training, test, and validation data, the model, and the algorithms to understand how the algorithm controls the clinical decision-making process?	SAF	DHT06 (23,55,56,57)
		Are expected direct and data usage costs made clear to the user to improve adherence rates?	SOC	H0203 (21, 32-34)

#	Attribute	Grouped issue questions	HTA Domain[a]	Issue ID[a] (Reference)
11	It is highly reliable and stable	How technically reliable and stable are the DHT and comparator(s): - Is there evidence of accurate and reliable transmission of unbiased data? - Does the DHT alert the user when working suboptimally or experiencing interference, e.g., low or no network connectivity? - Does it perform well outside the laboratory, and is it validated for use on multiple platforms? - Is it resilient to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions?	SAF	DHT08 (2, 20, 21, 38, 41, 51, 56, 57, 60, 63)
		How well are updates/continuity of the DHT managed: - Is there evidence that operating system updates and patches, service continuity, backup, and recovery mechanisms are well managed?	SAF	DHT08 (21, 63)
12	Helps health professionals respond quickly when changes in patient care are needed	- Does the DHT allow the user to communicate to the provider critical information about changes in their condition or information on risks of the DHT? - Is there a contact mechanism for technical support with a fixed response time? - Are there processes within the DHT to: o Correctly identify users? o Communicate changes to or transfer of a patient's care?	SAF	DHT09/10/11 (21, 36)
13	Has additional benefits – patients more confident in their managing condition, less travel and waiting, more connected health team	Have DHT specific outcomes been considered and measured where possible, e.g., improved access to health information and services, reduced waiting time, less burdensome travels, a feeling of security, transfer of skills, better-managed care through self-management and digitally connected healthcare professionals?	ECO	E0005 (20,29,48)
14	The health advice it provides is always up-to-date and correct	Is there evidence that the health information provided by the DHT is accurate, valid, up to date, sufficiently comprehensive, clear, tailored to the users' diversity, and that there are quality assurance processes in place?	EFF	DHT16 (2, 20, 21, 35, 36, 41, 51, 60, 63)
15	When trying to change patient habits, it uses best practice and respected methods	Are appropriate and best practice behaviour change techniques used in the technology? Is the targeted behaviour change apparent to the user, is the mechanism is credible, are the appropriate supports in place, and is it relevant for the target population?	EFF	DHT17 (2, 35, 39, 41, 43, 44, 47, 51)
16	Patients and caregivers helped design it and were happy with it	Were patients satisfied with the technology? - Is there evidence to show relevant stakeholders were involved in the design and satisfied with the DHT? - Is there ongoing data collected on user satisfaction that will be acted upon and available to decision-makers? - Has qualitative data been collected and analysed to evaluate the mode of action, differences between recipients and sites and identify barriers to uptake or implementation? - Does the DHT create additional burdens on the patient or caregiver, which may affect uptake or adherence?	EFF	D0017 (2, 20, 21, 35, 36, 41, 43, 44, 51,57, 59, 62)
17	Can be used anywhere	Can the results be transferred to other patient groups/settings/regions? - Will it work in regions where telecommunication infrastructure is poor, or there is low network connectivity?	EFF	DHT19 (20,35,59)
		Is there evidence of the DHT being used in hard-to-reach populations?	ETH	H0012 (2)
		- How much does the DHT improve the connectivity between the healthcare team and the patient? - Is access improved for remote patients?	SOC	H0201 (49)

#	Attribute	Grouped issue questions	HTA Domain[a]	Issue ID[a] (Reference)
18	Does not limit the user in their treatment options	Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT? Does the DHT use clear and simple language, providing: - Concise information how health information was chosen and who is responsible for content? - Controls to prevent behaviour change for purposes other than those stated, e.g., commercial purposes? - Information on potential conflicts of interest (funding, promotion) Is the DHT designed and used for clearly defined purposes that uphold the health system's social values or society's values?	ETH	F0004 (30) F0005 (41) F0011 (52)
19	Prevents patients misinterpreting test results or having a false sense of security	Could patients have a false sense of security if their DHT is collecting real-time data and not being contacted by physicians? Are there harms from the patient having access to the data without someone's assistance to help them interpret what it means? What will be done with any incidental findings?	ETH	F0003(45)
20	The new care pathway is mapped out, staff can adapt to it easily, and they have the resources they need	Have the steps in the proposed new care pathway or pathways incorporating the DHT intervention for the relevant population and setting been detailed? Have infrastructure and service-level changes to existing pathways and associated systems to implement, operate and maintain the new pathway been identified? What changes are required to staff work methods, staff communication and interactions, electronic communications, and information/reporting systems? How prepared is the health service to make these changes? How does removing the constraints of distance and sharing patient data impact staff work methods and the interactions between medical staff, patients, and their carers? Have all contextual barriers and enablers to DHT uptake: Infrastructure, clinical endorsement, champions of DHT, supplementary payments, etc been considered?	ORG	G0004 (20) G0100 (2, 23, 62) DHT21 (32-34)
21	Relevant health professionals have been involved in the design and they support its use	Does the DHT have credibility with health care professionals? Is there published or publicly available evidence documenting the relevant health care experts' role in the design, development, testing, or sign-off of the DHT? Enablers: Are there are champions of DHT within the health service?	ORG	G0010 (2, 21, 60) DHT21 (32-34)
22	It is clear who is legally responsible for what and who owns the data	Are parties responsible for medical advice, responsible for monitoring and reviewing patient data, and that own the data related to the DHT, clearly defined? Are litigation risks to the healthcare practitioners, and how insurance(s) (i.e., professional indemnity, life, health, income) and professional registrations could be affected through use or recommendation of the DHT, clearly defined?	LEG	DHT22 (63)
23	With patient consent, their data can be easily linked to existing medical records for clinician review	Does the DHT have processes to support the creation and maintenance of accurate healthcare records that can be integrated with multiple information systems using the relevant patient/ provider identifiers and standard terminologies?	TEC	DHT01 (21, 41, 48, 55, 57)
		How well is interoperability designed?	SAF	DHT03 (21, 41, 48, 55, 57)

#	Attribute	Grouped issue questions	HTA Domain[a]	Issue ID[a] (Reference)
24	At is at least as effective as usual (face to face) care	Has effectiveness been demonstrated: - Are accepted methods used to overcome common methodological problems in RCTs for DHTs, e.g., achieving blinding, biases from informed consent? - Is it clear whether the DHT was changed (bug fixes, content) during the trial? - Was digital literacy an implicit eligibility criterion? - Was the comparator group restricted in the DHT to which they had access? - Have DHT-specific and validated outcome measures been collected: i.e., the intensity of use (dose, exposure), online adherence, engagement? - Has data collection embedded in the DHT created systematic bias? - Is reporting of the RCT in accordance with CONSORT E-HEALTH?	EFF	DHT12 (22, 23, 35, 39) DHT13 (44, 47) DHT14 (2, 35, 50, 53)
		Are the results external valid/generalisable: - Have the actions taken to enhance the trial's internal validity, such as participant identity validation and obtaining offline contact details to promote good follow-up rates, skewed participant populations, and jeopardised external validity? - Are the results generalisable to the general internet population, to the general patient population, or other organisations?	EFF	DHT18 (44, 47) DHT19 (20, 59)

[a]From EUnetHTA's HTA Core Model version 3.0 or DHT specific issue identifier (1)
See Section 4.8 for references

Table A 11: Relative preferences of attributes and class allocation model for three latent class model

Relative preferences		Latent Class 1				Latent Class 2				Latent Class 3			
HTA Domain*	**Attributes**	***β***	**(95% CI)**	**Preference Score**	***p***	***β***	**(95% CI)**	**Preference Score**	***p***	***β***	**(95% CI)**	**Preference Score**	***p***
SAF	Helps health professionals respond quickly when changes in patient care are needed	0.41	(0.12, 0.69)	19.2	0.006	2.49	(2.03, 2.96)	77.4	<0.001	3.31	(2.61, 4.01)	100.0	<0.001
TEC/SAF	Always records the correct information about patients	0.70	0.42, 0.99)	27.5	<0.001	2.12	(1.76, 2.48)	67.0	<0.001	2.81	(2.32, 3.31)	86.3	<0.001
EFF	The health advice it provides is always up-to-date and correct	0.24	(-0.03, 0.52)	14.7	0.086	1.91	(1.56, 2.26)	61.1	<0.001	2.69	(2.24, 3.15)	82.9	<0.001
SAF	It is highly reliable and stable	0.72	(0.41, 1.02)	27.8	<0.001	1.87	(1.55, 2.20)	60.1	<0.001	2.61	(2.22, 3.01)	80.7	<0.001
EFF	It is at least as effective as usual (face-to-face) care	-0.27	(-0.52, -0.03)	0.3	0.030	0.47	(-0.06, 0.99)	20.9	0.085	2.14	(1.40, 2.88)	67.5	<0.001
EFF/ECO	Has additional benefits - patients more confident in their managing condition, less travel and waiting, more connected health team	0.49	(0.21, 0.76)	21.4	<0.001	1.41	(0.87, 1.96)	47.2	<0.001	2.12	(1.38, 2.86)	67.0	<0.001
ETH	Does not limit the user in their treatment options	-0.13	(-0.39, 0.13)	4.3	0.333	0.68	(0.32, 1.03)	26.7	<0.001	1.80	(1.28, 2.31)	58.0	<0.001
ETH	Prevents patients misinterpreting test results or having a false sense of security	0.01	(-0.26, 0.28)	8.1	0.957	1.35	(1.02, 1.68)	45.6	<0.001	1.78	(1.37, 2.19)	57.6	<0.001
TEC	Good training and technical support to keep users safe	0.46	(0.21, 0.71)	20.7	<0.001	1.26	(0.94, 1.58)	43.0	<0.001	1.59	(1.20, 1.99)	52.3	<0.001
TEC/SAF	With patient consent, their data can be easily linked to existing medical records for clinician review	-0.11	(-0.36, 0.13)	4.8	0.371	1.61	(1.13, 2.09)	52.7	<0.001	1.59	(1.05, 2.13)	52.3	<0.001
TEC	Shows patient information clearly and explains it	0.54	(0.30, 0.79)	23.1	<0.001	1.36	(0.97, 1.74)	45.7	<0.001	1.55	(1.11, 1.99)	51.2	<0.001
SAF	Ensures patient information is always kept private and safe from hacking	0.55	(0.24, 0.86)	23.3	<0.001	2.94	(2.44, 3.44)	89.7	<0.001	1.45	(0.97, 1.94)	48.3	<0.001
CUR/SAF/ EFF/ETH	Easy to access and use for everyone	0.68	(0.43, 0.94)	26.9	<0.001	0.87	(0.46, 1.28)	32.2	<0.001	1.29	(0.79, 1.78)	43.8	<0.001
ORG	The new care pathway is mapped out, staff can adapt to it easily, and they have the resources they need	-0.02	(-0.27, 0.22)	7.2	0.845	0.97	(0.58, 1.37)	35.0	<0.001	1.14	(0.62, 1.66)	39.6	<0.001
SAF	There is enough information for users to know how it works and what could go wrong	0.29	(0.05, 0.53)	16.0	0.018	0.59	(0.26, 0.92)	24.3	<0.001	1.05	(0.60, 1.49)	37.0	<0.001

Relative preferences		Latent Class 1				Latent Class 2				Latent Class 3			
HTA Domain*	**Attributes**	***β***	**(95% CI)**	**Preference Score**	***p***	***β***	**(95% CI)**	**Preference Score**	***p***	***β***	**(95% CI)**	**Preference Score**	***p***
ORG	Relevant health professionals have been involved in the design and they support its use	0.08	(-0.15, 0.30)	10.1	0.494	0.83	(0.53, 1.13)	31.1	<0.001	0.81	(0.46, 1.16)	30.6	<0.001
EFF	When trying to change patient habits, it uses best practice and respected methods	-0.05	(-0.28, 0.18)	6.5	0.665	0.75	(0.41, 1.09)	28.8	<0.001	0.81	(0.39, 1.23)	30.4	<0.001
EFF/ETH/ SOC	Can be used anywhere	0.07	(-0.19, 0.32)	9.7	0.610	0.10	(-0.29, 0.48)	10.6	0.615	0.62	(0.15, 1.09)	25.2	0.009
CUR	Low extra costs (data usage & personal technology) for users and carers	0.83	(0.55, 1.11)	31.1	<0.001	0.17	(-0.18, 0.53)	12.7	0.333	0.58	(0.12, 1.04)	24.0	0.013
TEC/ECO	Low extra costs (equipment, IT, services) for the health service to support it	0.48	(0.23, 0.73)	21.2	<0.001	-0.17	(-0.52, 0.18)	3.2	0.345	0.54	(0.03, 1.04)	22.9	0.036
TEC	The patient can download all their data in a useable format	0.01	(-0.23, 0.26)	8.3	0.911	0.54	(0.18, 0.89)	22.9	0.003	0.37	(-0.06, 0.80)	18.2	0.090
CUR	Lets the health service know how many patients are using it, so any improvements can be made	0.31	(0.07, 0.56)	16.6	0.012	-0.09	(-0.48, 0.30)	5.4	0.647	0.24	(-0.21, 0.69)	14.6	0.291
LEG	It is clear who is legally responsible for what and who owns the data	-0.28	(-0.52, -0.04)	0.0	0.020	0.85	(0.44, 1.26)	31.5	<0.001	-0.26	(-0.76, 0.25)	0.7	0.317
EFF	Patients and caregivers helped design it and were happy with it	Reference				Reference				Reference			

Class allocation model	Latent Class 1			Latent Class 2			Latent Class 3		
Variable	**OR**	**(95% CI)**	***p***	**OR**	**(95% CI)**	***p***	**OR**	**(95% CI)**	***p***
Respondent type									
Patient or carer (reference Community member)	1.32	(0.86, 2.05)	0.208	0.63	(0.41, 0.98)	0.041	Reference class		
Health professional (reference Community member)	0.80	(0.33, 1.94)	0.624	1.58	(0.56, 4.49)	0.392			
Gender									
Female (reference Male)	0.53	(0.33, 0.85)	0.008	1.47	(0.88, 2.45)	0.141	Reference class		
Age group									
40 to 69 yrs (reference 18 to 39 yrs)	0.44	(0.25, 0.75)	0.003	1.27	(0.67, 2.39)	0.467			
70yrs and over (reference 18 to 39 yrs)	0.16	(0.05, 0.46)	<0.001	1.07	(0.45, 2.55)	0.878			

Class allocation model	Latent Class 1			Latent Class 2			Latent Class 3		
Variable	**OR**	**(95% CI)**	***p***	**OR**	**(95% CI)**	***p***	**OR**	**(95% CI)**	***p***
Country of residence									
Canada (reference Australia)	0.98	(0.53, 1.81)	0.943	1.75	(0.89, 3.43)	0.104		Reference class	
NZ (reference Australia)	0.52	(0.27, 1.00)	0.051	1.07	(0.62, 1.85)	0.803			
UK and other countries (reference Australia)	0.89	(0.51, 1.57)	0.694	1.23	(0.68, 2.22)	0.493			
Speak a second language at home									
No (reference Yes)	0.55	(0.31, 1.00)	0.051	0.75	(0.38, 1.48)	0.411		Reference class	
Employment status									
Part-time/Casual/Student (reference fulltime)	0.49	(0.26, 0.93)	0.030	0.78	(0.41, 1.46)	0.431		Reference class	
Not employed/unable to work (reference fulltime)	0.81	(0.41, 1.60)	0.542	0.85	(0.38, 1.88)	0.686			
Retired (reference fulltime)	0.33	(0.15, 0.74)	0.007	0.82	(0.42, 1.61)	0.563			
How often do you need someone to help you when using your computer, mobile phone, tablet, or smart watch?									
Sometimes/Often/Always (reference None/Rarely)	5.30	(2.98, 9.42)	<0.001	1.48	(0.80, 2.73)	0.213		Reference class	
Average class probability		*0.30*			*0.38*			*0.32*	

Model Fit: AIC = 48254.47 (lowest out of all models with covariates added to class membership model), Respondents: n = 1,251, Pseudo r2 = 0.094, Proportion of participants classified in each latent class with a posterior probability above 75%: Class 1: 80%, Class 2: 66%, Class 3: 67%. Means of the posterior probabilities of belonging to the latent class among the subjects classified a posteriori in each latent class: Class 1: 88%, Class 2: 81%, Class 3: 81%. β = Regression model coefficient estimates

*HTA Domain = Health Technology Assessment (HTA) Domains of the EUNetHTA HTA Core Model version 3.0(31):

CUR: Describes the new technology's target population, target condition and current management, current and expected utilisation, and regulatory status

TEC: Describes the new technology's features in enough detail to differentiate it from comparators, and the investments, tools, and training required to use it

SAF: Identifies unwanted or harmful effects of the new technology important to patients or the decisions of health care providers and policymakers

EFF: Provides evidence of comparative effectiveness of the new technology in producing health benefits in the relevant health care setting

ECO: Provides information on the new technology's costs, health-related outcomes, and economic efficiency to inform value for money judgments

ETH: Considers potential harms to autonomy, respect for persons, justice, and equity from the use of the new technology or from performing the HTA

ORG: Identifies resources to mobilise or organise to implement the new technology and the consequences (Intra/inter-organisational and health system)

SOC: Considers issues related to the new technology relevant to patients, carers, and social groups

LEG: Identifies rules and regulations protecting patient's rights and societal interests for consideration when evaluating the new technology

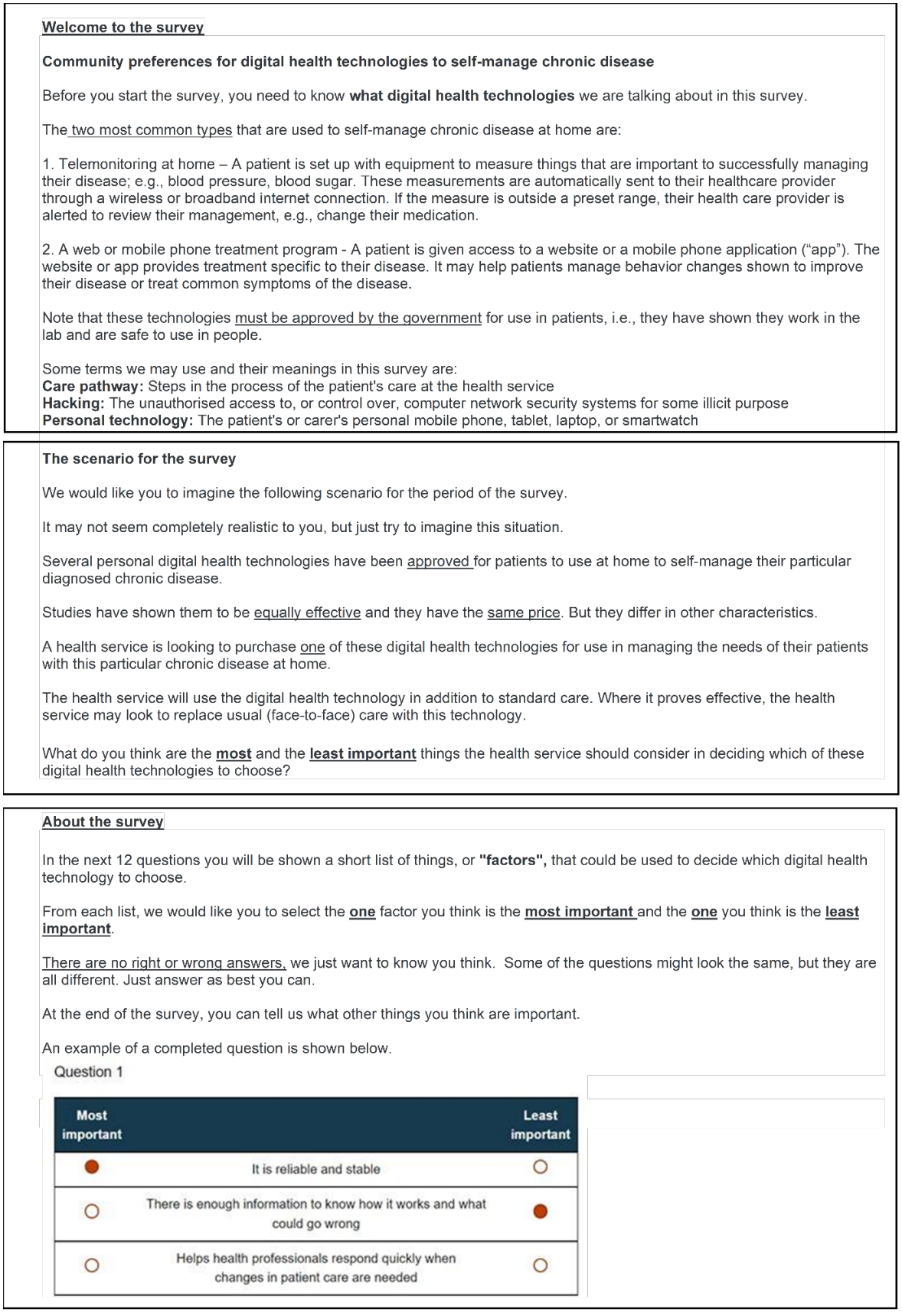

Figure A 4: Survey preamble with an example of a best-worst choice set

Figure A 5: Relative preferences for DHT attributes from the sequential best-worst latent class multinomial model

Chapter 5 supplementary materials

Table A 12: Suggested wording for chronic disease management digital health technology (DHT)-specific content to extend the HTA domain introductions of the Core Model[a]

Chronic disease management digital health technology (DHT)-specific content by HTA domain
Domain 1: Health problem and current use of technology (CUR)
Digital health technologies (DHTs) are often part of inventions that include human and other technology components (18); therefore, it is critical to specify the new health pathway and the existing care pathway that is the relevant comparator (8). Whether the DHT is complementary to, or a replacement of, usual care (5) should also be specified. Justification for the comparator, whether it be face-to-face care or another DHT should be given. Functions and risk profiles between DHTs differ widely. Refer to functional classifications for DHTs published by HTA agencies to assist in describing the function and risk profile of the DHT (7, 8).
Domain 2: Description and technical characteristics of technology (TEC)
Identifying the phase of development of the DHT is especially important. As DHTs can evolve rapidly, it may not yet have reached a state that is stable enough for the evidence of clinical effectiveness to be suitable for HTA (3). DHTs often involve storage and transfer of patient information. Training of personnel/caregivers to ensure patient and their own data is secure can minimise the risk of privacy breaches and cyber-attacks. Training of patients/family on technical skills, digital health literacy, and cyber safety skills, particularly with DHTs that may be used at home without clinician supervision, is critical to ensuring patient safety (4, 14, 19, 20). How well the DHT and comparators (when relevant) show patient information and explain it, e.g., visualisation and feedback (24), and integrate with existing health databases (interoperability) (19, 23, 25-27) is critical to describe.
Domain 3: Safety (SAF)
As face-to-face care can usually be used for the condition rather than the DHT, assessment of safety issues is necessary (51). Indirect harms specific to DHTs are: **Operator dependent:** Insufficient training of users can lead to serious harms such as death from incorrect use (4, 14, 19, 20) **Technology dependent:** • DHTs may not be technically reliable and stable outside of the laboratory, leading to incorrect diagnoses, treatment advice, or inadequate monitoring (3, 4, 8, 9, 23, 26, 27, 31, 36, 37) • Inadequate data quality management can lead to the DHT using incorrect information about a patient, misidentifying patients, or populating incorrect information in a patient's electronic medical record (19, 23, 25-27, 33) • Required health information may not be clearly displayed for the clinician to use (19, 23-27) • The health advice provided by the DHT may not be kept up to date and accurate (3, 4, 8, 9, 18, 23, 27, 31, 33) • Risk management procedures that ensure timely communication between the patient and health professionals to keep patients safe may not be adequate (23, 33) **Setting dependent:** DHTs may not work in low connectivity environments, or where digital infrastructure is poor, without alerting the user to potential error (3, 4, 8, 9, 23, 26, 27, 31, 36, 37) **Patient dependent:** • DHTs that monitor a patient may lead to a patient having a false sense of security that they are being continuously monitored and thus may be less alert to signs of deterioration in their health (18, 42) • Patients may misinterpret results or advice of the DHT in the absence of supervision by a clinician (18, 42) • Privacy and cyber-security breaches may threaten the welfare of vulnerable patients (27, 44) • Vulnerable patients may be more susceptible to DHTs that try to change behaviour for commercial purposes or that provide limited treatment options (27, 44) • Patients with less technical ability, low digital health literacy, or with limited economic resources may not be able to access and use the technology effectively (23, 26, 33)

Chronic disease management digital health technology (DHT)-specific content by HTA domain
Domain 4: Clinical Effectiveness (EFF)
Because DHTs can vary widely in their function and implementation, the importance of using reporting guidelines such as those recommended by the equator network https://www.equator-network.org/ (e.g., CONSORT E-HEALTH (15), TIDieR-telehealth (36)) is essential to ensuring complete, consistent, and transparent reporting of the intervention in DHT effectiveness trials. Evidence of patient satisfaction and effectiveness is highly correlated with DHTs being accessible to a diverse range of patients (3, 17, 20, 24, 26, 27, 31, 38). Patient satisfaction is especially important for DHTs where effectiveness relies on patients self-managing their condition and/or make behaviour changes. If DHTs provide health advice, there must be a quality assurance process to ensure this health advice is correct and kept up to date (3, 4, 8, 9, 18, 23, 27, 31, 33).
Domain 5: Costs and economic evaluation (ECO)
Resource use Consider DHT-specific resource use, e.g., device dimensions for physical storage costs, battery life and charging methods, calibration requirements, operational system compatibility, connectivity requirements (e.g., wired, Wi-Fi, Bluetooth), data access and storage, data security, technical and data support (3, 4, 18, 20, 24, 26, 27). Costs of supporting health care providers in using the DHT and costs to implement the DHT in the health system (licensing, platforms, hardware, helpdesk, compliance with security standards etc.) should also be considered (3, 4, 24, 39). Hardware and software costs may increase dramatically at a certain number of concurrent users, uploads or downloads frequency, or for processing speed/priority requirements (3). **Outcomes** DHTs have specific outcomes that should be considered in the assessment where possible, e.g., improved access to health information and services, reduced waiting time, less burdensome travels, a feeling of security, transfer of skills, better-managed care through self-management and digitally connected healthcare professionals (3, 19, 39).
Domain 6: Ethical analysis (ETH)
Ethical considerations are critically important to consider when assessing DHTs as: • They collect and store private information about patients that may be subject to cyber-attack (19, 23, 27, 30) • The information collected and communicated may endanger the welfare of patients if not kept securely (18, 42) • Being used by the patient without clinician supervision may lead to patient harm: misunderstanding results and advice, being influenced to change behaviour for reasons unrelated to health, being limited in treated options (27, 44) • DHTs that monitor the patient may cause the patient to have a false sense of security and be less alert to act on changes in their condition (18, 42)
Domain 7: Organisational aspects (ORG)
Moving from a face-to-face operating environment to a remote one is complex. The steps in the new health pathway and how they differ from the existing health pathway should be mapped out and clearly communicated throughout health care provider personnel. An assessment of required changes in infrastructure, service-levels, staff work methods, communications, and information/reporting systems is critical so staff can adapt to the new health pathway and be adequately resourced (3, 8, 14, 52-55). There are many contextual barriers and enablers to DHT uptake that need to be considered, e.g., appropriate infrastructure, clinical endorsement, champions of the DHT, and adequate reimbursement to health service provider. The DHT must have credibility with healthcare professionals and having champions within the health service is an important predictor of successful implementation (8, 9, 14, 23, 53, 55).

Chronic disease management digital health technology (DHT)-specific content by HTA domain
Domain 8: Patient and social aspects (SOC)
DHTs have the potential to improve access to health care for those in rural and remote communities, and patients with limited transport or mobility issues. However, DHTs also have the potential to limit access to health care if the costs of acquiring the personal technology to use the DHT or data usage fees are too high, the technology does not work in areas of poor connectivity or limited technical infrastructure, or the technology requires a high level of technical ability or digital health literacy skills.
Domain 9: Legal aspects (LEG)
DHTs will almost always have the possibility of producing additional information that is not directly related to the current care of the patient and may violate their right to respect for privacy. Evidence of compliance with relevant laws/binding rules for securing patient data should be provided. Issues of professional liability and ownership of data are often not addressed in the assessment process but are important for understanding the risks of the DHT to users. Parties responsible for medical advice, for monitoring and reviewing patient data, and that own the data related to the DHT, should be clearly defined. In addition, litigation risks to healthcare practitioners, and how insurance(s) (i.e., professional indemnity, life, health, income) and professional registrations could be affected through use or recommendation of the DHT, should be clearly defined (4).

[a]From EUnetHTA's HTA Core Model version 3.0 (6)
See Section 5.7 for references

Chapter 6 supplementary materials

Details of the costs considered in scenarios

Scenario 1: Technology costs comprised commercial versions of the database and web server software estimated using current market fees. Staff costs consisted of ongoing maintenance of the software to comply with security controls, clinician time to review and update clinical content, and a one-off implementation cost for software development to comply with state-wide standards and cybersecurity controls. Estimates of the one-off software development cost were based on the software developers' previous experience with the cost of programming and correspondence time with the state eHealth agency on similar work over the trial and were annualized using an estimated useful life of ten years. Hours for ongoing software maintenance and clinical review costs were estimated via project team interview, and applicable staff rates were applied.

Scenario 2: In addition to implementation costs, allowance was made to provide a tablet and data package for a six-month period at AUD40 per month and an enuresis alarm (average retail price AUD150) for the lowest socio-economic quintile (10%) of participants. The intervention software would also be upgraded to provide access for participants speaking one of the top ten most common non-English languages in NSW (10% of original development costs, amortized over a useful life of 10 years).

Figure A 6: Details of the costs considered in scenarios

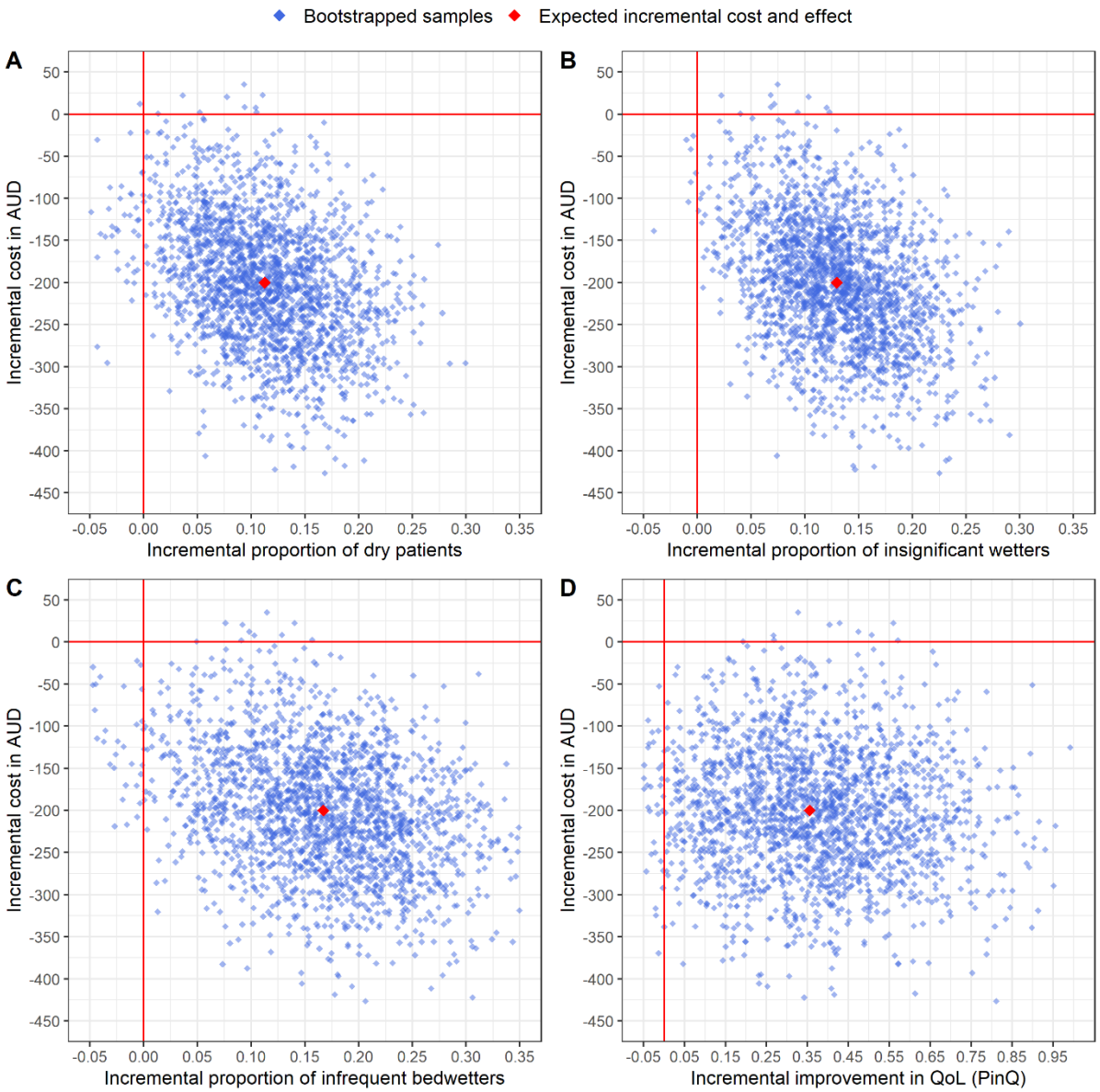

Figure A 7: Multiple imputation of missing data: Incremental cost-effectiveness planes for improvement in proportion (A) dry patients, (B) patients with insignificant* daytime urinary incontinence and enuresis, and (C) patients with infrequent* enuresis. Incremental cost-effectiveness planes for improvement in mean (D) Quality of Life (QoL) as measured by the Paediatric Incontinence Questionnaire (PinQ)

*Terms defined by the International Children's Continence Society (ICCS).

Chapter 7 supplementary materials

Table A 13: Testing of extended checklist on eADVICE

Item No	Issue ID[a c]: Issue	Clarification* for Digital Health Technologies	Able to be assessed? (Y/N/P)	Reported or will be reported in literature? (Y/N/P)	How assessed? Or Reasons not able to be assessed?
Domain 1: Health problem and current use of technology (CUR)[a]					
Topic: Utilisation (EUN)					
1	A0011: How much are the technologies utilised?	***Is it available to everyone?*** When estimating future utilisation rates for the technology, consider what may limit or improve usage over comparators in terms of DHT-specific design aspects.	Y	P	Confirmed no problems reported with the website when using different types of computers or operating systems. A mobile app version was not available
		Requirements for platforms and operating systems	*Y*	*N*	Confirmed no problems reported with the website when using different types of computers or operating systems A mobile app version was not available
		Requirements for network connectivity	*Y*	*Y*	Some families were unable to access Dr Evie because of the need for a reliable and fast connection. Families could access the program online or download it, so limited network access required
		Requirements for technical skills	*Y*	*Y*	eADVICE was developed and pilot tested with parents, children, clinicians, and information technology specialists, using evidence-informed guidelines and user centred design principles (11, 12) Website Usability and Usage: data were captured via a survey including questions on satisfaction, ease of use, structure, content (and appropriateness for parent or child); suggestions to improve the current design; frequency and timing of program access and whether the program was used by the parent, the child or both.
		Requirements for cost of personal digital technologies and data usage	*Y*	*Y*	Cost effectiveness scenario analysis: Personal digital technologies and data usage fees were subsidised for those in the lowest socioeconomic quintile
		Requirements for available languages	*Y*	*Y*	Cost effectiveness scenarios analysis: Program was translated into the ten most commonly spoken languages in NSW
2	A0012: What kind of variations in use are there across countries/regions/ settings?	***Is it available to everyone?*** Is the technology being used in settings where telecommunication infrastructure is poor or there is low network connectivity?	N	N	Not able to be assessed because the issue was not incorporated into testing plans. The trial was conducted with patients in metropolitan areas.

Item No	Issue ID[a c]: Issue	Clarification* for Digital Health Technologies	Able to be assessed? (Y/N/P)	Reported or will be reported in literature? (Y/N/P)	How assessed? Or Reasons not able to be assessed?
Domain 2: Description and technical characteristics of technology (TEC)[a?]					
Topic: Training & information needed to use the technology (EUN)					
3	B0013: What kinds of skills and training characteristics and information are needed for the personnel/caregivers using this technology?	***Is there training and technical support to keep personnel/caregivers safe?*** Do personnel/caregivers need training for digital skills, personal data handling, and cyber-safety along with 24-hour technical support to ensure efficacy and safety of the technology. Describe what training and support is provided and estimate whether it meets identified requirements.	P	N	***How assessed?*** • Identified the training and technical support provided to personnel/caregivers and incorporated this into the cost of intervention. • Confirmed no privacy breaches or cybersecurity attacks for general practitioners ***Reasons not able to be assessed?*** • There was no study undertaken of what general practitioners would need for digital skills, personal data handling, and cyber-safety along with 24-hour technical support • No adverse events reporting was planned in protocol for privacy breaches or cybersecurity attacks to test if training was adequate
4	B0014: What kind of training resources and information should be provided to the patient who uses the technology, or for his family?	***Is there training and technical support to keep patient and family safe?*** Do patients and their family need training for digital skills, digital health literacy, and cyber-safety along with 24-hour technical support to ensure efficacy and safety of the technology? Describe what training and support is provided and estimate whether it meets identified requirements.	P	N	***How assessed?*** • Identified the training and technical support provided to patients and family and incorporated this into the cost of intervention. • Confirmed no privacy breaches or cybersecurity attacks for patients and family ***Reasons not able to be assessed?*** • There was no study undertaken of what the patients and family would need for digital skills, personal data handling, and cyber-safety along with 24-hour technical support • No adverse events reporting was planned in protocol for privacy breaches or cybersecurity attacks to test if training was adequate
Topic: Features of Technology (EUN)					
5	DHT01: How well is the technology designed to overcome technical barriers in relation to comparator(s); e.g., interoperability, data visualisation and feedback	**How well is the technology designed to overcome technical barriers?**	P	P	Refer below
		With patient consent, can their data be easily linked to existing medical records for clinician review? Provide information on the technology's level of interoperability in relation to comparators, i.e., can the DHT be easily integrated with multiple information systems using the relevant patient/provider identifiers and standard terminologies, and does it use standardised access and extraction mechanisms?	*N*	*N*	• In terms of interoperability, the linkage with electronic Medical Records (eMR) records was discussed but not progressed in development or during the RCT. • Interoperability with the eMR is an objective for implementation in the NSW Health system

Item No	Issue ID[a c]: Issue	Clarification* for Digital Health Technologies	Able to be assessed? (Y/N/P)	Reported or will be reported in literature? (Y/N/P)	How assessed? Or Reasons not able to be assessed?
		Does the technology show patient information clearly and explain it well to <u>users</u>? Provide information on the technology's presentation of patient information. Is it easy to access and understand? Comment on DHT-specific features such as data visualisations and feedback mechanisms and how they may affect the efficacy and safety of the technology.			
		<u>Users: Personnel/Caregivers</u>	*N*	*Y*	• General practitioners were surveyed for useability, but not enough responded to the survey to be reported
		<u>Users: Patient /family</u>	*Y*	*Y*	• Website usability and usage data were captured via a survey including questions on satisfaction, ease of use, structure, content (and appropriateness for parent or child); suggestions to improve the current design; frequency and timing of program access and whether the program was used by the parent, the child or both • Extent of therapeutic alliance was captured using the 12-item version of the Working Alliance Inventory (WAI) (13) to determine whether the degree of therapeutic alliance between the child and eADVICE
Domain 3: Safety (SAF)[a]					
Topic: Quality & safeguarding (*NEW*)					
6	DHT02: How well does the technology manage data security and privacy?	***Is patient information always kept private and safe from hacking****?* Does it comply with General Data Protection Regulation (GDPR) principles of data minimisation/protection by default/design, and data protection legislation/binding rules? Does it allow users to manage access to their data? Does it employ authentication, encryption, and threat analysis to avoid unauthorised access to personal data? Is there safeguarding around peer-to-peer and other communications within the DHT?	Y	N	• eADVICE was subject to a NSW Health Privacy & Security Assurance Framework (PSAF) assessment to ensure security, privacy and legislative controls comply with NSW and Federal Government security requirements and legislation • Only provisional approval was gained under the PSAF for eADVICE during the RCT because not all requirements could be met • Developers of eADVICE are now conducting research on the most appropriate privacy, cybersecurity and cybersafety controls for the program, providing justifications, for discussion with NSW Health (eHealth NSW)

Item No	Issue ID[a c]: Issue	Clarification[*] for Digital Health Technologies	Able to be assessed? (Y/N/P)	Reported or will be reported in literature? (Y/N/P)	How assessed? Or Reasons not able to be assessed?
7	DHT03: How well does the technology manage data quality?	***Does the technology always record the correct information about a patient?*** Identify whether the DHT has processes to support the creation and maintenance of accurate healthcare records. Can it identify users correctly without human intervention? Is there evidence that uploading or downloading of patient information is correct on a consistent basis?	P	P	***How assessed?*** • eADVICE participants were given a unique identifier as a username and could set their own passwords, so that they could be identified uniquely when the entering the website ***Reasons not able to be assessed?*** • No testing of accurate capture and reporting of website collected data was undertaken as part of pilots or RCT • As interoperability with eMR function had not yet been developed, the quality of processes to map data accurately to health records could not be assessed
8	DHT05: Is the technology designed for accessibility and usability for safety?	***Is it designed to be easy to access and use for everyone?*** Is the DHT designed to minimise the barriers associated with hardware, software, data requirements, and platform services, or the language/location, age, culture, and ability of users?	P	P	***How assessed?*** • See responses to Item No. 1. Potential duplication. • For ability of users: Differences in eADVICE effectiveness were examined for parents with different scores in the: o eHEALS Health literacy survey o Newest Vital Signs test (functional health literacy) • The program is designed to allow access for those with hearing or visual impairments. The user can choose to hear the information through the speaking avatar, read the captions with the avatar, or read a written translation. • The website is compatible with common assistive technologies and meets relevant web application standards ***Reasons not able to be assessed?*** • Cultural barriers not examined in pilots or RCT
Topic: Technical safety (Reliability & stability) (*NEW*)					
9	DHT08: Is the technology reliable and stable?	***Is the technology reliable and stable?*** Is there evidence of accurate and reliable transmission of unbiased data? Does the DHT alert the user when working suboptimally or experiencing interference, e.g., low or no network connectivity? Does it perform well outside the laboratory? Is it validated for use on multiple platforms? Is it resilient to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions? Is there evidence that operating system updates and patches,	P	P	***How assessed?*** • Tested for effectiveness through multiple pilots and RCT • There were no complaints from participants about program dropouts • DHT does not alert the user when working suboptimally or experiencing interference • Any technical issues were relayed through the research officer to developers who would fix errors and redeploy the program • Website tested on multiple platforms by patients, but not yet developed as a mobile app ***Reasons not able to be assessed?*** • Our assessment of accurate and reliable transmission of unbiased data was limited by the loss of access to the website data, but no issues were identified in pilot testing

Item No	Issue ID[a] [c]: Issue	Clarification[*] for Digital Health Technologies	Able to be assessed? (Y/N/P)	Reported or will be reported in literature? (Y/N/P)	How assessed? Or Reasons not able to be assessed?
		service continuity, backup, and recovery mechanisms are well managed?			• No formal testing of resilience to erroneous data inputs, errors of precision, hardware problems, inappropriate use of devices, changes in other applications, and other interruptions. Only tested through pilot and RCT
Topic: Risk Management (EUN)					
10	C0062: How can one reduce safety risks for patients (including technology, user-, and patient-dependent aspects)?	***Does the technology help health professionals respond quickly when changes in patient care are needed?***	Y	P	Refer below
		Provide information on the defined parameters programmed within the technology to identify and respond to a patient's acute deterioration. How are they set, maintained, and changed?	*Y*	*Y*	Participants in the eADVICE program were children with urinary incontinence with a low risk of acute deterioration in their condition, so the setting of parameters to identify and respond to a patient's acute deterioration was not relevant. However, it was made clear to the participants when and if they should make an appointment with this physician to discuss these results
		Does the DHT allow the user to communicate to their healthcare team critical information about changes in their condition or information on risks of using the DHT?	*Y*	*Y*	While support was available through the research officer and supervising clinicians, the participant had to nominate a primary care physician to supervise them in the program, and their results were sent by the program to this supervising physician. eADVICE determined the information to be sent
		Is there a contact mechanism for technical support with a fixed response time?	*Y*	*P*	The research officer could be contacted for technical support and issues would be relayed to development team, but there was no fixed response time
		Are there processes within the DHT to communicate changes to or transfer of a patient's care?	*Y*	*Y*	There were no processes within eADVICE to communicate changes to or transfer of a patient's care, i.e., primary physicians could not send messages to patients through eADVICE
Domain 4: Clinical Effectiveness (EFF)[a]					
Topic: Patient Satisfaction (EUN)					
11	D0017: Were patients satisfied with the technology?	***Is it easy to use for everyone?*** Is there evidence that the DHT is usable for a diverse range of users, including those with disabilities or limited ability with digital technology or digital health literacy? Are there obvious design issues hindering usability, e.g., washable, durable, cause skin allergies?	P	P	***How assessed?*** Survey including questions on satisfaction, ease of use, structure, content (and appropriateness for parent or child); suggestions to improve the current design. feedback from the trial participants indicated a high degree of satisfaction with the program Differences in eADVICE effectiveness were examined for parents with different scores in the: eHEALS Health literacy survey and Newest Vital Signs test (functional health literacy) Patients raised the design issue of not being available on a mobile app. ***Reasons not able to be assessed?*** While effectiveness for different levels of digital health literacy and health literacy was examined, most participants scored highly, hence there was not

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					enough range of ability to evaluate this robustly. There also was too small a sample to evaluate effectiveness on participants with a disability. Digital health literacy was used as a proxy for limited ability with digital technology.
Topic: Reliable information content (*NEW*)					
12	DHT16: Does the technology always provide up-to-date and correct health advice?	***Is the health advice it provides always up-to-date, and correct?*** Evaluate whether the health advice provided by DHT is accurate, valid, up to date, comprehensive, clear, and tailored to the users' diversity. Provide evidence of an ongoing quality assurance process to maintain this accurate and up-to-date health advice.	Y	P	Whilst the eADVICE met these requirements currently, there was no evidence of a quality assurance process in place to keep this information up-to-date and accurate.
Domain 5: Costs and economic evaluation (ECO)[a]					
Topic: Measurement & estimation of outcomes (*EUN*)					
13	E0005: What is (are) the measured and/or estimated health-related outcome(s) of the assessed technology and its comparator(s)?	***Have DHT-specific benefits been considered?*** Provide information on DHT-specific outcomes such as improved access to health information and services, reduced waiting time, less burdensome travels, a feeling of security, transfer of skills, better-managed care through self-management and digitally connected healthcare professionals.	N	N	These outcome measures were not planned for in the study protocol so were not collected. These outcome measures are not typically collected in trials. Every additional outcome measure represents an extra cost in collection, analysing, and reporting to the research study. There is a need to encourage collection of this critical information in studies of DHTs that manage chronic disease.
Domain 6: Ethical analysis (ETH)[a]					
Topic: Benefit-harm balance (EUN)					
14	F0003: Are there any other hidden or unintended consequences of the technology and its applications for patients/users, relatives, other patients, organisations,	Hidden or unintended consequences of technology	Y	P	Refer below
		Is patient information always kept private and safe from hacking and tracking*?* Describe how the technology's data collection and communications may affect the patient's safety and welfare. Where are alerts about a patient's health reported?	*Y*	*Y*	Unique usernames and user passwords ensured security on the website. All patient information was kept separately in a secure hospital drive and could only be linked to patient by the research officer. Reports from eADVICE were sent to primary physicians securely by research officer.
		Is real-time data securely transmitted?	*Y*	*Y*	Real time data is not transmitted by the technology.

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	commercial entities, society etc.?	Have there been any perceived or real privacy breaches, technical problems, unexpected/unintended incidents created by the technology?	*Y*	*N*	No perceived or real privacy breaches, technical problems, or unexpected/unintended incidents were reported by participants in the trial.
		Consider tracking from other software on the platform/device, or operating system and malicious software (e.g., ransom ware, viruses, malware, etc.)	*Y*	*N*	Website use could be tracked by other software on computers or malicious software. However, the data collected by the website was kept to a minimum as identifying information kept on secure hospital drives.
		What prevents patients misinterpreting test results or having a false sense of security? Estimate the likelihood and severity of harm from patients having access to the data from the technology without assistance to help them interpret what it means, or a false sense of security that the data collected by the DHT is being monitored by a clinician. Describe the controls in place to minimise these risks.	*Y*	*Y*	In terms of patients misinterpreting test results or having a false sense of security, it was made clear when and if the patient should visit their primary physician. The risk is lowered for misinterpretation as no results given to patient, just advice to visit primary physician.
15	F0011: What are the benefits and harms of the technology for relatives, other patients, society, etc.?	***Does the technology help health professionals respond quickly when changes in patient care are needed?*** Explain how the DHT preserves and enhances direct contact between patients and healthcare professionals while supporting them to manage their health.	Y	Y	The eADVICE program aims to make this connection between primary health professionals while patients wait for specialist appointments. This is effective and patients and family are satisfied with the technology.
Topic: Autonomy (EUN)					
16	F0004: Does the implementation or use of the technology affect the patient´s capability and possibility to exercise autonomy?	***Does the technology limit the user in their treatment options?*** Is the user always able to make independent and authentic decisions based on an adequate range of options given by the DHT? For DHTs targeting behaviour change, what controls limit the DHT influencing behaviour for purposes other than those stated, e.g., commercial?	Y	Y	The design of the DHT with the relevant health experts employing best practice research helps to mitigate this risk. The direction to consult with the primary physician is also another mitigant - it is solely the decision of the primary physician the medications they prescribe. Although patients might have to buy a wetting alert alarm, there is no financial support or relationships with sellers of these products.

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17	F0005: Is the technology used for individuals that are especially vulnerable?	***Does the technology limit the user in their treatment options?*** Estimate the likelihood that the technology may influence a person's behaviour for commercial purposes when they are most vulnerable, i.e., consider the degree to which the DHT has access to a large amount of personal data, behavioural-economic insights, algorithmic predictive analyses, and can communicate with the patient continuously. Describe the controls in place to minimise this risk. For example, does the DHT use simple and understandable language? Does it provide concise information on how health information was chosen, who is responsible for the content, and information on potential conflicts of interest (funding, promotion)?	Y	Y	The DHT was designed with children, so high risk of vulnerability. However, it uses best practice advice built with health professionals, The health information chosen is referenced to the literature. There are many controls in place to reduce the risk, such as being designed with children and parents to be easy to understand, and having a supervising primary physician, and the advice to always consult with the primary physician. There are no conflicts of interest, and these statements are reported in the literature.
Topic: Respect for persons (EUN)					
18	F0101: Does the technology invade the sphere of privacy of the patient/user?	***Is patient information always kept private and safe from hacking and tracking?*** Does the DHT clearly identify who holds any personal data? Is the supplier's cookie policy stated and clear? Is only data necessary for a particular treatment shared with the doctor, and then only after explicit consent that the patient can revoke? Can patients opt-out if they are not able or unwilling to manage their data? Does the DHT provider have privacy policies that are easy to understand, uphold users' rights and choices, and are readily available to users before and while using the DHT, compliant with privacy laws, privacy principles, and best practices? Are changes to privacy policies communicated to users in a timely way? Is the DHT regularly audited for transmissions with third parties that include linkable identifiers and is the user informed of this risk?	N	N	These decisions will be dependent upon NSW Health's policies and standards for the implemented solution.

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Topic: Justice & Equity (*EUN*)					
19	H0012: Are there factors that could prevent a group or person from gaining access to the technology?	***Is it easy to access for everyone?*** Is there evidence that the DHT is accessible for a diverse range of users, including those with a lack of economic resources, disability, limited ability with digital technology, or limited digital health literacy? Is the DHT compatible with common assistive technologies, meet relevant web page or web application standards, and available in a wide number of languages and platforms?	Y	Y	There is a high risk that children in lower socio-economic groups will not be able to access the technology due to not having the required personal digital technology. The cost to subsidise the provision of these technologies and data usage fees for the lowest socioeconomic quintile was considered in a cost-effectiveness scenario. People who do not speak English should be catered for by translation of the program into several commonly spoken languages. This was considered in cost-effectiveness scenario. The program is designed to allow access for those with hearing or visual impairments. The user can choose to hear the information through the speaking avatar, read the captions with the avatar, or read a written translation. Use in those with poor IT skills digital literacy and health literary has been considered in the design phase and testing.
Domain 8: Patient and social aspects (SOC)[a]					
Topic: Social group aspects (*EUN*)					
20	H0201: Are there groups of patients who currently do not have good access to available therapies?	***Is it easy to access for everyone?*** Does the technology improve access for those on lower incomes, disabled, elderly, neurodiverse, indigenous populations, ethnic minorities, rural and remote patients? Is there evidence of the DHT being used, or being designed to be used in hard-to-reach populations?	N	N	The specialist incontinence clinics are all located in metropolitan areas, so patients in rural and remote areas are restricted in access. Children in rural and remote areas may be reached better by this technology but may struggle with internet connection. It is crucial to have more testing in these locations. No studies are yet planned for whether the technology is being used in hard-to-reach populations.
Domain 9: Legal aspects (LEG)					
Topic: Privacy of the patient (EUN)					
21	I0007: Is there a possibility that the use of the technology produces additional information that is not directly related to the current care of the patient and may violate their right to respect for privacy?	***Is patient information always kept private and safe from hacking and tracking?*** This possibility exists with almost all DHTs – refer to the content listed in F0101, DHT02, and F0003 for consideration. Consider General Data Protection Regulation (GDPR) principles (e.g., data minimisation and purpose limitation). Has a data protection by design and default approach been used?	Y	N	It is often difficult to decide what data needs to be collected in the trial period, so more information than needed for implementation has been collected. A data protection by design and default approach has not been used and a data protection impact assessment has not been completed.

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		Has a data protection impact assessment been completed?			
22	I0009: What do laws/binding rules require with regards to appropriate measures for securing patient data and how should this be addressed when implementing the technology?	***Is patient information always kept private and safe from hacking and tracking?*** Review GDPR principles and data protection legislation/standards and provide evidence of compliance. Does the manufacturers' cyber-insurance policy cover privacy breaches and privacy law violations?	Y	N	Assessment against the laws/binding rules will occur in the PSAF. This should consider residual risk and whether NSW Health cyber-insurance covers the risk of privacy breaches and privacy law violations.

[a]From EUnetHTA HTA Core Model version 3.0 (1)
[b]New topic
[c]DHT prefixes denote new issues (i.e., *DHTXX*)
[*]Clarification = A more detailed description of what the issue addresses (1)
[**]Content relations = A list of Issue IDs that deal with similar themes as this Issue ID (1)
GDPR = General Data Protection Regulation
See Section 7.8 for references

Appendix B: Publications and statements of contribution

Chapter 2

Chapter 2 was published as follows:

Von Huben A, Howell M, Howard K, Carrello J, Norris S. Health technology assessment for digital technologies that manage chronic disease: A systematic review. *Int J Technol Assess Health Care*. 2021;37(1), e66. doi:10.1017/S0266462321000362.

The co-authors made the following contributions to this manuscript (roles defined by CRediT (Contributor Roles Taxonomy), https://credit.niso.org/):

Von Huben A Conceptualisation, Data curation, Formal Analysis, Investigation, Methodology, Project Administration, Software, Validation, Visualisation, Writing original draft, Writing – review and editing

Howell M Conceptualisation, Formal Analysis, Investigation, Methodology, Supervision, Validation, Writing original draft, Writing – review and editing

Howard K Conceptualisation, Formal Analysis, Investigation, Methodology, Supervision, Validation, Writing original draft, Writing – review and editing

Carrello J Investigation, Validation, Writing – review and editing

Norris S Conceptualisation, Formal Analysis, Methodology, Supervision, Validation, Visualisation, Writing original draft, Writing – review and editing

Acknowledgments. We thank Ms. Bernie Carr, Academic Liaison Librarian, Fisher Library, University of Sydney, for assisting with the search strategy.

Chapter 3

Chapter 3 was published as follows:

Von Huben A, Howell M, Carrello J, Norris S, Wortley S, Ritchie A, Howard K. Application of a health technology assessment framework to digital health technologies that manage the chronic disease: A systematic review, *Int. J. Technol. Assess. Health Care.* 2022;38(1):e9. doi: 10.1017/S0266462321001665.

The co-authors made the following contributions to this manuscript (roles defined by CRediT (Contributor Roles Taxonomy), https://credit.niso.org/):

Von Huben A Conceptualisation, Data curation, Formal Analysis, Investigation, Methodology, Project Administration, Software, Validation, Visualisation, Writing original draft, Writing – review and editing

Howell M Conceptualisation, Formal Analysis, Investigation, Methodology, Supervision, Validation, Writing original draft, Writing – review and editing

Carrello J Investigation, Validation, Writing – review and editing

Norris S Conceptualisation, Formal Analysis, Methodology, Supervision, Validation, Visualisation, Writing original draft, Writing – review and editing

Wortley S Conceptualisation, Writing original draft, Writing – review and editing

Ritchie A Conceptualisation, Writing original draft, Writing – review and editing

Howard K Conceptualisation, Formal Analysis, Methodology, Supervision, Validation, Writing original draft, Writing – review and editing

Acknowledgments. We thank Ms. Bernie Carr, Academic Liaison Librarian, Fisher Library, University of Sydney, for assisting with the search strategy.

Chapter 4

Chapter 4 was published as follows:

Von Huben A, Howell M, Norris S, Wong KC, Tang J, Kazi S, Laranjo L, Chow KC, Howard K. Stakeholder preferences for attributes of digital health technologies to consider in health service funding. *Int J Technol Assess Health Care.* 2023;39(1):e12. doi: 10.1017/S0266462323000089.

The co-authors made the following contributions to this manuscript (roles defined by CRediT (Contributor Roles Taxonomy), https://credit.niso.org/):

Von Huben A, Conceptualisation, Data curation, Formal Analysis, Investigation, Methodology, Project Administration, Software, Validation, Visualisation, Writing original draft, Writing – review and editing

Howell M, Conceptualisation, Formal Analysis, Methodology, Software, Supervision, Validation, Visualisation, Writing original draft, Writing – review and editing

Norris S, Conceptualisation, Methodology, Resources, Investigation, Supervision, Visualisation, Writing original draft, Writing – review and editing

Wong KC, Conceptualisation, Resources, Investigation, Validation, Writing – review and editing

Tang J, Methodology, Resources, Investigation, Validation, Writing – review and editing

Kazi S, Resources, Investigation, Validation, Writing – review and editing

Laranjo L, Resources, Investigation, Validation, Writing – review and editing

Chow KC, Conceptualisation, Resources, Supervision, Writing – review and editing

Howard K, Conceptualisation, Formal Analysis, Funding acquisition, Methodology, Supervision, Validation, Visualisation, Writing original draft, Writing – review and editing

Chapter 6

Chapter 6 has been submitted as a manuscript to *Pediatrics* and is under review as follows:

Von Huben A, Howell M, Richards D, Hamilton S, Howard K, Teixeira-Pinto A, Craig JC, Seton C, Waters K, Deshpande A, Scott K, Caldwell PHY. eADVICE: an economic evaluation of a web-based program for children with incontinence. 2023, *[Manuscript submitted for publication]*.

The co-authors made the following contributions to this manuscript (roles defined by CRediT (Contributor Roles Taxonomy), https://credit.niso.org/):

Von Huben A, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualisation, Writing original draft, Writing – review and editing

Howell M, Formal analysis, Methodology, Investigation, Resources, Supervision, Writing original draft, Writing – review and editing

Richards D, Conceptualisation, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Writing original draft, Writing – review and editing

Hamilton S, Data curation, Investigation, Project administration, Validation, Writing – review and editing

Howard K, Formal analysis, Funding acquisition, Methodology, Supervision, Writing original draft, Writing – review and editing

Teixeira-Pinto A, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – review and editing

Craig JC, Formal analysis, Methodology, Supervision, Visualisation, Writing original draft, Writing – review and editing

Seton C, Writing – review and editing

Waters K, Data curation, Writing – review and editing

Deshpande A, Data curation, Writing – review and editing

Scott K, Conceptualisation, Writing – review and editing

Caldwell PHY, Conceptualisation, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing original draft, Writing – review and editing

Acknowledgments: We thank Mr Frank Jin, Clinical & Finance Partner, New South Wales Health Service, Sydney Children's Hospital Network (SCHN), for assistance in estimating the cost of paediatric specialist continence clinic encounters.