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Review

Health Technology Assessment for Cardiovascular Digital Health Technologies and Artificial Intelligence: Why Is It Different?

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ABSTRACT

Innovations in health care are growing exponentially, resulting in improved quality of and access to care, as well as rising societal costs of care and variable reimbursement. In recent years, digital health technologies and artificial intelligence have become of increasing interest in cardiovascular medicine owing to their unique ability to empower patients and to use increasing quantities of data for moving toward personalised and precision medicine. Health technology assessment agencies evaluate the money spent on a health care intervention or technology to attain a given clinical impact and make recommendations for reimbursement considerations. However, there is a scarcity of economic evaluations of cardiovascular digital health technologies and artificial intelligence. The current health technology assessment framework is not equipped to address the unique, dynamic, and unpredictable value considerations of these technologies and highlight the need to better approach the digital health technologies and artificial intelligence health technology assessment process.

RÉSUMÉ

Les innovations dans le domaine de la santé sont en croissance exponentielle, ce qui se traduit par une amélioration de l'accès aux soins et de leur qualité, mais aussi par une augmentation des coûts sociétaux des soins et des remboursements variables. Ces dernières années, les technologies de santé numérique et l'intelligence artificielle ont suscité un intérêt croissant en médecine cardiovasculaire en raison de leur capacité unique à responsabiliser les patients et à utiliser des quantités croissantes de données pour avancer vers une médecine personnalisée et de précision. Les agences d'évaluation des technologies de santé quantifient les sommes dépensées pour une intervention ou une technologie de soins de santé en vue d'obtenir une retombée clinique donnée et formulent des recommandations sur des considérations de remboursement. Cependant, les évaluations économiques des technologies de santé numériques cardiovasculaires et de l'intelligence artificielle sont rares. Le cadre d'évaluation actuel des technologies de la santé n'est pas outillé pour prendre en

Health technology is evolving at an exponential rate with the advent of connected medical devices, digital health, and precision medicine. The enthusiasm associated with this surge in technologies and innovations in health care has been tempered by rising costs and great variability in impact and reimbursement eligibility. Digital health technologies (DHTs), in the context of cardiovascular medicine, can be defined as "information and communication technologies to treat patients with cardiovascular diseases, develop appropriate cardiovascular disease surveillance, conduct technology-based clinical research, and educate peers and colleagues."[1] They can empower patients to take care into their own hands, improve monitoring and rehabilitation, and expand access to care.[1] Similarly, artificial intelligence (AI) is increasingly used in modern health care for diagnostic and therapeutic purposes.[2,3] AI carries distinct definitions depending on its purpose or use, but can largely be described as learning systems that mimic human intelligence, including comprehension, analysis, adaptation, self-correction, and interaction.[4] It can be categorised as a narrow system (also referred to as "closed") whereby an algorithm or model is developed from data, only once through machine-learning processes, or a broad system (also referred to as "open"), which allows data to accumulate and the algorithm "learns" in real time.[5] The latter in particular provides the opportunity to improve models as data become more available (eg, wearable-linked databases collecting clinically relevant variables) and thus constantly iterate and improve.

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In this review, we compare digital health technologies and artificial intelligence with traditional health care technologies, review existing health technology assessment frameworks, and discuss challenges and opportunities related to cardiovascular digital health technologies and artificial intelligence health technology assessment. Specifically, we argue that health technology assessments for digital health technologies and artificial intelligence applications must allow for a much shorter device life cycle, given the rapid and even potentially continuously iterative nature of this technology, and thus an evidence base that maybe less mature, compared with traditional health technologies and interventions.

considération l'aspect original, dynamique et imprévisible de ces technologies, soulignant la nécessité de mieux aborder le processus d'évaluation des technologies numériques de la santé et de l'intelligence artificielle. Dans cette étude, nous comparons les technologies numériques de la santé et l'intelligence artificielle par rapport aux technologies traditionnelles des soins de santé, nous examinons les dispositifs d'évaluation des technologies de santé existants et nous discutons des défis et des possibilités liés à l'évaluation des technologies numériques de la santé et de l'intelligence artificielle dans le domaine cardiovasculaire. Plus précisément, nous soutenons que les évaluations des technologies de la santé pour les technologies numériques de la santé et les applications de l'intelligence artificielle doivent tenir compte d'un cycle de vie des dispositifs beaucoup plus court, étant donné la nature rapide et même potentiellement itérative et continue de ces technologies, constituant alors une base de données factuelles peut-être moins mature, en comparaison avec les technologies et interventions traditionnelles de santé.

Although DHTs and AI are distinct entities, they share common issues. Currently, their costs remain high, the quality of evidence is variable, and their clinical significance debated.[6-8] This presents a clear need for rigorous health technology assessment (HTA) to evaluate these new technologies and determine their value, balancing innovation and market entry opportunities with cost containment and adequacy of evidence.[9] However, conventional HTA practices may not suffice owing to the large number of technologies being developed, the reliance on small pilot proof-of-concept studies, and the iterative adaptation of DHTs and broad AI systems. Each of these properties potentially disrupt the traditional approach to HTA.

Accordingly, in this review, we discuss HTA in light of DHTs and AI applications in cardiovascular medicine, describe existing DHT/AI HTA frameworks, and highlight unique opportunities for Canada to better evaluate, promote, and reimburse meaningful new technologic innovations. An in-depth HTA primer falls beyond the scope of the present review but has been described in previous work in this journal.[10,11]

Health Technology Assessment for Cardiovascular Medicine: The Basics

The adoption of novel technologies is typically accompanied by increased costs; given finite resources, determining if a technology has met a sufficient threshold of value is mandatory before system adoption. The American Heart Association/American College of Cardiology has, therefore, issued explicit guidelines to incorporate value within clinical guideline recommendations.[12] In health care, value can broadly be defined as the cost for outcome achieved.[13] In other words, value in health care equates to the amount of money spent to avert a defined quantity of morbidity and mortality, and/or to improve the quality of patients' life. Because health care payers often have to evaluate multiple different technologies simultaneously to make reimbursement decisions, the use of common metrics to evaluate value is necessary. This is clearly illustrated in cardiovascular medicine: For example, this allows decision makers to compare transcatheter aortic valve replacement (TAVR) in various surgical risk groups with the latest treatment for prevention of stroke in atrial fibrillation.[10,11,14] The value estimate from HTA is calculated as the incremental cost-effectiveness ratio (ICER) defined as amount of money spent per clinical impact. The clinical impact is typically calculated as quality-adjusted life-years (QALYs) gained. This can, therefore, inform resource allocation decision making in health systems agnostic to the specific condition. This is particularly important in publicly funded health care systems, such as in Canada, where health care budgets are often relatively fixed. Early review findings suggest favourable cost-effectiveness of cardiovascular DHTs, whereas economic evaluations and, in fact, real-world adoption of AI applications in cardiovascular medicine remain scarce.[15-20] Yet, the rapid adoption of these technologies in studies and introduction to the market suggests increasing evidence and value considerations in the near future.[7]

Quality of Life Estimations: Can Important Changes Be Captured?

Patient preference is incorporated in the calculation of QALYs through utility in achieving society's preferences for a particular health state that range from 0 for death to 1 for perfect health. QALYs are calculated by determining the change in utility from a treatment or intervention multiplied by the duration of the effect of the intervention. In other words, the greater the utility or the longer the effect, the greater the QALYs gained. Although life expectancy may remain constant, quality of life may be improved. For example, in lower-risk patients with aortic stenosis, there is no significant difference in life expectancy between TAVR vs surgical valve replacement; however, early healing and improved quality of life compensate for the higher procedural costs of TAVR.[21] Similar quality of life improvements may be seen with DHTs and AI, such as the use of remote monitoring devices or self-management smartphone applications. However, depending on the method of utility derivation, there may not be enough fidelity, or responsiveness in current tools to capture the patient preference considerations for DHT.

Currently, utilities for QALY calculations are often determined through EuroQol-5D (EQ-5D) questionnaires, as preferred by major HTA agencies.[22] The domains of the EQ-5D include mobility, self-care, usual activities, pain and

discomfort, and anxiety and depression, which may not adequately capture a patient's preference for novel technologies that improve satisfaction with their overall health. For a DHT, where decisional satisfaction may be the key improvement, this may not be readily or consistently captured.

This is particularly relevant because it has been shown that patients have a low marginal willingness to pay more for DHT.[23] In other words, society is only accepting of small incremental costs for the gains from DHT. This highlights the need for new tools to capture the nuances of patient preference and satisfaction in considering new technologies. Societal considerations in the adoption of new technologies, including DHTs, AI, and other such innovative developments, must, therefore, place greater value on patients' decision satisfaction. In addition, it reinforces that low acquisition costs of these technologies will be particularly important for developers to ensure.

Rapid Iteration With a Hypothetical Future State

The most challenging aspect of AI is that its very promise may conflict with our approach to the assessment of value. The value in AI may be unknown or difficult to grasp by decision makers, because there is the opportunity for rapid model iteration in broad AI systems with potentially increasing value over time (eg, clinical significance, earlier detection, improved health recommendations). There is both uncertainty in whether this promise of improvement will be met and, if so, its magnitude. For that reason, some have called for the consideration of AI as a health system transformation rather than a specific technology *per se*.[4] While most conventional health care technologies and developments incrementally improve outcomes, AI may be able to radically change traditional health care delivery and entire health care systems. For example, based on recommendations by the National Institute of Health and Care Excellence (NICE), the National Health Service England has mandated the adoption of HeartFlow Analysis in hospitals across the country. HeartFlow Analysis is a noninvasive AI-powered diagnostic technology that converts computed tomographic scans into 3-dimensional images to help detect coronary artery disease instead of using coronary angiography, thereby minimising unnecessary procedures, reducing health care spending, and shortening wait times.[24,25] This highlights the difficulty of how such health system transformations should be considered in HTA processes, as novel technologies with hypothetical and unpredictable future value propositions require vastly different evaluations.

However, equally so, there is the risk that new technologies are overvalued merely due to their novelty and that the perceived value does not reflect their true impact. Recent reports suggest that published AI health care models are either difficult to replicate (eg, because datasets are small, low quality, or not open source) or rife with flaws that limit their adoption in the real world (eg, biases and nonrepresentative samples).[26,27] In addition, while iterative potential is a strength of broad AI, many current applications consist either of narrow AI, constrained by its development on a primary dataset introduced into an ever-changing world. Conversely, the promise of broad AI is constrained by the limited interoperability of health care data sets and therefore difficulty implementing such applications in health care. Indeed, in the United States, the Food and Drug Administration has required approved AI applications to remain "locked" (ie, narrow) to avoid performance changes since their approval, for which traditional regulatory approval processes were not designed.[28] Moreover, AI models are nearly impossible to independently verify by individuals unless the algorithm and data are made available in the public domain. These factors hinder HTA recommendations and risk the approval of applications that are flawed, are untrustworthy, and may even negatively affect patient care.[29]

Finally, and importantly, HTA is time intensive to properly conduct, requiring the necessary data, economic evaluations, and expert review and validation. The increasing rate of new technologies or indications, such as the use of TAVR in increasingly lower-risk patients, has illustrated the seemingly inevitable mismatch between different stages of HTA, whereby research generation rapidly outpaces HTA recommendations and reimbursement decisions. Conventional HTA takes approximately 1 year to complete, which is too long a timeline for rapidly changing technologies such as DHTs and AI applications. Specifically, in Ontario, despite practice guidelines recommending TAVR for the treatment of aortic valve stenosis in high-risk and intermediate-risk patients in 2014 and 2017, respectively, provincial funding after the completion of HTAs did not follow until 2016 and 2020. Such delays will be exacerbated when considering DHTs and AI, especially broad AI, owing to the development of either marginally different DHTs or iteratively progressive broad AI applications.

Is a new approach to HTA needed?

Conventional HTA vs HTA for DHT and AI

Although many similarities exist between conventional HTA and HTA processes for DHTs and AI, there are unique considerations for the latter that are worthy of discussion and presented in Table 1 and Figure 1.[4] Love-Koh et al. previously presented distinct challenges related to HTA processes for precision medicine by the 4 principal stages of HTA appraisal[30]:

1. Scoping: There are a vast and growing number of DHT and AI technologies, of which the technologic complexity is variable and not typically easily understood by HTA agencies, necessitating complex decision making.
2. Modelling: The advent of multiple distinct technologies limits strong evidence, mostly relying on observational data with small sample sizes per DHT or AI intervention. Moreover, DHT/AI—specific decision modelling requires expert elicitation to address the limited evidence, existing uncertainty, and the potential absence of appropriate key variables to better inform models and interpret findings. The specific challenges to modeling DHT/AI HTA compared with conventional innovations are summarised in Table 1.
3. Decision making: There is increased uncertainty regarding technologic efficacy and technologies' effects on patient-doctor relationships. In addition, inequity in technologic uptake or resulting access to care may manifest itself.

Table 1. Comparison between conventional HTA and HTAs for DHTs and AI

	Traditional HTA	DHT/AI HTA	Issues
Perspective	Third-party payer (ie, Ontario Ministry of Health Long-Term Care)	Third-party payer and/or end-user (ie, consumer or patient)	
Time horizon	Relevant to the disease	Variable (eg, disease duration, lifetime)	
Comparator	Standard care	May not have a comparator, or may have many comparators depending on the market	
Discounting	Costs (3%-5%) and health benefits (1.5%-5%)		Uncertainty of future health benefits
Effectiveness	Assumed to be constant	May change with time especially with broad AI	Modelling uncertainty
Evidence base	Typically derived from randomised controlled trials	May not have solid evidence	Variable strength of evidence depending on quality of data and (un)known biases
Relevant outcomes	Cost per QALY	Quality of life, patient preference	
WTP thresholds	Controversial and several ways to determine this, benchmark of $50,000/QALY cited in literature	May depend on the consumer's own WTP rather than an aggregate WTP threshold	
Framework	Utilitarian	Microeconomic theory (technology may be priced to meet the demand of the individual)	Equity issues (not everyone may be able to pay for the new technology)
Value determination	Government agencies	Individual consumers	Unknown or unquantifiable value

AI, artificial intelligence; DHT, digital health technologies; HTA, health technology assessment; QALY, quality-adjusted life year; WTP, willingness to pay.

4. Reviewing and updating: The rapid developments in technologies require frequent updates of guidelines and/or frameworks to remain relevant. Considering the rapid iteration of DHTs and broad AI, this may require the development of HTA models that rapidly iterate similarly to the technologies they evaluate.

In addition, it may be argued that full HTA processes are not necessary for selected DHTs, such as those sold directly to the consumer, even though they may provide additional health benefits. For example, the Apple Watch tracks users' heart rhythms and notifies the user via its associated smartphone application in case of an irregular rhythm that may suggest atrial fibrillation.[31] In such cases, microeconomic theory suggests that individuals themselves decide individually whether they are willing to spend money (eg, to buy a smartwatch) to maximise utility (eg, to increase the chance of detecting an irregular heart rhythm). Because most single-payer health systems and commercial insurers do not normally reimburse DHTs that are not indicated for specific patient populations and that are largely commercial, such DHTs are likely not reviewed by HTA agencies.

HTA Frameworks

The availability of comprehensive HTA frameworks to evaluate DHTs and broad and narrow AI applications remains

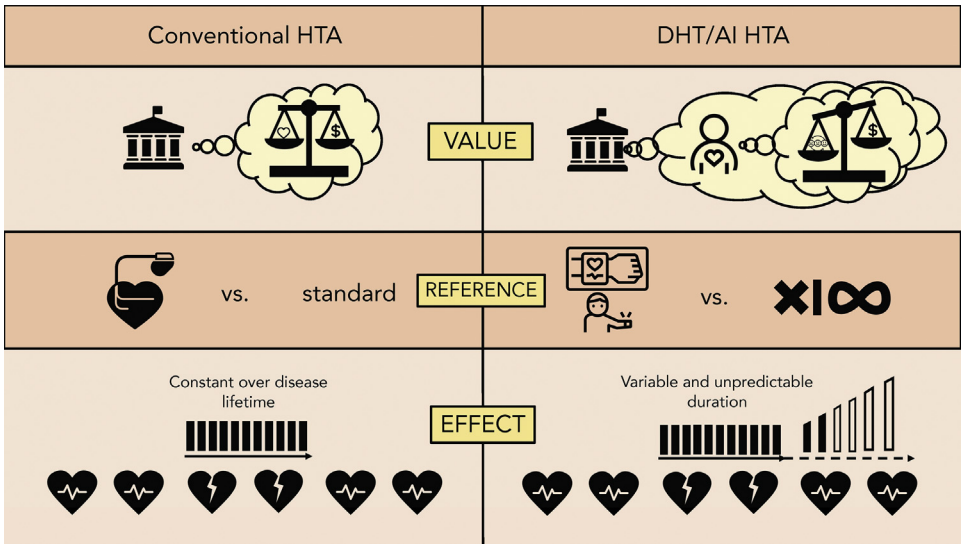

Figure 1. Rethinking value and impact in health technology assessment (HTA) for digital health technologies (DHTs) and artificial intelligence (AI). Conventional HTA, traditionally comparing a novel intervention or technology with a standard of care, considers the cost relative to the constant clinical impact achieved over the course of a disease from a societal perspective. In contrast, DHT/AI HTA compares a DHT or AI application with no, one, or numerous comparators with variable and unpredictable future impact and value, whereby both the societal and, especially, patient perspective are prioritised.

Table 2. Examples of HTA frameworks for DHTs and/or AI

	England and Wales	South Korea	Germany	France	Finland	Israel
Framework	Evidence Standards Framework for DHT	Assessment Guideline for National Health Insurance Coverage Eligibility of Innovative Medical Technology	The Fast-Track Process for Digital Health Applications	Guide to the Specific Features of Clinical Evaluation of a Connected Medical Device in View of its Application for Reimbursement	Digi-HTA	Digital Health Technology Evaluation for Health Organisations: an evaluation framework for early-stage technologies
Scope	DHT, narrow AI	AI imaging, non-DHT medical technologies	DHT	DHT	DHT, AI,* robotics	DHT, AI*

AI, artificial intelligence; DHT, digital health technologies; HTA, health technology assessment.
*The frameworks do not distinguish between broad and narrow AI applications.

limited and fragmented.[32] The Canadian Agency for Drugs and Technology in Health (CADTH) serves as an independent pan-Canadian not-for-profit agency funded by Canada's federal, provincial, and territorial governments to issue HTA recommendations for health care decision makers for the use, pricing, and reimbursement of medical drugs, tests, devices, and procedures. Although CADTH has issued individual evidence syntheses and recommendations of DHTs and AI applications, to date no standardised framework has been developed. In England and Wales, NICE guides access to new health care technologies in the National Health Service. Specifically, NICE developed an Evidence Standards Framework for Digital Health Technologies,[33] which provides recommendations on the levels of evidence and risk assessment of DHTs and narrow AI applications. The framework, though not incorporating adaptive algorithms (ie, broad AI applications), can currently be considered the most comprehensive DHT/AI—specific HTA framework, as it was developed by representatives of NICE, National Health Service England, Public Health England, and other government, academic, and private sector stakeholders and actively commissioned public input.[34] In addition, the framework was updated iteratively based on pre- and post-launch feedback, allowing for adaptation based on changing perceptions or developments over time. Other countries, such as South Korea, Germany, France, and Finland, have recently developed similar HTA frameworks for DHT and/or AI, as summarised in Table 2.[35,36]

The United States and Israel produce the majority of the world's medical AI applications that are on the market. In the United States, the Food and Drug Administration has approved more than a dozen cardiology AI applications, although its regulations have forced algorithms to be inherently "narrow," limiting real-time and real-world learning.[28] The Food and Drug Administration, however, started adopting a "total product life cycle—based regulatory framework" for AI applications that may allow for faster (in days) post-release contextual adaptation compared with traditional regulatory timelines. However, the Food and Drug Administration does not perform HTA; instead, this is conducted by various independent interest groups.[37] In Israel, driven by the example and frameworks set by the Israeli Center for Technology Assessment in Health Care, HTA has become decentralised and supported by multiple institutions and stakeholders.[38] In June 2021, the Israeli Ministry of Health released an evaluation framework for early-stage DHTs and AI applications that was developed and tested on approximately 400 early-stage technologies considered by the Ministry's Digital Health Division (Table 2).[39]

From Health Technology Assessment to Policy

The purpose of HTA is to inform health policy decision making by critically evaluating the best available evidence and presenting recommendations to policy makers based on these assessments. Typically, HTA processes are initiated as a result of an existing policy question which decision makers seek to address, for example, when Health Canada's Medical Device Bureau approves a new health technology for which reimbursement policies need to be formulated at the provincial/territorial levels. HTA products are developed by researchers

who are able to objectively develop assessment reports in order to ensure that policy makers are less influenced by context (eg, political considerations or personal values) or colloquial (ie, nonscientific) evidence.

Challenges and Unique Opportunities in the Canadian Health System

In the absence of existing DHT/AI–specific HTA frameworks or guidelines in Canada, unique challenges arise. As it is a single-payer health system, decision making for reimbursement of certain technologies, especially novel, costly, and rapidly developing ones such as DHTs and AI applications, requires consideration of allocative justice, nondiscrimination, and equality of opportunity for all Canadians.[10] The Canada Health Act emphasises 5 core conditions that must be met in the delivery of health care: public administration, accessibility, comprehensiveness, universality, and portability. Access to novel technologies is likely to be associated with geographic variation (eg, rural and remote regions), violating the accessibility condition, or financial considerations (eg, smartphone-linked DHTs), contradicting universality. However, the supply of DHTs to remote populations has the unique potential to improve universality and deliver health care to remote regions and provide expertise that would otherwise not readily be available. In addition, limited digital literacy and variable access to broadband or high-speed internet, either because of costs or living in remote regions, may exacerbate inequity concerns by limiting the adoption of DHTs in more vulnerable populations such as the elderly, socioeconomically disadvantaged, and indigenous communities. The governmental "Connecting Canadians" program seeks to bridge the digital divide in Canada by building broadband infrastructure in remote and rural parts of the country, aiming to connect nearly 300,000 Canadian households, most notably indigenous peoples.[40] More recently, the Canadian Radio-television and Telecommunications Commission launched the Broadband Fund to invest up to $750 million over 5 years in projects aiming to expand mobile wireless internet in underserved parts of Canada.[41] Such expansions could ultimately facilitate the adoption of DHTs in remote communities. Finally, the growing connectivity of DHTs and AI applications implies the continuous data generation and health information collection in one or multiple central databases. This raises ethical questions regarding who owns the data (ie, the patient using, the private sector supplying, or the government reimbursing the technology), who can use it for what, and how such benefits or harms are valued. This, for example, directly conflicts with the First Nations concept of ownership, control, access, and possession whereby First Nations determine how their communities' data are collected, processed, and used in order to safeguard their self-determination and preserve their cultures. As such, there may exist a fine line between precision medicine and potential harmful practices targeting vulnerable patient populations, such as variable private insurance policies, whereby life insurance payout and private insurance coverage may be less favourable for these populations. Although Canada has been a country leader in ethical adoption of AI across sectors, ethical-legal barriers, skepticism, and caution prevail regarding further adoption of AI in health care.[42,43]

Nevertheless, the opportunities are plentiful. Canada can follow other countries in adopting DHT/AI–specific HTA guidelines. The Canadian Network for Digital Health Evaluation (CNDHE) was recently launched in collaboration with pan-Canadian organisations, including CADTH, to expand capacity to formally evaluate DHTs.[44] This is critical, as DHTs and AI applications require unique and novel technical expertise to best inform guidelines and individual recommendations. Few existing HTA frameworks currently consider AI and often consider it only partially (eg, specific AI application, only narrow AI, no distinction between narrow or broad AI), providing room for innovation by CADTH and CNDHE. In addition, DHT/AI–specific guidelines must be developed with the flexibility and potential for iterative adaptability in light of rapidly changing technologies and accumulation of data. The Food and Drug Administration's example of adopting a total product life cycle–based regulatory framework may be followed to do so in an accelerated and adaptable manner. The future is unpredictable, but the exponential rise in DHTs and AI studies in cardiovascular medicine only scratches the surface of the overall market entry and looming innovation incubation of DHTs and AI applications. In addition, it is likely that the AI-related advances in health care will be catalysed by developments in other sectors, where AI may be more readily introduced and adopted, such as the financial sector, computer science, automotive industry, and other sectors. Guidelines must anticipate future developments to consider future potential value, either in terms of clinical significance (eg, improved models) or patient impact (eg, patient satisfaction). Finally, implementation of DHTs and AI applications may be considered either quantitatively (eg, cost of training or additional infrastructure) or qualitatively (eg, required technical expertise or ease of use), which may affect the ultimate value proposition from different perspectives.

Conclusion

The literature and frameworks supporting HTA for DHTs and AI applications remain scarce, particularly within the scope of cardiovascular medicine. Cardiovascular DHTs and AI present with unique technologic challenges and iterative demands that require defined and distinct HTA frameworks in Canada and beyond to contain costs while promoting equitable access to new technologies.

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