Artificial Intelligence-Based Medical Devices: A Scoping Literature Review of the Suitability of the current Health Technology Assessment for these technologies

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Submitted to: Journal of Medical Internet Research
on: August 02, 2023

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Abstract

Background: Artificial intelligence-based medical devices have garnered attention due to their ability to revolutionize medicine. There is a lack in the adaptation of their health technology assessment framework.

Objective: To analyze the suitability of each HTA domain for the assessment of AI-based MD

Methods: We conducted a scoping literature review following the PRISMA methodology. We searched databases including PubMed, Embase, Cochrane Library, and from the gray literature and from HTA agency websites

Results: 78 references were included out of 775 citations. Data quality and integration are vital aspects to consider when describing and assessing the technical characteristics of AI-based medical devices during a HTA process. When it comes to implementing specialized HTA for AI-based MD, several practical challenges and potential barriers could be highlighted and should be taken into account (AI technological evolution timeline, Data Requirements, Complexity and Transparency, Clinical Validation and Safety requirements, Regulatory and Ethical Considerations, Economic Evaluation).
Discussion: Adaptation of the HTA process through a methodological framework for AI-based MDs enhances the comparability of results across different evaluations and jurisdictions. By defining the necessary expertise, the framework supports the development of a skilled workforce capable of conducting robust and reliable HTAs of AI-based medical devices.

Conclusions: A comprehensive adapted HTA framework for AI-based medical devices can provide valuable insights into the effectiveness, cost-effectiveness, and societal impact of AI-based medical devices, guiding their responsible implementation and maximizing their benefits for patients and healthcare systems.

(JMIR Preprints 02/08/2023:51514)
DOI: https://doi.org/10.2196/preprints.51514

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Short title: AI-based MD: A scoping review of the Suitability of standard HTA

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ABSTRACT (212 words)

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Keywords: Artificial intelligence, Machine learning, health technology assessment, Medical devices, evaluation

INTRODUCTION

Artificial intelligence (AI) has emerged as a transformative technology with vast potential across various sectors, including healthcare [1,2]. In this field, AI-based medical devices (MDs) have garnered significant attention due to their ability to revolutionize diagnosis, treatment, and patient monitoring [3]. These devices utilize advanced algorithms and machine learning (ML) techniques to analyze complex medical datasets, thereby providing valuable insights and support to healthcare professionals in their decision-making. To meet the ever-increasing demand for integration of AI-

based MDs into clinical practice, heir efficient evaluation through adapted health technology assessment (HTA) is now crucial [4]. Several frameworks have been published showing an adaptation of items for reporting clinical trials related to AI-based MDs (Table 1). However, a much needed adaptation of the standard HTA framework to better suit the assessment of AI based-healthcare technologies is still lacking.

A HTA involves a systematic evaluation of a medical technology's clinical, economic, ethical, and social implications to determine its overall value and impact on healthcare delivery [9]. The European Union network HTA (EUnetHTA) has designed a HTA Core Model®, that provides a methodological framework for production and sharing of HTA information [10]. It evaluates the following nine domains including: (1) Health problem and current use of technology; (2) Description and technical characteristics of the technology; (3) Safety; (4) Clinical effectiveness; (5) Costs and economic evaluation; (6) Ethical analysis; (7) Organizational aspects; (8) Patients and Social aspects; (9) Legal aspects (Table 1 in supplementary file 1).

A full understanding of the capabilities, limitations and specificities of AI-based medical devices is paramount in order to complete these HTA domain assessments and thereby inform evidence-based decision-making, allow policy development and the responsible integration of these technologies into healthcare systems [11,12]. Much uncertainty remains with regards to the reliability of AI-based MD, data issues, and regulatory processes, resulting in multiple challenges faced by HTA agencies assessing new technologies and delivering their approval [4]. Nevertheless, AI-based MDs require strict regulations and specific legislations [13–15]. Over the last few decades, the evaluation of AI-based MDs through a HTA process has received growing interest, as shown by one published article in 1990 up to 64 in October 2023, with 401 articles in total (Figure 1).

The objective of this review is to critically assess the comprehensive suitability of the standard full HTA for AI-based MDs. By evaluating the performance and capabilities of AI-based MDs across multiple dimensions, the review aims to inform healthcare professionals, policymakers, and researchers about the challenges and opportunities associated with these technologies. Ultimately, the review seeks to facilitate evidence-based decision-making, promote responsible implementation, and maximize the potential benefits of AI-based MDs in improving healthcare quality, accessibility, and outcomes.

To this end, we analyze the suitability of each HTA domain for the assessment of AI-based MDs and propose an adapted HTA framework.

MATERIALS AND METHODS

Search strategies

A scoping literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology [16,17]. All articles related to HTA methods for AI-based MDs were selected. Data extraction focused on assessment criteria, methodological evaluations and results.

The following search terms and strategy were used for the scoping review (Table 2).

Databases

We searched multiple databases including PubMed (ncbi.nlm.nih.gov), Embase (Embase.com), the Cochrane Library (cochrane.org/fr/evidence). Additional sources were retrieved manually from the gray literature and from HTA agency websites (Bfarm, HAS, NHS, NICE, NIPH, INAHTA, and EUnetHTA).

Study selection process

The studies were selected by two reviewers (LF and AV). After removing duplicates, both reviewers independently screened the abstracts to select eligible articles, then analyzed full-text reports for eligibility. A third party (NM) resolved the possible discrepancies highlighted during the selection process should a consensus not be reached. An extraction database was used to list the selected articles meeting the inclusion criteria to ensure that all eligible articles were included.

The inclusion and exclusion criteria were: (i) Language (this research was limited to the English and French languages) ; (ii) articles type (Reviews and primary research were included, whereas others were excluded such as abstracts, commentaries, editorials, letters to the editor, case reports, case series, and animal studies, phase 1 and 2 studies, pilot studies, duplicate studies, irrelevant studies, studies with a wrong aim, availability in abstract form only) ; (iii) type of technology (Only AI-based medical devices were eligible) ; (iv) type of evaluation (health technology assessment articles were included).

Data extraction

Two analysts independently extracted the following items from the selected articles (LF and AV). A third party was involved to resolve any discrepancies highlighted during the selection process. The following data were extracted from each article: (i) General characteristics of the studies (authors, journal, publication date) ; (ii) Article objective ; (iii) HTA Assessment Domain for AI-based MDs related to the article

Methodological quality appraisal

Neither methodological quality nor risk of bias of the included articles were assessed, in consistence with scoping review guidance [16].

Application example of the HTA of an AI-based MD

Concerning each HTA domain, we added a case study of the health technology assessment of several AI-based MD in diabetes to illustrate our recommendations.

RESULTS

1. Scoping review results

The literature search resulted in 775 citations summarized in the Prisma flowchart (Figure 2). After removal of 253 duplicates, we carried out an initial screening of the 522 potentially relevant publications resulting in 129 potentially relevant full-text papers. After further screening, we assessed 77 reports for eligibility based on which we excluded 11 for not referring to AI-based MD and 2 for not being a HTA. We then included a further 14 records from 59 potential citations available from HTA agency website and grey literature.

This gave a total of 78 included articles covering one or multiple HTA domains, the distribution of which is given in the bottom of Figure 2.

We then summarize the data collection for each selected article in the table 2 in the supplementary file 2.

2. Suitability of each HTA domain for the assessment of AI-based medical devices

As the domain 1 “Health problem and current use of technology” is suitable for any type of medical technology and systematically addressed for these technologies, we focused on the suitability of the HTA domains (from 1 to 9).

1. 1. *Domains 1& 2 – Health problem, current use, description and technical characteristics of*

technology

Data quality and integration are vital aspects to consider when describing and assessing the technical characteristics of AI-based medical devices during a HTA process [18]. These devices often rely on accessing and analyzing diverse healthcare data sources, including electronic health records, medical images, genetic data, and wearable device data. Therefore, it is essential to evaluate their ability to seamlessly integrate and exchange data with existing healthcare systems [19].

Firstly, interoperability refers to the ability of AI-based medical devices to interact and communicate with other healthcare technologies and systems [11]. This includes the ability to access and utilize data from different sources, such as laboratory systems, imaging archives, and patient health records. The assessment should consider whether the devices adhere to relevant data standards and protocols, ensuring efficient data exchange and compatibility with existing healthcare infrastructure [20].

Secondly, data integration involves the ability of AI-based medical devices to aggregate and analyze data from multiple sources to provide comprehensive and accurate insights [21]. The HTA should assess whether the devices can handle different data types, formats, and resolutions, and if they can effectively integrate and harmonize data from disparate sources.

Additionally, data privacy and security considerations are crucial when evaluating AI-based medical devices [22]. The assessment should examine whether the devices comply with relevant data protection regulations, employ appropriate data anonymization and encryption techniques, and have robust security measures in place to protect patient information [23].

A comprehensive HTA should therefore address both the interoperability and data integration capabilities of AI-based MDs, ensuring that they can seamlessly interact with existing healthcare systems, integrate data from multiple sources, and that they adhere to data privacy and security standards. By evaluating all these aspects, the HTA could determine the devices' feasibility, scalability, and potential impact on healthcare delivery.

1. 2. Domain 3 - Safety & Domain 4 - Clinical effectiveness

The assessment of clinical effectiveness and the impact on patient outcomes is a crucial aspect when evaluating AI-based medical devices through a comprehensive HTA [4]. While accuracy and performance metrics are important, it is essential to determine how these devices translate into tangible benefits for patients and healthcare delivery [24].

Clinical utility refers to the extent to which the AI-based medical device improves clinical decision-making, patient outcomes, and healthcare processes [25]. The HTA should examine whether the device provides actionable and reliable information that potentially helps healthcare professionals

make more accurate diagnoses, or improve treatment plans or monitoring strategies [26,27]. It should also evaluate the potential impact of the device on patient outcomes, by assessing such as improved survival rates, reduced complications, or enhanced quality of life [28].

To assess clinical utility, the HTA should consider the device's performance in relevant clinical scenarios and its ability to address specific clinical questions or challenges. This may involve evaluating the device's performance against established clinical guidelines or expert opinions, as well as considering the device's potential to fill gaps in clinical practice or enhance existing diagnostic or treatment methods.

Furthermore, the HTA should examine the broader impact of AI-based medical devices on healthcare systems and resource allocation [22]. This includes evaluating the devices' potential to optimize resource utilization, reduce healthcare costs, or improve workflow efficiency. Economic evaluations, such as cost-effectiveness analyses, can provide insights into the value for money and long-term cost savings associated with the adoption of these devices [29,30].

A comprehensive HTA should thoroughly assess the clinical effectiveness and impact on patient outcomes of AI-based medical devices, examining their performance in relevant clinical scenarios, their alignment with clinical guidelines, and their potential to improve healthcare processes and resource allocation. By evaluating these aspects, the HTA can provide a holistic understanding of the AI devices' effectiveness and their potential to positively transform healthcare delivery [22].

AI-based medical devices must undergo rigorous clinical validation to assess their performance and reliability in real-world healthcare settings [31,32]. Clinical validation involves evaluating the device's accuracy, sensitivity, specificity, and overall diagnostic or prognostic performance. Additionally, the devices should be tested across diverse patient populations and compared against gold standard reference methods or expert opinions [33].

Furthermore, the use of real-world evidence (RWE) is crucial for a comprehensive HTA [34]. RWE involves gathering data from routine clinical practice, electronic health records, and other sources to evaluate the device's effectiveness and safety in real-world settings [35]. These data can help assess the device's performance in a broader patient population and identify any potential limitations or biases that may arise in specific clinical scenarios.

Robust clinical validation studies and the integration of RWE provide critical evidence for the evaluation of AI-based medical devices in a HTA process [4]. These studies should include a sufficient sample size, appropriate study design, and statistical analysis to ensure the validity and generalizability of the results [36–39]. By considering adapted clinical validation and RWE to AI-

based medical devices, HTA can provide valuable insights into the clinical utility and impact in real-world healthcare settings, facilitating evidence-based decision-making for their adoption and use.

A lack of safety evaluation was highlighted in a systematic review showing that only 9% of AI-based medical devices studies evaluated safety criteria [4]. However, the safety is crucial for the confidence and the adoption of AI-based technologies for both patients and healthcare professionals [40]. While these devices have the potential to improve diagnosis and treatment outcomes, their integration into clinical practice must be accompanied by robust safety evaluations [2,41]. Identifying and mitigating potential risks, such as algorithmic bias, data privacy breaches, and algorithm failures, is essential to protect patient well-being and maintain trust in these innovative technologies [42].

To ensure safety in AI-based MDs, it is crucial to establish standardized evaluation frameworks and guidelines [40]. These frameworks should encompass rigorous testing methodologies, validation procedures, and continuous monitoring of AI performance. Collaboration among stakeholders, including manufacturers, regulatory agencies, healthcare providers, and researchers, is essential to develop and implement comprehensive safety evaluation protocols. Addressing the safety gap in AI-based MDs not only ensures patient welfare but also instills confidence in healthcare professionals to embrace and utilize these technologies effectively [41]. By prioritizing safety evaluation, we can unleash the full potential of AI-based medical devices, leading to transformative advancements in healthcare delivery [1].

1. 3. Domain 5: Costs and economic evaluation

Costs and economic evaluation play a crucial role in the comprehensive assessment of health technology adoption, particularly in the context of health technology assessment of AI-based MDs [4,9,43]. While AI technologies show huge potential to improve healthcare delivery, reduce time to diagnosis and save money, their economic impact requires careful consideration to ensure their successful integration and sustainability [24].

When assessing AI-based MDs through HTA process, economic evaluations involve analyzing the costs and benefits associated with the adoption and utilization of the technology [4]. These evaluations go beyond the upfront costs of acquiring the AI-based MD; they encompass various factors such as training, infrastructure modifications, maintenance, and ongoing operational costs

[44]. Cost analysis also includes improved patient outcomes, reduced hospital readmissions, and shortened hospital stays. By conducting economic evaluations, decision-makers can gauge the cost-effectiveness and cost-utility in order to weigh up the affordability of AI-based MDs for their particular usage, with potential mid- and long-term cost savings considered [45].

HTA evaluates the suitability of AI-based medical devices by considering their potential economic benefits, risks, and ethical implications [46,47]. By incorporating economic evaluation into the HTA process, decision-makers can make evidence-based choices about the allocation of limited healthcare resources and prioritize interventions that provide the greatest value for money [4,48].

Finally, considering cost savings and conducting economic evaluations as part of the HTA process helps to facilitate the adoption of AI-based MDs [38]. It provides decision-makers with the necessary information to determine the financial feasibility and potential return on investment associated with implementing these technologies. HTA ensures that AI-based medical devices are suitable for integration into the healthcare system, fostering confidence in their effectiveness, efficiency and cost-utility [4,44,49].

1. 4. Domain 6 - Ethical analysis / Domain 8- Patients and Social aspects

Ethical and societal implications are critical aspects that must be considered when evaluating the suitability of AI-based medical devices for a comprehensive HTA [46]. The integration of AI technologies in healthcare raises important ethical concerns that need to be addressed to ensure responsible and equitable use [50].

Data privacy and patient consent are primary ethical considerations [51]. The HTA should evaluate whether AI-based MDs adhere to strict data protection regulations, maintain patient confidentiality, and obtain appropriate informed consent for data usage. It is essential to assess whether the devices have mechanisms in place to handle sensitive patient information securely and protect against unauthorized access or data breaches.

Algorithmic fairness and bias are additional ethical concerns [52]. AI algorithms can inadvertently perpetuate biases present in the data used for training, resulting in unequal treatment or access to healthcare resources [53]. The HTA should assess whether the devices have been evaluated for fairness and bias and consider the steps taken to mitigate any identified biases [54].

Moreover, the HTA should examine the impact of AI-based medical devices on healthcare disparities

and access to care [55]. It is crucial to assess whether the devices have the potential to exacerbate existing inequalities or if they can contribute to reducing disparities by improving healthcare access, particularly for underserved populations.

Accountability and transparency in AI decision-making processes are also important ethical considerations [56]. The HTA should evaluate whether the AI devices provide clear explanations for their outputs and ensure that healthcare professionals and patients can understand and challenge the device's recommendations [22].

A comprehensive HTA should thoroughly examine the ethical and societal implications of AI-based medical devices, ensuring that they prioritize patient privacy, fairness, and equitable access to care, fostering trust and ensuring that these devices align with societal values and goals.

To ensure the adoption of AI-based MDs through a truthfully AI concept, explainability, interpretability and transparency are important considerations for their comprehensive HTA [57]. Indeed, these devices often employ complex algorithms and machine/deep learning techniques, resulting in their operating as "black boxes" that reach decisions and recommendations that are challenging to understand [56]. However, explainability and transparency are essential to ensure trust, accountability, and acceptance of AI-based technologies in healthcare.

(i) Explainability refers to the ability to understand and interpret the reasoning behind the device's outputs [57]. It involves providing clinicians and users with transparent explanations of how the AI algorithm processes input data and generates results. This enables healthcare professionals to trust the device's recommendations and make informed decisions based on the provided information. The HTA should evaluate the extent to which AI-based medical devices can provide interpretable and understandable explanations of their decision-making processes [18,47].

(ii) Transparency involves disclosing important information about the AI-based medical device, including the data used for training, algorithmic methodologies employed, and potential limitations or biases [58]. Transparency promotes trust and allows stakeholders to assess the device's reliability and potential risks. The HTA should assess whether the device manufacturers provide clear documentation and information to healthcare professionals and patients about the device's capabilities, limitations, and potential errors [22,59,60]. Transparency is closely linked to regulatory considerations [61,62]. The HTA

should consider whether the device complies with relevant regulatory standards and if the manufacturers have provided the necessary documentation and evidence to support their ethical claims [22,63,64].

A comprehensive HTA process should address concerns regarding explainability and transparency of AI-based MDs, trust, accountability, and ethical implications related to the use of AI in healthcare [46,47].

1. 5. Domain 7- Organizational aspects

Organizational aspects play a crucial role in the effective integration of AI-based medical devices into healthcare systems [65]. To ensure consistency, transparency, and comparability in the evaluation process, there is a growing need for a robust methodological framework that provides standardized guidelines for assessing the organizational impact of the implementation of AI-based MDs [66]. According to a descriptive analysis led in German hospitals, the main barriers to AI-based MDs were lack of resources (staff, knowledge, and financial) [67].

Clear indicators are needed to measure the organizational readiness and impact for AI-based MDs. [4,11,68] Several criteria have been highlighted such as (i) healthcare workplace readiness and stakeholders acceptance; (ii) AI-based MDs' organization alignment assessment and (iii) business plan (financing and investments) [65].

1. 6. Domain 9- Legal aspects

The roles and responsibilities of healthcare professionals are also impacted by these AI solutions [69]. It is necessary to evaluate whether they complement or replace healthcare professionals' expertise, and if additional training, supervision or support is required for their optimal use [70,71]. As AI technologies could evolve and become more prevalent in healthcare, it is crucial to ensure that these devices comply with existing legal frameworks and regulations [50,72]. HTA plays a pivotal role in evaluating the legal implications of AI-based medical devices by assessing factors such as data privacy, security, liability, and regulatory compliance [73].

One key legal aspect to consider is data privacy and protection [74,75]. AI-based MDs often rely on vast amounts of patient data for training and decision-making. Therefore, it is essential to evaluate whether these devices adhere to relevant data protection laws, such as the General Data Protection

Regulation (GDPR) in the European Union [76,77]. HTA examines the measures taken by AI-based MDs manufacturers to safeguard patient privacy, including data anonymization, encryption, and secure data storage practices [38]. These issues are highlighted by the Artificial Intelligence Act published in June 2023 by the European Commission [78,79].

Cybersecurity is another critical consideration [22,80]. As AI-based MDs handle sensitive patient data and make critical healthcare decisions, it is crucial to assess the security measures implemented to prevent unauthorized access, data breaches, or tampering [81]. HTA evaluates the robustness of the security protocols implemented by device manufacturers and their compliance with industry standards and regulations [22,82].

Liability is also a significant legal aspect to be addressed in the context of AI-based MDs [83,84]. When errors or adverse events occur due to the use of these devices, determining liability can be complex [85]. HTA examines the legal frameworks and liability guidelines pertaining to AI technologies, including whether clear guidelines exist regarding the responsibility of manufacturers, healthcare providers, and users in case of device malfunctions or errors [86]. Assessing liability aspects within the HTA process helps establish accountability and ensures that legal frameworks adequately address potential risks [87].

Regulatory compliance is a crucial consideration when assessing the suitability of AI-based MDs for HTA [88]. Depending on the jurisdiction, AI devices need to undergo regulatory approval processes before being introduced into the market [89]. HTA examines whether AI-based MD manufacturers have obtained the necessary regulatory approvals, such as clearance from the relevant health authorities or certification from regulatory bodies like the Food and Drug Administration (FDA in the USA) or Notified Bodies in Europe [90]. This evaluation ensures that AI-based MDs comply with existing regulations and are fit for clinical use [62].

DISCUSSION

1. *Recommendations to adapt the nine HTA domains for AI-based MDs*

Taking into account the previous considerations, some recommendations could be proposed to adapt and to personalize the health technology assessment of these standard HTA domains to AI-based

MDs specificities. We therefore suggest four main recommendations by domain in table 3.

Adaptation of the HTA process through a methodological framework for AI-based MDs enhances the comparability of results across different evaluations and jurisdictions [91–93]. It promotes consistency in the assessment methodologies, reporting formats, and presentation of findings, enabling decision-makers to make informed choices based on reliable and comparable evidence. This standardization contributes to the overall credibility and acceptance of HTA outcomes related to AI-based medical devices [94]. Additionally, a methodological framework would address the need for appropriate expertise and skills to conduct the HTA of AI-based medical devices [95–100]. It would outline the qualifications and competencies required for the individuals involved in the assessment, including knowledge of AI technologies [47]. By defining the necessary expertise, the framework supports the development of a skilled workforce capable of conducting robust and reliable HTAs of AI-based medical devices (Figure 3).

Evaluating the trade-offs and weighing different features of AI-based MD is indeed a complex and important task, especially in domains like healthcare where the impact on human lives is significant. The acceptability of AI-based MD should be assessed on a case-by-case basis, considering various factors, including for instance performance, accuracy, cost, explainability, and the specific context in which it is being used.

Trade-offs between accuracy and cost are common in AI. It may be acceptable for AI to increase follow-up care costs if it significantly improves accuracy and patient outcomes. For example, if an AI system can detect diseases at an earlier stage, it might lead to more effective treatment and ultimately lower overall healthcare costs in the long run.

The balance between explainability and performance is a critical consideration. While explainable algorithms are preferred for safety and transparency reasons, there may be cases where a highly complex, unexplainable algorithm outperforms explainable ones. In such cases, the trade-off between transparency and performance should be carefully evaluated based on the specific use case and potential risks.

The minimum performance for adding this technology to the human clinician available tools depends on the specific task and the level of trust that patients, healthcare providers, and regulators have in the technology. Some key factors to consider include:

(i) The complexity of the task: AI-based MD should excel in tasks that are well-defined and data-driven, but it may not replace human clinicians in tasks requiring complex decision-making, empathy, or ethical considerations.
(ii) Safety and reliability: AI-based MD should demonstrate a high level of safety and reliability, ideally surpassing the performance of human clinicians in terms of avoiding errors.
(iii) Ethical considerations: AI-based MD should adhere to ethical standards, including patient privacy, informed consent, and unbiased decision-making, which are often considered even more important than performance metrics.
(iv) Regulatory approval: Regulatory bodies often establish performance thresholds for AI-based MD. Compliance with these thresholds is essential for market acceptance.

In general, AI should aim to complement and enhance the capabilities of human clinicians rather than completely replacing them. The specific threshold for acceptable performance will vary across applications and contexts, and it should be determined through a combination of rigorous testing, peer-reviewed studies, and input from healthcare professionals and patients.

It's important to note that ethical considerations, patient safety, and the potential for bias should always be at the forefront of these discussions, and AI-based MD should not be adopted solely for the sake of automation or cost reduction if it compromises these critical aspects of healthcare.

2. *Use case of the application of the previous HTA recommendations for AI: AI-based MD in diabetic patient pathways*

Concerning the HTA domain 3 on safety of an AI-based MD, the potential risk on patient injury of an insulin delivery AI-based MD system should be taken into account in the risk management process of the algorithm development.[97] In case of an evolutive deep learning-based MD without continuous ongoing safety assessment, a wrong dosage administration due to an AI error, for instance, could provoke serious adverse event such as an acid ketosis coma for a diabetic patient.
A risk management plan should be available for users and regularly updated with AI changes impact on safety plan.

In relation to the HTA domain 4 which focuses on effectiveness of an AI-based MD, the FDA in the USA proposed a regulatory Framework for modifications to evolutive AI/ML-based Software as a

MD with modifications guidance focuses on the risk to users/patients resulting from the AI change [101]. They asked for Algorithm Change Protocol with specific methods in place to achieve and control the risks of the anticipated types of modifications related to performance, use, or inputs. The continuous clinical effectiveness assessment could be an interesting approach for a detection AI-based MD system of diabetes foot ulcer for patient needing adaptative treatment modifications to prevent ulcer development [102].

Concerning the HTA domain 5, to evaluate diabetic retinopathy screening AI-based MD, clinical effectiveness is not sufficient. The cost-effectiveness of different AI diabetic retinopathy screening should be compared with no screening and ophthalmologist screening. A recent study demonstrated that the AI-based screening was the most cost-effective, which not only saved costs but also improved the quality of life of diabetes patients [45]. In this case, the long-term assessment of economic impact of AI introduction in diabetic retinopathy screening highlighted the added value of this technology.

The HTA domain 7 on organizational impact has to assess how the AI-based MD can be effectively integrated in the healthcare pathway and prevent wasteful spending. More thorough attention must be paid to the following aspects: (1) Evaluating needs and determining the added value of the implementation of the AI-based MD; (2) Assessing workplace preparedness, including stakeholder acceptance of the introduction of the AI-based MD and involvement; and (3) Analyzing the alignment between AI technology and organizational structure [65]. Decision-makers and technology advocates need to address the complexities of AI more comprehensively and understand the systemic challenges that its adoption poses in healthcare organizations and systems.. As an example, consider an AI tool used for diagnosing diabetic retinopathy in a primary care setting, such as by a family doctor or nurse [103]. In theory, this could lead to shorter waiting times for patients. However, if the healthcare organization faces challenges like a shortage of specialized staff (for example, ophthalmologists), insufficient organization of care pathways, and lack of specialized facilities for proper management and follow-up after diagnosis, the introduction of AI might adversely affect the quality of care and patient experience. In such a scenario, the AI application might merely transfer the delay from primary to secondary care, failing to address the fundamental issue.

Finally, concerning the last domains 6, 8, 9 about ethical, patient, social and legal aspects, continuous glucose monitoring and insulin pumps represent additional applications [104]. While citizen juries

have generally shown support for AI in research and treatment, concerns remain. The risks of data theft and privacy breaches necessitate careful consideration of ethical and legal issues to patients. Although AI can aid in decision-making, it cannot wholly substitute a physician's expertise. Effective regulations and systems designed to ensure safety, reduce bias, and enhance transparency are essential.

By implementing these recommendations, stakeholders can foster the responsible integration, regulation, and evaluation of AI-based medical devices. These measures can enhance the evidence base, address ethical concerns, and maximize the potential benefits of these AI technologies in improving healthcare outcomes, while safeguarding patient safety, privacy, and equity.

3. *Practical challenges and potential barriers to implementing HTA specific for AI-based MD*

When it comes to implementing specialized HTA for AI-based MD, several practical challenges and potential barriers could be encountered and should be taken into account:

1. AI technological evolution timeline: AI technologies evolve at a much faster pace compared to traditional medical devices, making it challenging for HTA frameworks to keep up with the latest developments and assess their long-term impact effectively. The AI-based MDs has short product lifetime, between 12 and 18 months, contrary to drug products. This shorter lifetime cycle highlighted the need of evolutive and fast track HTA process for AI-based MDs.
2. Data Requirements and Quality: AI systems rely heavily on large datasets for training and validation. Ensuring the availability of high-quality, representative data is a significant challenge. There is also the issue of data privacy and security, which must be addressed. The availability and quality of data and evidence required for conducting HTA on AI-based MDs present a complex and evolving landscape. Assessing the feasibility and challenges associated with gathering such data is crucial for robust evaluations. Firstly, the availability of data can vary significantly depending on the AI-based MD. While some devices may have access to vast amounts of high-quality real-world patient data, others might face limitations due to the novelty of the technology or issues related to data privacy. Secondly, the quality of data is paramount, as inaccurate or biased data can lead to flawed assessments. Ensuring data accuracy, representativeness, and relevance is a constant challenge in AI-based MD evaluations [105]. The rapid pace of AI development can result in limited long-term data,

making it difficult to assess the device's sustained performance and safety [106]. Balancing the need for robust evidence with the dynamic nature of AI technologies is a significant challenge that HTA organizations must address to provide valuable insights for informed decision-making in healthcare.

3. Complexity and Transparency: The complex algorithms used in AI-based MDs can be difficult to understand and assess, leading to issues with transparency and explainability [107]. This complexity can pose a challenge for regulators and assessors in HTA processes.
4. Clinical Validation and Safety requirements: Generating robust clinical evidence to demonstrate the safety, efficacy, and effectiveness of AI-based MDs can be challenging. This includes proving that these devices perform consistently across diverse patient populations. Moreover, to account for a lifecycle that would include updates that may improve performance, one solution to investigate could be the Food and Drug Administration in the USA proposition in 2019 to experiment a “dynamic certification” [101]. It allows to re-evaluate the AI-based MD if the AI algorithm could impact a substantial modification of the indication, or the way to deliver the diagnosis, for instance
5. Regulatory and Ethical Considerations: Adapting existing regulatory frameworks to accommodate AI-based MDs, addressing ethical concerns like bias, and ensuring equitable access are critical challenges [108].
6. Economic Evaluation: Determining the cost-effectiveness of AI-based MDs, especially when benefits might be indirect or long-term, poses a unique challenge for HTA [94].
7. Stakeholder Engagement and Trust: Building trust among healthcare providers, patients, and policymakers regarding the reliability, trustworthiness and usefulness of AI-based MDs is crucial but challenging [109].
8. Integration into Healthcare Systems and interoperability: The integration of AI-based MDs into existing healthcare workflows and systems can be complex and resource-intensive [19].
9. Global and Local Applicability: Ensuring that AI-based MDs are effective and appropriate for use in different global and local contexts, considering varying healthcare systems and population needs, is another significant barrier.

Practically, one suggestion to implement such framework could be to implement these recommendations in the future European clinical joint assessment guidelines. As it is being currently discussed in a European project on a common HTA process for connected medical device which includes AI-based MDs, it could be the opportunity to tackle these challenges at the European level [110].

Addressing these challenges requires a concerted effort from regulators, healthcare providers, technology developers, and other stakeholders in the healthcare ecosystem.

CONCLUSION

AI-based medical devices have the potential to transform healthcare delivery, but the suitability of the current comprehensive HTA requires careful adaptation of the evaluation across the 9 dimensions. While these AI devices show promise in improving accuracy, safety, and efficiency, there is a need for robust clinical validation, integration into workflows, economic evaluation, and addressing ethical and legal implications. A comprehensive adapted HTA framework for AI-based medical devices can provide valuable insights into the effectiveness, cost-effectiveness, and societal impact of AI-based medical devices, guiding their responsible implementation and maximizing their benefits for patients and healthcare systems.

Conflict of interest disclosure: The authors declare no conflict of interest with this work.
Funding statement: This research received no external funding.
Ethical Approval: not applicable
Author Contributions: Conceptualization: L.F., AV; methodology: L.F. and A.V.; articles selection: L.F., A.V., N.M., I.B., writing – original draft preparation: L.F. and A.V.; writing-review and editing: N.M., I.B., validation: L.F. and A.V. The authors have read and agreed to the published version of the manuscript.
Acknowledgement: not applicable

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Figure 1: Occurrences of “technology assessment” AND “medical device” AND “artificial intelligence” from inception to October2023 in Pubmed literature

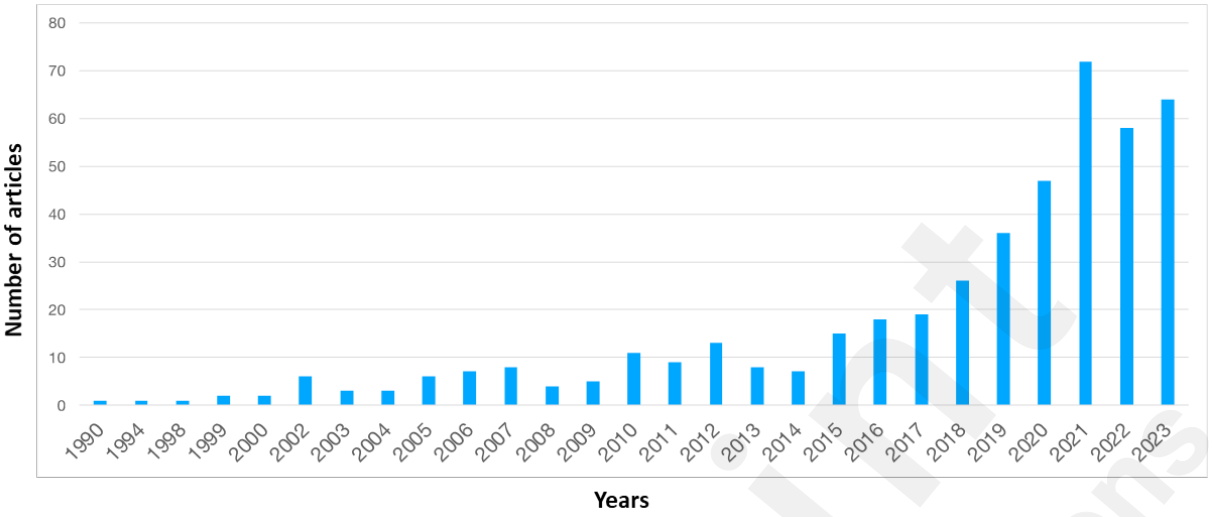


Figure 2: PRISMA flow chart for study selection process

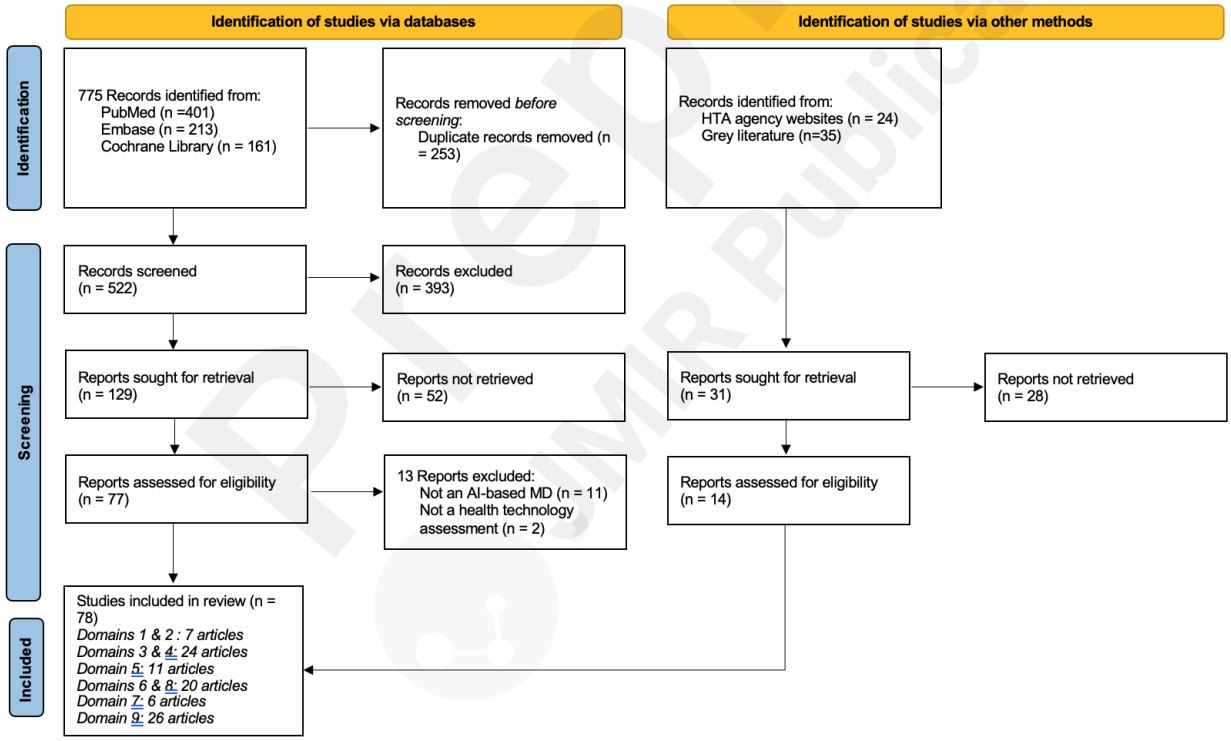
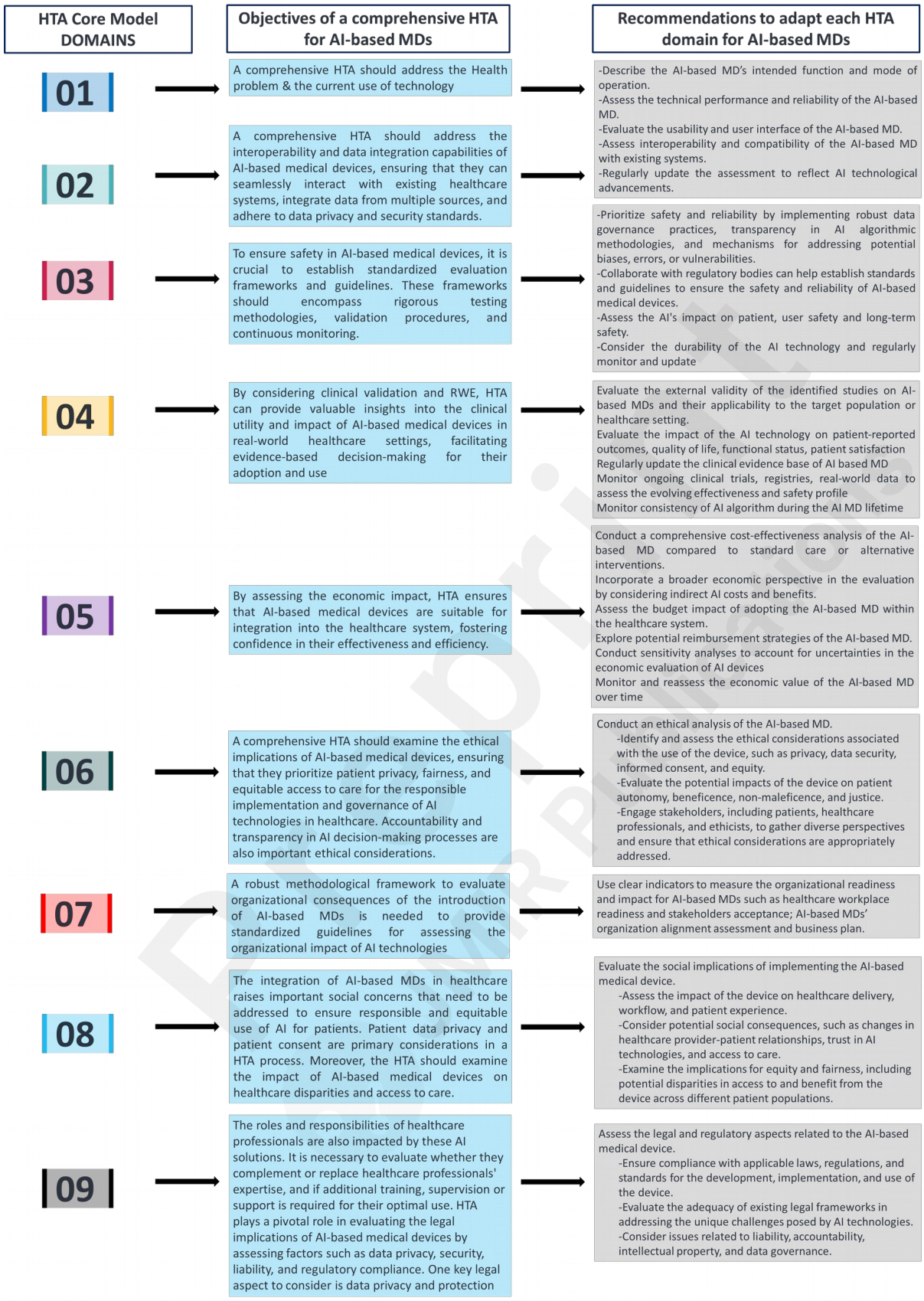


Figure 2: PRISMA flow chart for study selection process

From: 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. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Figure 3: Suggested recommendations to adapt each standard Health Technology Assessment (HTA) domain for the evaluation of Artificial Intelligence-based Medical Devices



*Supplementary file 1 - Table 1: Nine health technology assessment domains for the assessment of AI-based medical devices, adapted from the Health Technology Assessment (HTA) Core Model® proposed by European network HTA**

HTA Domain	Title
Domain 1	Health problem and current use of the technology
Domain 2	Description and technical characteristics of technology
Domain 3	Safety
Domain 4	Clinical effectiveness
Domain 5	Costs and economic evaluation
Domain 6	Ethical analysis
Domain 7	Organizational aspects
Domain 8	Patients and Social aspects
Domain 9	Legal aspects

*Reference: HTA Core Model® - EUnetHTA. 2018.https://www.eunethta.eu/hta-core-model/ (accessed 3 Jun2023)

Supplementary file 2: Table 2: Summary results of the scoping review and general characteristics of the studies included in the scoping review

General characteristics of the studies included in the scoping review

Authors	Publication date	Journal	Objective	HTA Assessment Domain for AI-based MDs related to each article
Bajwa J. et al.	2021	Future Healthc J	To examine how artificial intelligence (AI) is transforming the practice of medicine and to discuss the implications of AI in healthcare.	Domains 3 & 4
Bohr A. et al.	2020	Artif Intell Healthc	To explore the emergence and rise of AI in healthcare applications and its potential impact on the sector.	Domains 3 & 4
Farah L. et al.	2023	Artif Intell Med	To evaluate whether current clinical studies on AI-based medical devices are comprehensive enough to support a full health technology assessment.	Domains 3 & 4, 5, 7
Chen Y. et al.	2022	Integr Med Res	To discuss if the principles of health technology assessment and economic evaluation are applicable to traditional medicine.	Domain 5
He J. et al.	2019	Nat Med	To provide insights into the practical implementation of AI technologies in medicine.	Domains 1 & 2, 7
Farah L. et al.	2023	Mayo Clin Proc Digit Health	To assess the performance, interpretability, and explainability of AI-based health technologies and to inform healthcare stakeholders about what they need to know	Domains 1 & 2, 6&8
Lehne M. et al.	2019	NPJ Digit Med	To argue why digital medicine requires interoperability to succeed.	Domain 1 & 2
Esmaeilzadeh P. et al.	2020	BMC Med Inform Decis Mak	To investigate consumers' perspectives on the use of AI-based tools for healthcare purposes.	Domain 1 & 2
Zia A. et al.	2022	J Pers Med	To delve into the application of AI in medical data mining.	Domain 1 & 2
Ming J. et al.	2022	Cost Eff Resour Alloc	To provide an overview of the current landscape, challenges, and future directions in health technology assessment of medical devices.	Domains 1 & 2, 3& 4, 6&8, 9
Filkins BL. et al.	2016	Am J Transl Res	To discuss privacy and security concerns in digital health and what translational researchers should know and do about it.	Domain 1 & 2

Johnson KB. et al.	2021	Clin Transl Sci	To explore the implications of precision medicine and AI for personalized health care.	Domains 3&4,5
Sloane EB. et al.	2020	Clin Eng Handb	To examine the role of AI in medical devices and clinical decision support systems.	Domains 3 & 4
Steuten LMG. et al.	2016	OMICS J Integr Biol	To assess the early stages of health technology assessment for precision biomarkers in oral health and systems medicine.	Domains 3 & 4
Javaid M. et al.	2022	Int J Intell Netw	To highlight the significance of machine learning in healthcare and discuss its features, pillars, and applications.	Domains 3 & 4
Rowland SP. et al.	2020	NPJ Digit Med	To evaluate the clinical value of mobile health (mHealth) for patients.	Domains 3 & 4
Voets MM. et al.	2022	Value Health J Int Soc Pharmacoeconomics Outcomes Res	To conduct a systematic review of health economic evaluations focused on AI in healthcare.	Domains 3 & 4
Kirisits A. et al.	2013	Appl Health Econ Health Policy	To address the economic evaluation challenges ahead for medical devices.	Domains 3 & 4
Park SH, et al.	2021	Korean J Radiol	To discuss the key principles of clinical validation, device approval, and insurance coverage decisions for artificial intelligence in healthcare.	Domains 3 & 4
Tsopra R, et al.	2021	BMC Med Inform Decis Mak	To propose a framework for validating AI technologies in precision medicine, considering insights from the European ITFoC consortium.	Domains 3 & 4
Bolboacă SD	2019	Comput Math Methods Med	To review the anatomy of medical diagnostic tests, the phases involved, and the statistical treatment of data.	Domains 3 & 4
Hogervorst MA, et al.	2022	Front Pharmacol	To examine the use of real-world data in health technology assessment, particularly for complex health technologies.	Domains 3 & 4
Simon GE, et al.	2022	Clin Pharmacol Ther	To discuss when real-world data can be trusted for evaluating new medical treatments.	Domains 3 & 4
Pongiglione B, et al.	2021	Int J Technol Assess Health Care	To evaluate if existing real-world data sources are suitable for HTA of medical devices in Europe.	Domains 3 & 4
Pongiglione B, Torbica A	2022	Health Econ	To explore the potential of routinely collected administrative data for generating real-world evidence for medical device evaluation.	Domains 3 & 4
Zemplényi A, et al.	2023	Front Public Health	To offer recommendations for overcoming barriers in using AI-driven evidence in health technology assessment.	Domains 3 & 4, 5, 9
Daubner-Bendes R, et al.	2020	Front Public Health	To discuss the methodological challenges and recommendations for HTA of medical devices in Central and Eastern Europe.	Domains 3 & 4
Larson DB, et al.	2021	J Am Coll Radiol	To summarize and recommend regulatory frameworks for the development and evaluation of AI-based diagnostic imaging algorithms.	Domains 3 & 4
Choudhury A, Asan O	2020	JMIR Med Inform	To review the role of AI in improving patient safety outcomes.	Domains 3 & 4
Belenguer L	2022	AI Ethics	To explore discriminatory algorithmic decision-making models in AI and propose machine-centric solutions adapted from the pharmaceutical industry.	Domains 3 & 4
Binder L, et al.	2022	Curr Oncol	To assess the impact of changes in the Health Technology Assessment process for oncology drugs on public payer reimbursement recommendations.	Domain 5
Wolff J, et al.	2020	J Med Internet Res	To systematically review the economic impact of AI in healthcare.	Domain 5
Abràmoff MD, et al.	2022	NPJ Digit Med	To propose a reimbursement framework for healthcare AI technologies.	Domain 5
Bélisle-Pipon J-C, et al.	2021	Front Artif Intell	To discuss what makes AI exceptional in health technology assessment.	Domains 5, 6 & 8

Alami H, et al.	2020	J Med Internet Res	To anticipate the complexities that artificial intelligence brings to health technology assessment.	Domain 5, 6&8
Love-Koh J, et al.	2018	PharmacoEconomics	To evaluate the potential impacts of precision medicine on health technology assessment.	Domain 5
Gomez Rossi J, et al.	2022	JAMA Netw Open	To assess the cost-effectiveness of AI as a decision-support system in the detection and grading of melanoma, dental caries, and diabetic retinopathy.	Domain 5
Naik N, et al.	2022	Front Surg	To discuss legal and ethical considerations of AI in healthcare and who is responsible.	Domains 6 & 8, 9
Haynes CL, et al.	2007	J Med Ethics	To explore the legal and ethical considerations of processing patien - identifiable data without consent.	Domains 6 & 8
McCradden MD, et al.	2020	Lancet Digit Health	To address the ethical limitations of algorithmic fairness solutions in healthcare machine learning.	Domains 6 & 8
Gianfrancesco MA, et al.	2018	JAMA Intern Med	To identify potential biases in machine learning algorithms using electronic health record data.	Domains 6 & 8
Fletcher RR, et al.	2021	Front Artif Intell	To address fairness, bias, and the appropriate use of AI and machine learning in global health.	Domains 6 & 8
Tachkov K, et al.	2022	Front Public Health	To identify barriers to using AI methodologies in health technology assessment in Central and East European countries.	Domains 6 & 8
Durán & Jongsma et al.	2021	J Med Ethics	The objective is to explore the epistemological and ethical foundations of trust in medical AI, particularly addressing the fear of opaque algorithmic processes.	Domains 6 & 8
Amann et al.	2020	BMC Med Inform Decis Mak	To provide a multidisciplinary perspective on explainability in AI for healthcare, suggesting that comprehensibility of AI systems is crucial for their ethical and practical integration into clinical practice.	Domains 6 & 8
Kiseleva et al.	2022	Front Artif Intell	To provide input on the transparency of AI in healthcare, describing it as a multilayered system of accountabilities, and discusses the balance between legal requirements and technical limitations.	Domains 6 & 8
Baltaxe et al.	2023	J Med Internet Res	To assess medical device software used in chronic patient care at a tertiary hospital, aiming to evaluate its support of health care services.	Domains 6 & 8
Garfield et al.	2016	Value Health J Int Soc Pharmacoeconomics Outcomes Res	to addressthe practices, challenges, and recommendations for health technology assessment (HTA) of molecular diagnostics within the context of medical devices and diagnostics.	Domains 6 & 8
Fraser et al.	2023	Expert Rev Med Devices	The paper reviews definitions, expert recommendations, and regulatory initiatives regarding AI in medical device software and high-risk medical devices.	Domains 6 & 8
Beckers et al.	2021	Phys Medica PM	To discuss the implications of the EU medical device regulation for AI-based medical device software in medical physics.	Domains 6 & 8, 9
Melvin & Torre et al.	2019	EFORT Open Rev	To provide insights from the regulator's perspective on new medical device regulations.	Domains 6 & 8
Fleetcroft et al.	2021	BMJ Surg Interv Health Technol	To suggest use of the IDEAL framework as a guide to design clinical device studies in accordance with the new European Medical Device Regulation.	Domains 6 & 8
Alami et al.	2020	J Health Organ Manag	To investigate organizational readiness for AI in healthcare, providing insights for decision-making and practice.	Domain 7
Segur-Ferrer et al.	2022	JMIR Res Protoc	To outline methodological frameworks and dimensions for digital health technology assessment.	Domain 7
Weinert et al.	2022	JMIR Med Inform	To analyze the perspective of IT decision-makers on factors influencing the adoption and implementation of AI technologies in German	Domain 7

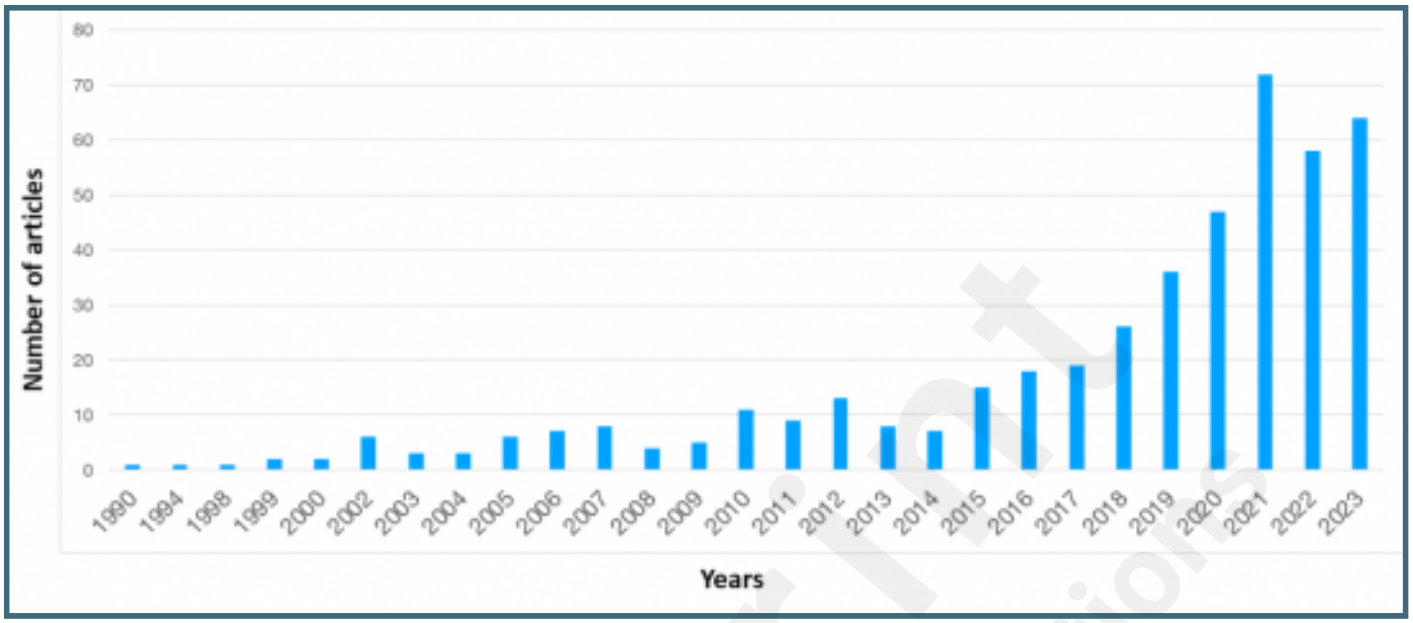
			hospitals.	
de Hond et al.	2022	NPJ Digit Med	To provide a scoping review of guidelines and quality criteria for AI-based prediction models in healthcare.	Domain 7
Ahuja et al.	2019	PeerJ	To examine the impact of AI in medicine on the future role of physicians.	Domain 9
Widrig & Tag et al.	2014	Int J Technol Assess Health Care	To propose a framework for identifying legal issues in health technology assessment.	Domain 9
Vella Bonanno et al.	2019	Expert Rev Pharmacoecon Outcomes Res	To reflect on opinions of policymakers, payers, and academics in the field of HTA concerning a proposal for a regulation on HTA in Europe.	Domain 9
McKee & Wouters et al.	2022	Int J Health Policy Manag	To discuss the challenges of regulating AI in healthcare.	Domain 9
Hordern et al.	2016	Eur J Health Law	To delve into data protection compliance in the context of digital health.	Domain 9
Stanberry et al.	1998	J Telemed Telecare	To discuss data protection, security, and European law in relation to telemedicine.	Domain 9
Poullet et al.	1991	Stud Health Technol Inform	To address legal aspects of data protection in medical informatics.	Domain 9
Dove & Chen et al.	2020	J Law Med Ethics J Am Soc Law Med Ethics	To discuss the extent to which the EU General Data Protection Regulation applies to citizen scientist-led health research with mobile devices.	Domain 9
Marovic & Curcin et al.	2020	JMIR Med Inform	To examine the impact of GDPR on health data management in Serbia, a European Union candidate country.	Domain 9
European commission	2023	European commission website	To promote regulation on AI at a european level	Domain 9
European parliament	2021	Eureopean parliament website	To act harmonised rules on AI in European Union	Domain 9
Camara et al.	2015	J Biomed Inform	To lead a survey focusing on security and privacy issues in implantable medical devices.	Domain 9
Migliore et al.	2009	Expert Rev Med Devices	To discuss the management of the introduction and use of medical devices in clinical practice in Italy, within the context of Health Technology Assessment.	Domain 9
Pisapia et al.	2022	Clin Chem Lab Med	To discuss the novelties of the regulation on health technology assessment and its importance for EU health policies.	Domain 9
MALIHA G et al.	2021	Milbank Quarterly	To discuss the balance between ensuring safety and fostering innovation in the application of artificial intelligence (AI) in medicine, with a focus on legal aspects and liability.	Domain 9
Jassar S et al.	2022	Healthcare Management Forum	To seem to be to explore the future of AI in medicine from a legal perspective, particularly regarding the implications for health leaders.	Domain 9
Samore MH et al.	2004	Journal of the American Medical Association	To discuss the surveillance of medical device-related hazards and adverse events in hospitalized patients, which may involve AI technology.	Domain 9
Bleher H, et al.	2022	AI Ethics Journal	To investigate how responsibility is assigned when AI-driven clinical decision support systems are used, addressing the concept of diffused responsibility.	Domain 9
Street J et al.	2020	International Journal of Technology Assessment in Health Care	To define the role of the public in Health Technology Assessment (HTA) and decision-making processes informed by HTA, potentially in the context of AI technologies.	Domain 9
Massella M et	2022	Health Technology	To discuss regulatory considerations for the use of machine learning	Domain 9

al.			tools in clinical trials, indicating a focus on compliance and regulatory frameworks.	
Marcus HJ et al.	2016	The British Medical Journal	To seem to be an examination of the processes for regulatory approval of new medical devices, which may include AI-powered devices.	Domain 9
Milam ME, et al.	2023	Clinical Radiology	To summarize the current status and future perspectives of FDA-approved AI tools in chest radiology within the United States.	Domain 9

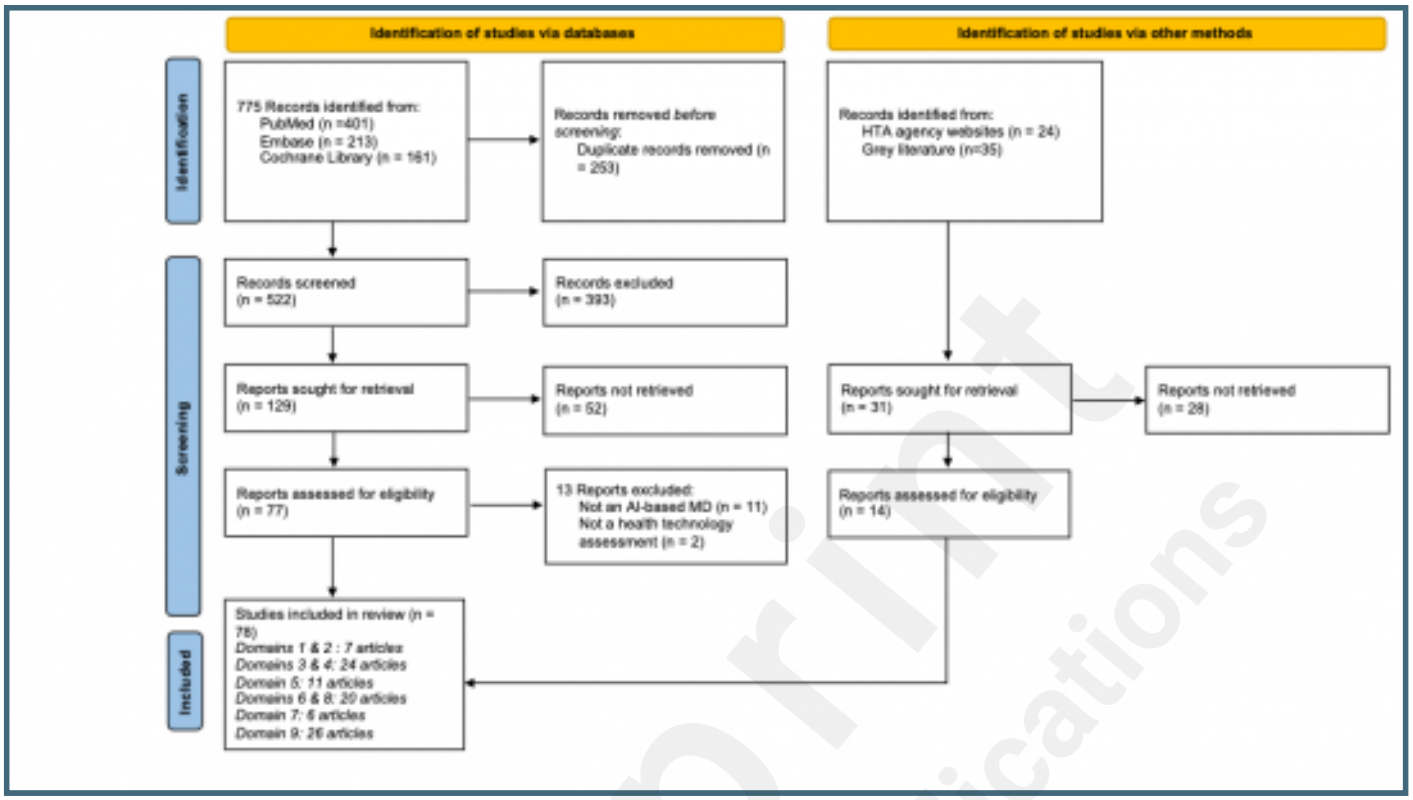
Supplementary Files

Figures

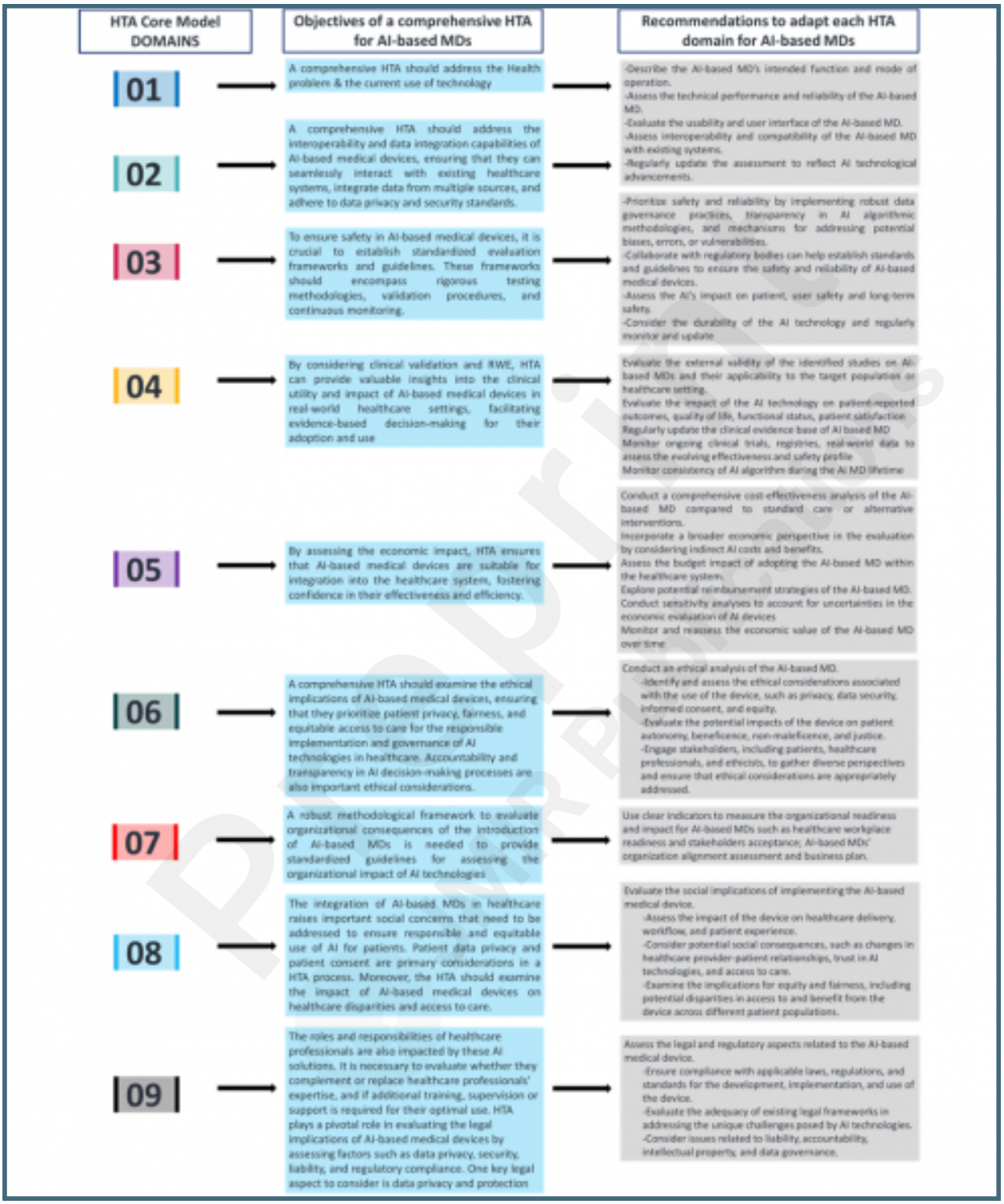
Occurrences of “technology assessment” AND “medical device” AND “artificial intelligence” from inception to October 2023 in Pubmed literature.



PRISMA flow chart for study selection process.



Suggested recommendations to adapt each standard Health Technology Assessment (HTA) domain for the evaluation of Artificial Intelligence-based Medical Devices.



Multimedia Appendixes

Table 1: Summary of different frameworks on AI-based health technologies.
URL: http://asset.jmir.pub/assets/e1d8ec3209f4723cd8d5bbe3326e59c7.docx

Table 2: Search strategies and MeSH terms used for the systematic literature review.
URL: http://asset.jmir.pub/assets/a595bbdcde56da092eaf81f21dc8b9bd.docx

Table 3: Recommendations to adapt and to personalize the health technology assessment of standard HTA domains to AI-based MDs specificities.
URL: http://asset.jmir.pub/assets/1da5cde2c798f5be717773730170fdd1.docx

Supplementary file 1 - Table 1.
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Supplementary file 2 - Table.
URL: http://asset.jmir.pub/assets/bbb8533a0031412aa256c643e16e0ea0.docx