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INTEGRATING ETHICAL ANALYSIS IN HEALTH TECHNOLOGY ASSESSMENT: OPPORTUNITIES AND CHALLENGES

Running title: The role of ethics in HTA

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Abstract

Ethics has been recognized as an integral part of Health Technology Assessment (HTA) since its beginning. However, the integration of ethical analysis in HTA practice has been limited and challenging. Members of the Health Technology Assessment international (HTAi) Interest Group (IG) for Ethical Issues in HTA reflected upon this situation, during a workshop and online meetings, to identify which challenges hinder integration of ethics in HTA and how to move the discipline forward. In this paper, we present the results of that discussion, describing different ways that ethical analysis can occupy a more central role in HTA practice. We also describe developments in HTA that create a momentum for reflecting upon such integral role for ethical analysis in HTA: artificial intelligence-based health technologies, changes in the evidence landscape, assessing the environmental impact of health technology, and the new EU regulation on HTA.

Keywords: health technology assessment, ethics, research ethics, health policy, artificial intelligence

Introduction

Since its origin, Health Technology Assessment (HTA) has been conceptualized as a multidimensional process extending beyond clinical and economic assessment, including ethical analysis as a fundamental component (1). The internationally accepted definition of HTA also underscores this central role of ethical analysis in assessing the value of a health technology and highlights its importance regarding the objectives of HTA itself, i.e., *to promote value* by ensuring an equitable, efficient, and high-quality healthcare system (2).

Despite these foundational premises and efforts of collaborative initiatives, such as the International Network of Agencies for Health Technology Assessment (INAHTA) and the EUnetHTA Core Model[®], the integration of ethical analysis (i.e., the systematic identification, articulation, and evaluation of ethical questions that arise in the assessment of health technologies) in HTA practice remains underdeveloped. Several reviews of published HTA reports showed an underrepresentation of ethics, a diversity of methods used, and unclarity about the role of ethical analysis in HTA (3-5).

This trend appears paradoxical for at least two reasons. First, an examination of its historical roots reveals that HTA emerged in response to ethical concerns arising from the rapid proliferation of health technologies (1).

Second, HTA is an *evaluative process* whose purpose is to assess the *value* of health technologies (6;7). This requires assessing potential changes, induced by health technology, *that matter*. Changes

generated by health technology can matter for all sorts of reasons. There may be less pain or suffering, preservation or restoration of function, less inequity, and there may be less waste. The relevance of these changes originates from moral commitments, e.g., we assess changes related to safety because we *want to avoid harm*. Therefore, it is an inherently normative type of inquiry because it is underpinned by an understanding of what makes a health technology (un)desirable (6;7). Because there are many modes of evaluation, and not all modes are equally suited for HTA, it also involves determining the norms by which we evaluate health technologies.

Therefore, the persistent underrepresentation of ethical analysis in HTA requires explanation. Several factors have been proposed (3-5;8-10). First, there is no consensus on the role of ethics in HTA. This is exaggerated by different mandates HTA agencies have to conduct substantive ethical analyses. Therefore, the discussion of ethical issues is often delegated to an appraisal committee or addressed implicitly throughout the HTA process, making it invisible in HTA reports. Second, the institutional and political context in which HTA operates – shaped by policymakers' demands for *objectivity* and preferably *quantifiable* outcomes – makes integration of ethical analysis challenging. Because ethics explicitly addresses value issues, it is sometimes positioned as oppositional to other disciplines involved in HTA that (apparently) deliver the required objective data (10). Third, integration of ethical analysis within HTA processes is methodologically complex, with no universally accepted framework. Finally, there are limited resources (time and expertise) available, or allocated by HTA agencies, to conduct substantive ethical assessments.

In this paper, members of the *Health Technology Assessment international (HTAi) Interest Group (IG) for Ethical Issues in HTA* reflect on this underrepresentation of ethics in HTA and propose that ethical analysis should play two central roles: (i) guiding value-laden decisions regarding appropriate HTA methods and frameworks, and (ii) revealing and justifying normative commitments underlying HTA practice. Rather than treating ethics as a separate domain, we argue for its integration across HTA domains and processes. For this purpose, IG members met to discuss best practices and identify opportunities and challenges.

Meetings to discuss the role of ethical analysis in HTA

During a workshop held in Rome, Italy, on March 30 – April 1, 2023, members of HTAi, including ten members of the HTAi IG for Ethical Issues in HTA, discussed current best practices of ethical analyses in HTA and associated challenges. Participants of the workshop represented an interdisciplinary group of experts in ethics, citizen and patient involvement, legal issues, and methodology of HTA. During the workshop, it was concluded that ethical analysis should address value-laden aspects of HTA itself, thus occupying more integral roles.

Building on that idea of more integral roles for ethics in HTA, the Ethics IG Steering Committee met in a series of virtual meetings in 2024-2025 to elaborate what these roles mean and identified opportunities and challenges for integrating ethics in HTA practice. The nine members of the Steering Committee are experts that either work in academia doing research on ethical aspects of HTA or work on ethical analysis at HTA agencies. This paper can be seen as a report from the HTAi Ethics IG on these issues.

Integration of ethical analysis into HTA

A central point of agreement is that ethical analysis should be an *integral*, not separate or additional, part of HTA – helping to identify and guide *value-laden decisions* throughout an HTA process. A decision can be value-laden when it (implicitly) reflects judgments about what is good, just, or important. In HTA, value-laden decisions are made when *scoping* (e.g., which questions should be addressed? Which evidence should be collected?), *conducting* (e.g., what methods should be used?), and *interpreting* (outcomes of) an assessment (e.g., what should we conclude about the value of this health technology?). Ethical guidance should support HTA practitioners in making these decisions.

This conceptualization of ethical guidance is broader than what is commonly characterized as ethical analysis in HTA, and we provide some examples of approaches that illustrate what we mean.

Firstly, the *VALues in Doing Assessments of health TEchnologies* (VALIDATE) approach, developed in an EU Erasmus+ funded project (<https://validatehta.eu>), provides a framework for integrating ethical considerations into HTA practice by conducting an in-depth normative analysis when scoping an assessment (7). By involving and analyzing relevant stakeholder perspectives (e.g., what is *valued* by patients, providers, etc.), different ways of framing the policy problem are uncovered and inform decisions about scope and protocol for an HTA.

Another example is the HTA Core Model[®] that includes ethics as a core domain, offering structured guidance for identifying and analyzing ethical issues raised by a technology but also by the HTA process (11). For example, in an HTA of medical treatments for gender dysphoria, ethical considerations were addressed throughout the HTA process, which demonstrated how ethical analysis could guide HTA and impact its final recommendations (12). Ethics was essential in considering the complexity of the topic and shaping the scope (e.g., definition of the population, identification of relevant outcome measures) of the assessment. It also influenced the final recommendations: by identifying and analyzing concerns regarding autonomy it highlighted that caution regarding irreversible treatment of adolescents should be advised.

Revealing the normative nature of HTA

A second point of agreement is the existence of a growing body of empirical research explicating the leading role of *normative commitments* in HTA practice. This points towards a second role for ethical analysis in HTA: to reveal normative commitments underlying a specific HTA practice, and help evaluating their implications.

Doing HTA inevitably involves *normative judgments* about what makes health technology valuable, how to establish that this value has been realized (e.g., which evidence to collect), and how to derive recommendations concerning the use of health technology (6; 7; 13; 14). Addressing this normative dimension of HTA requires competencies in conducting ethical analysis in HTA, which were developed earlier by members of our IG (15). This includes skills and knowledge for identifying and describing values in HTA, and to analyze and communicate the relative strengths and weaknesses of normative arguments in HTA (15).

We have recently published conceptual frameworks to identify and communicate *normative commitments* that guide HTA practice, clarifying that HTA involves moral and epistemological principles that its practitioners commit to following (13; 14). The next step is to apply these concepts in empirical research on HTA. For example, a comparison of published HTA reports of different HTA organizations on the same drugs showed how value judgments played a role in collecting and interpreting evidence, ultimately leading to divergent conclusions about the drugs' comparative effectiveness (16). Another empirical ethics study on the workings of an HTA agency was helpful in determining whether its methods are aligned with its (publicly communicated) normative commitments, which is a key step in providing moral justifications for its role in decision-making and highlighting areas for improvement (17). Future work could assess whether HTA decisions are aligned with normative commitments of stated policy, potentially illuminating instances where either HTA decisions or policy require revisions.

Current and emerging opportunities and challenges for integrating ethics in HTA

In current HTA ecosystems, several developments occur that create opportunities and challenges for the integration of ethics in HTA.

Artificial intelligence

The rapid development of artificial intelligence-based health technologies (AI-HTs) challenges existing HTA frameworks and processes (18). There is an ongoing discussion about whether and how HTA

should change in response to AI-HTs. Interestingly, this creates a momentum to reconsider the importance of ethics, with experts suggesting a larger role for the assessment of ethical issues (19; 20). In response, our IG is developing a position paper about the role of ethics in assessing AI-HTs.

A key question is whether AI-HTs require new assessment criteria. Scholars suggest that AI-HTs raise *novel issues* that require *new HTA frameworks* (18;19). Also, the European Union decided to fund two projects (<https://assess-dht.eu>; <https://edihta-project.eu>) aiming to develop frameworks for assessments of digital health technologies (DHTs), including AI-HTs, that consider the *addition of new value domains* specific for DHTs. This raises the question of whether these domains reflect truly novel normative commitments or extend existing ones. For example, while ‘explainability’ is often seen as a new ethical issue raised by AI-HTs, recent philosophical work suggests that it can be captured by existing moral principles (21). Such analysis would also benefit HTA: which normative commitments underlie established HTA domains and how do new domains relate to them? The normative relations between these domains remain often under-theorized and call for further analysis.

Ethical analysis could also help operationalizing frameworks for AI-HTs: e.g., what are appropriate evidence requirements? And what are potential implications of adapting HTA processes to developments in AI-HTs? Answering such questions implies a view about how HTA should be done and an explication of its normative commitments.

Changes in the evidence landscape

HTA typically determines the value of a technology by collecting information from randomized controlled trials (RCTs). However, recent progress in the generation, availability, and processing of data (e.g., by using AI) is transforming the evidence landscape of HTA (22; 23). The expansion of databases and platforms, alongside innovations in collecting real-world data (RWD), introduces unprecedented complexity into the debate on what constitutes *robust* evidence. New methods, such as pragmatic trials, observational studies enhanced by AI, and semi-automated systematic reviews, challenge traditional hierarchies of evidence and signal the emergence of a more pluralistic and dynamic evidence paradigm (23).

This raises several ethical concerns. Managing large-scale, fragmented, and heterogeneous datasets increases the potential for inaccuracies and uncertainty. Moreover, unequal data access across countries risks generating asymmetries in the quality, reliability, and comparability of HTA outcomes. Non-RCT evidence, more prone to bias and confounders, raises ethical dilemmas about its appropriate use. Furthermore, the growing reliance on algorithm-driven tools introduces issues of transparency, accountability, and trust. The inner workings of these systems are often opaque, making it difficult to evaluate how conclusions are reached (22).

In this evolving context, ethical analysis offers a critical space for reflecting on these challenges. Ethics may serve as a guiding framework for navigating methodological uncertainties, promoting fairness in the use of data, and strengthening legitimacy of decision-making.

Assessing environmental impact of health technologies?

With healthcare contributing around five percent of global carbon emissions, and environmental issues posing health risks, there is growing debate on whether and how HTA should assess environmental impact (24;25). Both an international HTAi working group and an INAHTA white paper highlight the need for guidance and consensus on when and how to integrate such assessments, including development of value frameworks that can guide its integration (24,25). This is precisely the type of work that can be informed by ethics analysis. It requires explicating normative commitments underlying established criteria in HTA, and how these may be expanded or modified by adding environmental sustainability impact assessments. Ethical analysis can play a crucial role in highlighting values involved and providing structured methods for how to transparently weigh different aspects of value of a health technology. It can support HTA by clarifying value tensions and help decision-makers reflect upon how environmental sustainability relates to other established criteria in HTA.

New EU regulation on HTA

EU Regulation 2021/2282 introduces Joint Clinical Assessments (JCAs) that Member States must accept without duplication, while leaving economic, organizational, ethical, social, and legal assessments to national agencies. This shift may free capacity for ethical analysis but also risks importing value judgments embedded in JCAs that may not reflect values of respective Member States. This import of value judgments in assessments of clinical effectiveness is not a mere theoretical possibility, as a previous comparison of clinical assessments across HTA bodies has shown (16). Therefore, while European countries are adapting their HTA processes to align with the JCA framework, ethical analysis can help individual countries identify and preserve their normative commitments.

Conclusion and recommendations

Ethical analysis in HTA should go beyond addressing ethical issues raised by a specific technology and take on two more integral roles: guiding value-laden decisions throughout the HTA process and clarifying HTA's underlying normative commitments. Our discussion highlighted opportunities and challenges for strengthening these roles.

Adopting these roles for ethical analysis in HTA practice requires capacity-building. This includes defining the necessary expertise for ethics in HTA (15). Given the integral role of ethics in HTA, this is a shared responsibility among all experts involved in HTA. Therefore, HTA practitioners should have a

basic understanding of how to recognize and evaluate value judgments. Ethicists, in turn, should be familiar with HTA processes to provide effective support (15).

Another key requirement is broader recognition among HTA practitioners and policy makers of the need to address value judgments in HTA and to position ethical analysis as cross-cutting element in HTA. Future empirical work on the normativity of HTA can support this shift.

Finally, the benefits of ethical analysis in HTA should be made more visible. Few studies document its real-world impact. Moreover, ethical issues are often addressed in a separate deliberative part of an HTA process, or implicitly in the process, leaving them unrecorded or mostly in confidential meeting minutes. Making these contributions of ethics in HTA more transparent would help to demonstrate its value and strengthen accountability.

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The authors declare none.

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