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Systematic Literature Review

What Is Next for Patient Preferences in Health Technology Assessment? A Systematic Review of the Challenges

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ABSTRACT

Background: Integrating patient preferences in Health Technology Assessment (HTA) is argued to improve uptake, adherence, and patient satisfaction. However, how to elicit and incorporate these preferences in HTA in a systematic and scientifically valid manner is subject to debate.

Objective: This article provides a systematic review of the challenges to integrating patient preferences in HTA that have been raised in the literature about patient preferences in HTA.

Methods: A systematic review of articles published between 2013 and 2017 addressing challenges to the integration of patient preferences in HTA was conducted in 7 databases. All issues with respect to the integration of patient preferences in HTA were extracted and divided into 5 categories: conceptual, normative, procedural, methodological, and practical issues. The issues were ranked according to how often they were mentioned.

Results: Of 2147 retrieved articles, 67 were included in the analysis. Thirty-seven unique research issues were identified. In the majority of the articles, methodological issues were posed (82%), followed by procedural (73%), normative (51%), practical (24%), and conceptual (9%) issues. Frequently posed methodological issues concerned preference heterogeneity and choice of method. Common procedural issues concerned how to evaluate the impact of preference studies and their degree of being evidence based.

Conclusions: This article provides an overview of issues with respect to the integration of patient preferences in HTA procedures. Most issues were of a methodological or procedural nature; yet, the large number of different issues points to the overall importance of further researching the different aspects concerned with patient preferences in HTA. Through its ranking of how many articles mention particular issues, this article proposes an implicit research agenda.

Keywords: health preference research, Health Technology Assessment, patient engagement, patient preferences, research agenda, systematic review.

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Introduction

Health Technology Assessment (HTA) informs reimbursement and coverage decisions on how to allocate healthcare resources to different health technologies by carefully assessing the costs and benefits of health interventions.[1] With the increasing focus on patient preferences in clinical practice guidelines,[2–4] academic research,[5,6] and regulatory decision making,[7–9] it is important that HTA not fall behind.[10] The US Food and Drug Administration defines patient preference information as "qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions."[11] In this context, qualitative assessments usually refer to exploring patient preferences and quantitative assessments for eliciting patient preferences. Not aligning the assessment of health intervention costs and benefits with patient preferences can cause adherence to be very different than expected, and it can explain why many health interventions that have developed throughout the medical product life cycle end up not being used.[12] Other arguments for integrating patient preferences in HTA are that it is considered ethical to listen to the

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patient voice,[13,14] it will increase patient satisfaction,[14,15] and that HTA decision making will be more informed and more transparent with the inclusion of patient-relevant value judgments and experiential data.[13–17]

Although the US Food and Drug Administration has provided guidance on how to use patient preference information in benefit-risk assessments,[11] HTA is still lagging behind. Patients are increasingly being involved in the HTA decision-making process,[18,19] but how to elicit and incorporate patient preferences in a systematic and scientifically valid manner is still subject to debate. For example, Weernink et al.[20] could not find a method that performed well from a statistical and patient burden point of view. Janssen et al.[21] suggested further researching validity and reliability tests for quantitative preference methods. Facey et al.[22] discussed whether and how qualitative, and quantitative, patient preference studies could be considered robust scientific evidence. Hansen and Lee[17] questioned the validity of qualitative research methods. In a recently published editorial, Mott[10] stated that HTA needs "substantive changes" to catch up with regulatory decision making in the incorporation of patient preferences. He mainly questioned how to weigh patient preference information in current HTA procedures. Facey et al.[23] highlighted the "substantial challenges to realizing the goal of informing evidence-based patient-centered policy." The variety of open questions concerning patient preferences in HTA raised by different researchers suggests the need for a comprehensive overview of all challenges in the field. Therefore, the objective of this article is to provide a systematic review of the challenges to integrating patient preferences in HTA raised by literature. By doing so, an implicit research agenda is proposed.

Methods

Study Design

To identify open questions concerning the use of patient preferences in HTA, the following study design was used. First, literature about patient preferences in HTA was identified. Second, the study characteristics of the included literature were elicited. Third, issues related to the integration of patient preferences in HTA, as raised in the literature, were derived. Last, the issues were categorized according to thematic differences and similarities. The results were analyzed on 3 different levels of categorization, namely from broad to specific: "categories," "topics," and "issues." An illustration of the study design can be found in Figure 1.

Identification of Literature

To identify literature about patient preferences in HTA, we conducted a systematic review using the databases Embase, Medline Ovid, Web of Science, Scopus, Cochrane CENTRAL, CINAHL EBSCOhost, and Google Scholar. The search terms can be found in Appendix A in supplementary materials found at https://doi.org/10.1016/j.jval.2019.04.1930.

Articles were deemed eligible if they met the following 6 inclusion criteria. The studies had to concern patient preferences, had to concern HTA, and had to discuss at least 1 issue concerning the integration of patient preferences in HTA. Further, the articles had to be English-language articles, the full text had to be available, and the articles had to be published between 2013 and 2017 because recent publication is inherent to providing a contemporary overview.

After excluding duplicates and articles outside the relevant publication years, 2 of the researchers (S.H. and C.W.) independently reviewed the remaining titles and abstracts for eligibility. If at least 1 of the researchers determined that an article met the eligibility criteria based on title and abstract screening, a full-text screening was done by the researchers. If no consensus could be reached about the eligibility of the full text, a third researcher (E.B.G.) was consulted. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement.[24]

Description of Study Characteristics

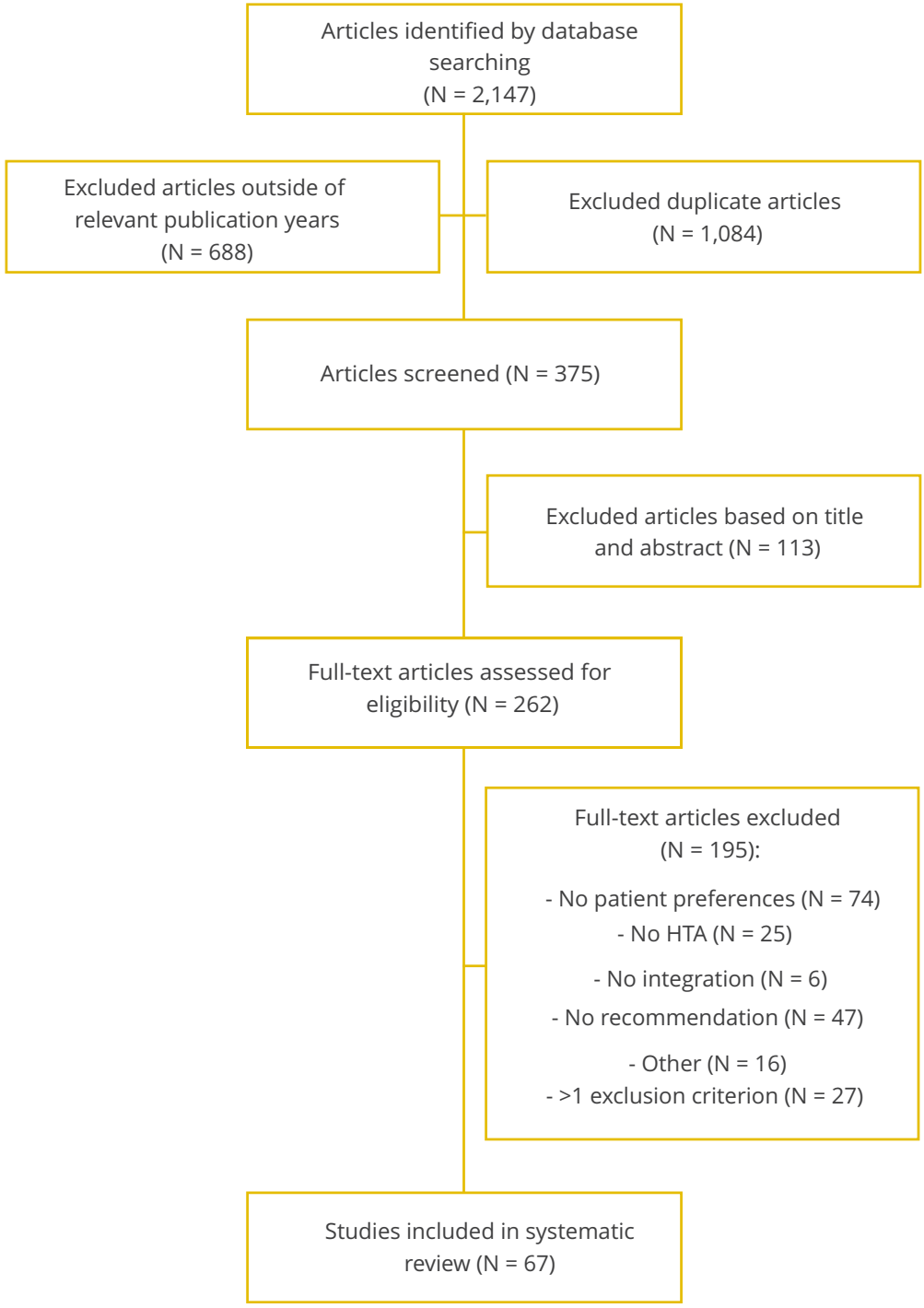
For all eligible articles, 6 study characteristics were extracted. Extracted data included the country in which the first author was employed, whether the study was a theoretical or applied study, the medical context (ie, general or disease-specific) in which the study was conducted, and whether the article concerned qualitative (exploring) or quantitative (eliciting) patient preferences. In addition, we extracted which type of stakeholders raised the issue (eg, respondents or the authors) and for which type of stakeholders the issue was relevant (eg, patients, HTA bodies, or academics). Data were extracted by 1 researcher, after which 2 other researchers validated the findings.

Elicitation of Issues

Issues concerning the integration of patient preferences in HTA were extracted from the literature in the broadest sense (ie, questions, concerns, barriers, facilitators, and areas for further research). All study-specific elements were deleted from the extracted issues to allow for comparison of the issues across

Figure 1. Study design. The 3 different levels of categorization, from broad to specific, were "categories," "topics," and "issues." Elicited issues were subdivided into topics; topics (and their issues) were also subdivided into categories.

Figure 2. Study selection.



studies. Data were extracted by 1 researcher, followed by confirmation of 2 other researchers.

Categorization of Issues

Two researchers (S.H. and C.W.) performed a 3-level categorization of the elicited issues, and a third researcher was consulted if no consensus could be reached. The 3 different levels, from broad to specific, were "categories," "topics," and "issues." Issues were subdivided into topics; topics (and their issues) were also subdivided into categories. Again, an illustration of the study design is presented in Figure 1. To enhance consistency of the categorization process, we defined, before analysis, whether a research issue would fall into only 1 category or topic, respectively. Consensus thus had to be reached on which category or topic best described the issue. As in Utens et al.,[25] we used the following 5 categories as the broadest level of categorization: conceptual, normative, procedural, methodological, and practical issues. Conceptual issues relate to the definition and characterization of patient preferences. Normative issues concern

which members of society should have their preferences elicited. Procedural issues relate to how to integrate patient preferences into the existing procedures of HTA. Methodological issues address establishing good and accurate research practice on the topic. Practical issues address all other concerns of a practical nature such as time and money constraints. The topics were the second level of categorization. Unlike the categories, topics were not predefined and were established using backward induction. The issues were grouped according to thematic similarities and differences; the exact name of the topic was determined after the issues were grouped. Included in the third level of categorization were the issues themselves. The categorized data were analyzed in 2 different ways. First, to give insight into the variety of issues in each category and topic, respectively, the number of issues in each category or topic (as % of the total number of issues) was established. Second, to measure frequency of occurrence of the issues, the number of articles that mentioned each issue (as % of total number of articles) was analyzed.

Results

Identification of Literature

The database search identified 2147 articles, of which 375 unique articles published in 2013 to 2017 were screened. Sixty-seven articles met the inclusion criteria and were subject to data extraction and analysis (Fig. 2).

Description of Study Characteristics

For most of the articles containing issues regarding patient preference in HTA, the first authors worked on behalf of organizations/universities in Canada (n = 13; 19%), the United Kingdom (n = 13; 19%), and Germany (n = 10; 15%) (Table 1). Other common countries of origin were the United States (n = 8; 12%), Australia (n = 7; 10%), and The Netherlands (n = 6; 9%). Three quarters of the articles (51 of 67 articles) discussed the integration of patient preferences in HTA theoretically rather than actually conducting a preference study. Almost two thirds of the articles (n = 44) concerned a general medical context rather than a disease-specific context. Thirty-one articles concerned the qualitative elicitation of preferences (46%), whereas 17 concerned quantitative preference elicitation (25%), 9 concerned both (13%), and 10 did not specify (15%).

Many of the research issues were raised by the authors or authors cited in the articles (n = 52; 78%). The vast majority of first authors (73%) worked in academia; the remainder worked for a variety of organizations (eg, patient organizations, HTA agencies, and private consultants). In the remainder of articles where study respondents were specifically asked about the advancement of patient preference integration in HTA (n = 15, 22%), respondents were HTA professionals (n = 5), patients (n = 4), and a variety of other respondents (eg, healthcare professionals, caregivers, and policy makers, n = 6). Most of the issues were relevant for HTA professionals and academics (n = 34; 51%). Other issues were relevant for HTA professionals only (n = 23; 34%) or for a variety of HTA professionals, clinical guideline developers, patients, patient organizations, or clinicians (n = 10; 15%). Table 1 summarizes these study characteristics; a more elaborate overview of the study characteristics per article is presented in Appendix B in the supplementary materials found at https://doi.org/10.1016/j.jval.2019.04.1930.

Categorization of Issues

Across the 5 categories of identified issues, 16 topics and 37 unique research issues were identified from the total selection of articles. The issues were the most specific level of categorization. These were subdivided into topics. In turn, the topics were subdivided into categories. Table 2 presents a broad overview of the research categories and topics. Table 3 presents the most specific level, namely, the issues. The analysis of the 3 levels of categorization is discussed ranging from broad to specific.

Table 1. Study characteristics—summary.

Item		N = 67*	%†
Country of origin	Canada	13	19
	United Kingdom	13	19
	Germany	10	15
	United States	8	12
	Australia	7	10
	The Netherlands	6	9
	Other	10	15
Type of study	Theoretical	51	76
	Application	15	22
	Both	1	1
Medical context	General	44	66
	Disease specific	23	34
Preference elicitation	Qualitative	31	46
	Quantitative	17	25
	Both	9	13
	Not defined	10	15
Issue raised by stakeholder	Authors and cited authors	52	78
	Respondents: HTA professionals	5	7
	Respondents: Patients	4	6
	Respondents: Other	6	9
Issue relevant for stakeholder	HTA professionals and academics	34	51
	HTA professionals	23	34
	Other	10	15

HTA indicates Health Technology Assessment.
*Absolute number of articles
†Relative number of articles (as % of total of 67 articles). Percentages may not add to 100 because of rounding error.

Categories of identified issues

Of the 37 issues, 1 was conceptual (3%), 5 were normative (14%), 9 were procedural (24%), 18 were methodological (49%), and 4 were of a practical nature (11%) (Fig. 3). In terms of how often the issues were mentioned, methodological issues arose relatively often in the literature—namely, in 55 of 67 articles (82%). Procedural issues were also mentioned frequently (n = 49; 73%). Normative issues were raised relatively less frequently (n = 34; 51%), followed by practical issues (n = 16; 24%) and conceptual issues (n = 6; 9%).

Topics of identified issues

The 16 research topics that were extracted can be found in Table 2. Each of these topics contains between 1 and 4 issues. The establishment of a taxonomy for patient preference studies was the only conceptual topic that was raised. It was raised in 6 of the

Table 2. Relative occurrence of issues, per category of issues and per topic of issues.

Category	Topic	# Issues		# Mentions	
		N = 37*	%†	N = 67*	%†
Conceptual		1	3	6	9
	Taxonomy	1	3	6	9
Normative		5	14	34	51
	Whose preferences	4	11	26	39
	Relevance of preferences	1	3	11	16
Procedural		9	24	49	73
	Weight	3	8	21	31
	Impact	1	3	21	31
	Patient education	3	8	20	30
	Evidence based	1	3	17	25
	HTA stage	1	3	16	24
Methodological		18	49	55	82
	Choice of method	3	8	30	45
	Internal validity	3	8	24	36
	Generalizability	4	11	19	28
	Sample selection	1	3	15	22
	External validity	2	5	9	13
	Patient characteristics	2	5	8	12
	Reliability	3	8	7	10
Practical		4	11	16	24
	Resources	4	11	16	24

HTA indicates Health Technology Assessment.
*Absolute number of issues identified and absolute number of articles mentioning each issue.
†Relative number of issues (as % of 37 issues) and relative number of articles mentioning each issue (as % of 67 articles). Percentages might not add up to 100% because most studies mentioned multiple issues or because of rounding error.

67 articles (9%; eg, Utens et al.,[25] Brooker et al.,[26] and DeJean et al.[27]). Normative topics included whose preferences to elicit and the relevance of preference studies to patients. Whose preferences to elicit was mentioned most—namely, in 26 of the 67 articles (39%; eg, Rashid et al.,[28] Gagnon et al.,[29] and Buck et al.[30]). Procedural topics concerned what weight to give patient preferences in current HTA procedures, how to evaluate impact, how to educate patients in preparation for preference studies, whether and how patient preferences are evidence based, and in which HTA stage to incorporate patient preferences. The most often mentioned procedural topics were how to weight preference studies in comparison to or in addition to current ethical, clinical, and cost-effectiveness (quality adjusted life year [QALY]) procedures (n = 21; 31%; eg, Dirksen,[14] Mühlbacher and Kaczynski,[31] and Mühlbacher and Sadler[32]) and how to evaluate the impact of preference studies on HTA decision making (n = 21; 31%; eg, Dipankui et al.,[33] Kreis and Schmidt,[34] and Abelson et al.[35]). Methodological topics concerned choice of method, internal and external validity, reliability, generalizability, and which patient characteristics affect preferences and how. The most prevailing methodological topic was choice of method (n = 30; 45%; eg, Utens et al.,[36] Wortley et al.,[37] and Brereton et al.[38]), followed by internal validity (n = 24; 36%; eg, Brooker et al.,[26] Wahlster et al.,[39] and Danner et al.[40]). The only practical topic that was raised concerned resource constraints in conducting preference studies, which was mentioned in 16 of the 67 articles (24%; eg, Utens et al.,[25] Hailey et al.,[41] and Single et al.[42]).

Issues

Table 3 gives an overview of the 37 unique research issues and their frequency of being mentioned. The most frequently posed normative issues concerned whether the preferences of representatives of patient organizations represent the preferences of a broader set of individuals (n = 13; 19%; eg, Rashid et al.,[28] Gagnon et al.,[29] and Buck et al.[30]) as well as whose preferences should be elicited (n = 12; 18%; eg, Kreis et al.,[43] Mott and Najafzadeh,[44] and Thokala et al.[45]) and whether patient-relevant outcomes and processes should be accounted for in preference studies and how this should be done (n = 11; 16%; eg, Evers et al.,[46] Mühlbacher et al.,[47] and Berglas et al.[48]). The most frequently posed issue of a procedural nature was how to evaluate the impact of preference studies (n = 21; 31%; eg, Dipankui et al.,[33] Kreis and Schmidt,[34] and Abelson et al.[35]), followed by whether preference studies can be considered robust scientific evidence (n = 17; 25%; eg, Iskrov and Stefanov,[49] Moreira,[50] and Tordrup et al.[51]) and in which HTA stage to incorporate them (n = 16; 24%; eg, Hämeen-Anttila et al.,[52] Weeks et al.,[53] and Husereau et al.[54]). The most frequently raised methodological issues were about which methods to use for preference elicitation (n = 29; 43%; eg, Utens et al.,[36] Wortley et al.,[37] and Brereton et al.[38]) and about heterogeneity in preferences (n = 18; 27%; eg, Wahlster et al.,[39] Di Paolo et al.,[55] and Doctor and MacEwan[56]). The most frequently mentioned practical issues with conducting preference studies were cost constraints (n = 13; 19%; eg, Wortley et al.,[37] Mossman et al.,[57] and Kievit et al.[58]) and time constraints (n = 11; 16%; eg, Buck et al.,[30] Brereton et al.,[59] and Scott and Wale[60]).

Discussion

In this study, from a selection of 67 articles, we identified 37 unique research issues that concern the integration of patient preferences in HTA. In most of the articles, methodological issues were raised (82%), followed by procedural (73%), normative (51%), practical (24%), and conceptual (9%) issues. Frequently posed methodological issues were about preference heterogeneity and choice of method. Common procedural issues concerned how to evaluate the impact of preference studies and their degree of being evidence based.

The relatively large number of unique issues shows that patient preference integration is by and large a relevant topic to be researched. This review includes theoretical and applied studies and includes studies in numerous medical contexts from various countries. Furthermore, the identified issues relate to qualitative (exploring) and quantitative (eliciting) preference methods that might vary in rigorousness and addressability depending on the research question concerning patient preferences in HTA. Given the variety of study characteristics, this review provides a comprehensive research agenda that is relevant for multiple stakeholders. The issues in the articles were relevant for HTA professionals, academic researchers, clinical guideline developers, patients, patient organizations, and/or clinicians. Nonetheless, the majority of the issues were raised by academic authors of the articles, and the articles provide little guidance on how to address the issues. Hence, we believe that to reach consensus on the way forward, involvement, coordination, and collaboration among the different stakeholders is warranted.

Table 3. Three-level categorization and relative occurrence of issues.

Category	Topic	#	Issue	N = 67*	%†	Article(s)
Conceptual						
	Taxonomy	1.	How should we define patient preferences and subsequently find and retrieve patient preference studies?	6	9	25–28,36,49
Normative						
	Whose preferences	1.	Do preferences of representatives of patient organizations/advocacies represent preferences of a broader set of individuals?	13	19	21,29,30,43,52, 57,59,60,62,64,82–84
		2.	Whose preferences should be elicited (eg, patients with or without treatment experience, carers, patient representatives)?	12	18	25,31,33,34, 43–45,64,68,82,84,85
		3.	Are patient preferences influenced by external factors (eg, media, family, or pharmaceutical companies)?	7	10	14,28,29,57,63,64,83
		4.	How can preferences from various samples (eg, clinicians, carers, and patients) be synthesized to be of value as a whole?	3	4	46,53,85
	Relevance	1.	What are patient-relevant outcomes (ie, health vs well-being), and should preference studies also focus on process?	11	16	14,25,36, 46–48,58,65,81,86,87
Procedural						
	Weight	1.	How should preference studies be evaluated in comparison/addition to clinical and economic evaluation studies?	15	22	14,25,27,29,31, 36,38,39,60,64, 65,82,84,88,89
		2.	How can preference studies add to or replace the QALY paradigm?	5	7	14,32,36,51,75
		3.	How should ethical issues concerning patient preferences be weighed in HTA?	4	6	13,42,60,63
	Impact	1.	How can we evaluate the impact of patient preferences studies on HTA decision making?	21	31	14,21,25,28,29,31, 33–35,37,43,49,52,53, 57,60,62,68,80,82,90
	Patient education	1.	How can patients be sufficiently trained to perform HTA studies?	14	21	21,29,30,43,52,55, 59,60,63,64,68,82,87,91
		2.	How can communication between researchers and patients be aligned in preference studies?	6	9	21,29,30,60,82,87
		3.	How should patients and caregivers be informed about HTA studies and the possibility of being involved?	12	19	37,46,52,53,60, 64,65,68,81,82,91,92
	Evidence based	1.	How is and should the quality and transparency of patient preference studies be assessed to be considered robust scientific evidence?	17	25	14,21,28,33,38,43, 46,49–51,58,59,63, 64,75,84,91
	HTA stage	1.	In which context and stage of HTA should preferences be used to inform decision making?	16	24	25,29,30,34,46, 48,52–54,62,65, 84,86,88,90,91
Methodological						
	Choice of method	1.	Which methods are preferable for eliciting preferences?	29	43	14,25–27,29,31, 32,34,36–40,45,51, 52,59,61,64,68,75,81, 84,85,90,91,93–95

continued on next page

Table 3. Continued

Category	Topic	#	Issue	N = 67*	%†	Article(s)
		2.	When should we use quantitative (eliciting) versus qualitative (exploring) research methods for patient preference studies?	3	4	14,25,26
		3.	Which methods to elicit patient preferences are preferable in which stage of HTA?	2	3	29,62
	Internal validity	1.	How do preferences on an individual level differ from those on a collective level (ie, preference heterogeneity)?	18	27	21,32,36,38–40,44, 47,55,56,58,60, 65,87,89,95–97
		2.	How does framing affect preferences?	4	6	26,31,40,66
		3.	How can validity of preference studies be tested?	1	1	47
	Reliability	1.	How stable are preferences over time?	4	6	14,47,48,81
		2.	How consistent are individuals in preference studies, how does this affect results, and how should inconsistent responses be handled?	3	4	21,40,47
		3.	How should uncertainty in patient preferences be modeled?	1	1	31
	Generalizability	1.	How representative are preferences from the recruited sample for the entire population?	9	13	21,28,34,47,59,60,64,68,85
		2.	Can preference studies be transferred across diseases and contexts (ie, as a generic instrument)?	7	10	14,25,33,39,46,51,81
		3.	Can preference studies be transferred across countries/sociocultural groups?	4	6	38,47,59,92
		4.	How representative are preferences for a singular intervention compared to when the intervention is administered alongside other interventions?	2	3	48,81
	Sample selection	1.	How (ie, via which channels and based on which characteristics) should the sample be selected?	15	22	28–30,41,43,46, 52,53,59,64,66, 68,82,90,98
	External validity	1.	What is the external validity of preference studies, and how can this be improved?	5	7	21,40,59,66,97
		2.	How can we merge real-world data (eg, adherence data) and stated preference studies?	4	6	14,48,49,56
	Patient characteristics	1.	Which sociodemographic patient characteristics (eg, sex, age, education, income, family, risk attitude, and beliefs) affect preferences, and how should we tailor these subgroups?	6	9	30,38,46, 55,56,97
		2.	Which disease-specific patient characteristics (eg, stage and severity of illness) affect preferences, and how should we tailor these subgroups?	6	9	46,55,56, 81,96,97

continued on next page

Table 3. Continued

Category	Topic	#	Issue	N = 67*	%†	Article(s)
Practical						
	Resources	1.	How can cost constraints of preference studies be overcome?	13	19	25,30,37,41–43,53,54,57–60,68
		2.	How can time constraints of preference studies be overcome?	11	16	25,29,30,41–43,54,59,60,68,98
		3.	How can staff/expertise constraints of preference studies be overcome (who should perform preference studies)?	6	9	25,29,42,60,67,68
		4.	How can location constraints of preference studies be overcome?	1	1	30

QALY indicates quality adjusted life year; HTA, Health Technology Assessment.
*Absolute number of articles.
†Relative number of articles mentioning each issue (as % of 67 articles). Percentages do not add up to 100% because most studies mentioned multiple issues or because of rounding error.

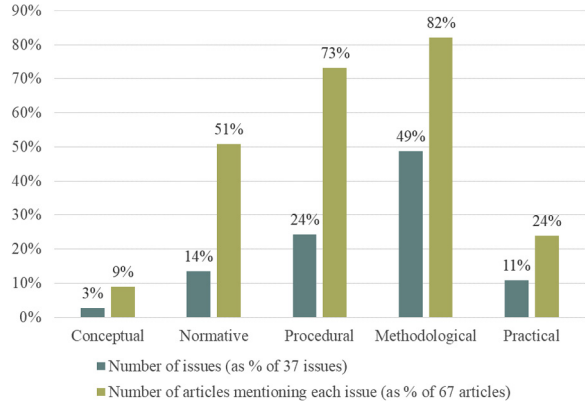
The issues identified in this review are very much in line with non-HTA specific literature[9,12] in which experts generally argue for the use of patient preferences in healthcare research. According to Ostermann et al.,[12] important issues are internal and external validity, reliability, and preference heterogeneity in addition to evidence-based prediction of uptake and adherence. In a research agenda concerning regulatory review of medical devices, Levitan et al.[9] stated that validity and reliability, the choice of method, sample selection, patient-relevant outcomes and processes, framing, patient education, and correcting for patient characteristics were important issues to consider. Within the HTA context, Mott[10] prioritized issues about weighting patient preferences in current HTA procedures. He discussed whether patient preferences should be incorporated within the QALY or beyond the QALY and proposed multiple-criteria decision analysis as a new methodological approach to HTA. The challenges mentioned by Facey et al.[23] include the impact of preference studies on HTA decisions, time and cost constraints, and how to weight preference studies alongside clinical and cost-effectiveness studies. The authors also strongly highlighted the need for patient preference studies to be evidence based. Despite the fact that the previously mentioned authors differed in their prioritization of issues, all of the issues in their articles were also identified in our review, advocating its inclusiveness.

Some aspects of this review require discussion. A first limitation is that articles outside the scope of our definitions may have been overlooked for various reasons. As mentioned in some of the included articles,[25–28,36,49] patient preferences are not clearly defined, and therefore studies concerning this topic are not easily retrievable. Furthermore, the integration of public preferences is sometimes discussed alongside the integration of patient preferences.[28,30,34,35,44,53,61–68] Although it is an important issue to address, it was not an explicit goal of this research to take a stance on or provide an overview of whether to use patient, public, or both preferences in HTA. For an overview of arguments for and against public and patient preferences in health valuation, other literature[10,69–74] can be consulted. Other reasons for potentially having overlooked important research questions that are inherent to reviewing literature are publication lag or bias and the inclusion of only English-language articles.

Second, the process of categorization should be interpreted with caution. For pragmatic reasons, study characteristics and issues were extracted by 1 researcher, followed by confirmation by 2 other researchers. The categorization of issues was performed by 2 researchers, followed by confirmation by a third researcher, yet the issues were subjectively categorized to put them into context. There could be discrepancies between what was originally meant by authors of the articles included in the analysis, how we interpreted the issues, and how other researchers would interpret them. In addition, we interpreted frequency of occurrence as a way to measure priority. The broader the issue, the more it is likely to occur; so it is possible that issues unintentionally became weighted according to their specificity in the extraction process. The current categorization is by no means intended to be definitive. However, it is a systematically retrieved overview and, we believe, an informative descriptive basis for a more extensive prioritization of issues to advance the integration of patient preferences in HTA. Other interesting research that goes beyond the scope of this article could be in-depth analysis about how knowledge accumulated on a particular issue or topic as listed in this review. In addition, it might be interesting to research how particular issues or topics trend together.

Thirdly, it should be noted that HTA studies vary in the degree to which patient preferences are meaningful. According to the articles included in this systematic review, integrating patient preferences in HTA is mostly relevant for the following situations: when there is no 1 treatment that is considered superior,[14,25,26] when the benefits of interventions are only marginal,[14] when uncertainty of the treatment outcome is high,[4] when there are

Figure 3. Relative occurrence of issues, per category of issues.



multiple alternatives that vary largely in terms of risk-benefit trade-offs,[4] when preferences of patients are expected to be very heterogeneous,[4] and when the treatment concerns a rare disease that would benefit from early HTA.[46]

Based on the literature and our interpretation of the data, we recommend 2 areas for further research that are fundamental to the advancement of integrating patient preferences in HTA. First, as addressed in articles included in this review[14,32,36,51,75] and beyond,[10,69,76] the discussion as to whether patient preferences should be incorporated within the QALY or beyond the QALY is essential to the integration of patient preferences in HTA. Second, in agreement with articles included in this review[32,45] and broader literature,[7,10,19,77–79] we recommend exploration of the possibilities of using multiple-criteria decision analysis to integrate patient preferences. Both of these procedural matters relate to normative changes to current HTA procedures, hence warranting further research. Other normative issues, such as whose preferences to incorporate in HTA, concern a choice rather than further research. To address the entire spectrum of issues identified in this review, especially the normative issues, better communication, collaboration, and consensus among the different stakeholders is required.[80,81]

Conclusion

In line with the increasing use of patient preferences in various medical contexts, the integration of patient preferences in HTA is expected to contribute to better decision making and to increase uptake, adherence, and patient satisfaction. So, what is next for patient preferences in HTA? Methodological and procedural issues were mentioned most; yet, the large number of different issues advocates the overall importance of a multi-stakeholder and holistic approach to the integration of patient preferences in HTA. By providing a contemporary overview of issues in the literature, this review is an important first step toward the integration of patient preferences in HTA in a systematic and scientifically valid manner. The next step requires coordination and collaboration among the different stakeholders to reach consensus on the way forward.

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Supplementary Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2019.04.1930.

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