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Implicit factors influencing the HTA deliberative processes in 5 European countries: results from a mixed-methods research

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ABSTRACT

Background: Health technology assessment (HTA) bodies across Europe rely on explicit factors for decision making. However, additional undefined factors play a role. This mixed-methods research aimed to identify the implicit factors involved in HTA deliberative processes in five European countries, and to analyze their impact on decision making.

Methods: Between February and May 2021, semi-structured interviews (n = 20) were conducted with HTA experts of three different profiles (chair, advisor, and committee member) from France, Germany, Italy, Spain, and the United Kingdom. The degree of influence of a set of implicit factors and attributes that play a role in the HTA deliberative process, as previously identified in a systematic literature review, was scored by the experts. Experts were also asked to make recommendations on ways of improving the deliberative process. A qualitative analysis and descriptive statistics of quantitative variables are reported.

Results: Most (18/20) experts concurred that implicit factors play a role in the HTA deliberative process. Recommendations for improving the process fell into three categories: transparency, methodology improvement, and stakeholder involvement. The results suggest a need for 1) increased external involvement HTA and 2) development of a methodology to mitigate the influence of implicit factors in the deliberative process. This could be achieved by updating the current frameworks to acknowledge these implicit factors and by developing methods to address them.

1. Introduction

Health technology assessment (HTA) is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision making and promote equitable, efficient, and high-quality health systems [1]. HTA relies on evidence-based medicine, which can be defined as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients [2,3]. When applying evidence-based medicine to HTA, facts or explicit criteria related to the use of health technologies like clinical effectiveness, safety, and cost-effectiveness (CE) are considered [4,5]. Additionally, throughout the HTA process, implicit values or value judgements on social, ethical, and legal aspects may influence decision making.

Detailed guidelines on the appraisal of new health technologies have

been published [6–10], providing clarity on the explicit factors that influence the deliberative process of HTA in different European countries [11,12]. All agencies include an assessment of clinical benefit in their approach. While France and Germany apply a comparative assessment of clinical benefit as the sole methodology, other countries incorporate economic evaluation as the key analytical method to determine the value of new technologies. In the United Kingdom (UK) the focus is on CE analysis, while HTA bodies in Spain and Italy focus on budget impact [12–14]. Further details of the explicit factors assessed in each country are shown in the [supplementary material \(Table S1\)](#).

In addition to explicit factors, implicit values or value judgments on social, ethical, and legal aspects may influence decision making [3,15]. In this context, implicit factors can be understood as any criteria playing a role in the deliberative process that have an impact on the output of the HTA process (decision or recommendation) [16,17]. The implicit nature

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of these other factors creates a lack of transparency and understanding of the basis of HTA recommendations. For example, in countries where there is explicit guidance on CE thresholds, e.g., the incremental CE ratio (ICER) thresholds used in the UK, there are cases where drugs with base case ICERs above the threshold were recommended. This suggests that, for some medicines, a weighting has been allocated to implicit factors [18].

There is a need to have a better understanding of the implicit factors that affect HTA [16]. The results of a systematic literature review (SLR) on the influence of implicit factors in the HTA deliberative process revealed a paucity of data and research on this topic [17]. Moreover, since HTA guidelines do not acknowledge the potential influence of implicit factors, there are a lack of methods in place to reveal and mitigate their impact on decision-making. Making explicit the factors that are entailed when assessing health technologies fosters transparency, clarity, and a higher degree of comprehensiveness and methodological robustness [14,17]. Understanding these factors would help different stakeholders to have a broader picture of the HTA deliberative process and understand often overlooked aspects involved in the recommendation and reimbursement of health technologies. The aim of this study was to identify the implicit factors influencing the HTA deliberative process and to analyze their impact on the decision-making process in five European countries.

2. Methods

2.1. Study participants and geographic scope

HTA experts from France, Germany, Italy, Spain, and the UK who had a minimum of three years' experience in HTA processes were recruited. The five countries in scope represent 73 % of the European Union (EU) population and all have established HTA agencies and recognized HTA processes [19,14]. Additionally, the healthcare expenditure of healthcare providers in these countries represented 72 % of the EU-28 total in 2019 [20].

Given the highly specialized area of research and the characteristics of the professional profile sought, the interviewees were recruited through the snowballing method [21]. Twenty-five experts were contacted via email and from those 20 participated in the interviews, resulting in an overall response rate of 80 %. Of the five experts who did not participate (Table S2), three experts refused to participate and two experts did not respond.

Interviewees were either HTA committee members with voting rights or subject matter experts present in the deliberation but without voting rights, who had been involved in the deliberative process in the 10 years prior to interview. Most of the experts contacted had experience at one of the following decision-making bodies: the Federal Joint Committee in Germany (G-BA); the National Institute for Health and Care Excellence (NICE) or the Scottish Medicines Consortium (SMC) in the UK; the French National Authority for Health (HAS); the Ministry of Health, Social Services and Equality in Spain (MSSSI); the Italian Agency of Medicines (AIFA); the Catalan Health Service (CatSalut) or advisory bodies such as the Andalusian School of Public Health in Spain (EASP).

2.2. Data collection

Interviews were conducted and recorded between February and May 2021 using Webex (version 41.5.0.18911) and lasted 60 min. Interviewees were briefed about the objectives of the research; all gave their consent to participate and for the interviews to be recorded.

Semi-structured interviews were used to encourage the interviewees to discuss openly their individual approaches to decision making when assessing medicines. A discussion guide and an interview checklist (supplementary material, Appendix S1) were developed by the authors following a standard methodology [22]. The interview guide was divided into two main sections: 1) perceptions on the HTA deliberative

process (12 questions) and 2) recommendations on how to improve the deliberative process (five open questions). The first section included 10 open questions, two of which focused on explicit factors and their importance in the HTA recommendations. These two questions were asked to highlight the differences between explicit and implicit factors, however, the responses were not analyzed nor reported. These were followed by two questions in which respondents were asked to score on a Likert scale, firstly, the degree of influence that 10 implicit factors play in the HTA deliberative process, and secondly, the strength of seven attributes related to the HTA deliberative process in their respective country. The scores ranged from 0 (lowest score) to 10 (highest score).

Since there is no formal definition of implicit factors related to the HTA deliberative processes in the public domain a definition was developed based on examples taken from the literature [2,16,23–28]. Implicit factors in HTA refers to all non-defined factors that are not explicitly collected or described in the HTA guidelines that may influence the HTA deliberative process and the subsequent recommendations. The implicit factors identified in the previously reported SLR [17], and subsequently assessed in this study, were related to contextual factors (functional role, qualification, professional experience, culture of the committee, sense of equity, conflict of interest, political and social influences, and appreciation of the burden of disease), and behavioral factors (value judgments and psychology). See Table S3 for a full list of the implicit factors identified in the SLR. The attributes of the HTA deliberative process assessed were transparency, objectivity, standardization, predictability, fairness, reproducibility, and inclusiveness. Each implicit factor and attribute were described in the discussion guide (Appendix S1).

2.3. Data analysis

All interviews were digitally recorded and transcribed into a Microsoft Word document. Two researchers independently coded the interviews. The researchers compared the code list and unified the codes. The unified code list was applied to all interviews, following the grounded theory approach [29,30]. Any coding divergence was resolved by discussion between the two researchers. The quotations were then extracted into a Microsoft Excel file.

For the questions focused on the experts' recommendations on improving the deliberative process, categories were created based on the frequency of topics that emerged from the answers. The final set of categories was illustrated with experts' quotations. For the questions involving scoring a descriptive quantitative analysis was performed (mean, median, interquartile range [IQR], and standard deviation [SD]). Country level median and IQR were calculated.

3. Results

A group of 20 experts, composed of individuals from different organizations across Europe (four per country), were interviewed (Table 1). The saturation point was reached after three interviews per country. The profile characteristics of participants who were contacted but did not participate in the interviews is detailed in Table S2.

3.1. Perceptions on the HTA deliberative processes across countries

3.1.1. Main explicit and implicit factors influencing the HTA deliberative process

Experts from all countries stated that clinical efficacy and safety were explicit factors influencing the deliberative process (Table S4). The experts in Germany specifically mentioned that mortality, morbidity, safety, tolerability, and quality of life were the outcomes assessed, and that clinical trial design and comparator were also relevant to decision making. Burden of disease was stated to be an explicit factor in both France and Germany. In terms of the economic case, budget impact was considered in Italy and Spain, while the ICER was the key determination

Table 1
Profiles of the study participants.

Country	Profile in the HTA deliberative committee	Years of experience (at time of interview)
SPAIN	Pharmacy Director	17
	External advisor	10
	Pharmacy Director	14
FRANCE	Committee member	25
	Committee member	9
	Chair	17
	Committee member	31
ITALY	Committee member	9
	External advisor	15
	Committee member	4
	Committee member	5
UK	Committee member	4
	External advisor	9
	Committee member	8
GERMANY	Committee member	17
	Committee member	5
	Committee member	20
	Chair	10
	Chair	10
	External advisor	25

of economic value in the UK. Finally, the experts from France mentioned that public health interest was also a key factor.

Most of the experts (18/20) concurred that, despite the process in each country being well defined with the key criteria published and available in the public domain, there are implicit factors that have not been integrated in the HTA frameworks or guidelines. They stated that it would be beneficial to acknowledge these factors.

Concerning implicit criteria that could influence decision making, experts identified unmet need (UK, France, and Germany), burden of disease (UK and Spain), patient perspective (UK), social pressure (UK and France), and epidemiology, (France) (Table S4). The interviewees from Spain also mentioned confidential discounts as having an influence. One expert from the UK highlighted the importance of quality-adjusted life year (QALY) weighting as a factor that may have been considered in the deliberative process in an unofficial way. In the case of Italy, one expert stated that the budget cap on the pharmaceutical expenditure was a factor that may influence the deliberative process.

3.1.2. Degree of influence of the implicit factors on the HTA deliberative process

The overall perceptions of the influence of implicit factors on the HTA deliberative process are shown in Fig. 1. The appreciation of burden of disease was the highest scoring factor (median score 6.8 [IQR 0.5]) whilst conflict of interest was rated as having the lowest influence from the HTA experts' perspective (median score 2.3 [IQR 1]).

The degree of influence of implicit factors (positive or negative) on the HTA deliberative process and outcome in each country are shown in Table 2. Overall, the experts from Germany gave least weight to implicit factors (scoring the lowest in seven factors out of 10) whereas the experts from Italy gave most weight overall (scoring the highest in seven factors out of 10). Individual responses within country are described in Table S5.

3.1.3. Attributes of the HTA deliberative process

The experts' perceptions of the strength of a set of attributes relating to the HTA deliberative process in their country of expertise are shown in Fig. 2.

Overall, the scores for each attribute were similar, being the attributes of "objective" and "transparent" the highest across all the countries (median score 7.5 [IQR 1 and 0]), whereas inclusiveness scored the lowest (median score 6 [IQR 1]). In terms of country-level responses (Table 3), the experts from Germany had the most positive perception of the HTA deliberative process, with median scores ranging from 7.5 to 10 and scoring the highest in six out of the seven attributes: standardization, reproducibility, objectivity, transparency, predictability, and inclusiveness. France scored lowest in standardization and Italy scored lowest in inclusiveness. Individual responses for each country are reflected in Table S6.

3.2. Recommendations for improving the HTA deliberative process

The experts were asked to provide recommendations on ways to acknowledge the implicit factors identified and improve the objectivity, transparency, and standardization of the HTA decision-making process. The recommendations from the experts were classified into the following categories: inclusiveness, methodology improvement and transparency.

Regarding the category of inclusiveness, most of the experts (17/20)



Fig. 1. Scores (median and IQR) given by experts to the degree of influence of implicit factors in the HTA deliberative process.

Table 2
Degree of influence of the implicit factors on the HTA deliberative process across countries.

Dimensions ^a	Spain	France	Italy	Germany	UK	Median	Interquartile range
Burden of disease	7.0	6.5	8.0	6.8	6.0	6.8	0.5
Professional experience	6.5	7.0	8.0	3.0	5.0	6.5	2
Functional role	6.0	5.0	6.8	1.0	5.5	5.5	1
Qualification	6.0	6.5	5.5	1.5	5.5	5.5	0.5
Equity	5.5	7.0	8.0	1.0	5.0	5.5	2
Committee's culture	4.5	5.8	5.5	1.0	5.3	5.3	1
Value judgments	3.0	4.5	8.8	5.0	5.0	5.0	0.5
Psychology	3.0	4.0	5.0	4.3	4.5	4.3	0.5
Politics and society	2.5	2.5	6.8	1.8	4.0	2.5	1.5
Conflict of interest	2.5	2.3	5.0	0.5	1.5	2.3	1

^a Country scores represent the median of all the responses per dimension.

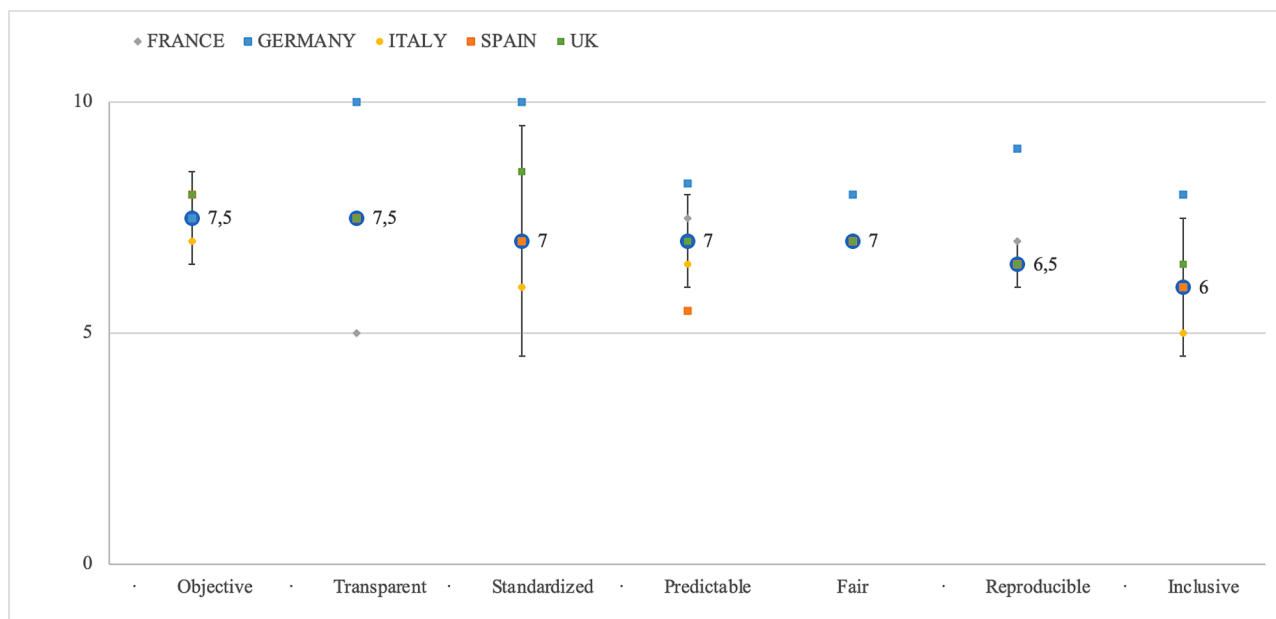


Fig. 2. Scores (median and IQR of medians) given by experts to a set of attributes pertaining to the HTA deliberative process.

Table 3
Quantification of a set of attributes in the HTA deliberative process across countries.

Dimensions ^a	Spain	France	Italy	Germany	UK	Median	Interquartile range
Objective	8	7	7	7.5	8	7.5	1
Transparent	7.5	5	7.5	10	7.5	7.5	0
Standardized	7	6	6	10	8.5	7	2.5
Predictable	5.5	7.5	6.5	8.25	7	7	1
Fair	7	7	7	8	7	7	0
Reproducible	6.5	7	6.5	9	6.5	6.5	0.5
Inclusive	6	5	5	8	6.5	6	1.5

^a Country scores represent the median of all the responses per dimension

agreed on the importance of expanding stakeholder involvement. This would provide a higher number of diverse, external perspectives to ensure that a broad range of values and their relative importance are understood. The range of stakeholders could include patients, caregivers, and specialist physicians, as well as politicians and defense counsels. Manufacturers, representatives of universities and specialized centers in HTA were other suggested stakeholders. For example, one of the experts from France stated “There could be the involvement of politicians and a defense counsel specialized in the disease, who could come from the side of the pharmaceutical company who is submitting the dossier, and on the other hand the Social Security could have another counsel expert in the disease. This would contribute to increased scrutiny and enhance the debate among the committee members to reach a fairer decision.”.

The next category of recommendations, provided by 14 of the 20 experts, was HTA methodology improvement. This would include methodologies like multi-criteria decision analysis (MCDA) or cost/QALY analysis [31], which define and document the implicit factors beforehand and assign weights to them. Experts stated that “The cost/QALY is a rough tool, but it allows to have all the diseases under an equal footing” (Expert from France) and “We could use a similar approach to MCDA, defining the implicit factors or criteria beforehand and introducing them progressively and in a consensual way after having been validated by the different members in the committee and then having weighted them” (Expert from Spain). Cost-utility analysis was suggested as another tool that could address the implicit factors relating to the perception of disease in some countries, since this method would also allow assessment of the

diseases on an even playing field. Mitigating cognitive biases (i.e., subjective feelings, authority biases) was also proposed as an approach to control some of the implicit factors.

Anonymous voting, especially in countries like France where the votes are made by a show of hands, was suggested as another way of improving HTA methodology. One expert from France noted that *“Every single opinion and vote should have the same weight in the decision. In countries like France where the votes are made by a show of hands, one way to reduce bias from seeing others’ vote is by making the vote anonymous. In all committees there are members who are dominant and members who are dominated. That is why the vote should be anonymous to avoid any kind of influence.”* Anonymous voting would reduce influences derived from seeing other committee members votes, notably those who are dominant in the committees. The final suggestion under this category related to the need for reassessment of health technologies when new evidence becomes available. The HTA assessments should ideally be equitable over time regardless of the committee culture or media pressure.

Finally, to improve transparency, the recommendation by most experts (17/20) was to provide greater external communication that would allow stakeholders to assess if the deliberative process and resulting recommendations were fair. To achieve this, minutes of meetings and draft committee reports with conclusions should be available to the public: *“The process would be more transparent if the deliberative discussions were open to the public with external observers. Then, the discussions would be approached in a different way”* (Expert from Italy). In terms of improving transparency, it was also suggested by some experts that time should be allocated to display all conflicts of interest and reveal the committee members’ perspectives on equity.

4. Discussion

The findings of this mixed-methods research suggest that implicit factors play a role in the HTA deliberative process. These implicit criteria, that do not form part of deliberative process frameworks, cannot be neglected. It has previously been acknowledged that implicit factors such as cognitive biases influence decision-making processes [32]. However, the literature on this topic is scarce and current checklists such as the Health Technology Assessment International (HTAi)/ and The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) taskforce do not account extensively for implicit factors [11]. Therefore, HTA practitioners may not always be fully conscious of the presence of these factors and their impact on final recommendations.

While empirical methods relating to clinical effectiveness, safety, and CE form the major element of the assessment of a health technology, value judgments also form a constituent part and permeate all levels of HTA, both in the assessment (i.e., the evaluation of relevant aspects of the technology to form a basis for decision) and appraisal (i.e., recommendation on the implementation of the technology, based on the assessment [33]).

Ignoring these value judgments can lead to situations in which HTA proves to be insufficient. Elements not easily quantified in the clinical and economic assessments such as equity should be documented to make the decision process more rational, better justifiable, and more transparent [15,23,34–37].

In the interviews performed, the experts perceived the process as fair, standardized, and reproducible. However, in terms of the perceptions on the standardization interviewees from France, Italy, and Spain scored the process low compared to Germany and the UK. This could be explained by the fact that G-BA and NICE assessments follow a standardized procedure based on evidence-based medicine, resulting in published guidance or guidelines [6,38–40]. The frequency in which implicit factors play a role might be higher in countries like Spain and Italy due to their decentralized healthcare system in which regions bear the largest decision-making component, in contrast to countries with a centralized system like Germany [41]. The influence of implicit factors

could therefore contribute to the inequality in access to innovations across regions [7].

Overall, it is recognized that patient involvement should occur at all stages to enhance trust in the HTA deliberative process [42]. In this study the importance of engaging with patients and patient organizations during HTA assessment was frequently highlighted by the interviewed experts. Other than those in Germany and the UK, the experts did not perceive that the HTA process was inclusive enough, explaining why stakeholder involvement was recommended to improve transparency, legitimacy, and objectivity. The higher score given by experts from Germany and the UK could be explained by the fact that the G-BA and NICE involve patient groups and take patients’ perspectives into consideration at different stages of the assessment [43]. The UK is one of the pioneers in patient engagement in the HTA processes, with active participation of caregivers and, where appropriate and possible, patients themselves in the committees’ deliberations [39]. Since 2004, patients or caregivers, patient group representatives, and advocacy groups have contributed to the G-BA HTA process through participation in committees and discussions in which they are entitled to submit petitions [43]. In France, even though patients have been involved in the deliberation of the Transparency Committee since 2015, there are areas for improvement regarding their level of engagement and influence on the deliberations. Since 2015, representatives of the pharmaceutical industry are no longer involved in the Transparency Committee as a consultative member, which means that the valuable expertise of the presenting company may not be considered [44,45]. In Italy and Spain, there is very limited patient participation in the HTA process, and any kind of involvement relies to a large extent on the patient organizations’ proactivity [41,43].

There has been rapidly growing interest in including not just patients but other stakeholders, including the broader public, in deliberative processes, in ways that add value to both the process and to the parties involved [46]. In some countries a range of different stakeholders are part of the HTA process, including industry representatives, patients, patient associations, and health professionals. Similarly, health professionals, medical associations, and payers are often involved in assessment or appraisal committees [47]. The G-BA includes members from associations of physicians, hospitals, and sickness funds, along with patient representatives, as do many of the governing boards and advisory panels of the Institute for Quality and Efficiency in Health Care (IQWiG) [48]. NICE, HAS, and IQWiG have established opportunities to engage with industry, healthcare managers, clinicians, and academics to discuss strategic challenges [39,49].

Preferences, concerns, and perspectives of a range of relevant stakeholders on socio-ethical aspects around the health technology should not be ignored in the HTA process, as illustrated in the assessment of cochlear implants in deaf children. Although the technology was advocated by some as effective and safe with additional benefits for deaf individuals, representatives of deaf organizations objected that the technology represented a negative value judgment on the deaf community. The two different perceptions were partially explained by the fact that both groups defined the problem from different perspectives [34,50]. This example showcases the importance of collecting, integrating, and documenting evidence that is not always objective nor easily quantifiable into the HTA assessment, such as values or norms; hence there is a need to involve stakeholders with different perspectives and values [15,23,37,50,51]. Additionally, there are some situation-specific contextual factors that are implicit in certain countries and that influence decision-making. The lack of transparency derived from not disclosing these factors or the way they influence the decision-making raises questions on decisions’ legitimacy. These factors need to be properly documented [51].

Broad stakeholder participation can serve to identify the full range of interests that society has by making the process more rational and contributing to the legitimacy of decision-making. A systematic approach and general principles to facilitate stakeholder participation in

the deliberative process have been described elsewhere [11]. The principles highlighted among others are transparency and impartiality. Stakeholder involvement deserves special attention in HTA reports, documenting who was involved in decision making as stakeholders, what they proposed, and how their feedback was used [35,34].

Another way to address objectivity and impartiality could be by conducting the HTA process independently from the institution that will ultimately be responsible for the pricing and reimbursement decision. The HTA bodies in Germany and in the UK have higher autonomy than in France and Spain where these institutions depend on the Ministry of Health, and as such there may be political influences on the decision-making process [14]. To increase the fairness and legitimacy of the process HTA bodies recognize the importance of making the process “independent” from the subjectivity of committee members [36]. On this note, accountability for the assessment and decision making should be determined to mitigate the influence that biases have in the decision-making. For example, HTA experts who are part of the assessment should not be part of the team responsible for making reimbursement decisions on the health technology [37].

Attempts have been made to develop pragmatic tools to take equity into consideration in HTA decision making processes [52,53]. However, this has not been extended to the whole range of implicit factors. Standardized methodologies like MCDA can serve as a tool to collect and document the implicit factors and raise awareness on their influence in the deliberative process. Nevertheless, complex methodologies can compromise the agility of decision-making [54,55].

4.1. Strengths and limitations

To the best of our knowledge, our research represents the first HTA mixed methods research focusing specifically on the implicit factors influencing the HTA deliberative process in Europe. A strength of our research is the high interview response rate (80 %), which is above the average for interviews conducted in the field of HTA, that ranges from 18 % to 90 % [42]. Another strength lies in the background of respondents, which included decision makers and payer advisors at national and regional level with at least three years of experience in deliberative processes.

The study has some limitations. Firstly, the factors assessed in the interviews were previously identified in a SLR [17], and there may be other factors not captured in the questions that may influence decision making. It is worth noting that in the implicit factors retrieved from the SLR and shared with the experts included factors that may not be considered implicit in some countries. This is the case for burden of disease which is an explicit factor in France and Germany. In the UK burden of disease is also now explicitly considered under the severity weighting introduced in 2022 [56]. However, in the SLR this distinction between countries was not considered.

In addition, the findings of this study may not be generalizable to other countries in Europe with less structured HTA processes, and in which implicit factors could represent a different weight in the deliberative process. Additionally, this research focused on medicines, meaning our findings cannot be extrapolated to other health technologies assessed through different processes. Another limitation lies in the fact that five experts did not participate in the interviews, and the impact of not gaining their insights is unknown. However, since saturation was reached after three interviews per country and the experts had robust experience in the HTA deliberative process it is unlikely that additional information would have been identified by interviewing additional experts.

It is possible that recall may have affected the results, however, the memory bias in the interviews may have been mitigated since a list of implicit factors were called out in the questions. Declaration biases may have impacted this research given the likely underestimation of the influence of implicit factors, i.e., in the case of Germany.

Finally, we did not perform specific research and analysis of each of

the categories of implicit factors (e.g. as it has been performed for equity) given the complexity of the concepts of each implicit factor.

5. Conclusions

The findings of this research expand the understanding of the impact of implicit factors on the HTA deliberative process. This is a call to action for decision makers from countries with established HTA processes to further characterize implicit factors and mitigate their impact on HTA decision making.

Further research should explore ways to acknowledge and systematically address implicit factors in the HTA deliberative process. This research may be complemented by deepening the findings in one of the countries in scope and/or by interviewing HTA experts from other countries. In every country the HTA process and individuals involved are unique, therefore, variability in the identification and weighting allocated to implicit factors could be expected. Studying the concepts and importance of each category of implicit factors, by first completing an SLR focusing on a specific category (e.g., equity) and then undertaking a qualitative study to determine the influence of this factor, may uncover further determinants of HTA decision making.

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Ethics approval

Not applicable.

Consent for publication The interviewees were informed about the use of this research as part of a PhD project and the aim to publish the results in an aggregated way in a peer-review journal.

CRediT authorship contribution statement

Clara Monleón: Conceptualization, Methodology, Investigation. **Hans Martin-Spáth:** Conceptualization, Methodology, Supervision, Validation. **Carlos Crespo:** Conceptualization, Methodology, Supervision, Validation. **Claude Dussart:** Supervision. **Mondher Toumi:** Conceptualization, Methodology, Supervision.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: CM was a full-time employee of Takeda Pharmaceuticals International AG during the time of performing the interviews. However, this research has been carried out independently from her affiliation. At the time of the performance of this research, MT was a consultant of Creativ-ceutical, a consulting firm specialized in health economics and market access. CC is the CEO of Axentiva Solutions, a consulting firm specialized in health economics and market access. HS and CD declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpopen.2023.100109>.

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