Supplementary material

Use of Patient Preferences in Health Technology Assessment: The Canadian, Belgian and German Perspective

van Overbeeke E, Forrester V, Simoens S, Huys I

Table of Contents

Supplementary material I COREQ Checklist

Consolidated Criteria for Reporting Qualitative Studies (COREQ): 32-item Checklist

No.	Item	Response
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Which author/s conducted the interview or focus group?	EvO (moderator) and VF (assistant).
2.	What were the researcher's credentials?	EvO holds a MSc in biomedical sciences, VF is a Master student in pharmaceutical sciences.
3.	What was their occupation at the time of the study?	EvO is completing her PhD in patient preference research at the University of Leuven and works on the IMI PREFER project, VF was completing her Master thesis.
4.	Was the researcher male or female?	The researchers are female.
5.	What experience or training did the researcher have?	EvO had previous experience and training in conducting interviews and focus groups. EvO trained VF (in preparatory sessions and on the job).
Relationship with participants		
6.	Was a relationship established prior to study commencement?	Two of the participants (one in BE and one in CAN) have been involved in previous PREFER work. Other participants were only contacted through e-mail on beforehand to agree on a time for the focus group.
7.	What did the participants know about the researcher?	The participants were informed that EvO is a PhD student and works on the PREFER project.
8.	What characteristics were reported about the interviewer/facilitator?	The researchers' background and the fact that the study was part of the PhD of EvO and studies of PREFER.
Domain 2: Study design		
Theoretical framework		
9.	What methodological orientation was stated to underpin the study?	Qualitative research evaluated through thematic content analysis.
Participant selection		
10.	How were participants selected?	Via purposive sampling.
11.	How were participants approached?	Central contact persons of the HTA bodies were contacted by the researchers via e-mail. Upon agreement to participate, the central contact persons forwarded the invitation to colleagues within their HTA body.
12.	How many participants were in the study?	15 participants.
13.	How many people refused to participate or dropped out? Reasons?	Of those that were invited to participate, 75% refused. 7/10 participated in Belgium, 5/7 in Canada, and 3/3 in Germany. The only reason to refuse participation, to our knowledge, was unavailability on the date of the focus group.
Setting		
14.	Where was the data collected?	At the office of the HTA bodies (BE/DE) or via teleconference (CAN).
15.	Was anyone else present besides the participants and researchers?	No, only the participant and one or both researchers were present.
16.	What are the important characteristics of the sample?	All participants were employees of HTA bodies.

Data collection		
17.	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Yes, a full focus group guide was prepared and provided to participants. It was not pilot tested.
18.	Were repeat interviews carried out? If yes, how many?	No.
19.	Did the research use audio or visual recording to collect the data?	Audio recording was used to collect the data.
20.	Were field notes made during and/or after the interview or focus group?	All audio recordings were transcribed vebatim and field notes were taken.
21.	What was the duration of the interviews or focus group?	Around 2 hours.
22.	Was data saturation discussed?	No.
23.	Were transcripts returned to participants for comment and/or correction?	Yes.
Domain 3: analysis and findings		
Data analysis		
24.	How many data coders coded the data?	Transcripts were coded by EvO and VF. VF then implemented the codes in NVivo upon agreement of EvO and VF on the coding tree and definitions.
25.	Did authors provide a description of the coding tree?	Yes, a codebook was developed including a definition of the code.
26.	Were themes identified in advance or derived from the data?	Both deductive and inductive codes were used.
27.	What software, if applicable, was used to manage the data?	Nvivo 12 was used to manage the data.
28.	Did participants provide feedback on the findings?	No.
Reporting		
29.	Were participant quotations presented to illustrate the themes/ findings? Was each quotation identified?	Yes, quotes are followed by the participant code.
30.	Was there consistency between the data presented and the findings?	Yes.
31.	Were major themes clearly presented in the findings?	Yes, results are presented per main theme.
32.	Is there a description of diverse cases or discussion of minor themes?	Yes, attention was given to statements mentioned by individual participants.

Supplementary material II Focus group guide

II.I Preparations

During recruitment

- Plan and set up a teleconference meeting with all participants via Skype for Business or a face-to-face meeting
    - Provide the information sheet and consent form to all participants in advance via email and ask participants to sign and send back the consent form a day before the focus group (send reminder a week before the focus group)
    - If via teleconference: Ask participants to call in separately, alone, in a quite space and with their camera and sound on
- Provide your and your assistants' phone number(s) to the participants

Day of the focus group

- Check if you received signed informed consent forms of all participants. If participants did not sign their consent form, they cannot participate in the focus group
- Have two audio recorders (+ extra batteries) with you and place these near your laptop/on opposite ends of the room
- Dress code for moderator and assistant(s): Business, formal

Moderator and assistant team

- A meeting between moderator and assistant should be planned before the focus group to go over the guide and discuss the moderator and assistant's tasks.

Attitude of moderator:

- If via teleconference: Calls into the teleconference separately from assistants (audio via telephone, not computer; video via computer)
- Exercise mild unobtrusive control (moderate the discussion but do not interrupt)
- Steering the focus group where needed
- Adequate knowledge of topic
- Appears like the participants
- Use purposeful small talk
- Do not complement or discourage stakeholders on the points they make
- Alert and free from distractions (put cell phone off and do not have your cell phone on you)
- Have the discipline of listening and apply active listening
- Familiar with questioning route (know the protocol very well)
- Consider the different types of participants and try to balance the conversation while addressing the obligatory topics: dominant talkers, shy participants, etc.

Tasks of the assistant:

- If via teleconference: Calls into the teleconference separately from the moderator and other assistants via telephone, not computer
- Takes careful notes (bring laptop)
    - Verbal reactions (Audio: Discussion, changes in attitude (voice)
    - Nonverbal reactions (Video: movements, attitudes, emotions)
- Controls for equal participation by all participants and informs the moderator if some participants are not getting the chance to participate
- Monitors audio recording equipment
- Time management via discrete signs or verbal communication to the moderator
- Gives a general summary of what has been said at the end of the focus group

II.II Focus group agenda

Introduction

Everything below in Italic is to be said to the participants, everything in black is guidance and if applicable can be told to the participants in your own words. In bold the timing of actions is given; however, this is an indication of time, it is more important to finish the two first topics than to rush through the focus group and complete all three topics.

00:00 Welcome the participants while they call in on the teleconference

- Try to get every participant's name directly and welcome them
- If participants try to participate without having signed the consent form, ask them if they can sign the consent form on the spot and send a scan per e-mail within a couple of minutes. If this is not possible, ask them to leave the teleconference
- Wait until all participants have joined till 5 minutes from start of teleconference

00:06 When all participants arrived and completed the forms, start the focus group with a general introduction:

- *Welcome, my name is* (your first name), *working as PhD/Master researcher at* (institute) *and I will be your moderator today. In addition, also* (first name of assistants) *called in to help me with the focus group*
- *My role as moderator will be to guide the discussion*
- *The discussion that we will have today is on the assessment and use of information on patient preference studies in HTA and reimbursement decisions*
- *Today's discussion is part of a study within a large European project called IMI PREFER. PREFER looks at how and when it is best to perform and include patient preferences in decision-making during the drug life cycle. The end-result of the PREFER project will be recommendations to support development of guidelines for industry, Regulatory Authorities and HTA bodies.*
- *We want to have this discussion with you as (name organization), since we think it is important to know how you feel about using these preferences in health technology assessment*
- *The opinions collected today will be used to write reports and publications to inform companies, health authorities, researchers and other parties on how to use patient preferences*
- *The focus group will take about 2 hours*

00:08 Explain the rules:

- *There are no right or wrong answers, only differing points of view*
- *We are looking for your opinions and hope for a good discussion*
- *It is possible that you do not agree with all opinions, but we ask you to listen to each other's points of view; each view is important to us and counts. Afterwards you are welcome to provide your view.*
- *We're audio recording, so it would be very helpful for the analysis if only one person is speaking at a time*
- *We will address each other only by their first name*
- *If there are any questions or terms that are used during the focus groups that are not clear to you, please let us know*
- *So, we will now start the recording. Is that OK for everybody?*
- *First, to get to know each other, could everybody state their name and job title?*

00:10 Introduce the topic of patient preferences:

- Definition of the FDA: *"The relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions"*
- *In other words, patient preferences are the basis of how patients choose a particular treatment over others. To make a choice, patients make trade-offs between a treatment's characteristics, weighing its advantages and disadvantages collectively.*
- Example: *A patient preference study asks patients about what they want from a flu vaccine (flu shot) by asking what different characteristics matters most to them, such as the probability that it is effective, how long it lasts, its side-effects, where patients can get it, or how much it costs. Some patients might say that the effectiveness of the vaccine is most important, while others think that a vaccine should have the lowest level of side-effects. Therefore, we ask patients to fill in a survey or take part in an interview for example, to in the end see what matters the most to each patient.*
- *From a patient preference study, we can learn what features of treatments are important to patients (attributes), how important these are in making a choice, how patients make trade-offs between attributes and treatment options, we can investigate the acceptability of products and we can identify subgroups within patient populations with different risk tolerances.*
- *We want to clarify that we know that it may not be necessary to take patient preferences into account in every evaluation and that in the HTA context often societal preferences are sought. However, when there is uncertainty in the available clinical evidence and it is unclear whether a health technology should be reimbursed or not, the HTA or reimbursement decision could be preference sensitive and patient preference studies might be able to further inform these assessment and decisions. (4 scenarios mentioned by EMA: unmet medical need, what matters most, acceptance of trade-offs, acceptance of uncertainty). All the questions we will ask you are on preference sensitive decisions and evaluations.*
- Ask if this is understandable to all
- *If there are any questions or terms that are used during the focus groups that are not clear to you, please let us know*

Current criteria used in the HTA procedure of the respective country

00:15 *Before bringing up patient preferences, let us begin with the criteria to assess the value of therapies that are currently used in the HTA procedure of your respective country. I will tell you what we found in literature and then I would like to ask you what criteria are missing.*

- *Germany:*
  In Germany, the Federal Joint Committee (G-BA) and IQWiG (the Institute for Quality and Efficiency in Health Care) can be seen as a tandem. The G-BA has the decision-making power and commissions IQWiG with technology assessments that are then appraised by the G-BA according to the principles of effectiveness, necessity, and cost-effectiveness. The main criterion however, is the added therapeutic benefit of the medicine (= relative therapeutic value). Economic factors are considered to be less important influential criteria.

- *Belgium:*
  In Belgium, the Drug Reimbursement Committee (*CTG*) was established in 2001 to assess the efficacy, safety, convenience, applicability, and effectiveness of a drug relative to existing treatment alternatives. Products can be granted an "added therapeutic value" class 1 label, this is a yes–no decision. It is only granted if there is at least one positive superiority trial on primary end points against an active control or against a placebo control if there is no alternative. For products with an added therapeutic value, a request for reimbursement has to be accompanied by an economic evaluation including a CEA and a budget impact analysis. For the other class 2 and 3 pharmaceutical products, only a budget impact analysis is requested.

- *Canada:*
  In Canada, the HTA infrastructure consists of a mix of centralized and decentralized structures and processes. HTA functions are carried out by national groups, provincial bodies, and hospital-based units. In 1989, CADTH was created as stakeholders felt that Canada needed a coordinated approach in assessing health technologies. The result was an organization that harnesses Canadian expertise from every region and produces evidence-informed solutions that benefit patients in jurisdictions across the country. A centralized review process exists at CADTH through the Common Drug Review and pan-Canadian Oncology Drug Review. Health technologies with the highest priority will be evaluated first based upon criteria such as comparative clinical effectiveness and cost-effectiveness, via a cost-utility analysis with outcomes captured as QALYs and budget impact assessment. Notable is that the assessment also focusses on the experiences and perspectives of patients. That is why patient input is currently used to inform and design assessment protocols; to interpret trial results; to identify use, equity, and ethical considerations; and to critique assumptions in economic models.

- **What would you have to add to this description to complete the list of criteria that are currently used in the HTA procedure in your country to assess the value of therapies?**
- Summarize (very briefly) with confirmation (list the criteria on a slide while sharing the screen to facilitate the discussion)
- Review purpose and ask if anything has been missed and move on to next topic

Integration of patient preferences

00:30 *There seems to be a consensus among stakeholders on the potential value of patient preferences in decision-making. However, actual application and integration of patient preferences in HTA and payer decision-making is limited and not systematic. In addition, the possibilities and processes to incorporate patient preferences in HTA and payer decision-making may be different per country. Therefore, we are conducting these focus groups in different countries. We will now ask you some questions to understand how patient preferences could be used in the HTA system in your country.*

- **We previously discussed what criteria are used in your country to assess the value of therapies. According to you, which of these criteria should be investigated in patient preference studies?**
    - **Which criteria (features of treatments – not of the population) should we ask patients their opinion on?**
        - Examples: Benefits, risk, administration, cost, etc.
        - If certain criteria are excluded from patient preference studies: Why should these criteria not be included in patient preference studies?
- **What elements of a value assessment do you believe patient preference studies inform?**
        - Examples: cost-effectiveness analysis, budget impact analysis
- **Where could they be integrated in evaluations or processes at your institution?**
        - Examples: Early dialogue/scientific advice; During submissions, evaluations and reimbursement discussions; Post-marketing approval
    - Would patient preferences serve as separate input to the deliberative process or could they be integrated in economic evaluations (cost-benefit analysis, cost-effectiveness analysis, or cost-utility analysis)?
        - How do you think that patient preferences be compared to, or combined with other decision criteria such as efficacy, safety risks, quality, cost, etc?
        - How do you think that patient preferences can be combined with or put next to QALY's?
- Multi-criteria decision analysis (MCDA) is any method that establishes criteria, weights them in terms of importance, and scores each alternative on each criterion to create an overall assessment of value. It has the potential to consider whatever criteria a decision maker judges relevant and, if done well, can support transparent and consistent decision-making. This is done by: (i) defining the decision context: identifying decision makers and the options to be evaluated; (ii) identifying the criteria to be used to assess the options; (iii) Measuring the performance of each option against the criteria; (iv) eliciting preferences for changes within and between criteria; (v) aggregating performance and preferences into an overall assessment of the value of the options. (9,68).
- **What is your opinion on incorporating patient preferences in MCDA's in the HTA context?**
    - **What is your opinion on weighing clinical and economic criteria in an MCDA according to their importance to patients?**
    - **What weight should patient preferences receive in HTA and payer decision-making compared to preferences of other stakeholders?**
- **What do you think the impact of patient preferences could be on HTA and payer decision-making?**
- Summarize (very briefly) with confirmation
- Review purpose and ask if anything has been missed and move on to next topic

Evaluation of patient preference studies

01:10 *The following topic deals with quality requirements for patient preference studies aiming to inform HTA and payer decisions.*

- **If a patient preference study would be submitted to you as part of a submission dossier, how would you evaluate it?**
- **What evaluation criteria would you use to assess the quality of the study?**
- **How do you think you could evaluate the impact of patient preferences on HTA and payer decision-making?**
- Summarize (very briefly) with confirmation
- Review purpose and ask if anything has been missed and move on to next topic

Case study

01:25 *Lastly, we would like to bring up a preference sensitive situation and discuss the possibilities for the integration of patient preferences in such a situation. The example we would like to discuss is gene therapy for the treatment of haemophilia. Haemophilia is an inherited bleeding disorder characterized by a deficit in coagulation factor VIII in haemophilia A or coagulation factor IX in haemophilia B. This causes bleeding in the joints or muscles, which leads to joint swelling, pain, stiffness and immobility of the limb. Today, haemophilia treatment is based on increasing factor concentrations through factor replacement therapy. The invasiveness of intravenous injections and the high administration frequency results in a high burden of treatment. Recently, gene therapy for the treatment of haemophilia is being studied as a new treatment option. A gene therapy medicinal product is a "biological medicinal product that contains a recombinant nucleic acid to regulate, repair, replace, add or delete genetic sequence and its effect relates directly to the recombinant nucleic acid sequence it contains or to the product of genetic expression of this sequence". Gene therapies are high-cost drugs, but one infusion can possibly replace lifelong administration of other high-cost drugs in the case of haemophilia. Gene therapy could potentially reduce the annualized bleeding rate to zero and eliminate the need for further factor replacement therapy in several patients. However, multiple challenges remain. Only a part of the patient population can be treated with gene therapy, as 30-50% of the population already possesses of antibodies against the vector/vehicle used in gene therapy to transport the gene into the target cells, in the case of haemophilia based on a virus. Besides, there is variability in outcomes after gene therapy administrations; some patients no longer have bleedings and don't need further factor administrations, while others still have some bleedings and need some additional factor administrations. The main adverse event that has been demonstrated is a light inflammation of the liver that can be treated with corticosteroids. In addition, current clinical data is insufficient to assess long-term safety and efficacy, therefore thorough follow-up of treated patients is crucial. In situations like this, performing patient preference studies could provide insights on the value of the product to patients and the acceptability to patients of benefits, risks and uncertainties.*

- **How valuable do you believe patient preferences can be in this situation?**
- **What would you like the patient preference study to investigate in this situation?**
- **How would you concretely integrate evidence from this patient preference study in the HTA process or reimbursement decision-making?**
- Summarize (very briefly) with confirmation
- Review purpose and ask if anything has been missed
- Thank participants for input

Ending

01:55 Final summary by the assistant to check if anything was misinterpreted by moderator or assistant
Ask if anything has been missed, or if anybody would like to add anything
02:00 Thank all participants for their participation and stop the teleconference

Supplementary material III Analysis plan

III.I Rationale behind the choice of the analysis method 'thematic analysis' (Howitt)

1. Thematic analysis focusses on what has been said rather than how it was said;
2. Thematic analysis is accessible to novice researchers, as it is less demanding than other methods (e.g. thematic analysis does not involve the same level of sophistication in data collection and theory building as grounded theory);
3. Useful technique when:
    a. Data collection has finished; thematic analysis, as opposed to grounded theory, does not have the requirement that the data being collected are reviewed part-way through the analysis and new approaches to data collection are initiated;
    b. Data consists of detailed textual material (e.g. focus group transcripts);
    c. A broad-brush approach to analysis is desired (as opposed to some fine-grained approaches which characterize some qualitative methods);

"How to do thematic analysis" (p.168-175, Howitt, 2016) has formed the basis of this protocol.

III.II Protocol

- Method: Thematic analysis based upon "Qualitative Research Methods in Psychology" – Howitt
- Core analyzing team ("CAT"): Valérie Forrester (VF) and Eline van Overbeeke (EvO)

Data familiarization

a. Howitt states that:
    i. Data familiarization can take place via several methods and will differ according to the details of the study. Ways of familiarizing with the data are: (i) being involved in the data collection stage, (ii) doing the transcription, (iii) playing the recordings repeatedly or (iv) re-reading the transcripts;
    ii. Start think about what is happening in the data during this stage. These early thoughts may suggest ways in which the data might be coded;
    iii. Use literal transcription (since thematic analysis is about what was said rather than how it was said);
    iv. Novice researchers to do all the data collection and transcription themselves;
b. Therefore, we will:
    i. Become familiar with the data by:
        1. Being present during the FGD as moderator or assistant;
        2. Doing the transcription and playing the recordings repeatedly
        3. Thoroughly reading the transcript several times;
    ii. Do the transcription done at verbatim (VF);
    iii. Have the transcripts checked for completeness and accuracy by moderator present during FGD (EvO);
    iv. Convene and discuss in order to agree together about what was said in that particular part of the FGD, should there be difficulties in understanding the transcript.

Initial coding generation

c. Howitt states that:
    i. This stage does not aim at identifying the themes that the research will generate; initial codes are nothing more than labels that will describe the content of 1 or 2 lines, they are not sophisticated analyses of the data. However, ideas as to what the themes might be can already occur (as during any stage of thematic analysis);
    ii. There are no "rules" describing that initial coding has to be done line-by-line. Coding frequency depends on circumstances, if every line is not possible then every 2/3 lines is "all right";
    iii. Best if these codes are based on an abstraction rather than something concrete, the more conceptual (i.e. the less concrete, the more abstract) the codes, the better the final themes;

iv. Researchers can choose:
    1. To work through the entirety of data or a subset of the data selected because it deals with a topic/matter of interest to the researcher;
    2. Between a theory-led or data-led approach;
v. During this stage, it may be appropriate to re-name codes that are covering the same meaning so they have the same wording;
vi. After the initial coding has been done, researchers should put together all of the transcript which has received a certain code. Reviewing all coded text of a certain code can reveal that:
    1. A coding label is not accurate/precise enough and needs to be renamed;
    2. New codes need to be formed as some of the data in a certain code "does not match";
    3. Certain codes need to be combined to one code as the coded text below two codes is too similar.

d. Therefore, we will:
    i. Aim for 1 initial code every 2/3 lines;
    ii. Use a data-led approach as described by Howitt, in which codes are primarily guided by careful analysis of what is in the data;
    iii. Independently code the entirety of the data (n=3 FGDs), since there are two core analyzers;
    iv. Convene after the independent coding of the data and perform steps vi.1, 2 and 3 together in order to agree upon the final list of initial codes

Search for themes based on initial codes

e. Howitt states that:
    i. This stage involves turning the initial codes into themes, which requires a lot of analytic work on the part of the researchers;
    ii. Searching for themes involves searching for patterns among the initial codes; as they will probably notice that some codes are more related than others;
    iii. Themes are the result of grouping and categorizing codes, which does not preclude that some codes might turn out to be very important and result in this code being an actual theme;
    iv. Some themes may be very obvious from the initial codes, whereas sometimes methods of sorting might help, e.g. by writing down all the initial codes on separate slips of paper and creating piles of related codes. NVivo or Word might be used in this stage.
f. Therefore, we will:
    i. Each independently search for themes based upon the initial codes;
    ii. Convene, discuss and agree upon the themes that we independently found.

Review of themes

g. Howitt states that:
    i. At this stage, there is a set of tentative themes which help to understand the data; In the case that these themes are not fully defined or refined at this stage, it is essential to examine these themes against the original data;
    ii. Reviewing of themes involves organizing the data around the set of themes just as previously the data was organized around the codes;
    iii. The possible scenarios of this stage are:
        1. Modifying or abandoning the theme if there is very little in the data supporting the theme;
        2. Dividing or subdividing the theme if the data in one theme actually imply two different themes or sub-themes;
        3. Find a new theme if some of the data you initially believed were part of the theme does not fit. If this is the case, a check for applicability of these themes to this data as well as the entire data set is advised.

h. Therefore, we will:
    i. Go back to each of the assigned transcript and organize the text that was captured by the initial codes around our identified themes;
    ii. Critically revise whether the theme should be abandoned, modified, (sub)divided or whether a new theme should be found;
    iii. Any modification to our initial found themes will trigger a discussion between EvO and VF and should this discussion lead to a modification of the initial list of themes, a check of the applicability of this modified list of themes to the entire data set will be done.

Theme definition and labelling

i. Howitt states that:
    i. Although it might be easy to give a label to a theme, it might be more difficult to define exactly what a theme is;
    ii. It is important to be able to conceptually distinguish one theme from another;
    iii. It is likely to continue developing sub-themes at this stage;
    iv. It is important to talk with other people about your analysis at this stage and allow them to question you and throw in ideas of their own.
j. Therefore, we will:
    i. Discuss and agree upon the final list of themes and sub-themes and our explanation to it. This will form the basis of the report;

Report writing

k. Howitt states that:
    i. The explanation and description of the themes in the final report of thematic analysis involve the selection of appropriate illustrations taken from the material which is associated with the theme;
    ii. Criteria that may be applied for this selection are:
        1. How ‘typical’ the material is of the data which belong to a particular theme;
        2. How ‘fit’ the material is in relation to the theme; some excerpts might illustrate particular features of the theme better than others;
        3. How ‘eye-catching’ the excerpt is; some data might be preferred to other excerpts as it is more vivid;
        4. Some might prefer using excerpts from just one of the participants to get into more detail about that particular case
    iii. It is helpful to indicate in the report the basis for your excerpt selection
l. Therefore, we will:
    i. Explain and describe in the final report the themes we identified;
    ii. Use appropriate excerpts to illustrate these themes;
    iii. Apply criteria ii.1, 2, 3 to select the excerpts we will use to describe the themes.

Supplementary material IV Definitions of codes

Themes	Definition
Current framework	
a. Current HTA process	The HTA process (including the different committees) of the respective HTA body
b. Current value assessment criteria	The criteria that are currently used to assess the value of health technologies by the HTA body
c. Other than value assessment	The criteria that are currently used to appraise health technologies by the HTA body
d. Current patient involvement	The way patients are currently involved in the HTA procedure
PPS design	
e. Criteria that should be investigated	Criteria that should be investigated in PPS
f. Criteria that should not be investigated	Criteria that should not be investigated in PPS
Organizational considerations	
g. HTA stage	Use of PPS in evaluations, value assessment and processes. The HTA stage in which patient preferences could be used to inform decision-making.
h. Weight	The weight of patient preferences in HTA in comparison to preferences of other stakeholders
i. Impact	The impact of patient preferences on decision-making in HTA and the evaluation of this impact on decision-making.
j. Quality requirements	The evaluation of the quality and transparency of patient preference studies to be considered robust scientific evidence
Gene therapy as a preference sensitive situation	
k. Value of pps for gene therapy	The value of PPS in examples like gene therapy for the treatment of haemophilia
l. Objectives of pps on gene therapy	The criteria that should be investigated in PPS in examples like gene therapy for the treatment of haemophilia
m. Integration of pps on gene therapy in HTA and payer decision-making	The way how HTA bodies would concretely integrate this evidence in the HTA process in examples like gene therapy for the treatment of haemophilia

Supplementary material V Value assessment criteria

This overview is based on focus group results and documentation provided by participants.

Table V.I Overview of criteria considered in the value frameworks of the respective countries (1-5)

		Assessment criteria			
		Clinical	Cost	Patient	Other
Canada	Canadian Drug Expert Committee	- Safety - Efficacy - Effectiveness - (dis)advantages compared to current therapy	- Cost - Cost-effectiveness - Budget impact	- Patient group input	/
	pCODR Expert Review Committee	- Effectiveness - Safety - Need - Burden of illness	- Cost-effectiveness	- Patient values	- Feasibility
	Health Technology Expert Review Panel	- Context (who requested the HTA and why) - Need - Benefits - Harms	- Economic impact (cost-effectiveness, budget impact)	- 'PP'	- Implementation - Legal - Ethics - Environmental impact
Germany	IQWiG's Drug Assessment Department	- Added patient-relevant benefits (mortality, morbidity, QoL) - Patient relevant harms	/	- Patient group input	/
	IQWiG's Non-drug Intervention Department	- Similar patient-relevant benefits - Patient relevant harms	/	- Patient group input	/
Belgium	Class 1	- Therapeutic value (efficacy, effectiveness, side-effects, user-friendliness, applicability) - Importance in clinical practice	- Price - Cost-effectiveness - Budget impact	/	/
	Class 2	- Therapeutic value (efficacy, effectiveness, side-effects, user-friendliness and applicability) - Importance in the clinical practice	- Price - Budget impact	/	/
	Class 3	- Importance in the clinical practice	- Price - Budget impact	/	/

1. Canadian Agency for Drugs and Technologies in Health. Health technology expert review panel [Internet]. 2015 [cited 2019 Nov 30]. Available from: http://www.cadth.ca/en/advisory-bodies/health-technology-expert-review-panel
2. Canadian Agency for Drugs and Technologies in Health. pCODR Expert Review Committee Deliberative Framework [Internet]. 2016 [cited 2019 Nov 30]. Available from: www.cadth.ca/pcodr
3. Canadian Agency for Drugs and Technologies in Health. Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review [Internet]. 2020 [cited 2019 Nov 30]. Available from: https://www.cadth.ca/sites/default/files/cdr/process/Procedure_and_Guidelines_for_CADTH_CDR.pdf
4. Ministry of Social Affairs; Public Health and the Environment. Royal Decree of 21 December 2001 (published 29 December 2001) [Internet]. B.S. [cited 2020 Jan 15]. Available from: http://www.ejustice.just.fgov.be/mopdf/2001/12/29_3.pdf#Page5
5. IQWiG. General Methods: Draft of Version 6.0 [Internet]. 2019 [cited 2020 Jan 20]. Available from: https://www.iqwig.de/en/methods/methods-paper.3020.html