Understanding Views around the Normative Decisions Made To Value Health-Related Quality of Life in Children and Young People: Study Protocol

Disclaimer: This research is funded by the National Institute for Health Research (NIHR) Policy Research Programme, conducted through the Policy Research Unit in Economic Methods of Evaluation in Health and Social Care Interventions, PR-PRU-1217-20401. The views expressed are those of the authors and not necessarily those of the National Institute of Health and Care Excellence, the National Institute for Health Research, the Department of Health and Social Care or its arm's length bodies, or other UK government departments.

1. Project Details

1.1. Investigator Details

Principal Investigator:

Name:	Dr Philip Powell
Post:	Research Fellow
ORCiD ID:	https://orcid.org/0000-0003-1169-3431
Employer:	University of Sheffield
Work address:	ScHARR University of Sheffield Regent Court 30 Regent Street Sheffield S1 4DA
Email:	p.a.powell@sheffield.ac.uk
Telephone:	+44 (0) 114 222 0794

Co-Investigators:

Name:	Dr Anju Keetharuth
Post:	Senior Research Fellow
ORCID ID:	https://orcid.org/0000-0001-8889-6806
Employer:	University of Sheffield
Work address:	ScHARR University of Sheffield Regent Court 30 Regent Street Sheffield S1 4DA
Email:	d.keetharuth@sheffield.ac.uk
Telephone:	+44 (0) 114 222 0884

Name:	Dr Clara Mukuria
Post:	Senior Research Fellow
ORCID ID:	https://orcid.org/0000-0003-4318-1481
Employer:	University of Sheffield
Work address:	ScHARR University of Sheffield Regent Court 30 Regent Street Sheffield

S1 4DA
Email: c.mukuria@sheffield.ac.uk
Telephone: +44 (0) 114 222 6395

Name: Professor Donna Rowen
Post: Professor of Health Economics
ORCID ID: https://orcid.org/0000-0003-3018-5109
Employer: University of Sheffield
Work address: ScHARR
University of Sheffield
Regent Court
30 Regent Street
Sheffield
S1 4DA
Email: d.rowen@sheffield.ac.uk
Telephone: +44 (0) 114 222 0728

Name: Professor Allan Wailoo
Post: Professor of Health Economics
ORCID ID: https://orcid.org/0000-0002-9324-1617
Employer: University of Sheffield
Work address: ScHARR
University of Sheffield
Regent Court
30 Regent Street
Sheffield
S1 4DA
Email: a.j.wailoo@sheffield.ac.uk
Telephone: +44 (0) 114 222 0729

1.2. URMS (University Costing) Reference Number
173657

1.3. External Advisors
Advisors from National Institute for Health and Care Excellence (NICE), including Dr Koonal Shah
Advisors from Department of Health and Social Care (DHSC), including Edward Aveyard

1.4. Project Title
Understanding views around the normative decisions made to value health-related quality of life in children and young people

1.5. Short Title
Perspectives on the normative decisions for valuing health in young people

1.6. Ethics Project Reference Number
046269

1.7. Protocol Version Number and date
Version 4.0, 21st April 2022

2. Research Question(s)

I. What are the opinions of the general public on whose preferences should be elicited and which perspective should be used when valuing the health-related quality of life (HRQoL) of children and young people?

II. Taking into account the evidence from (I), whose preferences and which perspective do experts think should be used when valuing the HRQoL of children and young people?

3. Abstract

Developing better methods for measuring and valuing health related quality of life (HRQoL) in children and young people is a priority area for NICE. One aspect of this is the normative decisions that are made around the valuation of HRQoL in children and young people for use in Health Technology Assessments (HTAs) for submission to NICE. There is limited evidence currently available about the public's views on how valuation studies should be designed to generate values for the HRQoL of children and young people. However, it can be argued that the normative decisions on how valuation studies should be conducted (whose health should be imagined, which tasks should be used) and who should be involved in them (adults, young people or both) should take societal preferences into account. Furthermore, little consensual insight has been observed or documented amongst experts involved in HTAs (including health economists and decision-makers) regarding their perspectives on who should be asked and under what conditions. Using a two-stage methodology, the proposed research seeks to produce novel evidence on the public's viewpoint on the normative decisions related to the valuation of health in children and young people using focus groups. These findings will then form part of the material for a Delphi process with key experts in an attempt to reach and report a consensus of views on who should be asked and which perspective used for child health valuation.

4. Policy relevance

- This topic in particular has been identified by NICE as a research priority (Health-related Quality of Life Task and Finish Group Report https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/chte-methods-consultation)
- This project has been proposed in response to a request from NICE.

5. Aim(s) of the Project

This project aims to better understand public and expert opinion around the valuation of the HRQoL of life of children and young people, in particular around the normative questions of whose preferences to elicit (adults, children or both) and from which perspective (who should be imagined is living with impaired health). This will be achieved in 2 stages detailed below:

5.1 Stage 1: Opinions of the general public

The opinions of the general public will be determined using semi-structured qualitative focus groups. Focus groups allow participants to clarify issues with the researcher, which is important given the complexity of health state valuation. They also enable participants to discuss their views with other members of the public which can enhance understanding and engagement. Five focus groups will be undertaken with 6 participants in each group. Each focus group will be led by a researcher, with another researcher co-facilitating where appropriate. The facilitators will provide information on the arguments around whose preferences and which perspective should be used, and will follow a topic guide to seek the opinions of the public. The focus groups will be audio-recorded and transcribed verbatim. The focus groups may be held face-to-face or online and this will be determined both by the COVID-19 situation at the time and latest recommendations about undertaking qualitative research during the pandemic. The sample will be restricted to adults (18+ years) and will be

purposively sampled to include a range of ages, genders, ethnicities and whether participants have children aged under 18 years. Focus group participants will be recruited via a market research agency and will be compensated for their time in accordance with the agency's standard compensation amount. Consent will be taken from the focus group participants. Prior to undertaking the focus groups, the Patient Advisory Group (PAG) (see section 10 below) will input into the education material and topic guide, to help ensure that the education material is appropriate and understandable. The data will be analysed using Framework analysis to generate themes and sub-themes. Quality of the analysis will be assured (see section 7.2) and research findings will be summarised, as described below.

5.2 Stage 2: Opinions of experts

A Delphi panel will be conducted with experts. Experts will be selected in consultation with NICE and the Policy Research Unit on the economic evaluation of health and care interventions (EEPRU) advisors, and it is proposed that these may include health economists, experts from the NIHR Child and Families Policy Research Unit, and representatives from NICE and DHSC. This stage will involve a minimum of 30 experts in the first round, who will be invited to be included across all three stages of the Delphi panel (though it is expected there will be some dropout across the three stages). The evidence from Stage 1 will be used to inform the information provided to the panel, alongside the theoretical, normative and practical arguments made in the published literature around whose preferences and which perspective. The findings of the Delphi panel will be summarised, as described below.

6. Scientific Background

In HTA, HRQoL can be assessed using utility values which represent the preferences for different health states. These values are generated for adult or child measures or vignettes in valuation or preference elicitation studies. Guidance on the valuation of adult health states is relatively well established (NICE, 2022; Rowen et al., 2017). Under UK guidance for HRQoL evidence submitted to NICE, utility values should have been generated using preferences elicited from a representative sample of the general population using a choice based technique (NICE, 2022). The standard perspective that is used is that the general public imagine themselves living in the impaired health state, but this is not specified in the NICE guidance. The guidance also does not specify that the sample should be adults, rather than children.

Guidance on valuing health for children and adolescents, however, is less well developed, with NICE guidance stating "there are methodological challenges when developing value sets for children and young people" (NICE, 2022, p. 182). In this context, at least two normative questions are apparent: 1) who should we ask to value child and adolescent health states, adults or children and adolescents themselves? And 2) what perspective should respondents be asked to adopt, with people valuing their own health or responding on behalf of others? Each of these questions raises a range of issues that need to be thought through. For example, if children and adolescents value the health states, what age range and methods are appropriate? If adults value health states for children, what perspective should be used (e.g. thinking about a hypothetical child of a certain age)? These questions matter, because different decisions made in response to these questions lead to different outcomes, which ultimately alters information used to inform HTA decisions.

In 2020 a standardised valuation protocol for the EQ-5D-Y-3L was developed (Ramos-Goñi et al., 2020) and since then two value sets for EQ-5D-Y-3L health states have been published accordingly (Prevolnik Rupel et al., 2020; Shiroiwa et al., 2021). In the standardised protocol it is stated that an adult general population should value health states for a 10-year-old child. This deviates from traditional valuation methodology of the EQ-5D, by asking adults to value health for someone else

(not themselves) and for a child (not an adult). Further, as recently noted by Lipman et al. (2021), while a normative justification for using members of the general public is provided (they collectively bear the costs of healthcare; the 'taxpayer perspective'), no additional rationale is given for using a child perspective. This is a difficult methodological decision and arguments exist for and against, which make it difficult to justify without drawing on further evidence or consultation. Following the logic of the 'taxpayer perspective' (advocated by Ramos-Goñi et al., 2020), more information regarding the public's views about what should be done in this situation would be beneficial.

Historically, the decision of who should be asked has been made based on arguments by health economists (see Helgesson et al., 2020), with little consultation with the members of the general population who bear the cost of, and potentially benefit from, health technologies. Ironically, this lack of consultation somewhat contradicts the 'taxpayer perspective' argument that is often used to justify the use of adult general public values (i.e. that the taxpaying public funding healthcare should have input into decisions in healthcare). Further, this stands in contrast to public and patient involvement and engagement (PPIE) and "nothing about us without us" initiatives now dominating health research (Versteegh & Brouwer, 2016).

There has been an increase in studies using utility values to describe child health (Kwon et al., 2019), and clearer guidelines have been requested to help facilitate choices for decision makers (Hill et al., 2020). While a decision has been made for the EQ-5D-Y-3L valuation protocol to have adults value health states in the context of a 10-year-old child (Ramos-Goñi et al., 2020), further empirical and normative work must be conducted to establish the appropriateness and acceptability of this approach, to provide feedback to decision makers, and to inform future guidance. Moreover, when this evidence is collected, distributing this to experts and key stakeholders in the decision-making process for their awareness and feedback is essential to ascertain their views and move towards consensus on an agreed approach towards the aforementioned normative decisions for valuing child and adolescent health. Delphi studies are particularly suited to such a purpose as they are designed to facilitate expert consensus on important research issues (Barrett & Heale, 2020).

This work will use a focus group methodology with members of the general public to elicit perspectives on who they think should value child and adolescent health and how (using what perspective). This will be followed by a Delphi study with experts and other key stakeholders in the HTA space, where the evidence from the focus groups will be combined with known theoretical, normative and practical arguments and presented to participants, with exercises to move towards a recorded expert consensus on these issues. The work is being conducted contemporaneously to another 18-month project led by the PI on 'Who should be asked in health state valuation exercises for children and adolescents? Views of the adult and adolescent general public' funded by the EuroQol Group and a cross-country collaboration with researchers in Sweden, which uses a different methodology involving a large online survey in both the UK and Sweden. The research questions are complementary and there is likely to be shared learnings between these two projects. However, this project makes two unique contributions through: i) rich qualitative data from the focus groups into public preferences; and ii) a consensus-based understanding of experts' preferences.

7. Plan of Investigation

7.1 Design

The overall project has a mixed design split into two sequential stages.

7.2 Methodology

Stage 1 involves focus groups with members of the general public in order to identify their views on who should be asked and using what perspective for valuing child and adolescent health states.

Stage 2 involves a Delphi study with experts in the valuation of health and HTA, which incorporates evidence derived from Stage 1. Experts will be selected in consultation with NICE and EEPRU advisors, and it is proposed that these may include health economists, experts from the NIHR Child and Families Policy Research Unit, and representatives from NICE and DHSC.

The methodology of each stage is detailed below.

Stage 1 methodology

Five semi-structured qualitative focus groups will be conducted with 6 members of the adult general public in each group (total sample of 30 participants). Focus groups allow participants to clarify issues which is important given the complexity of valuation. They also enable participants to discuss their views with other members of the public which can enhance understanding and engagement. Each focus group will be led by a researcher, with another researcher co-facilitating where appropriate. Participants will be purposively sampled to include a range of ages, genders, ethnicities and whether participants have children aged under 18 years, based on the following sampling grid (Table 1):

Table 1. Sampling framework based on a sample size of 30 participants.

Sex		**Ethnicities?**		**Age (yrs) | Children < 18 years?**				
Male	Female	White	Non-white	18-30 | Yes	18-30 | No	31-65 | Yes	31-65 | No	66+ | No
15	15	20	10	7	6	7	6	6

Focus group participants will be recruited via a Market Research Agency and will be compensated for their time in accordance with the agency's standard compensation amount. Consent will be taken from the focus group participants. It is anticipated that the focus groups will last up to 90 minutes.

A topic guide (or "interview schedule") will be used to help provide structure to the semi-structured focus groups and ensure that all important information is covered in the session. This topic guide will be reviewed by the Public Advisory Group (PAG, see section 10), prior to the research. Following consent procedures and an introduction, the focus group will be divided into two phases:

a) *Informational phase*: Explanatory materials (developed as part of this research) will be shown to participants to explain the context and normative issues of interest, including health state valuation and its application in children and adolescents. This will take the form of a short video (i.e., narrated slides/animations). The educational resources will be developed and refined with feedback from the PAG to ensure the educational material is appropriate and understandable. Following the presentation of the educational resources in the focus groups, participants' understanding will be probed qualitatively and they will be encouraged to ask questions for clarification (see topic guide). It is anticipated that this clarification stage will last up to 15 minutes.

b) *Discussion phase*: Using the topic guide, the facilitator(s) will then initiate a discussion with study participants on key topics, with suggested questions and prompts used as appropriate. It is anticipated that the discussion will last up to 60 minutes. At the end of the discussion phase, participants will be asked to complete a brief questionnaire on Qualtrics with sociodemographic

questions and perceived understanding of the material provided during the informational phase. This level of perceived understanding can be fed into the Delphi exercise as further contextual information for participants.

The focus groups will be audio-recorded on an encrypted device, transcribed verbatim, and then analysed using Framework Analysis to generate themes and subthemes. Quality of the analysis will be assured in at least the following four ways:

I. Dual coding and interpretation. The first two transcripts (33%) will be dual-coded with a meeting to discuss coding and refine the analytic framework, a meeting between two researchers will also be held following coding of all transcripts to provide an opportunity for discussion and reflection on the analysis.
II. Peer debriefing from members of the public. Confirmation of the findings will be sought from the Public Advisory group, by presenting them with an overview of our analysis, the analytic decisions made, and supporting data, for feedback and discussion.
III. Audit trail and transparency. All methodological decisions made and coding will be recorded, allowing for a traceable audit trail from the raw data (transcripts) to the final framework. This will include any deviant or negative coding identified.
IV. Reflective diary. The primary researcher will keep a reflective diary throughout the qualitative research (i.e. prior to and after the focus groups and during coding) to facilitate reflexivity and enhance the audit trail of the research process.

While focus groups can be conducted both face-to-face and virtually, with pros and cons of each approach, our preference is for online focus groups for this project. This is due to the unknowns still present as a result of the ongoing COVID-19 pandemic and as it allows for the recruitment of individuals from throughout England (not just those resident to Sheffield for example). Online video interviews have been shown to be a valid alternative to face-to-face interviews in qualitative research (Iacono et al., 2016) and the PI has conducted qualitative interviews and focus groups online previously.

Stage 2 methodology

An online Delphi study will be conducted with a panel of stakeholders in HTA. The participants will be selected in consultation with NICE and EEPRU advisors, but it is proposed that these may include health economists and allied researchers, experts from the NIHR Child and Families Policy Research Unit, and representatives from NICE and DHSC. The Delphi method is recommended in areas where no clear and prima facie consensus exists (Murphy et al., 1998), which is the case for the normative decisions around valuing child health.

The research team in consultation with representatives from NICE and DHSC will draw up and agree upon a 'long list' of potential participants for the Delphi exercise, including affiliated stakeholder organisations and representatives to approach by email. The potential participants will be international in scope (but restricted to UK policymakers, given contextual differences across countries). They will be identified by a targeted search for authors who have published work in the area (i.e. in the last 5 years), the combined knowledge of the research team (i.e., of people working in the field), and the identification of relevant experts affiliated with key stakeholder groups (e.g. NICE, DHSC, EuroQol Group etc.). The modal amount of participants in the final round of a Delphi is approximately 11-25 (Diamond et al., 2014) and recruitment needs to take into account limited response rates and drop-out throughout the Delphi process. A minimum of 100 people randomly selected from the long list (after stratifying on stakeholder type and priority, to be agreed) will be contacted about participating, to meet a target of a minimum of 30 experts in the first round (assuming a 30% response rate). If necessary, additional people will be invited to meet this quota.

Participants who have taken part in initial rounds of the Delphi will be invited again to take part in subsequent rounds, with additional recruitment of potential participants from the long list if and as appropriate (e.g. in response to attrition).

The Delphi survey will be designed on Qualtrics (an online survey platform) and will be informed by the focus group findings and the theoretical, normative, and practical arguments made in the published literature around whose preferences and which perspective, identified via a targeted narrative review and from existing reviews. The survey will be designed by the research team, in consultation with NICE and EEPRU advisors and will be piloted in a small independent convenience sample (i.e. N=5) outside of the research team prior to launch. Following consent procedures, participants will be required to respond to a series of dichotomous and/or Likert scale questions (1-9) to indicate their preferences to a range of statements and/or attributes relevant to the normative choices made in valuing child health, the precise content of which will be agreed during the project. For example:

Adolescents (aged 16-18) should be included in samples valuing child and adolescent health states

1	2	3	4	5	6	7	8	9
	Do not agree			Neither agree nor disagree			Agree	

Participants will be asked to provide reasons for their responses in open-text questions and can opt to not answer a question if they would prefer not to. Furthermore, in the first round of the Delphi survey, participants will be asked to include any issues that they think are missing from the survey that they recommend we incorporate into future round(s) of the Delphi study (relevant to who we should ask and how in child health valuation).

Delphi studies are typically made up of multiple rounds (a minimum of two, with the majority lasting up to 3 rounds, Diamond et al., 2014). Using multiple rounds helps researchers move towards consensus (producing a convergence of individual judgments) by allowing them to present the results of prior Delphi rounds back to the participants, both in terms of measures of central tendency and qualitative supporting evidence for responses (Murphy et al., 1998). Participants then have the opportunity to adjust their responses to move towards a goal of consensus in the sample. Employing multiple rounds also allows researchers to assess stability / consistency in participants' ratings on key issues, using for example Cohen's kappa (weighted/unweighted; Dimairo et al., 2018). Participants will be given approximately 3 weeks to complete the Delphi, with reminders sent 1 week, 72 hours, and 24 hours before the deadline.

This study will use percent agreement in order to define consensus to Delphi survey responses, with ≥ 75% of responses being the median threshold used to define consensus in Delphi studies (Diamond et al., 2014). For binary items, this is consensus in one of the options selected, for the 9-point scale Likert-type items, responses are usually reduced into groups (in this case 1-3 = do not agree; 4-6 = neither agree nor disagree; 7-9 agree) and consensus is defined by ≥ 75% in either the first or last category. Extent of agreement/support can be further ascertained by using the full information on the 9-point scale, but will not be used for consensus judgments. The Delphi will run for a maximum of 3 rounds or until consensus is reached on all issues (whichever occurs first). The limit of 3 rounds is practical, but means that there may be some issues where consensus is not reached and these will thus identify particular areas of disagreement amongst experts for exploration in further work. To this end, degree of percentage agreement will be a useful yardstick for how much agreement or disagreement exists on core issues, even if they do not reach the consensus defined a priori.

The data from the Delphi exercise will be descriptively analysed (e.g. N responses, median, mean, and estimates of dispersion) and presented for reach round separately. Open-ended (qualitative) feedback will be qualitatively synthesised and summarised using thematic analysis (Dimairo et al., 2018). Brief background data on participants will be collected at the start of the Delphi survey and will include questions such as gender, age, profession, years of expertise related to topic in question, country of location. Results can be clustered by limited, but key participant characteristics, such as profession (e.g. researcher, policy-maker etc.) and country of location (e.g. UK, US).
To ensure quality assurance of the Delphi process, the work will be designed, conducted and reported in compliance with the Recommendations for the Conducting and Reporting of Delphi Studies (CREDES) Checklist (Junger et al., 2017).

7.3 Setting

Stage 1 (Focus groups)
Given the unknowns as a result of the ongoing COVID-19 pandemic and the benefit of online focus groups for a wider breadth of recruitment, it is our preference to hold the focus groups for this project online, using University of Sheffield approved platforms, such as Blackboard Collaborate and/or Google Meet (as appropriate). Online meeting platforms and associated technologies have been shown to be valid alternative ways of generating qualitative data (Iacono et al, 2016).

Stage 2 (Delphi study)
The Delphi survey will be hosted online (using the Qualtrics survey platform), as is common in modern applications of this methodology. This allows for an international reach in recruitment and facilitates the timely collection and processing of digital data.

7.4 Participants

Stage 1 (Focus groups)
Stage 1 of this project will involve members of the adult general public, recruited via a Market Research Agency. Participants will be purposively sampled to include a range of ages, genders, ethnicities and whether participants have children aged under 18 years (using the sampling grid detailed above in Table 1). The following inclusion criteria will be applied:

Inclusion criteria:

a) Resident in England (the devolved nations of the UK have separate health services)
b) Age (18+ years)
c) Participants who are fluent in English
d) Consent to participate in the research

Exclusion criteria:

a) People lacking the capacity to consent
b) To ensure informed consent and useful and reliable data, in the absence of translation, participants must have a good understanding of English

Potential participants will be sent information about the research by the Market Research Agency and interested participants will be asked to provide an electronic copy of a completed consent form prior to the focus group.

Stage 2 (Delphi study)
Stage 2 of this research will involve expert stakeholders in HTA and child health valuation, to be identified in consultation with NICE and EEPRU representatives, using the methodology detailed above. Participants will be recruited internationally (i.e., policymakers will be restricted to the UK given the difference in context across countries, but experts that are qualified to comment on the UK system can be recruited worldwide). Participants will be a mixture of convenience and purposively sampled in an attempt to ensure a sufficient degree of representation from different stakeholder types (e.g. researchers, policy makers etc.) in the Delphi exercise. The following inclusion criteria will be applied:

Inclusion criteria:

a) Expert stakeholder in HTA/child health valuation (as defined by the research team and advisors)
b) Age (18+ years)
c) Participants who are fluent in English
d) Consent to participate in the research
e) If a policymaker, then based in the UK

Exclusion criteria:

c) People lacking the capacity to consent
d) To ensure informed consent and useful and reliable data, in the absence of translation, participants must have a good understanding of English
e) Policymakers in other countries

Potential participants identified for the Delphi exercise (i.e. the 'long list') will be approached by email with an invitation to participate in the study. This email will contain copies of the study Information Sheet and consent form and a link to the Delphi survey hosted on Qualtrics. Interested participants can then consent to take part on the survey pages themselves, before proceeding with the study.

7.5 Sample size

Stage 1 (Focus groups)
As the focus groups are intended to inform a wider Delphi exercise into consensus over normative decisions in child health valuation, the number of groups (and sample size) has been determined to balance both literature recommendations and practical considerations. Five focus groups with 6 people has been selected (i.e., a total of 30 participants). This is proposed because 3-6 groups, with 6-8 people is typically sufficient to provide an adequate degree of data saturation, with up 90% of themes coded (Guest et al., 2017). While achieving data saturation at the coding level is not a prerequisite of the number of focus groups that will be conducted, saturation will be monitored and reported as a quality indicator of the work.

Stage 2 (Delphi study)
While there are no formal recommendations for sample sizes in Delphi studies, the modal sample size is estimated to be between 11 to 25 participants (Diamond et al., 2014). While involving more people may increase the reliability of group judgments, particularly when ensuring different key stakeholder groups are represented, larger sample sizes can provide diminishing returns (Vogel et al., 2019). Taking this into consideration, a minimum of 30 participants will be recruited for the first round of the Delphi exercise, with top-up sampling for further rounds as needed.

7.6 Recruitment

Stage 1 (Focus groups)
Recruitment for Stage 1 will be facilitated by a Market Research Agency based on their standard procedures. Stage 1 participants will be approached by the Market Research Agency with full information about the study and an option to provide written (electronic) consent to take part. Verbal consent will also be taken at the start of the focus groups for those participating.

Stage 2 (Delphi study)
Recruitment for Stage 2 will be directly by email to people identified as potential participants in the Delphi exercise. The email will contain information about the study, with an attached Information Sheet and a link to the online Delphi survey, which will contain more information and the study consent procedures.

7.7 Incentives

Stage 1 (Focus groups)
People will be reimbursed for their time for participating in the focus group, based on accepted rates by the Market Research Agency.

Stage 2 (Delphi study)
No incentives will be used in Stage 2. However, participants will be acknowledged in the resulting publication, unless they prefer otherwise.

7.8 Outcome measure(s)

Stage 1 (Focus groups)
The primary outcome for Stage 1 of the project is indexed themes nested within categories that emerge from the qualitative focus groups related to research question 1: What are the opinions of the general public on whose preferences should be elicited and which perspective should be used when valuing the health-related quality of life (HRQoL) of children and young people?

Stage 2a (Delphi study)
The primary outcomes for Stage 2 of the project are descriptive quantitative data and supporting qualitative statements detailing consensus (or the lack of consensus) on statements/questions designed relating to research question 2: Taking into account the novel evidence from the general public, whose preferences and which perspective do experts think should be used when valuing the HRQoL of children and young people?

7.9 Analysis

Stage 1 (Focus groups)
The focus group transcripts in Stage 1 will be subjected to thematic content analysis using Framework, an approach developed by the National Institute for Health Research (NIHR) for the analysis of qualitative data (Ritchie & Lewis, 2003). The analysis will follow six stages, adapted from Gale et al. (2013): i) familiarisation; ii) coding; iii) developing a working framework; iv) applying the framework (indexing); (v) charting the data into a matrix; and (vi) interpretation (see Powell et al., 2021 for a worked example). Coding for stages (i-iii) will be conducted in hard copy, while Nvivo and Microsoft Excel will be used to manage the qualitative analysis from stages (iv-vi)

Stage 2a (Delphi study)
For the quantitative data, descriptive and aggregative analysis will be conducted (e.g. calculating measures of central tendency, percentage agreement, and stability using Kappa) using R. The qualitative data will be extracted into Word and a simple thematic analysis will be conducted.

7.10 Data Plan

The primary custodian for the data will be the project Chief Investigator, Dr Philip Powell.

Stage 1 (focus groups) will generate the following sources of data:

- Digital consent forms
- Sociodemographic data (such as age, gender, ethnicity, having children under 18, location within 9 ITL1 statistical regions of England)
- Quantitative (questionnaire) data on understanding of the educational materials/issues presented
- Encrypted audio files
- Anonymised transcripts
- Anonymised framework matrix
- Anonymised reflective diary entries

Stage 2 (Delphi study) will generate the following sources of data:

- Digital consent forms
- Personal contact details (i.e. name, affiliation, and email)
- Sociodemographic data (such as age, gender, profession, years of experience in role or related to HTA/child health valuation)
- Quantitative (survey) data in response to statements/questions on normative issues around valuing child health
- Written qualitative data to open-ended questions, explaining quantitative responses and/or giving additional comments on the survey

Personal contact details (i.e. identifying data) that is in the public domain will be collected in order to practically organise Stage 2 of the research (i.e. to invite people to take part in the Delphi survey and to track people's responses throughout the three rounds of the survey). They will also be used to generate an acknowledgement on any resulting publication, as is typical in Delphi studies. These personal contact details will be stored in a separate database to any other data produced, for only as long as they are needed (in line with the Data Protection Act).

All raw quantitative data that are collected (i.e. sociodemographic and questionnaire/survey data) will be transferred and stored in .csv files and read directly into R software for quantitative analysis. The data in these databases will not contain any direct identifying information, but for the Delphi study a unique alphanumeric ID will be used to link data back to respondents details. This link will be deleted from the database when no longer needed. Any raw data (such as in questionnaire files) will be deleted immediately after being transferred to the .csv file.

Encrypted audio files will be generated from the focus groups, using an encrypted Dictaphone. These will be uploaded to the University X Drive for transcription and deleted once the audio data has been transcribed and all coding is complete. Anonymization will take place during the process of transcription so that any potential identifying details are omitted. Transcripts will be stored as .docx files and in Nvivo files during analysis. The anonymised framework matrix will be stored as an .xlsx

file. Reflective diary entries will be made digitally by the researcher(s) (.docx files) and will not contain any identifiable participant data. Any paper notes from the focus groups to support these diaries will also not contain any identifiable data and will be destroyed as soon as possible after the focus group.

The qualitative data obtained during the Delphi survey will be transferred to Word documents and a degree of anonymization will be assured at this point (in case people have included any identifying information). However, a unique alphanumeric ID will be used to link data back to respondents for the purposes of the Delphi study. This link will be deleted from the files when no longer needed.

All data collected in Qualtrics will be deleted once fully downloaded and stored in the aforementioned file formats. All data will be stored on the University X drive, with access restricted to the research team. All university computers are password protected and have virus protection and firewalls to prevent access from external sources. University of Sheffield codes of practice for data management and storing the data will be adhered to throughout this research. All data generated through the project will adhere to the University of Sheffield information security policy: http://www.shef.ac.uk/cics/policies/infosecpolicy. The University of Sheffield is not an accredited ISO27001 institution. However, the university's information standards and procedures comply with this standard. All members of the research team have completed the University of Sheffield and ScHARR's training modules in information governance, which are renewed annually.

All non-identifying data generated in the course of the project will be archived and stored for 10 years after the study is over.

7.11 Project Plan

The proposed timescales assume a start date of January 2022 and are subject to timely recruitment of participants.

Task	Timeline
Stage 1	
(1) Develop protocol	January 2022
(2) Get quotes for recruitment to focus groups from MRA(s). Finalise methods	January 2022
(3) Videoconference with NICE and DHSC liaison officer on study design	Approx. 31st January 2022
(4) Design of study materials	February - March 2022
(5) PPI input into study and materials	March 2022
(6) Ethics application and approval process	April 2022
(7) Piloting of study materials and any revisions	April - May 2022
(8) Focus group data collection	May - July 2022
(9) Transcription	June - August 2022
(10) Data analysis	June - August 2022
(11) Videoconference with NICE and DHSC liaison officer on interim progress	Approx. 30th June 2022
(12) Member checking with PPI group	September 2022
(13) Write-up	September 2022
(14) Videoconference with NICE and DHSC liaison officer on findings	Approx. 30th September 2022
(15) Draft report submission	30th September 2022

Stage 2	
(1) Collation and design of materials for Delphi exercise, including information and survey	October - November 2022
(2) Identification of target expert(s) for the Delphi survey	October - November 2022
(3) Pilot of Delphi survey materials	October - November 2022
(4) Videoconference with NICE and DHSC liaison officer on progress and decisions	Approx. 16th November 2022
(5) Distribution of Delphi Stage 1 survey and response time (including write-up time)	November - December 2022
(6) Analysis of Stage 1 results and refinements to materials for Stage 2	January 2023
(7) Distribution of Delphi Stage 2 survey and response time (including write-up time)	January - February 2023
(8) Videoconference with NICE and DHSC liaison officer on progress and emerging findings	Approx. 1st February 2023
(9) Analysis of Stage 2 results and refinements to materials for Stage 3 (if necessary)	February 2023
(10) Distribution of Delphi Stage 3 survey and response time (if necessary) (including write-up time)	February - March 2023
(11) Final analysis of Delphi results	March 2023
(12) Final write-up	March 2023
(13) Videoconference with NICE and DHSC liaison officer on findings	Approx. 31st March 2023
(14) Draft final report submission	31st March 2023
(15) Final report submission following feedback	Expected 30th April 2023

8. Project Management

The Principal Investigator, Dr Philip Powell, will have general overview and management of the project and will ensure that the project progresses in accordance with the timetable provided above.

Co-investigators at the University of Sheffield include Dr Anju Keetharuth, Dr Clara Mukuria, Professor Donna Rowen, and Professor Allan Wailoo.

Strategic advisors from NICE and DHSC include Dr Lizzie Coates, Dr Koonal Shah, and Edward Aveyard. Further advisors may be involved later on in the project, as appropriate.

9. Ethical Issues

This is a relatively low risk project involving participation in focus groups, a Delphi study, and the collection of routine, aggregated socio-demographic data from participants themselves. Nevertheless, we acknowledge two primary ethical issues to consider.

The first is the capacity for potential distress or upset as a consequence of involvement in the qualitative research, for example, as a result of participants reflecting on child health and the value placed on this, including their own experiences. We will manage this potential for distress in a number of ways. First, in the information sheet and consent forms participants will be made

explicitly aware of their right to withdraw at any time up to the end of their participation in the study without reason or consequence, particularly if the focus group causes them to feel any distress. Second, it will be made explicitly clear to participants as part of the focus group that answering any question is not mandatory and individuals or the group are able to say if they do not want to talk about a particular issue or topic. Confidentiality between group members will be noted as a condition of participation. Finally, an experienced qualitative interviewer will undertake the focus groups, who has experience of working with the general public in similar studies around the valuation of health (e.g. Powell et al., 2021). If distress occurs during the focus group, we will stop the group and check with the participant that they are OK to continue or if they would prefer to stop participating at that point.

Participants will be advised to contact their GP or the NHS 111 service if they wish to seek advice or reassurance about their own or their child's health at any time. This information will be detailed on the Information Sheet.

A second ethical issue is the treatment of participants' data, such as personal contact details, and the appropriate handling of data to avoid identification. We already have a plan in place for the confidential, secure handling, and anonymization of the project data (see section 7.10 above). In particular, identifying (personal contact) details will be stored only for as long as necessary and will be stored separately from any other research data. Research data will remain confidential until published or shared for further research purposes in an anonymised form. Publications and reports will report data in an aggregated form. No personally-identifiable data will feature in reports and publications, so it will not be possible to identify anyone who has taken part from these documents. Special care will be taken to make sure no combination of data could be used to identify a particular participant who has taken part in the research (e.g. via combination of infrequent demographic characteristics in the patient group or from direct quotations). Participants will be made explicitly aware of what will happen to any data they provide in the consent process to taking part in the research. Only university computers will be used to analyse data, which are password-protected and have virus protection and firewalls to prevent access from external sources.

All data generated through the project will adhere to the University of Sheffield information security policy: http://www.shef.ac.uk/cics/policies/infosecpolicy. The University of Sheffield is not an accredited ISO27001 institution. However, the University's information standards and procedures comply with this standard.

Ethical approval for the project will be obtained from the School of Health and Related Research Ethics Committee at the University of Sheffield, prior to commencement of the study.

10. Public Involvement

The project will include Public Involvement, involving 3-4 participants from the EEPRU public involvement programme and 3-4 participants from the NICE public involvement programme. It is anticipated that the Public Advisory Group (PAG) will input into at least the following:

- Plan and topic guide for focus groups
- Educational resources/material for the focus groups
- Member checking/feedback on qualitative results

11. Dissemination

The following plans for dissemination have been made for this project, with the opportunity for additional dissemination (e.g. conference presentations) should stakeholders see fit:

- Stage 1 draft project report (expected 14th October 2022)

- Stage 2 draft project report (expected 31st March 2023)
- Final project report following feedback, for potential inclusion on EEPRU website (expected 30th April 2023)
- Submission of paper (combined across Stages 1 and 2) for journal publication (expected May 2023)

12. Intellectual Property

Any potential outputs will be the intellectual property of the University of Sheffield.

13. Funding Arrangements

This research is funded by the National Institute for Health Research (NIHR) Policy Research Programme, conducted through the Policy Research Unit in Economic Methods of Evaluation in Health and Social Care Interventions, PR-PRU-1217-20401.

14. References

- Barrett D, Heale R. What are Delphi studies? Evid Based Nurs. 2020 Jul;23(3):68-69. doi: 10.1136/ebnurs-2020-103303. Epub 2020 May 19. PMID: 32430290.
- Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, Wales PW. Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. Journal of clinical epidemiology. 2014 Apr 1;67(4):401-9.
- Dimairo M, Coates E, Pallmann P, Todd S, Julious SA, Jaki T, Wason J, Mander AP, Weir CJ, Koenig F, Walton MK. Development process of a consensus-driven CONSORT extension for randomised trials using an adaptive design. BMC medicine. 2018 Dec;16(1):1-20.
- Helgesson, G., Ernstsson, O., Åström, M., & Burström, K. (2020). Whom should we ask? A systematic literature review of the arguments regarding the most accurate source of information for valuation of health states. Quality of Life Research, 29(6), 1465-1482.
- Hill H, Rowen D, Pennington B, Wong R, Wailoo A. A Review of the Methods Used to Generate Utility Values in NICE Technology Assessments for Children and Adolescents. Value Health. 2020 Jul;23(7):907-917.
- Iacono VL, Symonds P, Brown DHK. Skype as a tool for qualitative research interviews. Sociological Research Online 2016; 21:12
- Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: Recommendations based on a methodological systematic review. Palliative medicine. 2017 Sep;31(8):684-706.
- Kwon J, Kim SW, Ungar WJ, Tsiplova K, Madan J, Petrou S. Patterns, trends and methodological associations in the measurement and valuation of childhood health utilities. Qual Life Res. 2019 Jul;28(7):1705-1724.
- Lipman, S. A., Reckers-Droog, V. T., & Kreimeier, S. (2021). Think of the Children: A Discussion of the Rationale for and Implications of the Perspective Used for EQ-5D-Y Health State Valuation. Value in Health.
- Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CF, Askham J, Marteau T. Consensus development methods, and their use in clinical guideline development. Health technology assessment (Winchester, England). 1998 Mar 1;2(3):i-88.
- NICE (National Institute for Health and Care Excellence) (2022). NICE health technology evaluations: the manual. NICE: London.
- Powell PA, Rowen D, Rivero-Arias O, Tsuchiya A, Brazier JE. Valuing child and adolescent health: a qualitative study on different perspectives and priorities taken by the adult general public. Health and quality of life outcomes. 2021 Dec;19(1):1-4.

- Prevolnik Rupel V, Ogorevc M; IMPACT HTA HRQoL Group. EQ-5D-Y Value Set for Slovenia. Pharmacoeconomics. 2021 Apr;39(4):463-471.
- Ramos-Goñi, J. M., Oppe, M., Stolk, E., Shah, K., Kreimeier, S., Rivero-Arias, O., & Devlin, N. (2020). International valuation protocol for the EQ-5D-Y-3L. Pharmacoeconomics, 38(7), 653-663.
- Ritchie J, Lewis J (Eds). Qualitative Research Practice: A Guide for Social Science Students and Researchers. Thousand Oaks, CA: Sage; 2003.
- Rowen, D., et al., International Regulations and Recommendations for Utility Data for Health Technology Assessment. PharmacoEconomics, 2017. 35: p. 11-19.
- Shiroiwa T, Ikeda S, Noto S, Fukuda T, Stolk E. Valuation Survey of EQ-5D-Y Based on the International Common Protocol: Development of a Value Set in Japan. Med Decis Making. 2021 Mar 23:272989X211001859. doi: 10.1177/0272989X211001859. Epub ahead of print.
- Versteegh, M. M., & Brouwer, W. (2016). Patient and general public preferences for health states: A call to reconsider current guidelines. Social science & medicine (1982), 165, 66–74. https://doi.org/10.1016/j.socscimed.2016.07.043.