VALUING CHILD HEALTH: EXPLORING THE USE OF A MIXED SAMPLE OF ADOLESCENTS AND ADULTS TO VALUE CHILD AND ADOLESCENT HEALTH STATES

REPORT BY THE DECISION SUPPORT UNIT

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EXECUTIVE SUMMARY

NICE and other international Health Technology Assessment (HTA) agencies have clear recommendations around the generation, source and usage of utility values for adults, but recommendations relating to health utilities for children are less prescriptive across all international agencies. The valuation of any preference-based measure requires decisions around whose preferences to elicit (e.g. patients vs. general population), using which perspective (e.g. one's own vs. that of another), and choice of preference elicitation technique (e.g. time trade-off (TTO) vs. discrete choice experiment (DCE)). In addition, where the elicitation technique does not produce values on the 1-0 full health-dead scale required to generate quality adjusted life years (QALYs), methods to do so are required. There may be good reasons to take different approaches when considering the valuation of child health compared to the approaches used for adults. The preferences for child and adolescent-specific health states used to generate value sets can be elicited from adults (members of the general public, parents, patients with comparable conditions to the child or healthcare professionals), young adults (e.g. 18-19 year olds), adolescents and children (including general public and/or patients). Previous research has shown that different populations provide different preferences. To date, no studies have explored the use of a sample that purposively includes both adults and adolescents to elicit preferences, using the same preference elicitation tasks, to generate a value set for a preference-based measure that reflects the values of adults and adolescents combined, despite this being a potentially attractive option.

The purpose of this report is to provide an overview of the ethical, practical and theoretical issues and implications arising from the use of a "joint" or "mixed" sample of adolescents and adults to value child and adolescent health states. In this report we define children as age below 11, adolescents as age 11-17, and adults as age 18 and over.

First, the report provides an overview of the literature on the methodological considerations of the valuation of child and adolescent health states, summarising the literature on the issues of whose preferences (adults or adolescents), which perspective, elicitation technique and mode of administration, and generating utilities

on the 1-0 full health-dead scale. An overview of existing published studies using the TTO elicitation technique with adolescents is also presented, since TTO is the method used to value adult EQ-5D and use of this technique would provide comparability in methods.

Second, the report presents a critical examination of the idea of using a mixed population of adults and adolescents to value child and adolescent health states, examining the practical, ethical and theoretical issues that arise. What is discussed is the use of a mixed sample comprised of both adolescents and adults, where all participants complete the same preference elicitation task and all preferences are modelled to generate a combined value set that reflects the preferences of both adolescents and adults. The discussion includes adolescent understanding and psychosocial maturity, ethical concerns, perspective, elicitation tasks, the selection of sample proportions across adolescents and adults and weighting of modelled results, and the empowerment of adolescents.

The existing evidence supports the use of methods such as TTO in adolescents, which would facilitate the use of a mixed sample to value child/adolescent health states. However, the minimum age where such a method could be applied is not clear. The evidence on whether adolescents are impacted adversely by considerations of death is also limited. The use of the same elicitation method for both adolescents and adults does not necessarily address concerns regarding perspective and the description of health states to ensure that the same states are being valued by adolescents and adults. There is a concern that the use of a mixed sample of both adolescents and adults does not address the crucial issue that this sample still does not contain children. The preferences that are elicited will therefore not reflect preferences of the full age range of the children and adolescents that the measure and value set are intended to be used for.

Third, the report summarises the only identified study reporting on public opinion around which perspective to use when eliciting preferences for child and adolescent health states from adults, which found that responses were split on this issue. A systematic search of the literature was undertaken to identify studies that report on

public opinion around whose preferences to elicit for the valuation of child and adolescent health states, but no relevant studies were identified.

In summary, the use of a mixed adolescent and adult sample to value child and adolescent health states has the advantage that it includes both the population who can potentially experience the health states, thus enabling adolescents to express their views around matters that may affect them, and the population that are taxpayers and voters. Overall, it appears feasible to use a mixed adolescent and adult sample to value child and adolescent health states. Valuation of health states from a person's own perspective (imagining yourself living in the health state) throughout the sample is suggested, but this is not without its limitations. TTO may be selected as the elicitation task, since TTO is a widely used and accepted approach in adult valuation samples. However, the evidence is limited around the minimum age of adolescents where it is appropriate and feasible to use tasks such as TTO, and no study was identified that purposively assessed acceptability, feasibility and framing of TTO in interviews with adolescent participants, exploring the issues by age of respondent. The published evidence has also focussed more on usage and feasibility than appropriateness, and there has not previously been consideration around the psychosocial maturity of survey participants that will impact on their choices. Therefore it is not straightforward to recommend a minimum age for use of TTO in a mixed sample of adolescents and adults using existing evidence. The selection of the proportion of adults and adolescents in a valuation study sample, and how to weight the sample and/or the modelled value set regarding adolescent participants relative to adults requires careful consideration in any mixed sample for valuation.

The report is limited by the paucity of academic literature on this topic, yet this is an important and relevant issue. The report reflects both the little literature that is available and the authors' opinions.

Summary of proposed recommendations, for consideration by NICE

Use of a mixed adolescent and adult sample to value child and adolescent health states has the advantage that it includes both the population who can potentially experience the health states, thus enabling adolescents to express their views around matters that may affect them, and the population that are taxpayers and voters. There

is evidence of the requisite cognitive capacity and prior administration of TTO in participants aged under 18, suggesting that undertaking a TTO valuation study of child and adolescent health states using a mixed sample of adolescents and adults may be feasible.

However, the use of a mixed adolescent and adult sample faces the disadvantage that there may be a discrepancy between the health state self-reported by children and adolescents and the health state that is valued, when adults value states imagining themselves living in the state (for example usual activities differ for adults and children). There is also a concern that the use of a mixed sample of both adolescents and adults does not address the crucial issue that this still does not contain children. In addition, prior to undertaking a valuation study using a mixed adolescent and adult sample it is recommended that research purposively designed to assess the acceptability, feasibility and framing of TTO in participants aged under 18 is more fully explored, and that the proportion of adolescents and adults that comprise the sample is given careful consideration.

Future potential research to address evidence gaps on these issues

- To explore the acceptability and feasibility of TTO in participants aged under 18, in particular by age in years. Qualitative research using focus groups and quantitative studies could be undertaken to examine adolescent views using a general population sample. If acceptable, the format and framing of tasks could also be explored.
- To better understand public opinion around the valuation of child and adolescent health states, in particular around the normative questions of whose preferences to elicit and from which perspective. Qualitative research using focus groups could be undertaken. However, the report authors were divided on whether this would be beneficial for NICE, and the value of doing this should be weighed up against whether this information is informative for NICE and whether this would be used to inform policy recommendations.
- To explore public opinion around the valuation of adult health states, in particular around the normative questions of whose preferences to elicit and whether this could potentially include adolescents and adults. The use of a

mixed sample for both adult and adolescent health states would mean consistency in the population providing preferences to score QALYs.

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TABLES

ABBREVIATIONS AND DEFINITIONS

ABBREVIATIONS	DEFINITIONS
16D	16 Dimensions
17D	17 Dimensions
AHUM	Adolescent Health Utility Measure
AQoL-6D	Assessment of Quality of Life- 6 Dimensions
CHU9D	Child Health Utility- 9 Dimensions
DCE	Discrete Choice Experiment
EQ-5D-Y	EQ-5D Youth Version
EQ-5D-Y-3L	EQ-5D Youth Version with 3 levels
EQ-5D-Y-5L	EQ-5D Youth Version with 5 levels
HTA	Health Technology assessment
HUI	Health Utilities Index
HUI2	Health Utilities Index Mark II
HUI3	Health Utilities Index Mark III
NICE	National Institute for Health and Care Excellence
QALY	Quality-adjusted life year
QWB	Quality of Well Being
ScHARR	School of Health and Related Research
TTO	Time trade-off
VAS	Visual Analogue Scale

1. INTRODUCTION

1.1. BACKGROUND

NICE and other international Health Technology Assessment (HTA) agencies have clear recommendations around the generation, source and usage of utility values for adults[1, 2]. NICE recommend the use of EQ-5D in particular, and that the preferences used to generate value sets of preference-based measures are elicited from the UK general public using a choice-based technique[2]. However, recommendations relating to health utilities for children are less prescriptive across all international agencies. It is likely that this is in part due to the limited research around these issues in relation to children.

There are at least nine child and adolescent-specific generic preference-based measures[3]: AHUM[4], AQoL[5], CHU9D[6-8], EQ-5D-Y (3L[9-11] and 5L[12]), HUI2[13], HUI3[14], QWB[15], 16D[16], and 17D[17], and one for infants[18]. EQ-5D-Y is related to EQ-5D with wording adapted to make it child/adolescent appropriate. Many measures include the provision of proxy versions for younger children. Across these measures there is no common approach used for valuation, with differences across the population valuing the health states, the perspective used in the preference elicitation task, and the preference elicitation technique[19]. In addition there is no UK value set for the EQ-5D-Y (3L or 5L)[20, 21], though there is a recently published international protocol for the valuation of the EQ-5D-Y-3L [22].

The valuation of any preference-based measure requires decisions around whose preferences to elicit (e.g. patients vs. general population), using which perspective (e.g. one's own vs. that of another), and choice of preference elicitation technique (e.g. TTO vs. DCE). In addition, where the elicitation technique does not produce values on the 1-0 full health-dead scale required to generate quality adjusted life years (QALYs), methods to anchor onto the 1-0 full health-dead scale are required. There may be good reasons to take different approaches when considering the valuation of child health compared to the approaches used for adults. Whilst many of the methodological choices around valuation can be informed by research, some methodological choices are normative and ultimately require a value judgement. In particular, the selection of

the population used to value child and adolescent-specific health states is a normative decision, that is likely to be informed by consideration of the practical, ethical and theoretical issues and implications. In addition, this decision can also be informed by consideration of the views of the general public, and potentially other stakeholders, about whose preferences should be elicited to value child and adolescent health states.

The preferences for child and adolescent-specific health states used to generate value sets can be elicited from adults (members of the general public, parents, patients with comparable conditions to the child or healthcare professionals), young adults (e.g. 18-19 year olds [23]), adolescents and children (including general public and/or patients). Previous research has shown that different populations provide different preferences (for example [24]), and theoretical, practical and ethical arguments can be made in favour of selecting any of these populations to value child and adolescent health states for use to inform public policy. There is little research involving the elicitation of preferences from younger children (rather than adolescents), as they are often considered to have greater difficulty in completing preference elicitation tasks. Previous studies have either elicited preferences from adults (general public or parents) or adolescents. Where adolescent preferences have been elicited using techniques that do not directly generate utility values on the 1-0 full health-dead scale, these have been anchored onto the 1-0 scale using young adult preferences (for example [23]). In these latter studies, adolescents provide the relative weightings of the dimensions and severity levels using one preference elicitation technique, and young adults anchor these relative weightings onto the 1-0 scale using a different preference elicitation task (for example [23]). Some studies have elicited preferences from adolescents and adults combined for own health, and for a small number of bespoke health states. For example, one study elicited adolescent and parent (as proxy) preferences using standard gamble and VAS for own health state and a small number of health states[25]. Other studies have elicited preferences for own health across a population that includes both adolescents and adults (see for example [26]). However, to date, no studies have explored the use of a sample that purposively includes both adults and adolescents to elicit preferences, using the same preference elicitation tasks, to generate a value set for a preference-based measure that reflects

the values of adults and adolescents combined, despite this being a potentially attractive option. This report aims to address this evidence gap.

1.2. AIMS AND OBJECTIVES

The purpose of this report is to provide an overview of the ethical, practical and theoretical issues and implications arising from the use of a mixed sample of adolescents and adults to value child and adolescent health states. This will be informative for considerations around the choice of population for the valuation of child and adolescent-specific preference-based measures. In this report we define children as age below 11, adolescents as age 11-17, and adults as age 18 and over.

This report aims:

- To provide an overview of issues to consider when choosing to recommend whether child and adolescent health states are valued by only adults, only adolescents, or a mixed sample of both adolescents and adults;
- To identify evidence gaps and make recommendations about future research that may be informative on these issues;
- To help inform NICE's future considerations about recommendations of the population used to value child and adolescent health states.

The study objectives are:

1. To provide an overview of the methodological choices required when valuing child and adolescent health states, focussing on whose preferences to elicit, from which perspective and using which elicitation method;
2. To critically examine the novel idea of using a mixed population of adults and adolescents to value child and adolescent health states to generate the value set for a preference-based measure, examining the practical, ethical and theoretical issues that arise;
3. To identify previous studies reporting on public opinion around the valuation of child and adolescent health states, in particular around the normative questions of whose preferences to elicit and from which perspective.

2. OVERVIEW OF CONSIDERATIONS IN THE VALUATION OF CHILD AND ADOLESCENT HEALTH STATES

This section provides an overview of the literature on the methodological considerations of the valuation of child and adolescent health states, for a more detailed review see [19].

2.1. WHOSE PREFERENCES

As stated above, preferences for child and adolescent-specific health states used to generate value sets can be elicited from adults and/or adolescents. Since previous research has shown that adult and adolescent preferences differ [24, 27-29], the choice of whose preferences to elicit impacts on the value set and the two are not interchangeable. The arguments discussed here are also summarised in Box 1.

Box 1: Arguments for and against the exclusive elicitation of adult or adolescent preferences for child and adolescent health states

	Adults	**Adolescents**
For	• Tax payers and eligible to vote • Consistency with the adult population used to value adult measures • Capacity to make decisions and legal age for other important decisions • No ethical concerns around the administration of tasks mentioning death or trading life years • Potential understanding of how ill health impacts on the lives of children and as they progress into adulthood (using child perspective) • Veil of ignorance (impartial and unbiased when using own perspective since they do not have a vested interest)	• Potential understanding of impact of health state on lives of adolescents (though questionable whether understand impact for children) • Veil of ignorance (impartial and unbiased) • Empowerment of adolescents (though can be argued this may not be a relevant consideration in this context) • Consistent with the United Nations Convention on the Rights of the Child, 1989 stating that the views of a child should be given weight in accordance with their age and maturity[30] • Age group that the preference-based measure is intended for (though the measures are also intended for use in children) • Age group that are impacted by resource allocation decisions informed by the elicited preferences (though the decisions will also impact children)
Against	• Do not fully understand the health state as experienced by children and adolescents • May not be impartial or unbiased when valuing health states that are framed as experienced by children and adolescents (i.e. using a child perspective) as they may have a vested interest (e.g. may be	• Adolescents are not regarded as autonomous legal, social and economic agents by society and the government. For example, adolescents are unable to vote and many adolescents are not tax payers • Ethical concerns are often raised around the administration of tasks mentioning death or

	Adults	Adolescents
	the parent of the child) and/or reasoning may be emotive • May find it difficult to imagine the health of a child or adolescent (if asked to value health states using a child perspective)	trading life years (particularly in younger adolescents) • May not have the psychosocial maturity to meaningfully complete preference elicitation tasks • May not be able to understand more cognitively challenging tasks (this will differ by age and the individual) • May not be able to imagine themselves in ill health (this will differ by age and the individual)

2.1.1. Adult preferences

Value sets for adult preference-based measures are typically elicited from adult members of the general population aged 18 and over. Preferences are elicited for hypothetical health states, and participants are typically asked to imagine that they themselves are in the health state. Arguments are provided for the elicitation of preferences from members of the general population rather than patients, including that they are voters in a democratic system, tax payers funding the health care system, and that due to a veil of ignorance around whether they will experience the health state they are impartial and unbiased. However, there is a value judgement about preferring those who may (or may not) have experienced health states over those who have (i.e. patients) and not all jurisdictions require general population values, for example Sweden recommend experienced utility values[31].

The use of adult preferences for child and adolescent health states can also be rationalised by similar arguments, in that children and adolescents are generally not voters and tax payers (though 16 and 17 year olds may pay tax). Counterarguments include that the health states are for children or adolescents, so members of the adult general population cannot experience these exact health states, unlike the valuation of adult health states. However, with child and adolescent states, adults will have had experience of being children and adolescents and may have experienced states similar to the child and adolescent states. Nevertheless, recall may depend on how

much older they are e.g. young adults vs. elderly, and, depending on the perspective that is used, respondents may not be aware the states are child and adolescent states. It is unclear whether adults are impartial or unbiased when valuing health states that are framed as experienced by children and adolescents. For example, adults may have pre-existing biases towards child health and the trading of life years for children, and may be more emotionally invested than when considering adult health, and this is an issue we will return to in section 3.

Nevertheless, the elicitation of preferences from adults to generate value sets for child and adolescent health states would provide consistency with the population selected to elicit preferences, but crucially this does not guarantee comparability in the elicited preferences, as discussed in section 2.2. There are also practical arguments for the elicitation of preferences from adults over adolescents. Adults arguably have greater understanding of preference elicitation tasks that can be cognitively challenging to understand and complete [32], though that they may have less understanding of the health state and how it impacts on children and adolescents. In addition, there are concerns around asking adolescents to complete preference elicitation tasks involving the consideration of being dead, and this is discussed in detail in section 3.

2.1.2. Adolescent preferences

The elicitation of preferences from adolescents is typically advocated on the grounds that it is children and adolescents, not adults, who can potentially experience the health states, and further that they better understand the impact on adolescents and children. Preferences differ for adults and adolescents, and arguably it is the preferences of the population who could experience the health states (i.e. the ages of people who the measure is intended for) that should be used to generate the values for these health states. The use of adolescent preferences to generate value sets ensures that the utility values used to inform resource allocation decisions reflect the preferences of the age group that are impacted by these decisions.

The United Nations Convention on the Rights of the Child states that children/adolescents who are capable of forming their own views should have the right to express their views in all matters affecting them, and further that their views should

be given weight in accordance with the age and maturity of the child/adolescent[30]. The UK abides by this treaty. Some institutions emphasise the importance of involving adolescents' opinions in decisions related to their health [30, 33-35]. There are also arguments around the empowerment of adolescents to make decisions for themselves[36].

However, adolescents are not regarded as autonomous legal, social and economic agents by society and the government. Older adolescents in particular can make many decisions for themselves, as from age 16 they can give sexual consent, consent to treatment in the NHS and join the Army and from age 17 they can drive a car. However this is contrary to other important decisions, such as voting, consumption of alcohol and marriage, which are only legally allowed for individuals aged 18 and over in the UK (with the exception of Scotland where marriage is legal at age 16 and in England marriage is legal at 16 with parental consent) and restricted films and videogames [37]. Further, it is likely that there are individual differences in the extent to which adolescents themselves want to be involved in decision-making about health (see for example [38]). However it is worth noting that even at age 18 people may not be considered full responsible, since you cannot adopt a child until age 21.

A counter-argument to adolescent empowerment is that the capacity of adolescents to engage in societally-impactful decision-making is potentially limited, with neurobiological arguments suggesting that while a typical adolescent may possess the necessary cognitive capacity for decision-making, they may need additional support to do so when compared to a typical adult. For example, on average, adolescents are more likely to take risks[38] and be less resistant to peer influence[39] during decision-making than adults. Research suggests that levels of psychosocial maturity (restraining oneself when exposed to emotional, exciting, or risky stimuli) lags behind cognitive capacity in the developing adolescent [40]. The extent to which levels of psychosocial maturity influence decision-making in health preference elicitation tasks has yet to be determined. However, research suggests that differences between adolescents and adults in decision-making may be less pronounced in tasks that promote more deliberative than emotional decision-making [41]. Preference elicitation tasks however may involve both deliberative and emotional decision-making, and this may differ by elicitation technique. Elicitation tasks involving consideration of death or

trading time such as time trade-off (TTO) are likely to involve both deliberative and emotional decision-making, whereas best-worst scaling which involves only selecting the best and worst aspects of a health state may only involve deliberative decision-making. Ultimately, this is a question for future research.

In attempting to elicit preferences from adolescents, there are further practical issues to consider as different preference elicitation techniques have different cognitive and ethical burdens. Studies that have successfully elicited adolescent preferences for hypothetical health states typically use ordinal tasks such as best-worst scaling that are both arguably cognitively simpler than TTO and do not involve consideration of death (see section 3). The appropriateness of different preference elicitation techniques for adolescents is discussed in section 2.3.

The elicitation of preferences for health states from children aged 10 and below is usually avoided, since they are unlikely to understand the task or be able to make the choice required. One issue raised with the elicitation of preferences from adolescents but not children is that adolescents may not understand child health states any better than adults, since they also cannot exactly experience the health state as lived by a younger child. In addition, adolescents may not share children's values or priorities. Children's own preferences cannot be meaningfully taken into account, so the decision of whose preferences are used to generate value sets for child health states is a normative one that cannot be based on who potentially experiences the health state.

The arguments for the elicitation of preferences from adolescent members of the general population rather than adolescent patients are the same as those for elicitation of adult preferences from members of the general population rather than patients. Accordingly, there would be issues of comparability and consistency if the preferences of patients were used to generate value sets for child and adolescent health states and the preferences of the general population were used to generate value sets for adult health states.

2.2. PERSPECTIVE

In preference elicitation tasks for hypothetical health states, participants are asked to imagine a particular health state and are then asked how good or bad they think the health state would be. Where preferences are elicited to generate value sets for preference-based measures the health states are described using the classification system for the health state. For example, for CHU9D this would be: worry; sadness; pain; tiredness; annoyance; school; sleep; daily routine; activities[6-8].

The term ‘perspective’ is used to indicate the person whom the participant is imagining living in the health state[19]. Preference elicitation tasks undertaken by adolescents would typically use an ‘own’ perspective, where they imagine that they themselves live in the health state. Preference elicitation tasks undertaken by adults for adult health states also use an ‘own’ perspective. For the elicitation of preferences for child health states tasks could involve several different perspectives including ‘other’ perspectives, such as imagining a child, or imagining themselves as a child. Emerging evidence suggests that the choice of perspective impacts on elicited preferences[21, 42].

2.2.1. Adult valuation using an ‘own’ perspective

Adult valuation using an own perspective, where respondents imagine they are living in the health state, is consistent with the approach used to value adult preference-based measures. This perspective can be advocated on the basis that the adult is under a veil of ignorance where they cannot be influenced by views around children or child health.

There are practical reasons that present challenges to the use of this approach, since many child and adolescent-specific preference-based measures involve wording that does not apply to or make sense to adults. For example, CHU9D has one dimension around schoolwork and homework which would need to be reworded to make it applicable. Whilst CHU9D has an adult version that instead refers to work[24], an adult’s work and a child’s schoolwork and homework may not be equivalent in terms of their impact on their life. The rewording of any dimension that is not applicable for adults means that the definition of the dimension is not the same in the aspect of health that is reported for the child (self-report or proxy-report) and the aspect of health that is valued to generate the value set[21, 43]. The same argument can be made around

dimensions that could be interpreted differently by adults, such as daily routine, and ability to self-care.

2.2.2. Adult valuation using an 'other' perspective to imagine a child

The use of an 'other' perspective is typically where adults are asked to imagine that the health state is experienced by, for example, a 10 year old child as recommended in the EQ-5D-Y protocol[22]. One recent quantitative interview study (n=299) found that 81.9% of respondents reported found preference elicitation tasks about health for a 10 year old child more difficult that the equivalent tasks about their own health, [44]. This suggests that preference elicitation tasks using an 'other' perspective to imagine a child are complex tasks to complete, yet this does not imply that respondents could not answer them nor that the responses they gave were not fully considered. The study also found that 49.5% of respondents were thinking about their own child or a child they knew, whereas 40.8% of respondents were not thinking of a particular child[44]. Ongoing research is examining the impact of which child is imagined - their own child, child they know, or an unspecified child – and also the age of the child that is specified, since it is possible that preferences may be impacted by this. The impact can also differ depending on whether the preference elicitation tasks involve a trade-off between length of life and quality of life (such as TTO) or not (e.g. visual analogue scale or best-worst scaling). There are concerns that whilst emerging research findings indicate that the choice of perspective impacts on preferences, there is as yet no published research examining qualitatively the reasoning for these differences (though this is reported in two recent unpublished qualitative studies [45, 46]). In addition, the use of an 'other' perspective, whether it is for a child or another adult, may involve different considerations since some participants may feel uncomfortable about making these types of choices on behalf of another[45].

Adults could be asked to imagine themselves experiencing the health state as if they were a child, but this is likely to be cognitively complex and potentially prone to recall bias and potentially impacted by other factors such as their own childhood and generational changes (though this may also be true of the 10 year old perspective).

2.3. ELICITATION TECHNIQUE AND MODE OF ADMINISTRATION

This section discusses the more commonly used preference elicitation techniques (TTO, standard gamble, discrete choice experiments, best worst scaling and visual analogue scales (VAS)) and their relationship to valuing child and adolescent health.

2.3.1. Time trade-off (TTO)

TTO is a widely used technique that asks participants to trade between years of life and quality of life (for a more detailed overview see[47]). TTO therefore relies on the assumption that individuals will be prepared to sacrifice years of life to improve their quality of life. At the start of a TTO task, participants are asked whether the health state is better than, worse than, or equivalent to being dead. For health states considered as being equal to being dead, their utility value is calculated as 0. For health states considered as being better than dead, the TTO task provides participants with a choice between (a) health state *h* for t_h years, after which they will die, or (b) full health for *x* years ($x \leq t_h$), after which they will die. Typically t_h remains fixed and years in full health, *x*, is varied to determine the point where the respondent is indifferent between the two options. The utility for health state *h* is then calculated using$^{x}/_{t_h}$. For states worse than dead, different approaches have been used to value the states. The current EQ-VT protocol for EQ-5D-5L uses a lead time approach where states worse than dead have an added 'lead time' of 10 years in full-health. The comparison is then (a) living for 10 years in full-health followed by health state *h* for t_h years, after which they will die, or (b) full health for *x* years (*x* <10 years), after which they will die. The utility for health state *h* is then calculated using$^{(x\ -\ 10)}/_{10}$. TTO is commonly used for adults and has been used to generate the value sets for many adult preference-based measures.

Since TTO requires consideration of death, there may be concerns about the acceptability and appropriateness of administering TTO in an adolescent sample[19], though it has been used[48]. The appropriateness of including consideration of death in preference elicitation tasks undertaken by adolescents depends upon whether adolescents have the ability to understand and state their preferences in these types of tasks, and whether the tasks cause upset or distress for adolescents[19]. In

addition, the framing in some studies has been amended to focus on years “left to live” rather than explicitly mentioning death (see for example[49]).

The combination of TTO with perspective also requires careful consideration. Studies have found that the use of different perspectives impacts upon elicited preferences, where in general participants appear less willing to trade quantity of life for children than for themselves[21]. If respondents are less willing to trade life years for children and adolescents, the health state utility value will be higher for child and adolescent states than for equivalent adult states. This has wider implications for the generation and usage of QALYs for adults, adolescents and children, where it is assumed that the generation of QALYs is comparable. Therefore the reasons why participants appear less willing to trade quantity of life for children than for themselves or potentially other adults, and the conditions under which this is found, are being explored in ongoing research[45, 46]. These studies will help to understand whether TTO administered using an ‘other’ perspective generates results that are appropriate for use for generating utilities for child and adolescent health states. Nevertheless, the use of TTO with an ‘other’ perspective of a 10 year old child is currently included in the international valuation protocol of the EQ-5D-Y to anchor the modelled DCE utilities onto the 1-0 full health-dead scale required to generate QALYs [22].

2.3.1. Standard gamble

Standard gamble asks participants to choose between an uncertain outcome and a certain outcome. For states better than dead, participants choose between (a) a certain impaired health state, *h*, or (b) the uncertainty of a gamble with two possible health states, full health (with probability *p)* or the worst health state (with probability 1-*p*). The probabilities in the uncertain outcome are varied until the respondent is indifferent between the certain and uncertain option, or until the respondent changes their choice of either the certain or uncertain option as the probabilities in the uncertain option are changed. Standard gamble has foundations in expected utility theory, meaning that it is sometimes portrayed as the gold standard because it mimics the uncertainty that can occur in medical decisions[50], though arguably in an unrealistic way[51].

Standard gamble has been used to generate value sets for HUI2 and HUI3, preference-based measures that can be used to generate utilities for children, adolescents and adults, as well as CHU9D, a child and adolescent-specific preference-based measure. For HUI2 value sets preferences were elicited using standard gamble and VAS from parents[13] or adults[52, 53] using the child perspective, whilst for HUI3 and CHU9D preferences were elicited from adults using their own perspective[14, 54]. Standard gamble has also been used to elicit preferences from adolescents[32, 55]. The authors are not aware of any evidence around the impact of perspective on utilities elicited using standard gamble by adults using the child perspective in comparison to their own perspective or an other perspective. However, since the child perspective asks participants to risk death of a child, insights from time trade-off studies suggest that different perspectives may impact on responses.

Standard gamble is rarely used in more recent studies, both for adults as well as children. The standard gamble technique has been criticised as being cognitively complex, which may mean that participants do not understand the tasks and or accurately interpret the probabilities.

2.3.2. Discrete choice experiment (DCE)

Discrete choice experiments (DCE) involve participants choosing between two or more alternatives. Each alternative is made up of a number of attributes, and for health state valuation these attributes are the dimensions in the classification system, with different severity levels. Typically this involves a pairwise choice where participants choose between two health state profiles (e.g. A and B), where these vary in the severity levels of most or all of the dimensions, and participants choose which profile they prefer. The modelling of DCE data generates latent utility values where the choices, as the proportion selecting profile A over profile B, allow the relative weights for each dimension and level to be modelled. However, these latent utility values are not anchored on the 1-0 full health to dead scale that is needed in order to be able to generate QALYs.

DCE can be undertaken by adolescents and adults with no concerns raised around its acceptability for use in adolescents on ethical grounds since there is no mention of

death. However, whilst the DCE task is cognitively simple to understand it does not necessarily follow that it is cognitively simple to complete. For example, a DCE task for EQ-5D-Y would involve simultaneous consideration of 2 health states each with 5 dimensions, involving 10 pieces of information in total. Larger descriptive systems such as CHU9D involve more information. One qualitative study found that pairwise comparisons (such as those in a DCE) were not feasible and reliable for younger adolescents (age 7 to 13 years), but were feasible and reliable for older adolescents (age 14 to 17 years)[56], whereas another qualitative study raised concerns around whether adolescents fully understand the DCE task[57]. However, it should be noted that the authors are not aware of equivalent qualitative studies assessing understanding in an adult population, that the same may be true of other elicitation techniques that have not been assessed in this way, and that the findings may be only be relevant to the measure and preference elicitation protocol used in these studies. For example, evidence from a recent quantitative study assessing EQ-5D-Y health states suggests that DCE with adolescents is feasible and produces valid latent estimates[28]. DCE studies with adults have been designed to reduce the amount of information that participants need to consider to make the choice cognitively simpler by allowing severity overlap in some of the dimensions, for example making the severity level the same for 6 of 10 dimensions[58], though this may mean that respondents do not consider the full health profile.

DCE data can be anchored directly on the 1-0 full health-dead scale if duration is included as an additional attribute in the DCE[59]. For example, life years can be included in the health state profiles, where the participant is told that they will die at the end of the specified number of life years. This method is often referred to as DCE_{TTO} since it can be interpreted as being similar to a TTO exercise, though note that TTO always compares an impaired health state to full health where the impaired health state lasts for 10 years. In contrast, in DCE with duration typically the participant chooses between two impaired health states and the duration of either can vary.

The concerns raised around the use of an ‘other’ perspective in TTO are expected to also apply to DCE with duration, since this involves the same trade-off between length of life and quality of life. DCE with duration using an own perspective has been completed with adults and used to generate a value set for a child and adolescent-

specific preference-based measure[43]. DCE with duration has not to our knowledge been administered in an adolescent sample, and may be too cognitively complex given that making the choice in the DCE through considering all information is already cognitively complex and DCE with duration has the additional requirement that there is a trade-off between quality of life and length of life. Although there is no evidence to support this hypothesis, it is recommended that prior to administration of DCE with duration in an adolescent sample careful piloting should be undertaken to ensure its appropriateness.

2.3.3. Best-worst scaling

Best-worst scaling is an ordinal technique where participants are presented with a health state and are asked to choose the best part and the worst part of the health state. Best-worst scaling estimates are modelled and generate latent estimates that are initially anchored to the least valued attribute level (e.g. mobility at its lowest level), and coefficients are estimated for every level of every other dimension. These estimates are not anchored directly on the 1-0 full health-dead scale, and deviate from the modelled preferences using other elicitation techniques since they estimate coefficients for all levels of every dimension with the exception of one.

Best-worst scaling can be undertaken by adolescents and adults with no concerns raised around its acceptability for use in adolescents on practical grounds since there is no mention of death and the task is cognitively simple. Studies have found that best-worst scaling is appropriate for use in adolescent populations [24, 29], though one of the studies found that best choices were more consistent than worst choices (for CHU9D health states[24], this was not found for EQ-5D-Y health states[29]). Qualitative research has found that best-worst scaling is a feasible technique for younger and older adolescents [56, 57].

Concerns, however, have been raised in the literature around the appropriateness of the best-worst scaling technique as a method for eliciting preferences for adult health states. Best-worst scaling has been argued to elicit values not preferences, since it does not involve a trade-off or sacrifice, as choices are made within a health state not across health states. For this reason, it is unlikely be considered an acceptable method for NICE, who require the use of a choice-based technique (which can be interpreted

as involving sacrifice or trade-off)[60]. One study found similar patterns of preferences for DCE and best-worst scaling[61], though two other studies have found that preferences generated using best-worst scaling differ to preferences elicited using DCE[62, 63], and argued that the data was of lower quality regarding stability and logical consistency.

2.3.4. Visual analogue scale (VAS)

VAS asks participants to assign health states a value between 0 and 100, where 0 can be labelled as 'best imaginable' and 100 can be labelled as 'worst imaginable' which is usually presented as a vertical rating scale with increments of 5 or10 (though there are several different variants of VAS). Typically, participants would use the same scale that is visually presented to place several states simultaneously onto the 0-100 scale. VAS is feasible for use both with adolescents and adults, yet to be able to generate values anchored onto the 1-0 scale required to generate QALYs the state 'dead' also needs to be considered alongside the other states. Concerns have been raised in the literature around the appropriateness of VAS since it does not involve a trade-off, sacrifice or choice, meaning that it is unlikely to be considered an acceptable method for NICE[60], though there is not consensus in the literature[64]. There are also concerns that participants may spread the health states that they value across the scale, meaning that the health states they are valued alongside may have a relative impact on their values. Participants often also typically assign numbers ending in 0 or 5 e.g. 80, 85, and avoid placing states at the ends of the scale. These biases indicate that although the task may be easy to complete, it is important to take into account the design of the task and participants need clear guidance in order to complete the task appropriately. VAS has been used to value health states for children and adolescents[15-17]. However, eliciting values using an adult population and 'other' perspective for a 10 year old child generated lower utilities than when participants provided values using the 'own' perspective[42].

2.4. GENERATING UTILITIES ON FULL HEALTH-DEAD SCALE

Best-worst scaling, DCE with no duration attribute and potentially VAS (if dead is not also valued in the VAS task) generate values that are not anchored onto the 1-0 full health-dead scale required to generate utilities. Several different methods can be used to anchor these values onto the 1-0 full health-dead scale[65]:

- Rescaling the modelled values for all health states using cardinal utilities (for example TTO) for a small number of health states or for the worst health state (typically the latent DCE values for the best state and worst state are linearly rescaled between 1 and the cardinal utility value for worst state);
- Mapping the modelled values onto cardinal utilities (for example TTO) for a number of states;
- Jointly modelling the ordinal and cardinal values (for example DCE and TTO) using a hybrid model (we are not aware that the hybrid model has been used in the valuation of child and adolescent health states).
- Personal utility function approach involving location of dead at the individual level via ranking of the best level of each dimension (to determine the relative importance of dimensions for the individual) and pairwise comparisons of severe health states and dead (states selected using the ranking information and tailored to determine where dead is located for the individual)[44].

The mapping and hybrid methods provide more accurate predictions of TTO utilities when mapping from DCE values in comparison to rescaling, though concerns have been raised with the estimation of hybrid models [66]. The personal utility function approach has not been compared to the other approaches in this context. It should be noted that all of these approaches require cardinal utility data, for example elicited using TTO or DCE with duration, or location of dead via a personal utility function, to be able to anchor the values generated from ordinal DCE or best-worst scaling data, or from VAS data where dead is not valued in the task. This means that whilst these techniques could be used in a sample of adolescents to elicit ordinal preferences, a sample of adults is required to be able to provide the cardinal values using a technique that does involve consideration of death (assuming this is something that health economists want to avoid when using a sample of adolescents, see section 3). This presents a discontinuity in that even if adolescent preferences are used to generate the ordinal preferences, adult preferences are still required to anchor them onto the 1-0 scale, if these cardinal tasks are not used in the adolescent sample. Some valuation studies have used a sample of young adults to provide the cardinal utilities used to anchor the ordinal adolescent preferences[23, 67], but it is unclear whether the use of young adults rather than a representative sample of adults is preferable.

2.5. OVERVIEW OF TTO VALUATION STUDIES WITH ADOLESCENT SAMPLES

TTO is the more widely used approach in adult valuation samples, is the method used to value adult EQ-5D, and is a choice-based technique which is likely to be acceptable to NICE[60]. Therefore, in this section we report on published TTO studies undertaken with adolescents. In 2017 a systematic review was published of studies eliciting preferences for health states using samples of adolescents[48], using a search conducted from January 1990 to May 2015. The review identified 26 studies.

- *Preference elicitation technique:* 14 studies used TTO, 11 studies used standard gamble, 8 studies used visual analogue scale and 2 used DCE (without a duration attribute).
- *Psychometric performance of TTO:* Out of the 14 studies using TTO, 2 reported validity[68, 69], 2 reported test-retest reliability[68, 70], and 5 reported feasibility[32, 68, 71-73] (one in a young adult sample[32]). Only 2 of the 14 studies reported on validity (both assessed this using correlations), and for the remaining studies validity was not assessed[48]. Feasibility was assessed in 5 of the 14 studies using completion rates, where completion rates varied from 12.5%[32], 73%[72], 82%[68], 99%[73] to 100%[71]. The two studies assessing test-retest reliability found evidence of this [68, 70].
- One study conducted since the published review examined feasibility, test-retest reliability and construct validity of TTO using an online survey of adolescents, finding evidence of feasibility but that test-retest reliability and construct validity was poor[49].

A targeted search in MEDLINE and supplementary citation searches of four key articles[3, 42, 74, 75] in the Web of Science were carried out in June 2020 to find studies reporting on child or adolescent studies using choice-based methods, in particular TTO, DCE and VAS. The full search strategies are reported in the appendix. Since the 2017 review we identified 4 relevant TTO studies [49, 76-78]. Below is a summary of the findings of all 18 TTO studies highlighted by the published review (n=14) and our updated review (n=4).

- *Perspective used in TTO studies*: Out of the 18 studies that used TTO one used ‘dental freetime’ trade-off in a sample of dental patients of their own

health[79]. Out of the remaining 17 studies, 8 involved the valuation of hypothetical health states [32, 49, 70, 71, 77, 80-82], 7 involved the valuation of their own health state[26, 55, 72, 73, 76, 78, 83], and 2 involved valuation of both their own health state and hypothetical health states [68, 69].

- *Sample used in TTO studies*: Of the 18 studies, 5 used general population adolescent samples ([32, 49, 69, 71, 82], one study recruited adolescents from the general population but only included participants who had acne [69], and one study recruited adolescents via clinics but there was no requirement that the participants had a health condition [82]), 10 studies used samples of adolescent patients[26, 55, 68, 72, 76-78, 80, 81, 83], and 2 studies used adolescent samples that included both patients and members of the general population[70, 73].
- *Age-range of participants in TTO studies*: There was a variety of age ranges in years across the studies: 8 years and over [68], age 9 to 18 years [78], 10 to 18 years[49], 11-13 years [32], 11-14 years [70], 11-19 years [72, 73], approximately 12 to 17 years [83], 12-18 years [55, 80], 12-19 years [82], 12 years and over[76], 12-25 years [26], over 13 years[77], 14-18 years [69], 15-18 years [71, 81]. The age range starts at 8 but this is for only one study with the majority starting from 11 or 12 years.

, . The overview indicates that TTO has been undertaken in both general population and patient adolescent samples using hypothetical health states and own health states. The elicitation of preferences for hypothetical health states using TTO was undertaken for all five studies involving a general population adolescent sample (as identified by the published 2017 review and our recent literature search) [32, 49, 69, 71, 82]).

2.6. SUMMARISING THE ISSUES

The use of either adult or adolescent populations to value child/adolescent health states is associated with different issues (Table 1). The use of question marks in the table indicates where this issue is unknown, and where research would contribute to better understanding of this.

Regarding the selection of valuation population, adults may be taxpayers and voters who are legally allowed to make decisions that adolescents cannot. Adults may understand elicitation tasks better and the cognitive burden for them may be lower, but there are elicitation tasks that adolescents can also complete. The consistency of valuation sample of adults across both child and adolescent and adult health states may not translate into consistency across values depending on the perspective used in the elicitation tasks. For the valuation of adult health states adults are asked about their preferences imagining they experience the health state, whereas for the valuation of child and adolescent health states by adults they can be asked to imagine themselves or, say, a 10-year old child is experiencing the health state.

Regarding the selection of perspective for adults, the use of an own perspective for adults valuing child health states may require changes in the wording of measures, whereas using a child perspective may have an impact on the values that adults give especially where techniques include life years.

Regarding the selection of preference elicitation task, there is limited evidence and little qualitative research to determine the ease of understanding and completing tasks by adolescents, and around the appropriateness of using tasks involving mention of dead. Future research examining this would be beneficial.

Table 1: Methodological issues in the valuation of child and adolescent health states

	Issues	Adults	Adolescents
Population	Tax payers and voters	✓ (although some adults will not be tax payers)	× (although some adolescents will be tax payers)
	Veil of ignorance (impartial and unbiased)	✓ members of the public	✓ members of the public
	Consistency with the adult population used to value adult measures	✓	×
	Experience and understanding of the *health state*	✓ potentially for adults who experienced childhood illness	✓ for patients
	Understanding the impact of the health state on the lives of children	? Questionable, though parents may have better understanding	? Questionable, and likely to differ by previous health and life experiences
	Understanding the impact of the health state on the lives of adolescents	? Questionable, though parents may have better understanding	? Unlikely
	Empowerment of adolescents	×	✓
	Capacity of decision-making	✓	**?** Questionable whether all adolescents have the psychosocial maturity that enables important decision-making
	Legal age for other important decisions	✓	×
	Responsible for other decisions around their own health	✓	**?** Likely to differ by age and between individuals
Perspective	Consistency with child/adolescent descriptions of health	✓ hypothetical/real child × own perspective (though not necessarily for all measures or dimensions)	✓ own health
	Consistency with adult valuation perspective of own health	✓ when using own perspective × when using child perspective	✓
Preference elicitation task	Ease of understanding the task	✓ TTO, BWS, DCE, VAS	✓ BWS **?** DCE, VAS, TTO
	Ease of completing the task	✓ TTO, BWS, DCE, VAS	✓ BWS **?** DCE, VAS, TTO
	Able to generate relative importance of dimensions and severity levels	✓	✓

	Issues	Adults	Adolescents
	Able to anchor values onto 1-0 full health-dead scale	✓	**?**
	Appropriateness of including dead in valuation tasks	✓	**?**
	Bias related to perspective	**?** potentially when using an other perspective	**×**

Notes: ✓=yes, **×**=no, **?**=unknown, TTO= time trade-off, BWS=best-worst scaling, DCE=discrete choice experiment, VAS=visual analogue scale.

3. ELICITING PREFERENCES FROM A MIXED SAMPLE OF ADOLESCENTS AND ADULTS

The previous section provided a brief overview of the methodological considerations in the elicitation of preferences for child and adolescent health states, in particular summarising the rationale behind the use of either adult or adolescent preferences for generating utilities for child and adolescent health states. This section will present a critical examination of the practical, ethical and theoretical issues arising from the novel idea of using a mixed population of adults and adolescents to value child and adolescent health states. What is discussed is the use of a mixed sample comprised of both adolescents and adults, where all participants complete the same preference elicitation task and all preferences are modelled to generate a combined value set that reflects the preferences of both adolescents and adults. Using mixed samples of adolescents and adults requires decisions to ensure that the same task is undertaken across both samples. Many of the choices are not independent of each other, for example the preference elicitation technique that is chosen may have an impact on the selection of perspectives. In addition, the elicitation task that is selected may be influenced by the age of the sample. Some of these choices will be informed by existing evidence.

3.1. MIXED ADOLESCENT AND ADULT SAMPLE FOR VALUING CHILD/ADOLESCENT STATES

The selection of the same elicitation task for use with both adolescents and adults should take into consideration the age-range of the adolescent group, the appropriateness of the elicitation technique, and the perspective to use. There are also further methodological issues related to sample size and modelling.

3.1.1. Age of participants and ensuring understanding

In a mixed sample, decisions need to be made regarding the age-range of adolescent participants. As noted in section 2, published TTO studies with child/adolescent samples range in age from 8 to 18 years. Preference elicitation tasks can be cognitively complex to understand and cognitively complex to make a choice, particularly since they require participants to imagine hypothetical health states.

It is recommended by an ISPOR taskforce that self-reporting of own health is recommended for adolescents aged 12-18 years, and that the reliability and validity of the self-report improves for children aged 8-11 years in comparison to children aged 5-7 years, where reliability and validity of self-report is often questionable[84]. In accordance with these age ranges, a minimum age of 12 would seem appropriate for self-reporting of own health and consideration of the ability to undertake preference elicitation tasks.

Whilst many of the concerns around the complexity of preference elicitation tasks to both understand and to complete (i.e. make a choice) arise for both adults and adolescents, one potential difference is the ability to be able to imagine one's self in a defined state of impaired health. There is a possibility that many adolescents will not have experienced severe health states, and as such may be unable to imagine them. However, the same argument can also be made for adults. Studies have found that often participants can better imagine health states through both their own related experiences of impaired health but also the experiences of family members [45]. Therefore, adolescents may have knowledge of the impact of health states vicariously from observing family members. It can also be argued that participants' ability to both understand and choose is affected by their educational level, intelligence and experience of impaired health rather than simply their age. Whilst some younger children may be able to successfully undertake some preference elicitation tasks, some adult participants may be unable to successfully undertake the same preference elicitation tasks, and age is not the only important factor.

Appropriate framing and design could be implemented to ensure the acceptability and appropriateness of these tasks, and further research assessing this and adolescents' views on the acceptability and appropriateness of these tasks directly may be informative for ethics committees making decisions around the conduct and acceptability of these types of studies. A key consideration of approval committees is that the research will yield results that are both meaningful and useful, and is not unnecessarily burdensome. Careful design of valuation studies including consideration of formatting, framing, number of dimensions in the health states, number of preference elicitation tasks and mode of administration can all impact on whether the valuation survey will appropriately elicit utility values.

Some studies use prompts to make the tasks cognitively simpler, such as smiley faces to indicate whether the state was mild or severe (see for example [49]), though the use of visual prompts must be carefully piloted to ensure that is not leading or able to influence preferences. In recent years the use of Computer-Assisted Personal Interviews (CAPI) has increased, meaning that tasks can be more interactive or potentially animated, and these techniques could be used to increase user experience and understanding, which may appeal more to younger participants. The use of touchscreen devices (for example tablets) that adolescents can operate themselves can also be used. In addition, the COVID-19 pandemic has also lead to the use of remote interviews conducted via videoconference, and this could be an attractive for the elicitation of adolescent (and adult) preferences since interviews can be scheduled to fit around school and homework requirements (and work).

The elicitation of preferences from adolescents raises the issue around whether their parent/guardian is present at that time, since for some adolescents this could influence their preferences. Parental consent is required for adolescents aged under 16 and, ethically, parents and participating adolescents should be allowed to decide together whether the parent is present during research participation of under 16s. Methodologically, we would recommend that the elicitation of preferences should be conducted without others present as the default option, to avoid confounding the participant's response.

Adult samples recruited for preference elicitation studies are typically aged 18 and over, but many people aged 18 will still be in education in the same class as 17 year olds, yet they are often given much more freedom and autonomy. A recent cross-national study featuring a range of decision-making tasks (note these were not preference elicitation tasks) reported that adolescents' cognitive capacity reached adult levels at around age 16, with psychosocial maturity (including sensation seeking, impulse control, future orientation, and resistance to peer influence) in decision-making reaching adult levels beyond age 18[40]. To the extent that preference elicitation tasks promote deliberative and reflective decision-making, rather than emotional or time pressured decisions, then a sample of 16 year olds and above should be able to complete the tasks as well as adults. Indeed, psychosocial maturity

did not peak in these data until the 20s, suggesting that young adults (who are already included in valuation studies) may be as liable to decision-making biases associated with psychosocial immaturity as a sample of adolescents. It is worth nothing that there were some cross-country differences observed in the study cited above and the UK was not sampled.

3.1.2. Age of participant and ethical concerns

As discussed in section 2, there are concerns around whether it is acceptable and appropriate to administer preference elicitation tasks due to the possibility that consideration of dead or trading between quality of life and quantity of life may cause upset or distress for adolescents.

The existence of TTO studies that have been undertaken with adolescents using preference elicitation tasks for both their own health and/or for hypothetical health states that involve consideration of being dead (potentially framed as trading of years left to live) suggests that these tasks may be acceptable and appropriate, though the authors are not aware of any qualitative work assessing this, and the studies were not designed to explicitly test this. In order to assess whether consideration of dead or trading between quality and quantity of life causes distress or upset, research must be conducted on this, though the possibility that this research itself may cause distress or upset challenges this and the argument may become circular.TTO is a hypothetical task and is different to talking to respondents about their views around a death in real-life and dying per se. Arguably, adolescents are used to making hypothetical choices that involve some risk of death, for example in computer games, and make other choices around their health including participating in high risk sporting activities, dietary decisions and other risk-based lifestyle choices. This issue would also benefit from direct research with adolescents that is appropriately and sensitively conducted to examine this issue. Given that a resolution to this issue may facilitate greater adolescent empowerment in health research, we believe it is ethically appropriate and prudent to conduct such research.

3.1.3. Perspective

A mixed sample valuing child/adolescent health states can be valued from ‘own’ or ‘other’ health perspective. All preference elicitation surveys undertaken in adolescents that the authors are aware of have been conducted from an ‘own’ perspective rather than an ‘other’ perspective, as this is cognitively simpler. The use of ‘own’ health perspective for the adults who are valuing child/adolescent health states raises challenges regarding the appropriate wording in the states. For some measures such as HUI2 and HUI3, the same set of questions and classification system is used for children, adolescents and adults (although completion of the questions to report own health may be supported in those who are younger or proxy- reported). Although the HUI2 and HUI3 measures have only been valued by adults, as the same questionnaire is used for patients across the age spectrum, then this may indicate that the same questions could be used in the valuation from an ‘own’ perspective of both adults and adolescents. Other measures, including the EQ-5D have different child/adolescent versions to make them appropriate for these younger populations both in terms of meaning (e.g. replacing anxiety/depression with worry/sadness) and content (e.g. providing appropriate examples for usual activities). These differences can have an impact on adult valuation, for example whether anxiety/depression is the same as worry/sadness/unhappiness, and usual activities, for example differ, such as the inclusion of school as a usual activity. This is supported by the literature where it has been found that utility values differ for the EQ-5D and EQ-5D-Y classification systems for adults imagining themselves living in the health state (though there were no significant differences when using the perspective of a 10 year old child)[21]. If examples are excluded or altered to make the states more relevant to adults, then adults will be likely to imagine a different impact on their lives from impaired health states, for example the impact on income rather than on school work. Adolescents valuing their own health may also consider support from family or carers whereas adults may not take this into account when they consider their own health, which may result in different values for the same states.

The second option where a mixed sample is used would be to use ‘own’ perspective for adolescents and an ‘other’ perspective for adults. Whilst it could be specified for the adult sample that they are to imagine an adolescent of, say 15 years, which would provide some consistency regarding age with the adolescent sample, there is still a

difference in imagining yourself in the health state at your current (adolescent) age versus imagining somebody else age 15 in the health state. The choice process is arguably conceptually different, where if you are making choices on behalf of another you may choose differently than if you were making the decision for yourself, and this may be particularly true in the case of sacrificing years of life of another, particularly an adolescent. In addition, making choices on behalf of another may bring in societal considerations that are not reflected in the same way if you are making choices for yourself. Further, adults and adolescents potentially differ systematically in the way they think about and make decisions for others versus themselves, with research suggesting that adolescents may be 'hard-wired' to be more selfish than adults, yet this difference flattens out over time[85].

A third option is to have a range of different aged children for adults to imagine (for example age 5-7 years, 8-10 years, 11-13 years, 14-15 years), and 16 to 17 year old adolescents answer using their own perspective. This raises the same concerns as the second option, but one advantage to this option is that all ages of children (whose health could be captured using the measure) are considered, albeit from a different (own) perspective for older adolescents. However, we are not aware of published evidence demonstrating the impact of preferences on utility values elicited for different ages of children, though we are aware of several ongoing studies examining this. If this option was pursued there would also need to be consideration on selection of sample representativeness around parental/guardian status and age of their child, as research is ongoing around whether and how this impacts preferences using the child perspective.

On balance, it seems preferable to use the own perspective throughout the sample to maintain consistency since we know that different perspectives generate different responses and involve different considerations for participants. However the use of the own perspective throughout the sample is not without its limitations.

3.1.4. Preference elicitation task

There are requirements both that the same elicitation task(s) are used for the entire sample and that the elicitation task(s) generate modelled utilities that are anchored onto the 1-0 full health-dead scale required to generate QALYs. TTO, DCE with

duration, and VAS (involving a dead state) tasks meet the requirement of being able to generate utilities on the 1-0 scale, but their appropriateness and acceptability in a mixed sample can be questioned. We focus on TTO and DCE with duration as they are methods that involve opportunity cost, and concerns have been raised in the literature around the use of VAS to generate utilities including its lack of theoretical foundations for generating utilities (see for example [47]).

TTO has an advantage that it has been used in adolescent samples and is widely used in adult samples, thus providing arguably the most comparability with the valuation of adult preference-based measures. One important consideration is that typically TTO tasks use a 10 year time frame for states that are better than dead, where participants are asked to trade between 10 years in an impaired health state and 10 or fewer years in full health, and at the end of either of the states the participant would be dead. There is an additional concern around the plausibility of a life expectancy of 10 years from today for adolescents and younger adults and potentially this could impact on preferences and the results (though the authors are not aware of any studies examining this). For this reason some studies have used different time frames, for example a 60 year time frame[49]. However, increasing the time frame beyond 10 years would be implausible for the elderly participants in the sample. The use of a 10 year time frame for the mixed sample will be equally implausible both for younger and elderly participants, though for different reasons since the young would expect to live longer and the elderly may not expect to live that long. The same criticism of implausibility can be applied to all valuation studies involving elderly people and potentially young adults, including studies using the DCE with duration technique that often use 10 years as the highest level of duration. However, if oversampling is undertaken of adolescents in the sample this may exacerbate this issue.

DCE with duration has not been used in a sample of adolescents to our knowledge. DCE with duration involves the simultaneous consideration of a large amount of information, since it asks participants to choose which they prefer of two impaired health profiles where each contain several dimensions as well as duration of the state. Techniques have been used in the literature to make DCE tasks easier to complete, including colour coding to identify where dimensions have the same severity across the health profiles[58, 86], and the fixing of attributes at the same level across the two health profiles in a DCE task to ensure there is less information that varies for each

DCE task[87]. However, qualitative research has cast doubt on the feasibility of conducting DCE (without duration) in adolescent samples[57], particularly at the younger end[56].

3.1.5. Health state descriptions

The report has focussed on generating a value set for a preference-based measure, and hence health state descriptions would be based on the classification system of the preference-based measure. The dimensions and severity levels need to be clear and comprehensible and applicable for adults and adolescents for the perspective that is selected. In preference elicitation tasks used to generate value sets for preference-based measures information on the wider impact of the life of the patient is not typically described beyond the health state description generated by the classification system. However, studies have examined the inclusion of wider impact on the life of the patient for adult health (for example the impact of self-management on quality of life [88]or the inclusion of satisfaction [89] and the elicitation of 'informed preferences' where participants are provided information about what patients report about how impaired health impacts on them and their lives. However, to our knowledge, this has not been undertaken with adolescents and therefore there is no evidence around whether this would be feasible or acceptable for adolescents.

3.1.6. Sampling and weighting of results

Table 2 below reports the age distribution in the UK as generated by the UK 2011 census. If a representative sample for age was obtained in a valuation study for the population aged 16 and over, the proportion of participants aged 16 and 17 would be 3.2%. This small percentage of participants would not be anticipated to have a substantial impact on the value set.

Table 2: UK age distribution according to the UK 2011 Census

Age	N	%
All usual residents	63,182,178	
Age 0 to 4	3,913,953	6.2
Age 5 to 7	2,158,947	3.4
Age 8 to 9	1,357,668	2.1
Age 10 to 14	3,669,326	5.8
Age 15	774,892	1.2

Age	N	%
Age 16 to 17	1,568,941	2.5
Age 18 to 19	1,652,619	2.6
Age 20 to 24	4,297,198	6.8
Age 25 to 29	4,306,340	6.8
Age 30 to 44	12,945,561	20.5
Age 45 to 59	12,351,632	19.5
Age 60 to 64	3,807,974	6.0
Age 65 to 74	5,480,225	8.7
Age 75 to 84	3,504,915	5.5
Age 85 to 89	918,343	1.5
Age 90 and over	473,644	0.7
Age 18 and over	49,738,451	78.7
Age 16 and over	51,307,392	81.2

One option is to oversample adolescents in the valuation study. However, there is then an issue of how to weight the sample, and/or the modelled value set, regarding adolescent participants relative to adults. An equal weighting of 50/50 adolescents/adults would mean a large oversampling of adolescents, but would be a true mixed sample rather than a representative sample of the population aged 16 and over. The selection of proportions of adolescents in the sample and any weightings in the modelled value set is a normative decision, though this could be informed by research into the impact of the differences, as well as the views of the general public and decision makers.

3.1.7. Meaningful involvement and empowerment of adolescents

Arguments for the empowerment of children can draw on theories relating to participation, empowerment, voice and emancipation, where they can even be empowered as active researchers where children undertake studies about other children [90]. However, there are counter-arguments that the empowerment of adolescents may not be regarded as a relevant consideration for obtaining accurate preference estimates for use in economic evaluation.

The use of a mixed sample should ensure adequate representation in order to be meaningful. If the mixed sample includes only a small sample of adolescents there is a concern that this will not impact on the value set for the child and adolescent-specific preference-based measure, and the inclusion of adolescents in the sample will not be

perceived as being given due weight and consideration and could be potentially regarded as tokenistic. Therefore, the selection of the proportion of the sample that are adolescents will impact on how the final value set is important.

There is still a concern that since children cannot meaningfully undertake preference elicitation tasks, meaning that adolescents and/or adult preferences – not child preferences - must be used to generate utilities for child health states. Therefore, at best, the use of a combined sample of adolescents and adults is only empowering for a subsection of the population that the measure is used to generate utility values for. In addition, the older adolescents who are most likely to be included in any mixed sample, may actually have their health measured using an adult measure not a child and adolescent-specific measure. This raises the issue of whether a mixed sample should be used to elicit preferences for adult health states, since adult measures can reasonably be administered to respondents aged 16 and over.

3.2. SUMMARY OF POTENTIAL OPTIONS FOR ELICITING PREFERENCES FOR CHILD AND ADOLESCENT HEALTH STATES

Table 3 summarises potential options for eliciting preferences for child and adolescent health states, summarising the similarity to EQ-5D methods (i.e. the UK EQ-5D-3L value set was generated using TTO values elicited from adults using their own perspective and utilities for different options of population[91]), and EQ-5D utilities. The use of TTO provides the greatest comparability both to EQ-5D methods and EQ-5D utilities.

Table 3: Considerations and study characteristics for eliciting preferences for child and adolescent health states

Sample	Perspective	Method	Similar to methods used to generate UK EQ-5D-3L value set	Expected similarity to adult UK EQ-5D-3L value set	Notes
Adult	Own	TTO	Yes	Yes	• Wording changes may be required to make states applicable to adults
		DCE with duration	Some similarity	No	
		Standard gamble	No	No	
		DCE	No	No	• Wording changes may be required to make states applicable to adults • Not choice based tasks that involve a trade-off or sacrifice • Typically require data elicited using another preference elicitation task to anchor onto the 1-0 full health-dead scale
		VAS			
		Ranking			
		BWS			
	Child[21, 42]	TTO	Some similarity	No	• Evidence showing participants find this more difficult than use of an own perspective, and that the child who is imagined varies across respondents (e.g. own child, no particular child)[45, 92]. Research is ongoing around the impact of whose child is imagined.
		DCE with duration	Some similarity	No	
		Standard gamble	No	No	
		DCE	No	No	• Not choice based tasks that involve a trade-off or sacrifice • Typically require data elicited using another preference elicitation task to anchor onto the 1-0 full health-dead scale
		VAS			
		Ranking			
		BWS			

Sample	Perspective	Method	Similar to methods used to generate UK EQ-5D-3L value set	Expected similarity to adult UK EQ-5D-3L value set	Notes
Adolescent	Own	TTO	Some similarity	Some similarity	• Ethical concerns around consideration of death and trading of life years
		DCE with duration		No	
		Standard gamble	No	No	• Ethical concerns around consideration of death and risk of death • Concerns around understanding of probabilities
		DCE	No	No	• Not choice based tasks that involve a trade-off or sacrifice • Typically require data elicited using another preference elicitation task to anchor onto the 1-0 full health-dead scale
		VAS			
		Ranking			
		BWS			
	Child	All	No	No	• No research examining the elicitation of adolescent preferences using a child perspective
Mixed sample of adolescents and adults	Own	TTO	Some similarity	Some similarity	• Wording changes may be required to make states applicable to adults. • Ethical concerns around consideration of death and trading of life years for adolescents
		DCE with duration	Some similarity	No	
		Standard gamble	No	No	• Wording changes may be required to make states applicable to adults • Ethical concerns around consideration of death and risk of death for adolescents

Sample	Perspective	Method	Similar to methods used to generate UK EQ-5D-3L value set	Expected similarity to adult UK EQ-5D-3L value set	Notes
					• Concerns around understanding of probabilities
		DCE	No	No	• Wording changes may be required to make states applicable to adults • Not choice based tasks that involve a trade-off or sacrifice • Typically require data elicited using another preference elicitation task to anchor onto the 1-0 full health-dead scale
		VAS			
		Ranking			
		BWS			
	Child	All	No	No	• Evidence showing adults find this more difficult than use of an own perspective, and that the child who is imagined varies across respondents (e.g. own child, no particular child)[44, 45]. Research is ongoing around the impact of whose child is imagined. • No research examining the elicitation of adolescent preferences using a child perspective

Notes: BWS: best-worst scaling; DCE: discrete choice experiment; VAS: visual analogue scale.
Similar to methods used to generate UK EQ-5D-3L value set: The UK EQ-5D-3L value set was generated using TTO values elicited from adults using their own perspective[91]. In this column the following is used: yes=TTO values elicited from adults using their own perspective; some similarity=values elicited either using TTO (but not also from adults and using the own perspective) or an elicitation technique that involves trading between quantity and quality of life, where this either undertaken by adults or adolescents from their own perspective; no=values are not elicited using TTO or an elicitation technique that involves trading between quantity and quality of life. Expected similarity to adult UK EQ-5D-3L value set: this takes into account relevant literature around the comparability of utility values elicited using different techniques (though typically this is for adults valuing health states from their own perspective, for an overview see [47]) and different perspectives.

3.3. SUMMARY ON MIXED ADOLESCENT AND ADULT SAMPLE

The existing evidence supports the use of methods such as TTO in adolescents, particularly older adolescents, which would facilitate the use of a mixed sample to value child/adolescent health states. The minimum age where such a method could be applied is not clear, but appears appropriate at least for respondents aged 16 and over. The evidence on whether adolescents are impacted adversely by considerations of death is also limited. The use of the same method does not necessarily address concerns regarding perspective and description of health states to ensure that the same states are being valued by adolescents and adults. Overall, there is a concern that the use of a mixed sample of both adolescents and adults does not address the crucial issue that this still does not contain children.

4. PUBLIC OPINION ON WHOSE PREFERENCES TO ELICIT

The selection of whose preferences to elicit and from which perspective is a normative decision that can be informed by a number of considerations including the views of the public on this issue. A targeted literature search was undertaken to identify previous studies reporting on public opinion around the valuation of child and adolescent health states, in particular around the normative questions of whose preferences to elicit and from which perspective. The search was undertaken in MEDLINE and supplementary citation searches of four key articles[3, 74, 75, 93] in the Web of Science were carried out in June 2020 to find studies reporting on public opinion around the valuation of child and adolescent health states. The full search strategy is reported in the appendix.

The search identified 267 records, and these were sifted using the title and abstract by one researcher (DR). No relevant studies were identified. However, one recent and unpublished study on this topic was conducted by some of the authors of this report, and this study is summarised below.

The study examined the views of members of the UK general population around which perspective should be used in valuation of child and adolescent health states by adults[45], but participants were not asked about their views around the elicitation of either adolescent or adult preferences. The study involved six focus groups with 30

members of the UK adult general population. In the focus group participants individually valued two EQ-5D-Y health states using TTO and DCE pairwise comparison tasks (without duration) using four perspectives: themselves; another adult; a 10-year old child; themselves as a 10-year old child. Following these exercises, a semi-structured discussion explored: task understanding and what informed responses; potential differences by perspective and task; views on the relative prioritisation of child/adult health; and which techniques should be used for informing policy.

The study found that differing views were raised. Whilst in general participants had a different willingness to trade-off life years for children versus themselves, this varied, such as by the dimension of ill health that was impacted and by which child participants they were imagining when they completed the tasks. Participants disagreed around whether ill health had more, less or the same impact on children and adults. Views were raised that ill health had lower impact on child utility with reasons provided that children are more resilient, may have been born with health problems (as opposed to adapting to ill health), and have an established and continuing support network. In contrast, views were raised that ill health has a larger impact on children, and that it is worse for a child to be in ill health for emotive reasons around a child being unhappy or suffering, and considerations around whether the life is worth living. Some participants stated that they would rather that their values were elicited using an own perspective, rather than a child perspective or any other perspective, raising concerns that otherwise the preferences could be impacted by other factors, including emotion and bias. However, other participants raised the counter-argument that knowing the health states were for children and adolescents would make responses more accurate and that people have a right to know that the health states are experienced by children. The study also identified that parental status impacted on preferences elicited from a child perspective, meaning that if a child perspective is used it is important that the sampling is representative for parental status of children aged below 18. The study results did not find evidence to support the prioritisation of child health over adult health for the allocation of healthcare resources.

Another study examined similar issues around the reasons why TTO health state values differ using the perspective of an 8 year old child or a 40 year old adult, but did not ask participants around which perspective they thought should be used[46].

5. CONCLUSIONS

The report has critically examined the use of a mixed sample of adolescents and adults to value child and adolescent health states. The report: summarised the literature around considerations in the valuation of child and adolescent health states; presented an overview of existing TTO studies undertaken with adolescents; explored the practical, ethical and theoretical issues arising from the novel idea of using a mixed population of adults and adolescents to value child and adolescent health states, and summarised the only identified study exploring public opinion on which perspective to use to elicit preferences for child and adolescent health states.

The use of a mixed adolescent and adult sample to value child and adolescent health states has the advantage that it includes both the population who can potentially experience the health states, thus enabling adolescents to express their views around matters that may affect them, and the population that are taxpayers and voters. Overall, it appears feasible to use a mixed adolescent and adult sample to value child and adolescent health states. TTO may be selected as the elicitation task, since TTO is a widely used and accepted approach in adult valuation samples. Valuation of health states from the own perspective (imagining yourself living in the health state) throughout the sample is suggested, but this is not without its limitations. However, the evidence is limited around the minimum age of adolescents where it is appropriate and feasible to use tasks such as TTO, and no study was identified that purposively assessed acceptability, feasibility and framing of TTO in interviews with adolescent participants, exploring the issues by age in years. The published evidence has also focussed more on usage and feasibility than appropriateness, and there has not previously been consideration around the psychosocial maturity of survey participants that will impact on their choices. Therefore it is not straightforward to recommend a minimum age for use of TTO in a mixed sample of adolescents and adults using existing evidence. The selection of the proportion of adults and adolescents in a valuation study sample, and how to weight the sample and/or the modelled value set

regarding adolescent participants relative to adults requires careful consideration in any mixed sample for valuation.

The report has not discussed the complex issues around measuring health across children, adolescents and adults and the challenges raised by the use of different measures for different ages and potentially the use of both self-report and proxy-report health for the generation of health state utility values for use in HTA. The use of a single measure across populations would make both measurement and valuation simpler, and this is something that could potentially be explored by instrument developers.

The report has also not discussed whether preferences used to generate the value sets for adult preference-based measures could be elicited from a mixed sample of adolescents and adults. The use of a mixed sample for both adult and adolescent health states would mean consistency in the population providing preferences used to score QALYs. This could also mean that the same preference elicitation techniques, perspective, and populations could be used to elicit preferences across both child/adolescent-specific and adult measures, providing comparability in the methodological decisions used to generate value sets for use in cost-effectiveness analyses. This could enable greater consistency in the elicitation methods used to generate health state utility values that inform cost-effectiveness models across children, adolescents and adults.

The report is limited by the paucity of academic literature on this topic, yet this is an important and relevant issue. The report reflects both the little literature that is available and the authors' opinions.

5.1. SUMMARY OF PROPOSED RECOMMENDATIONS, FOR CONSIDERATION BY NICE

- Use of a mixed adolescent and adult sample to value child and adolescent health states has the advantage that it includes both the population who can potentially experience the health states, thus enabling adolescents to express their views around matters that may affect them, and the population that are taxpayers and voters. There is evidence of the requisite cognitive capacity and

prior administration of TTO in participants aged under 18, suggesting that undertaking a TTO valuation study of child and adolescent health states using a mixed sample of adolescents and adults may be feasible.

- However, the use of a mixed adolescent and adult sample faces the disadvantage that there may be a discrepancy between the health state self-reported by children and adolescents and the health state that is valued, when adults value states imagining themselves living in the state (for example usual activities differ for adults and children). There is also a concern that the use of a mixed sample of both adolescents and adults does not address the crucial issue that this still does not contain children. In addition, prior to undertaking such a valuation study using a mixed adolescent and adult sample, it is recommended that research purposively designed to assess the acceptability, feasibility and framing of TTO in participants aged under 18 is more fully explored, and that the proportion of adolescents and adults that comprise the sample is given careful consideration.

5.2. FUTURE POTENTIAL RESEARCH TO ADDRESS EVIDENCE GAPS ON THESE ISSUES

- To explore the acceptability and feasibility of TTO in participants aged under 18, in particular by age in years. Qualitative research using focus groups and quantitative studies could be undertaken to examine adolescent views using a general population sample. If acceptable, the format and framing of tasks could also be explored.
- To better understand public opinion around the valuation of child and adolescent health states, in particular around the normative questions of whose preferences to elicit and from which perspective. Qualitative research using focus groups could be undertaken. However, the report authors were divided on whether this would be beneficial for NICE, and the value of doing this should be weighed up against whether this information is informative for NICE and whether this would be used to inform policy recommendations.

To explore public opinion around the valuation of adult health states, in particular around the normative questions of whose preferences to elicit and whether this could potentially include adolescents and adults. The use of a mixed sample for both adult

and adolescent health states would mean consistency in the population providing preferences to score QALYs.

6. REFERENCES

1. Rowen, D., et al., *International Regulations and Recommendations for Utility Data for Health Technology Assessment.* PharmacoEconomics, 2017. **35**: p. 11-19.
2. National Institute of Health and Care Excellence (NICE), *Guide to the methods of technology appraisal*. 2013, NICE: London.
3. Chen, G. and J. Ratcliffe, *A Review of the Development and Application of Generic Multi-Attribute Utility Instruments for Paediatric Populations.* Pharmacoeconomics, 2015. **33**(10): p. 1013-1028.
4. Beusterien, K.M., et al., *Development of the multi-attribute Adolescent Health Utility Measure (AHUM).* Health & Quality of Life Outcomes, 2012. **10**: p. 102.
5. Richardson, J., et al., *Measurement of the quality of life for economic evaluation and the Assessment of Quality of Life (AQoL) Mark 2 instrument.* Aust Econ Hist Review, 2004. **37**: p. 62–88.
6. Stevens, K.J., *Working With Children to Develop Dimensions for a Preference-Based, Generic, Pediatric, Health-Related Quality-of-Life Measure.* Qualitative Health Research, 2010. **20**(3): p. 340-351.
7. Stevens, K.J., *Developing a descriptive system for a new preference-based measure of health-related quality of life for children.* Quality of Life Research, 2009. **18**(8): p. 1105-1113.
8. Stevens, K.J., *Assessing the performance of a new generic measure of health related quality of life for children and refining it for use in health state valuation.* Applied Health Economics and Health Policy, 2011. **9**(3): p. 157-169.
9. Ravens-Sieberer, U., et al., *Feasibilty, reliability and validity of the EQ-5D-Y: results from a multinational study.* Quality of Life Research, 2010. **19**: p. 887-897.
10. Wille, N., et al., *Development of the EQ-5D-Y: a child-friendly version of the EQ-5D.* Quality of Life Research, 2010. **19**: p. 875-886.
11. Devlin, N. and R. Brooks, *EQ-5D and the EuroQol Group: Past, Present and Future.* Applied Health Economics and Health Policy, 2017(127-137).
12. Kreimeier, S., et al., *EQ-5D-Y-5L: developing a revised EQ-5D-Y with increased response categories.* Quality of Life Research, 2019. **28**: p. 1951-1961.
13. Torrance, G., et al., *Multiattribute utility function for a comprehensive health status classification system: Health Utilities Index mark 2.* Medical Care, 1996. **34**: p. 702-722.
14. Feeny, D., et al., *Multiattribute and Single-Attribute Utility Functions for the Health Utilities Index Mark3 System.* Medical Care, 2002. **40**(2): p. 113-128.
15. Seiber, W.J., et al., *Quality of Well Being Self-Administered (QWB-SA) Scale: Users Manual.* 2008, Health Services Research Center, University of California: San Diego.
16. Apajasalo, M., et al., *Quality of life in early adolescence: a sixteen-dimensional health-related measure (16D).* Quality of Life Research, 1996. **5**: p. 205-211.
17. Apajasalo, M., et al., *Quality of life in pre-adolescence: a 17-dimensional health-related measure (17D).* Quality of Life Research, 1996. **5**: p. 532-538.
18. Jabrayilov, R., et al., *Valuing Health Status in the First Year of Life: The Infant Health-Related Quality of Life Instrument.* Value in Health, 2019. **22**(6): p. 721-727.
19. Rowen, D., et al., *Review of Valuation Methods of Preference-Based Measures of Health for Economic Evaluation in Child and Adolescent Populations: Where*

are We Now and Where are We Going? Pharmacoeconomics, 2020. **38**(4): p. 325-340.
20. Kreimeier, S. and W. Greiner, *EQ-5D-Y as a Health-Related Quality of Life Instrument for Children and Adolescents: The Instrument's Characteristics, Development, Current Use, and Challenges of Developing Its Value Set.* Value in Health, 2019. **22**(1): p. 31-37.
21. Kreimeier, S., et al., *Valuation of EuroQol Five-Dimensional Questionnaire, Youth Version (EQ-5D-Y) and EuroQol Five-Dimensional Questionnaire, Three-Level Version (EQ-5D-3L) Health States: The Impact of Wording and Perspective.* Value in Health, 2018. **21**(11): p. 1291-1298.
22. Ramos-Goni, J.M., et al., *International Valuation Protocol for the EQ-5D-Y-3L.* Pharmacoeconomics, 2020. **38**(7): p. 653-663.
23. Chen, G., et al., *Scoring the Child Health Utility 9D instrument: estimation of a Chinese child and adolescent-specific tariff.* Quality of Life Research, 2019. **28**(1): p. 163-176.
24. Ratcliffe, J., et al., *Nothing About Us Without Us? A Comparison of Adolescent and Adult Health-State Values for the Child Health Utility-9D Using Profile Case Best-Worst Scaling.* Health Economics, 2016. **25**(4): p. 486-496.
25. Saigal, S., et al., *Self-perceived health status and health-related quality of life of extremely low-birth-weight infants at adolescence.* JAMA, 1996. **276**(6): p. 453-459.
26. Tong, A., et al., *Quality of life of young adults and adolescents with chronic kidney disease.* Journal of Pediatrics, 2013. **163**(4): p. 1179-85.e5.
27. Saigal, S., et al., *Differences in preferences for neonatal outcomes among health care professionals, parents, and adolescents.* JAMA, 1999. **281**(21): p. 1991-1997.
28. Mott, D.J., et al., *Valuing the EQ-5D-Y using a discrete choice experiment: do adult and adolescent preferences differ?*, in *OHE Research Paper*, O.o.H. Economics, Editor. 2019: London.
29. Dalziel, K., et al., *Feasibility, Validity and Differences in Adolescent and Adult EQ-5D-Y Health State Valuation in Australia and Spain: An Application of Best-Worst Scaling.* Pharmacoeconomics, 2020. **38**(5): p. 499-513.
30. Nations, U., *Convention on the rights of the child*. 1989, United Nation: London.
31. Pharmaceutical Benefits Board, *General guidelines for economic evaluations from the Pharmaceutical Benefits Board*. 2003, Pharmaceutical Benefits Board: Sweden.
32. Ratcliffe, J., et al., *Valuing Child Health Utility 9D health states with a young adolescent sample: a feasibility study to compare best-worst scaling discrete-choice experiment, standard gamble and time trade-off methods.* Applied Health Economics & Health Policy, 2011. **9**(1): p. 15-27.
33. Health, D.o., *Chief Medical Officer's annual report Our Children Deserve Better: Prevention Pays*. 2012, Department of Health: London.
34. Commission, N.H.a.H.R., *A healthier future for all Australians: final report of the National Health and Hospital Reform Commission*. 2009.
35. Consumo, M.d.S.y., *Ganar Salud con la Juventud*. 2008, Ministerio de Sanidad y Consumo: Madrid.
36. Wong, N., M. Zimmerman, and E. Parker, *A Typology of Youth Participation and Empowerment for Child and Adolescent Health Promotion.* Am J Community Psychol, 2010. **46**: p. 100–114

37. Grootens-Wiegers, P., et al., *Medical decision-making in children and adolescents: developmental and neuroscientific aspects.* BMC pediatrics, 2017. **17**(1): p. 1-10.
38. Duell, N., et al., *Age patterns in risk taking across the world.* Journal of youth and adolescence, 2018. **47**(5): p. 1052-1072.
39. Steinberg, L. and K. Monahan, *Age differences in resistance to peer influence.* Developmental psychology, 2007. **43**: p. 1531.
40. Icenogle, G., et al., *Adolescents' cognitive capacity reaches adult levels prior to their psychosocial maturity: Evidence for a "maturity gap" in a multinational, cross-sectional sample.* Law and human behavior, 2019. **43**(1): p. 69.
41. Figner, B., et al., *Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task.* Journal of Experimental Psychology: Learning, Memory, and Cognition, 2009. **35**: p. 709.
42. Kind, P., et al., *Can adult weights be used to value child health states? Testing the influence of perspective in valuing EQ-5D-Y.* Quality of Life Research, 2015. **24**: p. 2519-2539.
43. Rowen, D., et al., *Estimating a Dutch Value Set for the Pediatric Preference-Based CHU9D Using a Discrete Choice Experiment with Duration.* Value in Health, 2018. **21**(10): p. 1234-1242.
44. Shah, K., et al., *An exploration of methods for obtaining 0 = dead anchors for latent scale EQ-5D-Y values.* Eur J Health Econ, 2020. **21**: p. 1091-1103.
45. Powell, P., et al., *Valuing child and adolescent health states: a qualitative study of adult general public perspectives and priorities*. 2020: In submission.
46. DeWilde, S., et al., *Exploration of the reasons why health state valuation differs for children compared to adults: a mixed methods approach*. 2020, Unpublished manuscript.
47. Brazier, J., et al., *Measuring and Valuing Health Benefits for Economic Evaluation*. 2016, Oxford: Oxford University Press.
48. Crump, R.T., et al., *Reliability, Validity, and Feasibility of Direct Elicitation of Children's Preferences for Health States: A Systematic Review.* Medical Decision Making, 2017. **37**(3): p. 314-326.
49. Crump, R.T., et al., *Testing the feasibility of eliciting preferences for health states from adolescents using direct methods.* Bmc Pediatrics, 2018. **18**.
50. Mehrez, A. and A. Gafni, *HYEs versus QALYs: in pursuit of progress.* Medical Decision Making, 1993. **13**: p. 287-292.
51. Richardson, J., *Cost-utility analysis - what should be measured.* Social Science & Medicine 1994. **39**: p. 7-21.
52. McCabe, C., et al., *Health state values for the HUI 2 descriptive system: results from a UK survey.* Health Economics, 2005. **14**: p. 231-244.
53. Le Gales, C., et al., *Development of a Preference-Weighted Health Status Classification System in France: The Health Utilities Index 3.* Health Care Management Science, 2002. **5**: p. 41-51.
54. Stevens, K., *Valuation of the Child Health Utility 9D Index.* Pharmacoeconomics, 2012. **30**(8): p. 729-747.
55. Yi, M.S., et al., *Health values of adolescents with cystic fibrosis.* Journal of Pediatrics, 2003. **142**(2): p. 133-40.
56. Stevens, K.J., *Because that's what matters to me". A pilot study to test the feasibility and reliability of ordinal valuation methods for health state valuation with children*, in *HEDS Discussion Paper*. 2015, University of Sheffield: Sheffield.

57. Rogers, H., et al., *Discrete choice experiments or best-worst scaling? A qualitative study to determine the suitability of preference elicitation tasks in research with children and young people*. 2020, In submission.
58. Norman, R., et al., *Using a discrete choice experiment to value the QLU-C10D: feasibility and sensitivity to presentation format.* Quality of Life Research, 2016. **25**(3): p. 637-649.
59. Bansback, N., et al., *Using a discrete choice experiment to estimate health state utility values.* Journal of Health Economics, 2012. **31**: p. 306-318.
60. (NICE), N.I.o.H.a.C.E., *Guide to the methods of technology appraisal 2013*. 2013, National Institute of Health and Care Excellence (NICE): London.
61. Potoglou, D., et al., *Best–worst scaling vs. discrete choice experiments: An empirical comparison using social care data.* Social Science & Medicine, 2011. **72**: p. 1717-1727.
62. Krucien, N., J. Sicsic, and M. Ryan, *For better or worse? Investigating the validity of best-worst discrete choice experiments in health.* Health Economics, 2019. **28**: p. 572-586.
63. Krucien, N., V. Watson, and M. Ryan, *Is best-worst scaling suitable for health state valuation? A comparison with discrete choice experiments.* Health Economics, 2017. **26**(12): p. e1-e16.
64. Parkin, D. and N. Devlin, *Is there a case for using visual analogue scale valuations in cost utility analysis?* Health Economics, 2006. **15**: p. 653-664.
65. Rowen, D., J. Brazier, and B. Van Hout, *A Comparison of Methods for Converting DCE Values onto the Full Health-Dead QALY Scale.* Medical Decision Making, 2015. **35**: p. 328-340.
66. Hernandez-Alava, M., S. Pudney, and A. Wailoo, *The EQ-5D-5L Value Set for England: Findings of a Quality Assurance*

Program. Value in Health, 2020. **23**(5): p. 642-648.
67. Ratcliffe, J., et al., *Valuing the Child Health Utility 9D: Using profile case best worst scaling methods to develop a new adolescent specific scoring algorithm.* Social Science & Medicine, 2016. **157**: p. 48-59.
68. Lee, J.M., et al., *Health utilities for children and adults with type 1 diabetes.* Medical Care, 2011. **49**(10): p. 924-31.
69. Chen, C.L., et al., *A community-based study of acne-related health preferences in adolescents.* Archives of Dermatology, 2008. **144**(8): p. 988-94.
70. Fox, D., E.J. Kay, and K. O'Brien, *A new method of measuring how much anterior tooth alignment means to adolescents.* European Journal of Orthodontics, 2000. **22**(3): p. 299-305.
71. Moodie, M., et al., *Predicting time trade-off health state valuations of adolescents in four Pacific countries using the Assessment of Quality-of-Life (AQoL-6D) instrument.* Value in Health, 2010. **13**(8): p. 1014-27.
72. Tong, A., et al., *Quality of life of adolescent kidney transplant recipients.* Journal of Pediatrics, 2011. **159**(4): p. 670-5.e2.
73. Yi, M.S., et al., *Health values in adolescents with or without inflammatory bowel disease.* Journal of Pediatrics, 2009. **154**(4): p. 527-34.
74. Thorrington, D. and K. Eames, *Measuring Health Utilities in Children and Adolescents: A Systematic Review of the Literature.* Plos One, 2015. **10**(8).
75. Petrou, S., *Methodological issues raised by preference-based approaches to measuring the health status of children.* Health Economics, 2003(12): p. 697-702.

76. Bharij, A., et al., *Health utility and quality of life in pediatric liver transplant recipients.* Pediatric Transplantation, 2020. **24**(4): p. e13720.
77. Borges, P.A., et al., *The influence of body image on surgical decisions in adolescent idiopathic scoliosis patients.* Clinics (Sao Paulo, Brazil), 2017. **72**(3): p. 130-133.
78. Dillman, J.R., et al., *Relationship of Bowel MR Imaging to Health-related Quality of Life Measures in Newly Diagnosed Pediatric Small Bowel Crohn Disease.* Radiology, 2016. **280**(2): p. 568-75.
79. Fyffe, H.E., et al., *The reliability of two methods of utility assessment in dentistry.* Community Dental Health, 1999. **16**(2): p. 72-9.
80. Cheng, S., et al., *Health-related quality of life anticipated with different management strategies for paediatric febrile neutropaenia.* British Journal of Cancer, 2011. **105**(5): p. 606-11.
81. Saw, S.M., et al., *Utility values and myopia in teenage school students.* British Journal of Ophthalmology, 2003. **87**(3): p. 341-5.
82. Trent, M., et al., *Adolescent and parental utilities for the health states associated with pelvic inflammatory disease.* Sexually Transmitted Infections, 2011. **87**(7): p. 583-7.
83. Sung, L., et al., *Health-related quality of life (HRQL) scores reported from parents and their children with chronic illness differed depending on utility elicitation method.* Journal of Clinical Epidemiology, 2004. **57**(11): p. 1161-6.
84. Matza, L., et al., *Pediatric Patient-Reported Outcome Instruments for Research to Support Medical Product Labeling: Report of the ISPOR PRO Good Research Practices for the Assessment of Children and Adolescents Task Force.* Value in Health, 2013. **16**: p. 461-479.
85. van den Bos, W., et al., *Changing brains, changing perspectives: the neurocognitive development of reciprocity.* Psychological science, 2011. **22**(1): p. 60-70.
86. Jonker, M., et al., *Effect of Level Overlap and Color Coding on Attribute Non-Attendance in Discrete Choice Experiments.* Value in Health, 2018. **21**(7): p. 767-771.
87. King, M., et al., *Australian utility weights for the EORTC QLU-C10D, a multi-attribute utility instrument derived from the cancer-specific quality of life questionnaire, EORTC QLQ-C30.* Pharmacoeconomics, 2018. **36**(2): p. 225-238.
88. Rowen, D., et al., *Estimating a preference-based single index measuring the quality of life impact of self-management for diabetes.* Medical Decision Making, 2018. **38**(6): p. 699-707.
89. Mulhern, B., et al., *Preparatory study for the revaluation of the EQ-5D tariff: methodology report.* Health Technology Assessment, 2014. **18**(12): p. vii-191.
90. Kellett, M., *Small shoes, big steps! Empowering children as active researchers.* American Journal of Community Psychology, 2010. **46**(1-2): p. 195-203.
91. Dolan, P., *Modeling valuations for EuroQol health states.* Medical Care, 1997. **35**(11): p. 1095-1108.
92. Shah, K.K., et al., *An exploration of methods for obtaining 0 = dead anchors for latent scale EQ-5D-Y values.* European Journal of Health Economics, 2020. **06**: p. 06.
93. Bahrampour, M., et al., *Developing a cerebral palsy-specific preference-based measure for a six-dimensional classification system (CP-6D): protocol for a valuation study.* Bmj Open, 2019. **9**(9).

7. APPENDIX

7.1. SEARCHES OF THE LITERATURE TO IDENTIFY RELEVANT PAPERS

Search 1: Focused search for studies reporting on public opinion around the valuation of child and adolescent health states

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to June 29, 2020
161 results

#	Searches	Results	Concept
1	consumer participation/	17125	Precise PPI filter
2	patient participation/	25717	
3	1 or 2	42476	
4	(patient* or public or lay or people or consumer* or user* or citizen*).ti,ab.	7482635	
5	(participat* or involv* or engag*).ti,ab.	2836100	
6	(health or research).ti,ab.	3001012	
7	4 and 5 and 6	230716	
8	(partners or partnership).ti,ab.	104938	
9	6 and 8	41866	
10	3 or 7 or 9	297789	
11	((child* or adolesc*) adj2 (health state or health states or preference* or value* or valuation)).tw.	4983	Child health states/preferences/values
12	10 and 11	165	PPI AND child health states/preferences/values
13	limit 12 to english language	161	

Supplementary citation search of 4 key references using the Web of Citation Cited Reference Search

Provided references	Citations
Chen G, Ratcliffe J (2015) A Review of the Development and Application of Generic Multi-Attribute Utility Instruments for Paediatric Populations. PharmacoEconomics 33:1013–1028.	34
Petrou S. Methodological issues raised by preference-based approaches to measuring the health status of children. Health Economics, 2003; 12:697-702.	85
Kind P, Klose K, Gusi N, Olivares PR, Greiner W. Can adult weights be used to value child health states? Testing the influence of perspective in valuing EQ-5D-Y. Quality of Life Research, 2015; 24:2519-2539	16

Provided references	Citations
Thorrington D, Eames K (2015) Measuring Health Utilities in Children and Adolescents: A Systematic Review of the Literature. PLoS ONE 10(8): e0135672. https://doi.org/10.1371/journal.pone.0135672	43
Unique reference in Endnote	149

Search 2: Focused search for child or adolescent studies using choice-based methods in particular time-trade-off, DCE and VAS.

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to June 29, 2020
118 results

#	Searches	Results	Concept
1	(child* or adolesc* or kid or kids or youngster* or teen* or youth* or pediatri* or paediatri*).tw.	1725885	Child terms
2	(time trade off or time trade-off or time tradeoff or tto or dcetto).tw.	1877	Methods (TTO, DCE and TTO/duration, choice based methods, VAS and valuation)
3	((discrete choice experiment* or dce) adj5 duration).tw.	31	
4	((choice-based or choice based) adj3 method*).tw.	41	
5	(visual analogue scale and valuation).tw.	98	
6	(eq-vas or euroqol visual analogue scale or vertical visual analogue scale).tw.	957	
7	5 not 6	91	Exclude EQ-VAS
8	2 or 3 or 4 or 7	1980	
9	1 and 8	121	Child and methods
10	limit 9 to english language	118	