EDITORIAL

EQ-5D-Y-3L Value Sets, Valuation Methods and Conceptual Questions

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The measurement and valuation of child health-related quality of life (HRQoL) is a rapidly evolving field. Research is responding to the challenging issues noted in health technology assessment (HTA) and decision making regarding child health interventions [1–4]. New methods and instruments are emerging to address how best to describe and collect HRQoL data from children and their proxies, and how to obtain preference weights to summarise that descriptive information, for use in priority setting.

Recognising that adult instruments and methods were not suitable for measuring children's health, the Euro-Qol Research Foundation published its first child HRQoL instrument—the EQ-5D-Y-3L—in 2010 [5, 6] (see Fig. 1) and since then evidence has built around its measurement properties. But valuation adds additional challenges when it comes to children's health, and it was nearly a decade until the first valuation protocol was published to facilitate the production of EQ-5D-Y-3L value sets [7]. That protocol has been the catalyst to a remarkable level of international effort to rapidly produce value sets [8]. In parallel, there has been an active programme of methodological research to address the many remaining methods issues.

This special issue of *Pharmacoeconomics* brings together current research on valuation of EQ-5D-Y-3L that has been supported by the EuroQol Research Foundation to advance knowledge in this area. It includes six new EQ-5D-Y-3L value sets from around the world—for Germany [9], Netherlands [10], Belgium [11], Hungary [12], China [13], and Indonesia [14], in addition to three papers on related conceptual and methodological issues [15–17].

The value sets for the EQ-5D-Y-3L reported in this issue add to the value sets already published for the EQ-5D-Y-3L for Japan [18], Slovenia [19], and Spain [20], which means there are now more value sets available to support use of EQ-5D-Y-3L than for any other paediatric measure of HRQoL. More value set studies are underway, including in Canada, Australia, Brazil, USA, UK, Singapore, Taiwan, Vietnam and Malaysia. While all these studies follow the protocol for valuation of EQ-5D-Y-3L [7], which sets out suggested *minimum* requirements for valuation studies, the research effort has welcomed experimentation to generate data around the impact of methodological choices and to accelerate learning about what works in child valuation. Hence, there are some methodological differences between the value set studies that are reported in this special issue.

Notable differences among the studies reported in this issue include the amount of composite Time Trade Off (cTTO) data that is collected and how it is used in combination with DCE data. The protocol suggested eliciting cTTO values for 10 EQ-5D-Y-3L states as a minimum; several study teams decided to collect cTTO values for a larger set of states (e.g., China, the Netherlands, Japan, and Indonesia). There are also differences in how the cTTO data are used to anchor the latent scale DCE preferences on the 0 and 1 scale required for estimation of quality-adjusted life years (QALYs). The EQ-5D-Y-3L value sets for Slovenia [19], Spain [20], Belgium [11], and Hungary [12] use the cTTO values for just one state—the worst state defined by the descriptive system (33333)—to anchor. Others, such as China [13], Japan [1], Germany [9], Netherlands [10], and Indonesia [14] make use of all the cTTO data collected, via hybrid modelling or mapping approaches. The implications of these anchoring method choices for EQ-5D-Y-3L values are the focus of the paper by Mott et al. (2022) in this issue [15], who illustrate the differences produced from these alternative ways of combining DCE and cTTO data. The authors provide grounds for arguing that anchoring just on 33333 is inferior to alternative approaches—while noting that it is difficult to conclude that definitively, since that depends in part on what characteristics are seen as desirable

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Fig. 1 EQ-5D-Y-3L questionnaire: descriptive system. © EuroQol Research Foundation. Source: EQ-5D-Y User Guide

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY *(walking about)*

I have <u>no</u> problems walking about ☐

I have <u>some</u> problems walking about ☐

I have <u>a lot</u> of problems walking about ☐

LOOKING AFTER MYSELF

I have <u>no</u> problems washing or dressing myself ☐

I have <u>some</u> problems washing or dressing myself ☐

I have <u>a lot</u> of problems washing or dressing myself ☐

DOING USUAL ACTIVITIES *(for example, going to school, hobbies, sports, playing, doing things with family or friends)*

I have <u>no</u> problems doing my usual activities ☐

I have <u>some</u> problems doing my usual activities ☐

I have <u>a lot</u> of problems doing my usual activities ☐

HAVING PAIN OR DISCOMFORT

I have <u>no</u> pain or discomfort ☐

I have <u>some</u> pain or discomfort ☐

I have <u>a lot</u> of pain or discomfort ☐

FEELING WORRIED, SAD OR UNHAPPY

I am <u>not</u> worried, sad or unhappy ☐

I am <u>a bit</u> worried, sad or unhappy ☐

I am <u>very</u> worried, sad or unhappy ☐

in a value set. While anchoring on 33333 may work in some contexts, some papers in this issue (e.g., Indonesia) [14] have noted that the value for 33333 seems disproportionately low and 'out of keeping' with other observed values. Where that is the case, anchoring only on 33333 is likely to yield lower minimum values than other anchoring approaches—information which potential users of these value sets should be aware of. The available data do not give a clear picture of what is causing this issue. Further research is needed to clarify whether this reflects non-linearities in the preference structure or is a method-induced gap effect.

Given the number of value sets now available for EQ-5D-Y-3L, it is timely to reflect on the similarities and differences apparent between these value sets and how the values compare with those for adult EQ-5D instruments, where both exist in a given country.

For example, it is notable that the most important dimension across all EQ-5D-Y-3L value sets published to date is pain/discomfort. There is less uniformity in the order of importance of other dimensions—but notable that in 8 out the 9 EQ-5D-Y-3L values sets, 'taking care of oneself' is the least important dimension. These patterns of dimension importance are different than those observed in values for adult instruments [21], and may have intuitive explanations, e.g., adults find it more acceptable to provide supportive care for children than to require assistance with self-care themselves. Notwithstanding, concerns about unwillingness to trade off life years in cTTO tasks concerning children, it is also worth noting that, of the EQ-5D-Y-3L value sets available for European countries, some have a substantial proportion of health states being worse than dead (the proportion of values < 0 varies from 3.3 to 20.6%), whereas for

Asian countries no or very few states (0.4% in Indonesia) have negative values.

In European countries, evidence to date suggests the overall distribution of values for the EQ-5D-Y-3L and EQ-5D-5L are very similar; the worst health state is typically assigned a somewhat higher value for the EQ-5D-Y-3L instrument compared to the EQ-5D-5L, although the differences are relatively small. For the Asian countries, however, the characteristics of the distributions of values differ considerably between the adult and youth instruments. Caution is required in generalising about these patterns and attributing them to regional or cultural differences. As further EQ-5D-Y-3L value sets are published, we will be in a position to fully investigate these differences and similarities in terms of both the published value set algorithms and in terms of the underlying respondent-level preferences data. This is a research agenda being actively pursued.

The EuroQol Research Foundation is in a unique position to explore possibilities for providing a suite of coherent, linked instruments which cover HRQoL 'from the cradle to the grave'. To date, these efforts have preliminarily focused on making available instruments that allow HRQoL of children to be measured and valued. In addition to the EQ-5D-Y-3L, instrument development has included a five-level version of it (EQ-5D-Y-5L) [22] to improve measurement precision and sensitivity; and an instrument for infants aged 0–3 years (Toddler and Infant Populations, EQ-TIPs) (formerly known as TANDI—see Verstraete et al. 2020) [23]. Researchers are also conducting experimental work to develop and test a modified version of the EQ-5D-Y proxy versions to allow its age range potentially to be extended to also include those aged 2–4 years. These instruments are experimental in nature, and are subject to further development and testing, but have the potential in future to enable measurement and valuation of HRQoL from birth through to adulthood. The exploration of whether analogous issues in measurement and valuation of HRQoL exist at the other end of the age spectrum—older people—is currently unexplored territory.

The availability of age-specific measures with accompanying values strengthens the evidence base on HRQoL but leaves us with new issues to resolve. Age-specific instruments seek to improve measurement within an age group, but this potentially comes at the cost of reduced consistency in what is measured and how it is valued *between* age groups. These differences, and ways to reconcile them, are important to consider in HTA. Incorporating age-dependent health state values will mean that analysts and decision makers face new challenges. Age-dependent pediatric value sets seem appropriate for assessing and comparing cost effectiveness of treatments exclusively targeting children, but how should they be incorporated in models that span the lifetime? And how can decision makers use and compare estimates of QALYs and cost-effectiveness ratios across age groups if

they are constructed on a different basis? It is also crucial to consider normative questions involved in using age-dependent health state values, which imply that we value health gains for children and adults differently. Is that aligned with societal preferences for priority setting? The introduction of age-dependent value sets raises a broader set of issues to reflect on than may have been anticipated when value sets for EQ-5D-Y-3L were introduced.

What stands out in this area of research, as Lipman et al. [16] emphasise, is that there are many choices to be made in valuation protocols that rely on value judgements, which exert a clear influence on the resulting value sets. That paper contributes to a growing body of literature about the effects of these methods' choices on values [24–30], but it is not clear how we choose between approaches and whose value judgements should guide those choices. A review of the state of play in EQ-5D-Y-3L valuation [8] emphasised the importance of undertaking stakeholder engagement on these decisions, to ensure value sets are 'fit for purpose'. One of the first papers reporting on this kind of consultation exercise—with stakeholders in the USA—is reported in this issue [17]. Different stakeholders, in different countries, may of course, reach quite different conclusions about the appropriate means of valuing child HRQoL. How best to undertake this kind of stakeholder engagement is a further area of work currently being pursued, building on lessons learned from the USA and elsewhere.

This special issue represents a remarkable achievement: to be able to report six new value sets for a single HRQoL instrument in one journal issue is unprecedented. It reflects the considerable investment of the EuroQol Research Foundation in promoting methods research, developing protocols and providing support for such studies. Our ability to report and compare the characteristics of these value sets, and to identify relevant differences, underlines the advantages of developing standardised protocols, while also retaining a degree of flexibility to address local user requirements.

The body of work reported in this issue of *Pharmacoeconomics*, together with other stated preference studies underway for EQ-5D-Y-3L and for other paediatric HRQoL instruments, means we have reached a turning point in our ability to assess child HRQoL, providing for much improved practice in the use and reporting of child HRQoL in clinical trials and economic evaluations of paediatric intervention.

Declarations

Data availability This is an editorial, and does not directly draw on any data.

Conflict of interest All authors are either members of the EuroQol Group or are directly employed by the EuroQol Research Foundation.

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