Generic preference-based health-related quality of life in children with neurodevelopmental disorders: a scoping review

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ABBREVIATIONS

ASD	Autism spectrum disorder
CUA	Cost–utility analysis
EQ-5D	EuroQoL 5D
EQ-5D-3L	Three-level EQ-5D
EQ-5D-5L	Five-level EQ-5D
EQ-5D-Y	Youth version of the EQ-5D
HRQoL	Health-related quality of life
HUI	Health Utilities Index
NDD	Neurodevelopmental disorders
QALY	Quality-adjusted life year
QoL	Quality of life

AIM To describe how generic preference-based health-related quality of life (HRQoL) instruments have been used in research involving children with neurodevelopmental disorders (NDD).

METHOD A systematic search of nine databases identified studies that used generic preference-based HRQoL instruments in children with NDD. Data extracted following the Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Review guidelines included type of NDD, instrument used, respondent type, justification, and critical appraisal for these selections.

RESULTS Thirty-six studies were identified: four cost–utility analyses; 15 HRQoL assessments; five economic burden studies; three intervention studies; and nine 'other'. The Health Utilities Index (Mark 2 and Mark 3) and EuroQoL 5D (EQ-5D; three-level EQ-5D, five-level EQ-5D, and the youth version of the EQ-5D) instruments were most frequently used (44% and 31% respectively). The relatively low use of these instruments overall may be due to a lack of psychometric evidence, inconsistency in justification for and lack of clarity on appropriate respondent type and age, and geographical challenges in applying preference weights.

INTERPRETATION This study highlights the dearth of studies using generic preference-based HRQoL instruments in children with NDD. The use of cost–utility analysis in this field is limited and validation of these instruments for children with NDD is needed. The quality of data should be considered before guiding policy and care decisions.

Neurodevelopmental disorders (NDD) are a heterogeneous group of conditions with onset in the first 5 years of life, characterized by impairments in personal, social, academic, or occupational functioning.[1–5] The prevalence of NDD is estimated to be 5% to 9% of all children or 75% of all childhood disability.[6–9] Over 90% of children with NDD experience limitations in activities throughout their lifespan that impact their quality of life (QoL).[10,11] The needs of children with NDD are heterogeneous, even within a single diagnosis, with varying support needs often extending beyond traditional health care to social services, rehabilitation, and education.[4,8,12,13] Compared with neurotypical children, children and young people with NDD have higher health care service utilization,[8,14] are more likely to be in the top 5% of most frequent health care users (43% of children with developmental delay are high users),[15] and are more prone to mental health problems.[16–18] To address these complex needs, specialized clinical, educational, and community-based interventions are designed to support children with NDD and their families. Consequently, health outcome measures that focus on specific conditions are most often used. However, use of condition-specific outcomes measures makes it difficult to compare study results across different clinical contexts for resource allocation purposes.

In publicly funded health care systems, economic evaluations are increasingly required to examine the value of interventions, informing resource allocation decisions by allowing for a comparative analysis of costs and health outcomes. Organizations such as the Canadian Agency for Drugs and Technologies in Health in Canada and the National Institute for Health and Care Excellence in the UK require health effects of an intervention to be captured using quality-adjusted life years (QALYs).[19,20] The QALY is a metric that combines length of life and QoL in a single outcome, and health-related QoL (HRQoL) instruments are often used to estimate the quality component. An economic evaluation with health benefits expressed in QALYs – a cost–utility analysis (CUA) – provides a standardized framework for making comparisons of the value of interventions across clinical areas.[21] CUA is the recommended type of economic evaluation in guidelines across the world, including Canada,[19] the UK,[20] and Australia.[22]

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The dominant method of estimating QALYs is through the use of generic preference-based HRQoL instruments (other names commonly used include multi-attribute utility instruments or preference-based health state classification questionnaires). These standardized instruments facilitate the estimation of health state values or preference weights. Although the primary purpose of these instruments is to provide estimates of health state valuations to generate QALYs, there are a number of other applications in health research, including determination of the individual domain scores of HRQoL or a generic measure of health status in population-based studies.[23]

Generic preference-based HRQoL instruments are made up of two parts: a descriptive classification system and a valuation system. The descriptive classification system consists of questions and response options, which enable respondents to describe their HRQoL in one of a finite number of health states. Given that generic preference-based HRQoL instruments are intended for use across clinical areas, questions and response options in the descriptive system should capture a board range of health dimensions, and accurately reflect respondents' experience in a health state. The valuation system is a method of scoring each health state defined by the descriptive system. The process of scoring usually involves using an existing value set, i.e. an off-the-shelf set of scores derived using preference elicitation methods such as time trade-off, standard gamble, or discrete choice experiments in a valuation study comprising a representative sample of the target population.[24] The numerical scores represent the relative value society places on living in each health state defined by the descriptive system, interpreted on a scale, where '1' represents full health and '0' indicates a health state equivalent to dead. Negative values are possible, representing health states worse than dead. The validity of the preference-based instrument for the population of interest is critical to inform cost-effectiveness analyses.

There are several generic preference-based HRQoL instruments, such as those developed by the EuroQol 5D (EQ-5D) Group (three-level EQ-5D [EQ-5D-3L] and five-level EQ-5D [EQ-5D-5L]) and Health Utilities Index Mark 2 and Mark 3 (HUI-2 and HUI-3 respectively), that have been developed and validated for use in adult populations in many clinical areas, ensuring that they provide reliable and valid estimates of health outcomes. For example, the HUI-3 scoring system provides health-state values that correspond to a classification system comprising eight domains (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain), with between four and six levels within each domain.[25] For the HUI-3, health-state valuations have been derived from a representative sample of the adult population in Hamilton, Canada, using a combination of visual analogue scale and standard gamble techniques. Responses to a preference-based instrument are sometimes referred to as defining a health profile. For example, the HUI-3 health profile of '11121131' indicates level 1 vision, level 1 hearing, level 1 speech, level 2 ambulation, level 1 dexterity, level 1 emotion, level 3 cognition, and level 1 pain. For the Canadian HUI-3 scoring algorithm, this health profile has the health-state valuation of 0.84. For the estimation of QALYs, periods of time are weighted by the respective health state value. For example, over a 2-year period, a person who spends the first 6 months in a health state of 0.72 and the remaining 18 months in health state 0.88 would be assigned a QALY estimate of 1.68. The results of a CUA are expressed as an incremental cost-effectiveness ratio, or cost per-QALY gained, which is calculated as the difference in costs between two interventions divided by the difference in QALYs produced by two interventions.[21,24] The incremental cost-effectiveness ratio can be used as a decision rule in resource-allocation decisions.

What this paper adds

- Limited use of generic preference-based health-related quality of life (HRQoL) instruments in studies on children with neurodevelopmental disorders.
- Only 11% of studies were cost–utility analyses.
- Inconsistencies in justification for choosing generic preference-based HRQoL instruments and respondent types.

The measurement and valuation of health states for children and adolescents is a developing field of research. There are many challenges in using preference-based instruments in this context, where the valuations of health state descriptions are typically elicited from adults (there is a paucity of research for valuations derived from children or adolescents). A recent systematic review and meta-analysis explored methodological concerns and considerations in measuring and valuing childhood health states, including the suitability of adult-centred or adult-derived values for childhood health states, bias from proxy assessment, and uncertainty regarding the relevance of descriptive classification systems to the experiences of children.[26]

Ideally, self-reports of HRQoL from children should be considered when using these instruments. However, there will be cases where children are too young and/or lack the necessary cognitive, linguistic, and communication skills to self-report HRQoL. In this case, proxy respondents such as parents, clinicians, and caregivers are often used.[12,27] Proxy assessments can be elicited by asking the proxy to assess how a child would rate their health (the proxy-patient perspective), or by asking the proxy to provide their own perspective on the child's HRQoL (the proxy-to-proxy perspective).[28] Parents or caregivers can be useful proxy respondents as they are the people most familiar with their child's health, but such valuations can be influenced by anxieties stemming from caregiving burden and competing priorities represented by other children in the family.[28,29]

In light of these challenges, some generic preference-based HRQoL instruments have been developed or modified for use specifically in children and adolescents, including the Child Health Utility 9D,[30] the Assessment of

Quality of Life 6D,[31] and the youth version of the EQ-5D (EQ-5D-Y).[32] However, the use of these instruments in children with NDD is currently unknown.[12,33] Researchers and analysts interested in using generic preference-based HRQoL instruments or conducting an economic evaluation of interventions for children with NDD can benefit from a review of these instruments in this population. The primary objective of this study is to describe the application of current generic preference-based HRQoL instruments in the context of research involving children with NDD. A secondary objective is to identify research gaps and highlight important areas for future research.

METHOD

A scoping review was conducted using a methodological framework developed by Arksey and O'Malley,[34] and further enhanced by the Joanna Briggs Institute.[35] This protocol was registered with the Joanna Briggs Institute.

Identifying the research question

This study was guided by the research question: 'What is the nature and extent of research about HRQoL in children with NDD based on generic preference-based HRQoL instruments?'

Defining the search strategy and study selection

A search of the following electronic databases covered literature published between January 1980 and September 2018: MEDLINE, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Methodology Register, Health Technology Assessment, and the NHS Economic Evaluation Database. A comprehensive search strategy was developed using search terms identified from published literature reviews,[33,36,37] combining aspects of the clinical context (children with NDD) and the specific type of outcome measurement (preference-based instruments) that were the focus of the study. Articles generated by all database searches were compiled using Endnote X8.2. The search strategy is provided in Appendix S1 (online supporting information).

Selection of NDD

The search strategy comprised 35 NDD used by Bishop (Appendix S2, online supporting information).[36] Rutter et al. used *Rutter's Textbook of Child and Adolescent Psychiatry, Fifth Edition*[38] and a review of behavioural phenotypes,[39] aiming for a broad NDD definition.

Selection of generic preference-based HRQoL instruments

Seven generic preference-based HRQoL instrument 'families' were selected for this review: 15D,[23,40,41] Assessment of QoL,[31] Child Health Utility 9D,[30] EQ-5D,[32,42,43] HUI,[25] Quality of Well-Being Scale,[44] and Short-Form 6D.[45–47] The term 'families' was used to reflect the fact that multiple formats exist for some preference-based instruments. For example, there are 16D and 17D variants of the 15D, and the HUI descriptive system can be scored using value sets that provide HUI-2 or HUI-3 index scores. Table SI (online supporting information) presents key features of some of the instruments within these seven-preference based HRQoL instruments families.

Inclusion criteria

Inclusion criteria were applied in two stages. In the first stage, titles and abstracts were screened independently, by two authors (RL, BF). Articles were retained during stage one if a review of the title and abstract gave an indication that the study included participants who were aged 18 years of age or younger, who had at least one of the NDD included in the study, and included reference to one or more of the generic preference-based HRQoL instruments described above (or alluded to broader terminology, such as 'QALY' or 'utility'). The requirement for studies to be published in a peer-reviewed journal and written in English were incorporated at this first stage. Full-texts of articles remaining after stage one were retrieved for closer inspection in stage two. The second stage involved the hierarchical application of exclusion criteria. First, articles were excluded if study participants did not have at least one NDD. Second, articles were excluded if study participants, or an identifiable subsample, were not children (≤18y). Finally, articles were excluded if at least one of the abovementioned generic preference-based HRQoL instruments was not used to obtain health state values. Review articles identified during the search process were not included in the final list of identified papers. However, these articles were used for a supplementary search, whereby the lead author manually searched their reference lists to identify potential inclusions. A second supplementary search, conducted by a single author (BF), examined the Pediatric Economic Database Evaluation for potentially eligible studies.[48] The same inclusion criteria were applied in both supplementary searches.

Charting the data

From the articles that met the study inclusion criteria, the following descriptive data were extracted (where available), independently, by two of the authors (RL, BF): lead author, year of publication, aim/purpose of the study, study design, NDD studied, generic preference-based HRQoL instrument(s) used, respondent type, age of study population, justification of instrument selection, justification of selecting the respondent type selection, authors' concerns regarding use of instruments or the respondent type, population from which preference weights were derived, country where the study was conducted, sample size, psychometric evidence of selected instruments, and mean health state valuations specific to children with NDD.

Analytic consideration and quality appraisal

The analytic focus comprised of identifying the types of NDD studied, the types of respondent used to assess

HRQoL for children with NDD, determining the frequency of use for different instruments, and cataloguing mean health-state valuations reported for different NDD. Further goals were to collect evidence on psychometric properties of these instruments in the identified studies, to explore how the authors justify instrument selection for a particular NDD and the respective group(s) of respondents, and to explore authors' concerns regarding the use of instruments and the respondent type. These latter considerations originated from the fact that few studies have examined the reliability and validity of existing generic preference-based HRQoL instruments in children with NDD, and there is no general agreement among researchers on what type of respondent is the most suitable for children with NDD.[12,29,33,49–51]

The quality of identified studies was assessed by a single author (RL) using the Quality Assessment Tool for Studies with Diverse Design.[49] The 14 Quality Assessment Tool for Studies with Diverse Design items relevant to quantitative studies were used. These items are rated on a 4-point scale from 0 to 3 (0=not at all described; 1=described to some extent; 2=moderately described; 3=described in full), with total scores ranging from 0 to 42 (with higher scores indicating higher quality). Total scores were converted into percentages for reporting.[49] This tool has been used in assessing the methodological QoL studies for NDD.[50,51]

Collating, summarizing, and reporting the results

Data were collected and summarized in a single spreadsheet. The results were reported using the same framework as established in the analytical consideration for the study's objectives and the research question.

RESULTS

A total of 3150 unique results were identified from the database search, with 32 articles meeting the inclusion criteria. An additional four articles were identified through supplementary searches (36 articles in total). Figure S1 (online supporting information) provides a flowchart describing the study selection process and the reasons for exclusion at each stage of screening.

Study characteristics

A summary of study characteristics for the 36 articles is provided in Table SII (online supporting information). The studies can be categorized as HRQoL assessments (n=15),[9,52–65] CUAs (n=4),[66–69] studies that describe economic burden and HRQoL assessment (n=5),[70–74] and intervention studies (n=3).[75–77] The remaining nine studies included validation or feasibility studies,[78–84] a mapping study,[85] and a study assessing agreement between self-reported versus proxy-reported HRQoL.[86] Studies looked at either a specific NDD, broad categories of NDD, or NDD as a part of other childhood conditions (see Table SII). Ten specific NDD were examined: attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), cerebral palsy (CP), Down syndrome, Duchenne muscular dystrophy, fetal alcohol spectrum disorders, Fragile X syndrome, Prader–Willi syndrome, intellectual disability, and speech disorder (stutter). Five broad NDD categories were examined: social and conduct disorders, specific language impairments, speech and language disorders, neurodevelopmental impairments, and neurodevelopmental disability. Two studies investigated HRQoL in a variety of conditions, of which at least one was an NDD.

The most frequently studied NDD were ADHD (n=9), CP (n=9), and ASD (n=8). Generic preference-based HRQoL was assessed by a number of different instruments (Table SII). The HUI (HUI-3: n=16; HUI-2: n=3) was the most frequently used instrument, followed by EQ-5D instruments (EQ-5D-3L: n=10; EQ-5D-5L: n=2; EQ-5D-Y: n=4), Quality of Well-Being Scale-Self-Administered (n=2), and the 16D (n=2). Four other instruments were used in one study only (17D, Child Health Utility 9D, Short-Form 6D [12-item Short Form], and Assessment of Quality of Life 6D). Three different types of respondents were used across the 36 studies: assessment by parents or primary caregivers of children (n=21), self-assessment by children or adolescents (n=8), and a mixed assessment, completed by both parents and children/adolescents (n=7).

Quality assessment

Quality rating of identified studies ranged from 52% to 79%, with an average quality rating of 68% (Table SII). In general, studies scored low with respect to the presence of an explicit theoretical framework, sample-size considerations, assessment of reliability and validity, and justification for analytical methods. Higher scores were observed on items related to the statement of aims/objectives, description of research setting, description of procedures for data collection, and the fit between the research question and the method of analysis. Finally, seven studies did not include critical discussion of strengths and weakness.

Justifications for instrument selection and type of respondent

Thirty-two studies provided some justification for selecting a particular generic preference-based HRQoL instrument (Table SIII, online supporting information). Generally, the justifications included reasons such as previous use of the respective instrument in children, adolescents, or children with NDD; the instrument had been developed or modified for use in children and adolescents; and instruments had been validated to measure generic preference-based HRQoL in adults. However, concerns were expressed regarding the ability of generic preference-based HRQoL instruments to capture domains relevant to children with NDD and the lack of age-appropriate generic preference-based HRQoL instruments. For instance, although Chevreual et al. used EQ-5D-5L, they state that the instrument may not accurately reflect the behavioural, social, and cognitive aspects of Fragile X syndrome.[71] Hoving et al. suggested that the EQ-5D-3L domains do

not capture HRQoL changes most relevant to children with CP.[67] Matza et al. commented that the EQ-5D-3L does not assess key HRQoL domains such as school behaviour, peer relations, or family functioning, which are directly affected by ADHD.[84] Similarly, Willems et al. state that domains in the EQ-5D-3L are insensitive to cognitive functioning and suggest using a disease-specific instrument simultaneously.[81]

Variability in the type of respondent (i.e. the child/adolescent, proxy respondent, or both) suggests a lack of consensus on who is best suited to complete generic preference based-HRQoL instruments. Twenty-one studies used proxy respondents (parents or caregivers or family members), eight studies used children/adolescents (self-report), and seven studies used both proxy and children/adolescents with NDD. In 25 studies, the authors provided a justification for the choice of respondent (Table SIII). For example, Payakachat et al.[85] justified the use of a primary caregiver to complete the HUI-3 on the basis that some children with ASD have limited cognitive ability to comprehend the questions. Stade et al.[58] justified their use of proxy assessments with the HUI-3 in children with fetal alcohol spectrum disorders by noting that the HUI-3 proxy report has been validated in children aged 5 years and older. Chevreul et al. cited a study by Balboni et al., which indicated that caregivers could reliably estimate the point of view of an individual with an intellectual disability.[71,87] The concern that proxy respondents might misrepresent the HRQoL of children with NDD was expressed as a limitation in 21 studies.

Psychometric properties and reporting the health state values

Seven studies examined the aspects of validity and feasibility of generic preference-based HRQoL instruments in children with NDD. Two studies concluded that the EQ-5D-3L proxy version is an appropriate and valid instrument for measuring HRQoL in children with ADHD.[78,84] On the contrary, one study concluded that the EQ-5D-3L and EQ-5D-3L proxy version might be less suitable for children who experience cognitive problems compared with children with a chronic physical condition, and recommend using an additional condition-specific instrument simultaneously.[81] Tilford et al. examined correlations of the HUI-3 and Quality of Well-Being Scale-Self-Administered domains with ASD-specific diagnostic instruments, behavioural measures, symptoms, and measures of cognitive functioning. The authors found that the HUI-3 is more sensitive to ASD symptoms in children than the Quality of Well-Being Scale-Self-Administered.[80] Furthermore, a study by Burström et al. showed that the EQ-5D-Y is valid in a Swedish sample of children and adolescents with functional disability (including CP); however, authors cautioned that further research is necessary to support their results.[83] Mok et al.[79] concluded that the Chinese version of the HUI (HUI-2 and HUI-3) is a valid instrument for measuring HRQoL in children with Down syndrome. Secnik et al.[82] used the EQ-5D-3L proxy version in a study that suggested the standard gamble is a valid technique for obtaining values from parents for health states experienced by children with ADHD.

Twenty-six studies reported at least one mean health state valuation for the respective NDD. Health state valuations were reported for seven specific NDD: ADHD (n=13), ASD (n=11), CP (n=7), Prader–Willi syndrome (n=2), Duchene muscular dystrophy (n=2), fetal alcohol spectrum disorders (n=1), and Fragile X syndrome (n=1). They were also reported for six broad NDD categories: neurodevelopmental impairments (n=4), neurodevelopmental disability (n=3), specific language impairment (n=2), speech disorder (n=2), learning disability (n=2), and language and speech disorder (n=1) (Table SIV, online supporting information). There is considerable variation in mean health state valuations across NDD: ADHD (0.43–0.81), ASD (0.43–0.75), CP (0.26–0.73), Prader–Willi syndrome (0.51–0.85), Duchene muscular dystrophy (0.24–0.75), learning disability (0.42–0.72), and neurodevelopmental impairments (0.36–0.87).

Eleven of the 26 studies applied preference weights from countries different to the country of the study population.[54,57,66,68,71,72,74,76,80,85,88] Five studies raised concerns about using preference weights derived from adults to value health state descriptions of children with NDD.[57,59,72,78,81]

DISCUSSION

This study reports a scoping review regarding the application of generic preference-based HRQoL instruments in children with NDD. Relative to other child health fields, the paucity of economic evaluation studies in the context of NDD is an important finding. Only four of the 36 studies identified were CUAs. This suggests a need for a greater understanding of barriers to conducting CUAs in this clinical context, particularly as economic evaluations are increasingly required to inform resource allocation decisions.[19] The psychometric properties of instruments, respondent type, and appropriate use of preference weights are important considerations that we discuss below.

While there was a range of different generic preference-based HRQoL instruments used across the studies, the HUI (HUI-2 and HUI-3) and EQ-5D (EQ-5D-3L and EQ-5D-5L) instruments were the most common. In contrast, the ED-5D-Y, Child Health Utility 9D, and Assessment of Quality of Life 6D, which were developed or modified for use specifically in children and adolescents, have been used less frequently. The lower frequency of use may be owing to that fact that these instruments were developed more recently, which also means there has been less time to explore the psychometric properties.

The dearth of psychometric evaluation of generic preference-based HRQoL instruments in the context of children with NDD highlights that more needs to be done to explore validity in existing tools and determine whether dimensions captured in the existing tools are

relevant to children with NDD. Regardless of the clinical context, there are between-measure discrepancies when comparing different instruments, such as the framing of questions and response options.[89] This highlights that instrument selection is a difficult task. Blanket justification is often used despite development behind and evidence in support of the instrument potentially not fitting the context. Further research in instrument validation in this population is needed to assist in understanding appropriateness, or to justify the amendment of existing instruments.

'Respondent type' is another important consideration, as there was a lack of consistency in how studies determined the use of self-report, proxy report, or both. Several studies have reported discordant results from parent-report and child-report for the same condition.[28,29,37] This is supported by the results of this review, as children with NDD reported higher HRQoL relative to parents or caregivers in four of the identified studies.[58,59,62,86] Some researchers in the paediatric health outcome literature have suggested using both parent and child reporting to measure HRQoL.[28] This may be an advisable approach to better understand appropriate respondent type. However, it is important to note that, in the context of economic evaluation, a decision would be required as to whose values would be used in the primary analysis.

Variation was observed in the mean health state valuations across NDD and across different generic preference-based HRQoL instruments. It is difficult to draw definitive conclusions about the observed variation in mean health state valuations within the same NDD or across NDD because of the differences in study characteristics. However, the collation of such data is useful for decision-modellers.

The use of country-specific preference weights is recommended when using generic preference-based HRQoL instruments, as these weights reflect the relative value a society places on living in different health states.[90–92] Evidence suggests that health state valuations from the general population could differ by country owing to differences in demographics, sociocultural factors, and economic systems.[90,93–95] Approximately 42% of studies used preference weights from countries other than the country of the study population. It is unclear how this affects the health state valuations in these studies.

Few studies (n=5) in our review raised concern over using preference weights derived from adults in children with NDD. One reason for this could be a lack of child-specific instruments. There is a substantial debate in paediatric economic evaluation studies about whose preferences should be used to value health states for the purposes of prioritizing resource allocation.[96–98] The choice of whose value to use (i.e. the child or the parent/caregiver/proxy respondent) may have important policy implications; results from empirical studies have found notable differences in adult and adolescent preferences for identical health states.[96,99]

A limitation of this review is the potential for relevant articles to be missed by the search strategy. Four of 36 articles were found through searches supplementary to the database search. Systematic searching can be challenging in this area given the absence of formal indexing standards within databases and the inconsistent reporting styles of authors. To provide structure to the scoping review, we opted to include only seven generic preference-based HRQoL instrument families. Our decision to select these instruments was based on the results of several previous reviews on paediatric HRQoL assessment;[12,26,100] however, it may have resulted in the exclusion of some studies. Lastly, the requirement for studies to be published in the English language and a peer-reviewed journal will have resulted in some studies being excluded.

Further research

This scoping review describes the current use of generic preference-based HRQoL instruments in research focusing on children with NDD. The methodological and practical challenges identified highlight three areas for further research to address the paucity of economic evaluation studies of interventions for children with NDD.

First, a better understanding of the psychometric properties of generic preference-based HRQoL instruments for NDD is needed. One approach may be to see how well existing generic preference-based HRQoL instruments align with the categorical epidemiological definitions of NDD. These definitions are focused on the medical model of disability relying on diagnosis, classifying neurological conditions with International Classification of Disease, 10th Revision codes that define disease disorders and health conditions.[101] For example, HUI-2 domains on emotion (irritability, anxiety, and anger) and cognition (learning disability) may be more applicable to children with ASD than children with CP.[102]

Alternatively, a more contemporary, non-categorical definition or classification emphasizes the functional limitations common to neurological conditions, as discussed in the International Classification of Functioning, Disability and Health.[101] Recently, a definition of NDD based on both diagnostic and functional status has been applied to population data and linked administrative data.[8,103] These studies have attempted to harmonize diagnosis or condition-based classification with functional domains conceptualized in the International Classification of Functioning, Disability and Health. Consideration of generic preference-based HRQoL dimensions relative to these International Classification of Functioning, Disability and Health domains may be a good approach when considering psychometric properties.

Second, children and young people with NDD may lack cognitive and communication skills, limiting their ability to comprehend and complete a preference-based HRQoL classification system. Developing instruments that make use of visual aids may help children with NDD to understand the intended meaning of the items and effectively

draw upon life experiences during self-evaluation.[104,105] Such instruments may help parents (proxy respondents) to understand what a child with NDD may be communicating through verbal or non-verbal means.[33]

Finally, it is important to acknowledge that proxy respondents for valuing HRQoL are essential in most cases involving children with NDD, as these children have difficulties in understanding abstract concepts of health and well-being used in generic preference-based HRQoL instruments.[12,28,99,102] Further research should explore ways to minimize bias from proxy respondents (parents/caregivers). Furthermore, it is important to acknowledge that a child's well-being is embedded in multiple contexts, including family, the child's peer group, the classroom, and the community. Each of these contexts affects their HRQoL. Understanding this dynamic relationship between a child's HRQoL and their family, friends, and community might help to create reliable and valid generic preference-based HRQoL instruments for children with NDD.

CONCLUSION

Compared with other clinical contexts, few studies have used preference-based HRQoL instruments in research involving children with NDD. This could be owing, in part, to the lack of evidence on psychometric properties. This scoping review identified inconsistencies across studies regarding the justification for choosing particular generic preference-based HRQoL instruments, and the type of respondent required to complete the chosen instrument. The low quality of data from existing studies suggests caution in informing policy and care decisions due to potential for measurement error. Validation of generic preference-based HRQoL instruments and potential adaptation for use in child populations with NDD is needed so these instruments can better inform policy-makers designing or funding programmes for children with NDD.

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SUPPORTING INFORMATION

The following additional material may be found online:

Appendix S1: Embase database strategy, searched via OVID.

Appendix S2: Name of 35 neurodevelopmental disorders selected for the review.

Table SI: Key properties of selected preference-based health-related quality of life instruments

Table SII: Study characteristics for the 36 identified articles

Table SIII: Justification for instrument selections and selection of the respondent type

Table SIV: Details of mean health state values reported in the 26 studies

Figure S1: Preferred reporting items for systematic reviews and meta-analyses flow diagram.

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