Author/s:
Tonmukayakul, U;Imms, C;Mihalopoulos, C;Reddihough, D;Carter, R;Mulhern, B;Chen, G

Title:
Health-related quality of life and upper-limb impairment in children with cerebral palsy: developing a mapping algorithm

Date:
2020-07-01

Citation:
Tonmukayakul, U., Imms, C., Mihalopoulos, C., Reddihough, D., Carter, R., Mulhern, B. & Chen, G. (2020). Health-related quality of life and upper-limb impairment in children with cerebral palsy: developing a mapping algorithm. Developmental Medicine and Child Neurology, 62 (7), pp.854-860. https://doi.org/10.1111/dmcn.14488.

MS UTSANA TONMUKAYAKUL (Orcid ID : 0000-0002-6464-744X)

PROFESSOR CHRISTINE IMMS (Orcid ID : 0000-0001-9055-3554)

Article type : Original Article

(Original article: 4 tables, 3 online tables, 5 online figures)

Health-related quality of life and upper-limb impairment in children with cerebral palsy: developing a mapping algorithm

UTSANA TONMUKAYAKUL[1]
CHRISTINE IMMS[2]
CATHRINE MIHALOPOULOS[1]
DINAH REDDIHOUGH[3]
ROB CARTER[1]
BRENDAN MULHERN[4]
GANG CHEN[5]

1 Deakin University, Institute for Health Transformation, Faculty of Health, Geelong, Melbourne, Australia; **2** Centre for Disability and Development Research, Australian Catholic University, Fitzroy, Melbourne, Australia; **3** Murdoch Children's Research Institute, University of Melbourne, Royal Children's Hospital, Parkville, Melbourne, Australia; **4** Centre for Health Economics Research and Evaluation, University of Technology Sydney, Haymarket, Sydney, Australia; **5** Centre for Health Economics, Monash Business School, Monash University, Melbourne, Australia.

Correspondence to Utsana Tonmukayakul, Deakin University, School of Health and Social Development, Faculty of Health, Locked Bag 20000, Geelong, Victoria 3220, Australia. E-mail: utsana.tonmukayakul@deakin.edu.au

PUBLICATION DATA
Accepted for publication 00th Month 2019.
Published online 00th Month 2019.

ABBREVIATIONS

CCC	Concordance correlation coefficient
CHU9D	Child Health Utility 9D
CPQoL-Child	Cerebral Palsy Quality of Life Questionnaire for Children
GLM	Generalized linear model
HREC	Human Research Ethics Committee
HRQoL	Health-related quality of life
MACS	Manual Ability Classification System
MAE	Mean absolute error
MAUI	Multi-attribute utility instrument
MITrial	Minimising Impairment Trial
NHDC	Neurological Hand Deformity Classification
QALY	Quality-adjusted life year

AIMS To: (1) investigate the relationship between upper-limb impairment and health-related quality of life (HRQoL) for children with cerebral palsy and (2) develop a mapping algorithm from the Cerebral Palsy Quality of Life Questionnaire for Children (CPQoL-Child) onto the Child Health Utility 9D (CHU9D) measure.
METHOD The associations between physical and upper-limb classifications and HRQoL of 76 children (40 females, 36 males) aged 6 to 15 years (mean age 9 years 7 months [SD 3y]) were assessed. The mean age was. Five statistical techniques were developed and tested, which predicted the CHU9D scores from the CPQoL-Child total/domain scores, age, and sex.

RESULTS Most participants had mild impairments. The Manual Ability Classification System (MACS) level was significantly negatively correlated with CHU9D and CPQoL-Child (r=−0.388 and r=−0.464 respectively). There was a negative correlation between the Neurological Hand Deformity Classification (NHDC) and CPQoL-Child with r=−0.476 (p<0.05). The generalized linear model with participation, pain domain, and age had the highest predictive accuracy.

INTERPRETATION The weak negative correlations between classification levels and HRQoL measures may be explained by the restricted range of impairment levels of the participants. The MACS and NHDC explained the impact of upper-limb impairment on HRQoL better than the other classifications. The generalized linear model with participation, pain, and age is the suggested mapping algorithm. The suggested mapping algorithm will facilitate the use of CPQoL-Child for economic evaluation and can be used to conduct cost–utility analyses.

[First page footer]
© Mac Keith Press 2020
DOI: 10.1111/dmcn.xxxxx
[Left page footer]
Developmental Medicine & Child Neurology 2020, 62: 000–000
[Right page footer]
Developing a Mapping Algorithm for CP *Utsana Tonmukayakul et al.*

What this paper adds

- The Manual Ability Classification System and Neurological Hand Deformity Classification were the best predictors of health-related quality of life measures.
- Age and Cerebral Palsy Quality of Life Questionnaire for Children participation and pain domain scores can predict Child Health Utility 9D scores.

[main text]

Many children with cerebral palsy (CP) have tightness or weakness in arm and hand muscles that can lead to structural changes resulting in long-term difficulty in performing day-to-day tasks, for example, dressing, feeding, and playing.[1] Significantly more children at lower

functioning levels reported pain than those at higher levels.[2] Upper-limb functional impairment can impact the health-related quality of life (HRQoL) of individuals with CP.[3]

HRQoL measures assess multiple subjective dimensions that address the impact of health or disease on physical and psychosocial functioning.[4] It is an important outcome measure in research and CP management since it describes and quantifies holistic changes. For instance, the New South Wales Ministry of Health guidelines for the management of childhood CP by allied health professionals recommends including HRQoL measures in routine assessments.[5]

There are two groups of HRQoL measures: (1) non-preference-based HRQoL profile measures that provide summary scores for individual dimensions (items), groups of dimensions (domains), or overall health; and (2) preference-based HRQoL instruments, known as multi-attribute utility instruments (MAUIs). MAUIs contain a list of dimensions and a scoring system to derive preference weights for individual dimensions relating to their relative desirability and severity levels. The preference weights, or utility scores, anchored on a 0 (death) to 1 (full health) scale, are used to calculate quality-adjusted life years (QALYs) for cost–utility analysis. The National Institute for Health and Care Excellence in the UK and the Pharmaceutical Benefits Advisory Committee in Australia recommend QALYs as an outcome measure.

One valid and reliable non-preference-based, CP-specific paediatric HRQoL profile measure, the Cerebral Palsy Quality of life Questionnaire for Children (CPQoL-Child), has been used in CP studies.[6] However, CPQoL-Child scores do not provide utility scores for a QALY calculation. Recent reviews have highlighted an absence of robust MAUIs specifically for the paediatric CP population.[7,8] A mapping technique that crosswalks the scores from a profile measure onto a MAUI can enable the use of HRQoL profile measures for cost–utility analyses.[9]

How appropriate the existing generic MAUIs (e.g. the Child Health Utility 9D [CHU9D], EuroQoL 5D youth version) are for use in children with CP has not been investigated sufficiently. There is also an absence of a mapping algorithm for children with CP that uses a child-specific generic MAUI. Given that there are some relevant items and/or overlapping domains between the CPQoL-Child and CHU9D (Table S1, online supporting information)—daily activity, physical health and functioning, psychological functioning, pain and discomfort—it is likely that a meaningful relationship between these two instruments exists. Thus, it was considered that a crosswalk transformation algorithm could be developed to enable QALY calculations where a MAUI is not collected in a CP study and where researchers want to investigate whether their intervention is cost-effective.

The aims of this study were: (1) to assess the relationship between gross motor and upper-limb functional classifications in children with CP and the CPQoL-Child and CHU9D; and (2) develop a mapping algorithm from the CPQoL-Child onto the CHU9D to facilitate cost–utility analysis studies when only the CPQoL-Child is administered.

METHOD

The Minimising Impairment Trial (MITrial; Australia New Zealand Clinical Trials Registry universal trial no. U1111-1164-0572) assessed the clinical efficacy and cost-effectiveness of the rigid wrist/hand orthosis to maintain muscle length and prevent hand deformity in Australian children with CP aged 6 to 15 years.[10] Details of the MITrial have been published elsewhere.[10] A brief summary of the functional classifications and data sets used in this study is provided here.

Functional classifications were the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS), Bimanual Fine Motor Function, and the Neurological Hand Deformity Classification (NHDC). The GMFCS and MACS comprise five levels of severity where level I represents least impairment and level V the most severe impairment. The NHDC consists of five flexion and two extension deformity levels. The Bimanual Fine Motor Function consists of five levels, but levels II to IV can be further subdivided into: (1) ability of one hand and (2) both hands.

Although the limitation of the proxy report HRQoL has been identified previously,[8] many participants had limited ability to self-report the CPQoL-Child and CHU9D. Therefore, 76 records from parents/carers, collected at baseline, were used to investigate the relationship between the classification systems and HRQoL. The effectiveness of the orthoses is presented in a separate paper. The records of 43 participants who completed both the CPQoL-Child and CHU9D were used to develop and identify the best performing mapping algorithm.

HRQoL instruments

Commented [SC1]: Typesetter: B head

The CPQoL-Child proxy comprises 65 questions across seven domains: social well-being and acceptance; feelings about functioning; participation and physical health; emotional well-being; access to services; pain and feelings about functioning; and family health. Each item has nine response levels. The CPQoL-Child proxy is designed to be completed by the parents/carers of children with CP aged 4 to 12 years. The responses of the CPQoL-Child proxy are then transformed to scores between 0 and 100 for each domain.[11] Higher scores represent better HRQoL. The overall score was the mean across all domains. The CPQoL-

Child has excellent psychometric properties[12] and high test–retest reliability ranging from 0.76 to 0.89 across all seven domains.[13]

The CHU9D captures nine dimensions: worry; sad; pain; tired; annoyed; school work/homework; sleep; daily routine; and ability to join in activities, with five response levels per dimension where 1 represents no problem to 5 which represents a severe problem.[14] The CHU9D provides utility scores between −0.1059 and 1 (negative values indicate health states considered to be 'worse than dead').[15] The CHU9D has been validated in a population of 6- to 17-year-olds.[16] A child or a parent/carer can complete the CHU9D. The Australian adolescent population-specific scoring algorithm was used in this study.[17]

Statistical analysis

Assessing the relationships between classification systems and HRQoL measures

Commented [SC2]: Typesetter: C head

Negative correlations between the four classifications and HRQoL were expected because higher levels of classification indicate lower levels of functioning. Positive correlations between the CPQoL-Child and CHU9D were expected. The original classification levels were regrouped into two categories: (1) mild; and (2) moderate and severe. For example, GMFCS levels I and II were 'mild', while levels III to V were 'moderate and severe'.

The CPQoL-Child and CHU9D scores were tested for normality using the Shapiro–Wilk normality test. Since utility values were not normally distributed, the non-parametric Spearman's rank correlation (r_S) was used to analyse the correlations between the classifications and HRQoL. The Kruskal–Wallis test was used to investigate the statistical difference in HRQoL according to the reclassified severity levels. A correlation coefficient greater than 0.7 represented a strong correlation, 0.5 to 0.7 moderate, and less than 0.5 weak.[18]

Mapping the CPQoL-Child onto the CHU9D

Two core models, based on a direct additive mapping to regress the CHU9D utility score on the CPQoL-Child overall, or domain scores were used. An item response level mapping approach was not chosen because it requires a large sample size with an adequate number of responses for each response level, which was not available in this study. A recent mapping study on CHU9D utilities reported larger prediction errors with the indirect response mapping approach than with the direct mapping approach.[19]

In addition to the two core models, and consistent with previous mapping studies,[19,20] we included the squared term, interaction term, and socio-demographic variables, particularly age and sex, with the aim of improving predictive performance.[9]

The two core models can be presented in regression algebraically as:

$$CHUD9=\propto+\beta_1\times CPQoL\_total+\beta_2\times CPQoL\_total^2+\delta_1\times age+\delta_2\times sex \text{ (model 1)}$$

$$CHUD9=\propto+\sum_{j=1}^{k}\gamma_1\times CPQoL\_domain_j^{sw}+\delta_1\times age+\delta_2\times sex \text{ (model 2)}$$

where age is in years, sex is a binary variable (1: male, 2: female), CHU9D is the CHU9D utility score, CPQoL_total is the CPQoL-Child total score rescaled from 0 to 100 to 0 to 1, $CPQoL\_total^2$ is the CPQoL-Child total score squared, $CPQoL\_domain_j^{sw}$ represents the selected CPQoL-Child domains based on statistical significance ($p<0.05$) using the stepwise regression, and k is the number of selected CPQoL-Child domains.

Five econometric techniques were used: (1) the ordinary least squares estimator, which is a widely used technique.[9] It demonstrated good mapping performance despite the presence of heteroscedasticity and non-normality of residuals. (2) The generalized linear model (GLM) allows for the non-normal distribution of dependent variables, which was the case in this study (Fig. S1, online supporting information); the Gaussian family with logit link was chosen as the best fit for these data; (3) the robust MM-estimator is used to deal with heteroscedasticity and the presence of outliers (the MM-estimator demonstrated good performance in prior mapping studies in adolescents and adults);[20,21] (4) the Tobit model considers the bounding issue found in this study where the utility score is truncated to 1 (full health); and (5) beta regression, which can handle skewed data and restricts the range of the data set between 0 and 1.

Assessment of predictive ability

Commented [SC3]: Typesetter: C head

Model goodness of fit was determined using the mean absolute error (MAE) and concordance correlation coefficient (CCC). Smaller MAE values indicate better model performance. Larger CCC values indicate a better-performing predictive model.

Validation of primary models

Given the absence of a data set for external validation, internal validation using the cross-validation approach was conducted. The full sample was randomly divided equally into five groups. Each time, four random groups (80% of the sample) were assigned as the 'estimation sample', which was used to generate the mapping algorithm, while the remaining group

(20%), the 'validation sample', was used to predict the CHU9D scores based on the estimated algorithm. This procedure was repeated five times so that each of the five random groups served as a validation sample. The predicted CHU9D scores from these five groups were used to calculate the goodness of fit.

Ethical approval

Commented [SC4]: Typesetter: B head

The MITrial received ethical approval for conduct within all clinical sites (Monash Health HREC 14199B; Royal Children's Hospital site governance 34280A; Perth Children's Hospital HREC 2014060EP; Cerebral Palsy Alliance HREC 20150428) and was registered at the Australian Catholic University HREC 2014 318V and Deakin University HREC 2016-231). Each parent, and where appropriate participating adolescent, provided written informed consent to take part in the trial and for the trial findings to be published.

RESULTS

Table 1 presents the characteristics of the 76 children. Fifty-five parents completed the CPQoL-Child proxy and 43 completed both the CPQoL-Child and CHU9D proxies. The CHU9D utility score was not normally distributed ($p<0.05$), with a large number (19.15%) valued at 1. The normality test was not rejected for the CPQoL-Child total score; the distribution was left-skewed (Fig. S1). The mean (SD) of the CHU9D utility was 0.863 (0.124) and the mean of the CPQoL-Child total scores was 68.134 (8.590). Approximately half (52.6%) of the children were female. The mean age was 9 years 7 months (SD 3y). Right- and left-hand functional limitations were reported in 41.3% and 29.3% of children respectively. The remaining children (29.3%) had bilateral presentation. At least half of the children were at levels I or II of the classifications: 64.9% for GMFCS; 50.0% for MACS; 60.0% for NHDC; and 73.4% for Bimanual Fine Motor Function.

Commented [SC5]: Typesetter: Please insert Table 1 here.

Relationship between HRQoL and the classification systems

Table 2 shows that MACS was significantly negatively but weakly correlated with CHU9D and CPQoL-Child (r_S=−0.388 and r_S=−0.464 respectively). There was a significant negative but weak relationship between NHDC and CPQoL-Child (r_S=−0.476).

Commented [SC6]: Typesetter: Please insert Table 2 here.

Assessment of correlation between HRQoL measures

A positive but weak correlation (r_S=0.393; $p<0.05$) between the CHU9D utility scores and CPQoL-Child total was found (Fig. S2, online supporting information). At the domain level,

a moderate correlation was found between the CHU9D and the participation domain (r_S=0.560, p<0.05). Table S2 (online supporting information) presents the correlation coefficients for each domain. Figure S3 (online supporting information) presents the correlations between each CPQoL-Child domain and the CHU9D.

Mapping model performance

Commented [SC7]: Typesetter: B head

Table 3 presents the goodness of fit results of the different models. Almost all estimators overpredicted the mean CHU9D utility score except the ordinary least squares estimator, which produced similar predicted mean scores to the observed values. All estimators overpredicted the lowest boundary of the CHU9D. For the highest boundary, all estimators, except the model 2 MM-estimator, underestimated the maximum CHU9D utility.

Regarding goodness of fit, the model 2 GLM had the best predictive ability (lowest MAE: 0.0621 and highest CCC: 0.7450) followed by the model 2 ordinary least squares estimator (MAE=0.0626, CCC=0.7050). While the model 2 GLM predicted the closer minimum CHU9D score to the observed value, the model 2 Tobit estimator had a closer predicted maximum CHU9D score.

Validation of mapping algorithms

The model 2 GLM was the best predictive model (Table 4; lowest MAE: 0.0689, and highest CCC: 0.6620). The model 2 MM-estimator had the second lowest MAE and the model 2 beta regression had the second highest CCC.

Commented [SC8]: Typesetter: Please insert Table 4 here.

Mapping algorithms

The regression results based on the full sample are presented in Table S3 (online supporting information). The CPQoL-Child total score was a significant predictive variable (p<0.05) in all five methods. The CPQoL-Child participation and the physical health domain was consistently significant across all five methods. The CPQoL-Child pain and impact of disability domain was significant in the GLM and beta regression, while age was significant in the GLM and Tobit estimators.

The model 2 GLM, the best predicting algorithm based on its predictive property and cross-validation results, can be presented as:

$$\text{Predicted CHU9D} = \frac{\exp(-1.0206 + 0.0314 \times \text{CPQoL participation} - 0.0129 \times \text{CPQoL pain} + 0.1476 \times \text{age})}{1 + \exp(-1.0206 + 0.0314 \times \text{CPQoL participation} - 0.0129 \times \text{CPQoL pain} + 0.1476 \times \text{age})}$$

where CPQoL participation is the CPQoL-Child participation and physical health domain score, CPQoL pain is the CPQoL-Child pain and impact of disability domain score, and age is in years.

The scatter plots for the observed and predicted CHU9D utility scores of all mapping models are shown in Figures S4 and S5 (online supporting information).

DISCUSSION

Commented [SC9]: Typesetter: A head

Valid and reliable preference-based HRQoL measures are important for economic appraisal. Recent systematic reviews found that the existing generic MAUIs do not cover all aspects related to the HRQoL of children/adolescents with CP and there is a lack of information demonstrating their responsiveness and reliability.[7,8] While CP-specific HRQoL has been recommended for inclusion in routine CP management, preference-based HRQoL measures are not commonly used. The CPQoL-Child does not provide utility scores, so it cannot be used to estimate QALYs.

In this study, we assessed the relationship between the classifications of gross motor and upper-limb functioning and proxy reported in the CPQoL-Child and CHU9D and developed a mapping algorithm that can be used to predict CHU9D utility scores from the CPQoL-Child score. Ideally, collecting MAUIs is strongly recommended for cost–utility analysis studies. Mapping algorithms are an alternative approach when a MAUI measure is missing. Our suggested mapping algorithm leverages the use of the CPQoL-Child proxy from a clinical to an economic purpose. In a CP study that does not collect a MAUI, but collects the CPQoL-Child proxy, researchers can estimate QALYs by using the participation and pain domains and age of the children with CP in the provided mapping algorithm. There is no immediate impact for clinical practice, but the information about which health interventions/treatments are effective and good value for money should assist clinicians in selecting the best care, particularly when they are faced with budget constraints.

This study has two strengths. First, it validates the CPQoL-Child proxy and CHU9D against a range of functional classification systems. While this study hypothesized a negative relationship between the classification systems and HRQoL scores (i.e. greater impairment associated with lower HRQoL), this expected relationship was identified only in the MACS and NHDC. Negative weak correlations between MACS and NHDC and the CPQoL-Child

total scores, and MACS and CHU9D utility scores, were reported. It is possible that the upper limb is more important for HRQoL than gross motor function. However, our data do not allow further exploration of this assumption. A possible explanation for the weak relationship was that more than half of participants had mild upper-limb impairment (i.e. were classified at MACS/GMFCS levels I or II). This proportion is consistent with population averages.[22] Park[23] reported negative relationship between MACS and GMFCS levels and the Korean version of the Childhood Health Assessment Questionnaire in 71 Korean children with CP aged 6 to 15 years.

Second, a mapping algorithm transforming the CPQoL-Child score into the CHU9D utility index was developed using a direct mapping approach. The strength of this mapping technique relies on the degree of overlap between the two HRQoL measures. The correlations between the CPQoL-Child domains and the CHU9D (see Table 2) are stronger than found in a previous study, which mapped the Pediatric Quality of Life Inventory scores (a generic paediatric HRQoL) onto to the CHU9D,[19] although our sample size is smaller. This provides reassurance of the feasibility of developing the mapping algorithm from the CPQoL-Child domain scores onto the CHU9D.

Previous studies using the direct mapping approach found that deriving transformation algorithms from generic HRQoL measures to generic preference-based measures had adequate predictive validity; mapping from a disease-specific HRQoL to a generic preference-based measure had relatively poorer predictive validity.[9,24] Our preferred mapping algorithm has good predictive performance and better performance than the previous mapping study (MAE=0.0621–0.0836 compared to 0.1261–0.1317).[19]

The model 2 GLM with CPQoL-Child participation, CPQoL-Child pain scores, and age was the preferred mapping model based on the original full-sample lowest MAE and highest CCC; it was confirmed by the fivefold internal cross-validation. It is important to highlight that model performance was validated using the internal data set only. External validation is ideal if data are available; this is a limitation of this study and the vast majority of previous mapping studies.[19,20] However, recent work found that mapping algorithms that were originally only internally validated, had acceptable predictive accuracy when they were subsequently externally validated.[25]

The suggested mapping model was developed from a specific group of the CP population who fitted the inclusion criteria of the MITrial; this impacts on the generalizability of the mapping algorithms to individuals with differing presentations. Although our mapping algorithm was derived using a small sample and external validation was not possible, the

recommended mapping algorithm can be useful to conduct cost–utility analyses in similar populations.

Further research is required to better elicit health state utilities from young people with CP, such as the development of a CP-specific MAUI or the validation of the mapping algorithm using a large sample with an external data set.

CONCLUSION

Weak negative correlations between functioning levels and HRQoL measures were found in children with CP and mild upper-limb impairment. The MACS and NHDC explained the impact of the upper-limb impairment on the HRQoL better than the other classifications. This study has produced a mapping algorithm to generate CHU9D index scores from the CPQoL-Child responses. The preferred algorithm is the GLM model, which uses CPQoL-Child participation, CPQoL-Child pain scores, and age as the predictors according to its MAE, CCC, and cross-validation results.

ACKNOWLEDGEMENTS

We thank Sophy Shih for her support in drafting the MITrial study protocol, ethics applications, and data acquisition. We thank Alice Ames for her assistance with database access and support. Utsana Tonmukayakul received a PhD scholarship from the Centre of Research Excellence in Cerebral Palsy (NHMRC no. APP1057997). The upper-limb trial orthoses were funded through a five-year grant from the Australian Catholic University (no. 2013000413), a small grant from the Princess Margaret Hospital Foundation and support from the Centre of Research Excellence in Cerebral Palsy (no. APP1057997), and in-kind support from the Princess Margaret Hospital, The Ability Centre, Monash Children's Hospital, the Royal Children's Hospital, and the Cerebral Palsy Alliance.

The authors have stated that they had no interests that might be perceived as posing a conflict or bias.

Commented [SC10]: Typesetter: A head

Supporting information

The following additional material may be found online:

Table S1: Comparison between the dimensions and items of the CHU9D and CPQoL-Child proxy.

Table S2: Correlation coefficients of each CPQoL-Child domain and CHU9D utility scores.

Table S3: Mapping algorithm from CPQoL-Child scores to CHU9D utility scores.

Figure S1: Distribution of CHU9D utility scores and CPQoL-Child total scores.

Figure S2: Scatter plot of CHU9D utility scores and CPQoL-Child total scores.

Figure S3: Correlation matrix of CHU9D utility scores, CPQoL-Child total scores, and each domain of the CPQoL-Child.

Figure S4: Scatter plots of observed and predicted CHU9D utility scores from the CPQoL-Child total scores (model 1).

Figure S5: Scatter plots of observed and predicted CHU9D utility scores from the selected CPQoL-Child domain scores (model 2).

REFERENCES

Commented [SC11]: Typesetter: A head

1. Kerr Graham H, Selber P. Musculoskeletal aspects of cerebral palsy. *J Bone Joint Surg Br* 2003; **85**: 157–66.
2. Alriksson-Schmidt A, Hägglund G. Pain in children and adolescents with cerebral palsy: a population-based registry study. *Acta Paediatr* 2016; **105**: 665–70.
3. Tarsuslu T, Livanelioglu A. Relationship between quality of life and functional status of young adults and adults with cerebral palsy. *Disabil Rehabil* 2010; **32**: 1658–65.
4. Tsiros MD, Olds T, Buckley JD, et al. Health-related quality of life in obese children and adolescents. *Int J Obes (Lond)* 2009; **33**: 387–400.
5. Agency for Clinical Innovation. Management of cerebral palsy in children: a guide for allied health professionals [Internet]. Sydney, NSW: New South Wales Ministry of Health, 2018. Available at https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/GL2018_006.pdf (accessed 8 January 2020).
6. Sakzewski L, Carlon S, Shields N, Ziviani J, Ware RS, Boyd RN. Impact of intensive upper limb rehabilitation on quality of life: a randomized trial in children with unilateral cerebral palsy. *Dev Med Child Neurol* 2012; **54**: 415–23.
7. Mpundu-Kaambwa C, Chen G, Huynh E, Russo R, Ratcliffe J. A review of preference-based measures for the assessment of quality of life in children and adolescents with cerebral palsy. *Qual Life Res* 2018; **27**: 1781–99.
8. Tonmukayakul U, Le LK, Mudiyanselage SB, et al. A systematic review of utility values in children with cerebral palsy. *Qual Life Res* 2019; **28**: 1–12.

9. Brazier JE, Yang Y, Tsuchiya A, Louise RD. A review of studies mapping (or cross walking) non-preference based measures of health to generic preference-based measures. *Eur J Health Econ* 2010; **11**: 215–25.

10. Imms C, Wallen M, Elliott C, et al. Minimising impairment: protocol for a multicentre randomised controlled trial of upper limb orthoses for children with cerebral palsy. *BMC Pediatr* 2016; **16**: 70.

11. Waters E, Davis E, Boyd R, et al. Cerebral palsy quality of life questionnaire for children (CP QOL-Child) manual. Melbourne, VIC: University of Melbourne, 2013.

12. Carlon S, Shields N, Yong K, Gilmore R, Sakzewski L, Boyd R. A systematic review of the psychometric properties of Quality of Life measures for school aged children with cerebral palsy. *BMC Pediatr* 2010; **10**: 81.

13. Waters E, Davis E, Mackinnon A, et al. Psychometric properties of the quality of life questionnaire for children with CP. *Dev Med Child Neurol* 2007; **49**: 49–55.

14. Stevens K. Developing a descriptive system for a new preference-based measure of health-related quality of life for children. *Qual Life Res* 2009; **18**: 1105–13.

15. Ratcliffe J, Huynh E, Chen G, et al. Valuing the Child Health Utility 9D: using profile case best worst scaling methods to develop a new adolescent specific scoring algorithm. *Soc. Sci. Med.* 2016; **157**: 48–59.

16. Ratcliffe J, Stevens K, Flynn T, Brazier J, Sawyer M. An assessment of the construct validity of the CHU9D in the Australian adolescent general population. *Qual Life Res* 2012; **21**: 717–25.

17. Ratcliffe J, Couzner L, Flynn T, 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. *Appl Health Econ Health Policy* 2011; **9**: 15–27.

18. Hinkle DE, Wieersma W, Jurs SG. Applied statistics for the behavioural sciences. Boston, MA: Houghton Mifflin, 2003.

19. Mpundu-Kaambwa C, Chen G, Russo R, Stevens K, Petersen KD, Ratcliffe J. Mapping CHU9D utility scores from the PedsQL™ 4.0 SF-15. *Pharmacoeconomics* 2017; **35**: 453–67.

20. Chen G, Stevens K, Rowen D, Ratcliffe J. From KIDSCREEN-10 to CHU9D: creating a unique mapping algorithm for application in economic evaluation. *Health Qual Life Outcomes* 2014; **12**: 134.

21. Chen G, Khan MA, Iezzi A, Ratcliffe J, Richardson J. Mapping between 6 multiattribute utility instruments. *Med Decis Making* 2016; **36**: 160–75.

22. Hedberg-Graff J, Granström F, Arner M, Krumlinde-Sundholm L. Upper-limb contracture development in children with cerebral palsy: a population-based study. *Dev Med Child Neurol* 2019; **61**: 204–11.

23. Park EY. Path analysis of strength, spasticity, gross motor function, and health-related quality of life in children with spastic cerebral palsy. *Health Qual Life Outcomes* 2018; **16**: 70.

24. Mortimer D, Segal L. Comparing the incomparable? A systematic review of competing techniques for converting descriptive measures of health status into QALY-weights. *Med Decis Making* 2008; **28**: 66–89.

25. Mpundu-Kaambwa C, Chen G, Huynh E, Russo R, Ratcliffe J. Mapping the PedsQL™ onto the CHU9D: an assessment of external validity in a large community-based sample. *Pharmacoeconomics* 2019; **37**: 1139–53.

Table 1: Sample characteristics

CHU9D utility score	0.863 (0.124)
CPQoL-Child total score	68.134 (8.590)
CPQoL-Child social well-being and acceptance domain score	82.862 (10.092)
CPQoL-Child feelings about functioning domain	68.222 (14.785)
CPQoL-Child participation and physical health domain	68.296 (16.782)
CPQoL-Child emotional well-being domain	81.933 (10.820)
CPQoL-Child access to services domain	71.627 (17.425)
CPQoL-Child pain and feelings about functioning domain	30.691 (18.597)
CPQoL-Child family health domain	73.304 (16.731)
Age, y:mo	9:7 (3:0)
Females, *n*=76 (%)	40 (52.6)
Right hand functional limitation, *n*=75 (%)	31 (41.3)
Left hand functional limitation, *n*=75 (%)	22 (29.3)
Functional limitation in both hands, *n*=75 (%)	22 (29.3)
GMFCS, *n*=74 (%)	
Mild (levels I and II)	48 (64.9)
MACS, *n*=74 (%)	
Mild (levels I and II)	37 (50.0)

Commented [AB12]: Au: please confirm

Commented [AB13]: Au: please confirm

NHDC, *n*=68 (%)	
Mild (F1, F2, E1)	42 (60.0)
BFMF, *n*=64 (%)	
Mild (levels I and II)	47 (73.4)

Data are mean (SD) unless otherwise stated. CHU9D, Child Health Utility 9D; CPQoL-Child, Cerebral Palsy Quality of Life for Children; GMFCS, Gross Motor Function Classification System; MACS, Manual Ability Classification System; NHDC, Neurological Hand Deformity Classification; BFMF, Bimanual Fine Motor Function.

Table 2: Mean of CHU9D and CPQoL-Child total scores by regrouped classification and Spearman's rank test

		CHU9D utility scores				CPQoL-Child total scores			
		n	Mean (SD)	Kruskal–Wallis test	Spearman's rho (*p*)	*n*	Mean (SD)	Kruskal–Wallis test	Spearman's rho (*p*)
MACS	Levels I and II (mild)	21	0.918 (0.084)	0.010[a]	−0.388 (0.008[a])	23	72.778 (7.728)	0.001[a]	−0.464 (0.004[a])
	Levels III and IV (moderate and severe)	25	0.825 (0.133)			31	64.509 (7.608)		
BFMF	Levels I and II (mild)	30	0.901 (0.816)	0.080	−0.278 (0.079)	33	69.876 (8.572)	0.354	−0.138 (0.360)
	Levels III–VIII (moderate and severe)	11	0.813 (0.143)			13	66.846 (5.761)		
NHDC	Levels F1, F2, E1 (mild)	20	0.872 (0.118)	0.650	−0.075 (0.656)	24	71.205 (8.014)	0.002[a]	−0.476 (0.001[a])
	Levels F3, F4, F5 (moderate and severe)	18	0.858 (0.119)			19	63.659 (5.378)		
GMFCS	Levels I and II (mild)	30	0.891 (0.108)	0.444	−0.122 (0.449)	33	69.716 (8.705)	0.225	−0.177 (0.229)
	Levels III–V (moderate and severe)	11	0.839 (0.160)			15	64.796 (9.038)		

[a]$p<0.05$. CHU9D, Child Health Utility 9D; CPQoL-Child, Cerebral Palsy Quality of Life for Children; MACS, Manual Ability Classification System; BFMF, Bimanual Fine Motor Function; NHDC, Neurological Hand Deformity Classification; GMFCS, Gross Motor Function Classification System.

Table 3: Goodness of fit results

Model specification	Differences between predicted and observed mean	Mean predicted CHU9D	Minimum predicted CHU9D	Maximum predicted CHU9D	MAE	CCC
Observed (*n*=43)		0.8699	0.5143	1.0000	–	–
Method 1: ordinary least squares estimator						
Model 1	0.0000	0.8699	0.6810	0.9954	0.0836	0.4780
Model 2	0.0000	0.8699	0.5750	0.9973	0.0626[a]	0.7050[b]
Method 2: generalized linear model: Gaussian family logit link						
Model 1	0.0007	0.8706	0.6810	0.9944	0.0763	0.5650
Model 2	−0.0001	0.8698	0.5637	0.9581	**0.0621**[c]	**0.7450**[d]
Method 3: MM-estimator						
Model 1	0.0140	0.8838	0.6810	0.9954	0.0836	0.4780
Model 2	0.0138	0.8837	0.5936	1.0000[e]	0.0655[e]	0.6600[e]
Method 4: Tobit estimator						
Model 1	0.0153	0.8851	0.6518	1.0000[e]	0.0838[e]	0.4780[e]
Model 2	0.0134	0.8833	0.5428	1.0000[e]	0.0632[e]	0.7040[e]
Method 5: Beta regression						
Model 1	0.0130	0.8829	0.4523	0.9758	0.0775	0.5640
Model 2	0.0125	0.8823	0.4835	0.9754	0.0659	0.7000

Key findings are indicated in bold type. [a]Second smallest value in the mean absolute error (MAE) column. [b]Second largest value in the concordance correlation coefficient (CCC) column. [c]Smallest value in the MAE column. [d]Largest value in the CCC column. [e]Adjusted goodness of fit results obtained by specifying the maximum predicted utility score to be 1. Model 1 used total Cerebral Palsy Quality of Life for Children (CPQoL-Child) scores to predict Child Health Utility 9D (CHU9D) utility scores. Model 2 used CPQoL-Child domain scores to predict CHU9D utility scores.

Table 4: Goodness of fit results using a fivefold cross-validation technique

Model specification	Differences between predicted and observed mean	Mean predicted CHU9D	Minimum predicted CHU9D	Maximum predicted CHU9D	MAE	CCC
Observed (*n*=43)		0.8699	0.5143	1.0000	–	–
Method 1: ordinary least squares estimator						
Model 1	−0.0023	0.8676	0.6786	1.0000[a]	0.0858[a]	0.4230[a]

Model 2	−0.0016	0.8682	0.5411	0.9931	0.0724	0.6260
Method 2: generalized linear model: Gaussian family logit link						
Model 1	−0.0046	0.8652	0.4664	0.9517	0.0818	0.5240
Model 2	−0.0023	0.8676	0.5805	0.9986	**0.0689**[b]	**0.6620**[c]
Method 3: MM-estimator						
Model 1	0.0133	0.8831	0.6934	0.9621	0.0873	0.4600
Model 2	0.0117	0.8815	0.5805	1.0000[a]	0.0694[a,d]	0.6220[a]
Method 4: Tobit estimator						
Model 1	−0.0007	0.8692	0.6786	1.0000[a]	0.0874[a]	0.4150[a]
Model 2	0.0103	0.8802	0.4652	1.0000[a]	0.0759[a]	0.6150[a]
Method 5: Beta regression						
Model 1	0.0059	0.8758	0.3482	0.9774	0.0847	0.5060
Model 2	0.0024	0.8722	0.2901	0.9778	0.0801	0.6460[e]

Key findings are indicated in bold type. [a]Adjusted goodness of fit results obtained by specifying the maximum predicted utility score to be 1. [b]Smallest value in the mean absolute error (MAE) column. [c]Largest value in the concordance correlation coefficient (CCC) column. [d]Second smallest value in the MAE column. [e]Second largest value in the CCC column. Model 1 used the total Cerebral Palsy Quality of Life for Children (CPQoL-Child) scores to predict the Child Health Utility 9D (CHU9D) utility scores. Model 2 used the CPQoL-Child domain scores to predict the CHU9D utility weight scores.