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Health state preference scores of children with spina bifida and their caregivers

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Abstract

Cost-effectiveness evaluations of interventions to prevent or treat spina bifida require quality of life information measured as preference scores. Preference scores of caregivers also may be relevant. This study tested whether the preference scores of children with spina bifida and their caregivers would decrease as disability in the child increased. Families of children aged 0–17 with spina bifida ($N = 98$) were identified using a birth defect surveillance system in the state of Arkansas. Primary caregivers of children with spina bifida identified other families with an unaffected child ($N = 49$). Preference scores for child health states were determined using the Health Utilities Index – Mark 2 (HUI2). Caregiver preference scores were determined using the Quality of Well-Being (QWB) scale. Children with spina bifida were categorized into three disability levels according to the location of the child's lesion. Mean preference scores declined for both affected children and the primary caregiver as disability in the child increased. In multivariate analysis, the preference score of the child was a significant and positive predictor of the primary caregiver's preference score. A more modest association was found for caregiver health preference scores by lesion location. The findings can inform cost-effectiveness evaluations of interventions to treat or prevent spina bifida.

Key words: Caregiver quality of life, Economic evaluation, Preference-weighted health states, Spina bifida

Abbreviations: CEA – cost-effectiveness analysis; HUI – health utilities index; PCHM – panel on cost-effectiveness in health and medicine; QALY – quality adjusted life year; QWB – quality of well-being

Introduction

The U.S. Public Health Service Panel on Cost-effectiveness in Health and Medicine (PCHM) sought to improve the comparability of cost-effectiveness analysis (CEA) by developing recommendations for analysts to implement in reference case analyses [1]. One recommendation of the PCHM was that all CEAs should measure health outcomes using the metric of the quality adjusted life year (QALY). This metric allows cost-effectiveness ratios to be compared across interventions affecting disparate outcomes.

The PCHM report included a worked example of the cost-effectiveness of strategies to prevent pregnancies affected by neural tube defects [2]. Neural tube defects result from delayed closure of the neural tube; they may be prevented by adequate intake of folic acid [3–5]. The two most common forms of neural tube defects are anencephaly and spina bifida. Anencephaly is the absence of all or a large part of the cranium and

central nervous system and is uniformly fatal. Spina bifida results from the incomplete closure of the tissue and bone surrounding the spinal cord. Children born with spina bifida can have mild to severe disabilities depending on the location of the lesion along the spinal cord. Children with lower or sacral malformations may only have bowel and bladder dysfunction while higher lumbar or thoracic lesions can cause varying degrees of limb paralysis among other disabilities.

As recommended by the PHCM, health state preference scores of children with spina bifida relative to children without spina bifida are needed to conduct CEA of prevention strategies. Prevention strategies should be expressed as the costs per QALY gained as a result of the program. QALYs are calculated as the number of life years gained multiplied by a preference score that typically is bounded by 0 (death) and 1 (perfect health). As no such scores were available, the PHCM analysts used expert opinions of doctors who treat children with spina bifida in their worked example. Doctors were asked to complete generic instruments suggested by the PCHM based on three lesion locations and three age ranges. The resulting preference scores were used in the economic analysis that concluded fortification of food with folic acid would add QALYs and reduce costs relative to no fortification.

The analysts did not include the potential health impact on the caregivers of children with spina bifida, but did include an estimate of the economic impact of caregiving based on the opportunity cost of time taken away from paid employment. Although there is a large literature suggesting caregivers are affected by caring for a child with disabilities [6–9], there is little information on caregiver health-related quality of life impacts that can be used in economic evaluations of birth defects [10]. To be useful in economic evaluations, caregiver impacts need to be measured as costs or QALYs. PCHM analysts summarized the current state of measuring caregiver quality of life impacts by the following:

> Although quality-of-life impacts on these parties are clearly important, their inclusion is not recommended in a Reference Case analysis because the methods for capturing these impacts are in early stages of development. Also, data on these quality-of-life impacts are not available. Including these QALYs would increase the benefits of all interventions (Kelly et al., p. 320).

A cost-benefit analysis of folate fortification also did not value caregiver quality of life impacts, but suggested such costs may be substantial [11].

To address the potential impact of disease on caregivers, Neumann et al. [12] conducted the first evaluation of caregiver quality of life using a generic *preference-weighted* instrument. Using the Health Utilities Index – Mark 2 (HUI2) [13–15], they hypothesized that the health utilities (or preference scores) of the caregivers would change in relation to the stage of disease for patients with Alzheimer's. They found significant differences in the preference scores of the patients by disease stage, using caregivers as proxy respondents for the patient's health state, but the preference scores of caregivers did not decline with worsening disease stage.

The Neumann et al. study may be limited by the use of the HUI2 to study changes in caregiver health states. The HUI2 may not be sufficiently sensitive to changes in caregiver health states to capture important differences. In subsequent work using the same database, Bell et al. [16] reported differences in a caregiver burden scale and the mental health component summary score of the SF-36 across disease stage and setting for patients with Alzheimer's, but no differences in the HUI2. They concluded that generic preference-weighted instruments may not adequately capture caregiver impact associated with Alzheimer's and suggested the need for developing condition-specific instruments for obtaining preference scores of caregivers.

The present study was developed to provide information on the preference scores of children with spina bifida aperta and to measure the impact of caring for a child with spina bifida consistent with economic evaluations. In particular, we assess the preference scores of children and their caregivers relative to the disability of the affected child and a control group to estimate impacts in QALY terms. We considered three lesion locations consistent with prior economic evaluations of neural tube defects: sacral, lower lumbar, and higher lumbar/thoracic. In contrast to previous studies, we measured caregiver health states using the

Quality of Well-Being (QWB) scale [17, 18], The QWB scale has been shown to predict mental health outcomes better than other generic instruments [19–21] and may be more appropriate for preference-weighting caregiver health states. We hypothesized that (1) the preference-weighted health states of children with spina bifida would decrease with the location of the lesion and (2) the health state preference scores of caregivers as measured from the QWB scale also would diminish as the disability of the child increased.

Methods

Study design and sample

Subjects for this study were obtained from a birth defects surveillance system in place in the state of Arkansas for more than 20 years. Patients were identified from the surveillance system and mailing addresses located. Potential subject families were mailed a letter notifying them of the study and indicating that they would be contacted about whether they would be interested in participating. Families were then contacted by telephone and asked to consent to participate in the study. Families that consented were then interviewed by telephone. As part of the interview, the respondent was asked to provide information on up to three families that lived nearby and had an unaffected child of similar age. The institutional Human Research Advisory Committee approved the study design.

The surveillance system identified 342 children with spina bifida aperta less than age 18. Of these children, 134 children were no longer living in the state of Arkansas, leaving 208 families that were sent an introductory letter describing the study. Of the 208 families that were sent a letter, 88 could not be contacted by phone leaving 120 families that received a letter and a phone call. From these families, 98 agreed to participate in the study and 22 refused, resulting in a response rate of 82%. Among sampled households, including those unreachable, the participation rate was 47.1%. Of the case caregivers contacted, 96% were the biologic mother of the child and 4% were either the grandmother or the biologic father (3 grandmothers and 1 father; 1 father responded as a caregiver from control families).

Caregivers of case participants provided the names of up to three families that might be interested in participating in the study. Names and addresses for 78 control families were obtained from 41 case respondents. Letters describing the study were sent to the 78 control families and contact was made with 57. Four control families refused to participate resulting in a response rate of 93% and an overall participation rate for control families of 68%.

Because of the potential for case families to name control families with a child with disabilities, we asked control families four questions to assess disability in the control child. The questions asked about restrictions in activities of daily living, having special needs, being referred to special education classes, and having physical limitations. A review of this information found 10/53 responses indicated at least one limitation. If the caregiver answered positive to any of the questions, they were asked to explain. Further review found one control had just broken his leg prior to the interview and they answered he had special needs. Excluding this child left 9/53 (17%) indicating some disability. Two children had needs for speech therapy, two children had needs with feeding, one child had attention deficit hyperactivity disorder, and 4 children had severe disabilities (Down's syndrome, cerebral palsy, muscular dystrophy, and blindness).

Because control children with severe disabilities can bias the analysis towards the null hypothesis, these children were dropped from all analyses.

Measures

The main measures used in this study included the interviewer-assisted QWB scale and the HUI2 [13–15, 22]. The QWB scale was used to measure the primary caregiver's health-related quality of life while the HUI2 was used to measure the child's health-related quality of life. Both instruments are widely used in economic evaluations. For the QWB scale, respondents (the primary caregivers) were asked to report on their health state across four subscales over a 6-day period. The subscales include a symptom/problem complex (CPX) subscale and three functional subscales, physical activity (PAC), social activity (SAC), and mobility (MOB). Each of the subscale scores is determined

by preference weights (scores) derived from a representative community sample by the QWB scale developers. The algorithm for preference-weighting health states uses a categorical rating scale method and a multi-attribute utility model. The preference-weighted subscale scores are then subtracted from 1.0 (perfect health) to determine the total QWB score. The higher the subscale score, the greater the impairment associated with that subscale. Analyses presented below used total and subscale scores based on subject responses for the most recent 6-day period.

A similar approach was adopted for obtaining preference scores of children. The caregivers reported the health states of the children based on the HUI2 for an average day. Published algorithms developed for use with the HUI2 were then applied to the reported health states to derive preference scores. Algorithms for assigning preference scores to the HUI2 health states also were developed by the HUI2 developers using community samples.

Other measures included information on the age and education level of the child, the marital status of the caregiver, the number of people living in the household, the number of children aged 5 or less, the age and educational level of the caregiver, the race of the child and the caregiver, labor market outcomes of the caregiver and their spouse, number of hours of sleep, and annual family income. We did not obtain information on health conditions other than descriptions provided by the QWB or HUI2 in either caregivers or children, respectively. In addition, we did not obtain information from the medical record or in the interview describing various clinical procedures such as the placement of shunts or other surgical procedures. Concerns over respondent burden with no compensation for interviews limited the amount of information obtained.

Statistical analysis

We used a non-parametric trend test [23, 24] to assess whether the preference scores of caregivers from the QWB scale varied by control children and lesion location and across specific domains of the HUI2. Linear regression analysis was used to test whether a relationship exists between the preference scores of the caregiver and the child and by location of lesion relative to controls. The use of linear regression analysis follows recent work that compared a number of alternative models [25]. Tests of alternative specifications indicated that both child age and caregiver age were modeled best using a non-linear relationship. Thus, caregiver age, child age, and their squared terms were included in the regression models. Other predictor variables were tested including education level, whether the respondent was divorced, the number of adults in the household, the total size of the household, and other characteristics, but none of these predictors was significant or influenced the estimated relationships. All analyses were conducted using Stata Statistical Software: Release 8.0.

Results

Table 1 provides a summary of the characteristics of the caregivers and their children for both case and control families. Significant differences were noted in the characteristics of case and control families. Caregivers and children in case families tended to be older relative to controls. The range in age for children was similar (2–17), but caregivers of case children included grandmothers and ranged in age from 24 to 70 whereas control caregivers ranged in age from 25 to 60 (with the eldest control caregiver being a father). Children in the case families were less likely to be under 5 years of age (18.4% vs. 36.7%; $p < 0.05$). Because children must be at least age 5 to calculate HUI2 scores, this difference influenced the number of children included in analyses involving the HUI2. Control caregivers were also more likely to have graduated from college (38.8% vs. 17.4%; $p < 0.01$) and more likely to be married (88.6% vs. 77.5%; $p < 0.05$).

Mean preference scores for children and their caregivers by case and control families and by the three lesion locations are presented in Table 2. Mean scores are provided because of their use in economic evaluations. The preference scores for children with spina bifida range from 0.09 to 1.0 and exhibit the expected step function across the three lesion locations. For children with the least severe lesion (sacral), the estimated mean preference score is 0.61 with a standard deviation of

0.26. As the severity of the lesion increases, the estimated mean preference score falls to 0.54 for lower lumbar lesions and to 0.45 for thoracic and higher lumbar lesions. In comparison, the mean preference scores for control children were 0.93 with a standard deviation of 0.11. The trend test among case children for differences across lesions is significant at the 0.01 probability level as is the comparison with the control children. Placed in context, previous research on a sample of extremely low birth weight children using the HUI2 generated mean preference score estimates of 0.82 and standard deviation 0.21 while a reference group of school children scored 0.95 with a standard deviation of 0.07 [22].

Table 1. Characteristics of caregivers and their children

Characteristics	Case	Control
Caregiver age	37.7 (8.9)	34.2 (6.4)*
Child age	9.3 (4.6)	7.1 (4.0)**
Child age <5 (%)	18.4	36.7**
Child gender		
Female (%)	61.2	55.1
Caregiver race		
Black (%)	6.1	4.1
White (%)	90.8	93.9
Other (%)	3.1	2.0
Education		
< High school ed. (%)	11.2	2.0
High school grad. (%)	41.8	36.7
College or trade (%)	29.6	22.5
College grad. (%)	17.4	38.8*
Marital status		
Divorced (%)	13.3	5.7
Married (%)	77.5	88.6**
Other (%)	9.2	5.7
N	98	49

Notes: Values are presented as mean (sd); * Significant at 0.01 level; ** Significant at 0.05 level.

The preference scores for the caregivers of children with spina bifida also differed across lesion locations with the trend test indicating significant differences across the four groups (control children, sacral lesion, lower lumbar lesion, and thoracic/higher lumbar lesion). The mean QWB score for control caregivers is close to prior reports for the same age group [26]. The differences across the four groups are relatively small with the exception of caregivers of children with thoracic/higher lumbar lesions. Caregivers of children with these lesions had a mean preference score that was 0.08 points lower than control caregivers and 0.05 points lower than other caregivers of children with spina bifida.

Table 3 provides the results of linear regression analyses using the preference scores of the caregiver (based on the QWB scale) as the dependent variable. Two sets of analyses are performed. In analysis #1, the child HUI2 scores are inserted as the primary independent predictor of interest. In analysis #2, child HUI2 scores are replaced by lesion location as the primary predictor of interest with control children, who have no lesion, serving as the reference group. Additional covariates include child age, caregiver age, their squared terms, and whether the caregiver graduated from college.

Results of analysis #1 in Table 3 indicate a significant relationship between the preference scores of children and the preference scores of their caregiver ($\beta = 0.135$; $p = 0.001$). In addition, the relationship has the expected sign indicating that

Table 2. Health state preference scores for children with spina bifida and their caregivers relative to controls

Characteristics	Mean Score	SD	Range	N
Case children (HUI2)	0.55	0.24	0.09–1.00	80
Sacral lesion	0.61	0.26	0.15–1.00	34
Lower lumbar lesion	0.54	0.19	0.10–0.93.	27
Thoracic lesion	0.45	0.25	0.09–1.00	19
Control children (HUI2)	0.93	0.11	0.47–1.00	30
Case caregivers (QWB)	0.76	0.11	0.54–1.00	98
Sacral lesion	0.77	0.10	0.57–1.00	41
Lower lumbar lesion	0.77	0.12	0.56–1.00	33
Thoracic lesion	0.72	0.10	0.54–1.00	24
Control caregivers (QWB)	0.80	0.10	0.59–1.00	49

Note: Child preference scores measured by caregiver reported Health Utilities Index (HUI2) for children aged 5 and above. Caregiver preference scores measured by Quality of Well-being (QWB) scale.

less disability in children is associated with higher preference-weighted health states in the caregiver. Because the HUI2 applies to children age 5 and above, children less than 5 years of age (N = 38) are not included in the analysis. The second analysis includes all children and provides estimates of the impact of the three lesion locations (relative to control children) on the preference scores of the caregivers. While all of the coefficients on the three lesion locations are negative and exhibit a step function in relationship to severity, this analysis indicates that only caregivers of the most severely affected children with spina bifida (upper lumbar/thoracic) have QWB scores significantly different from caregivers of control children. The marginal impact is −0.072 points, which is significant at the 5% level.

Table 4 provides insight into the overall caregiver QWB scores by providing mean estimates of the four subscale scores. The QWB preference score is calculated by subtracting the four subscale scores from 1. Thus, a higher subscale score is indicative of lower health-related quality of life and a lower QWB preference score. Estimates are provided for control caregivers and by the lesion location of the child for case caregivers. Because there were little difference in caregiver health states for case caregivers of children with sacral and lower lumbar lesions, these two categories were combined in Table 4 and Table 5. The data in Table 4 indicate that the CPX symptom subscale accounts for most of the decrement in the QWB preference score. On average, caregivers of control children had a 0.195 point reduction in their QWB score based on symptoms reported over the 6-day period. Caregivers of children with the most severe lesions had larger decrements (0.239 points) in the CPX symptom subscale, which was significantly different at the 0.05 level relative to control caregivers.

Examination of the other subscales indicates significant differences for caregivers of children with higher lumbar and thoracic lesions in the PAC subscale and the SAC subscale relative to control caregivers. Caregivers of children with sacral and lower lumbar lesions also had significantly different decrements in the SAC scale relative to control caregivers, but the difference was small (0.005 points).

Table 5 provides details on the individual components of the CPX symptom subscale in the QWB by control caregivers and by the lesion location of the child for case caregivers. Data are presented as the percentage of respondents indicating the presence of a particular symptom or problem at any time over a 6-day period. Caregivers of children with higher lumbar or thoracic lesions indicate the presence of substantially more symptoms relative to control caregivers. For example, 16.7% of these caregivers report 'trouble

Table 3. Linear regression analyses predicting caregiver QWB score according to child HUI2 score and lesion location

Variable	Analysis #1			Analysis #2		
	Coefficient		*p*-value	Coefficient		*p*-value
HUI2 score	0.135	(0.037)	0.001	–	–	
Lower lumbar lesion	–		–	−0.015	(0.024)	0.525
Sacral lesion	–		–	−0.022	(0.024)	0.373
Upper/thoracic lesion	–		–	−0.072	(0.028)	0.012
Child age	0.023	(0.017)	0.176	0.020	(0.009)	0.028
Caregiver age	−0.024	(0.008)	0.004	−0.015	(0.008)	0.042
Child age squared	−0.001	(0.001)	0.258	−0.001	(0.000)	0.062
Caregiver age squared	0.000	(0.000)	0.005	0.000	(0.000)	0.062
College graduate	0.018	(0.024)	0.448	0.024	(0.021)	0.259
Constant	1.080	(0.179)	0.000	1.034	(0.148)	0.000
N	108			145		
Adjusted R^2	0.137			0.050		

Notes: Dependent measure in both analyses is caregiver QWB score. Child health states measured by caregiver reported HUI2 scores and caregiver health states measured by self-reported QWB scores. Lesion location estimates relative to controls in Analysis #2. Standard errors in parentheses.

Table 4. Quality of Well-Being (QWB) subscale scores for caregivers of children with spina bifida relative to controls

QWB subscale	Caregiver subscale score		
	Mean	SD	*p*-value
CPX symptom scale			
Control	0.195	0.094	
Sacral/ L. lumbar	0.214	0.095	0.295
H. lumbar/Thoracic	0.239	0.060	0.042
Mobility scale			
Control	0.002	0.009	
Sacral/ L. lumbar	0.001	0.004	0.391
H. lumbar/Thoracic	0.003	0.013	0.696
Physical activity scale			
Control	0.006	0.017	
Sacral/ L. lumbar	0.008	0.020	0.450
H. lumbar/Thoracic	0.017	0.030	0.050
Social activity scale			
Control	0.000	0.003	
Sacral/ L. lumbar	0.005	0.016	0.035
H. lumbar/Thoracic	0.015	0.030	0.002

Notes: Subscale scores subtracted from 1 to obtain overall QWB score; significance probability obtained by *t*-test relative to controls.

learning, remembering, or thinking clearly' compared to 2.04% of controls. Other symptoms also were more likely to be present including excessive worry or anxiety, general tiredness, weakness, or weight loss, and headache or dizziness, ringing in ears, or spells of feeling nervous/shaky. In contrast, no caregiver of children with the most severe lesions indicated an absence of symptoms compared to 10% of controls.

Finally, Table 6 provides preference scores of the caregiver in relation to the child health domains from the HUI2. Caregiver preference scores were significantly different across the first four domains reported in Table 6. Caregiver preference scores in the pain and emotion domains indicated a declining step-function as caregiver-reported child pain levels increased or emotional states worsened. For caregivers reporting no pain in their children, mean preference score scores were 0.788 with a standard deviation of 0.13 while caregivers reporting their children were in the most severe pain levels had mean preference scores of 0.698 with a standard deviation of 0.07. Similar findings are evident for the emotion domain with a declining step-function in caregiver preference scores as they report worse emotional states for their children. In general, the preference scores for caregivers were highest when the child's health state level indicated no disability.

Discussion

This study provides new information on two important measures for economic evaluations of the prevention and treatment of neural tube defects. Primary data on the health state preference scores of children with spina bifida are important for estimating QALY gains from prevention efforts. The PCHM has called for the collection of preference-weighted health-related quality of life information based on generic systems that could be used 'off the shelf', recognizing that most investigators do not have the resources to collect original data on preference-weighted health states [27]. HUI2 preference scores from the perspective of the caregiver of the child with spina bifida fall within the range estimated previously by physicians [2]. Analysts can now use these scores in economic evaluations of novel interventions to treat or prevent neural tube defects.

Table 5. Percentage of caregivers reporting quality of well-being scale symptom measures over a 6-day period by child lesion location (cases) and controls

Quality of well-being symptom scale description	Child lesion location		
	Controls	Sacral/ L. lumbar	H. lumbar/ Thoracic
Loss of consciousness (seizure, fainting, or coma)	0.00	1.35	0.00
Burn over large area of face, body, arms, or legs	2.04	1.35	0.00
Pain, bleeding, itching or discharge from sexual organs	4.08	5.41	4.17
Trouble learning, remembering, or thinking clearly	2.04	9.46	16.67**
Missing, deformed, paralyzed, or broken hands, feet, arms, or legs	2.04	2.70	0.00
Pain, stiffness, weakness, numbness or discomfort in chest, stomach, side, neck, back, hips, or any joints of hands, feet, arms, or legs	24.49	27.03	25.00
Pain, burning, bleeding, itching with rectum, bowel movements or urination	2.04	0.00	4.17
Sick or upset stomach, vomiting or loose bowel movements	24.49	5.41*	12.50
General tiredness, weakness, or weight loss	12.24	25.68	37.50**
Cough, wheezing, or shortness of breath	4.08	13.51	12.50
Spells of feeling upset, being depressed, or of crying	14.29	22.97	25.00
Headache or dizziness, or ringing in ears, or spells of feeling nervous/shaky	12.24	31.08**	37.50**
Burning or itching rash on large areas of face, body, arms, or legs	0.00	2.70	12.50**
Trouble talking (lisp, stuttering, hoarseness, or inability to speak)	0.00	2.70	4.17
Pain or discomfort in one or both eyes; Trouble seeing after correction	8.16	4.05	4.17
Overweight or underweight for age/height; skin defect of face, body, arms, or legs (scars, pimples, warts, bruises)	40.82	51.35	66.67**
Pain in ear, tooth, jaw, throat, lips, tongue; missing or crooked teeth; stuffy, runny nose; any trouble hearing (includes wearing hearing aid)	30.61	35.14	54.17
Taking medication or on medically prescribed diet for health reasons	32.65	35.14	45.83
Wore eyeglasses or contact lenses	51.02	50.00	50.00
Breathing smog or unpleasant air	2.04	9.46	12.50
No symptoms	10.20	8.11	0.00
Trouble sleeping	24.49	24.32	37.50
Intoxication	2.04	0.00	4.17
Problems with sexual interest or performance	2.04	5.41	12.50
Excessive worry or anxiety	14.29	16.22	37.50**

Notes: significance probability based on Fisher's exact test relative to controls. $^{**}p < 0.05$; $^{*}p < 0.01$.

The paper also extends the literature on the inclusion of caregiver impacts in economic evaluations. Previous studies have failed to demonstrate differences in the *preference scores* of caregivers across stages of disease *using generic measures* such as the HUI2. Use of the QWB scale generated differences in health state preference scores for caregivers of children, even in this limited sample. Preference score deficits averaging 0.072 points were reported for caregivers of children with the most severe lesions. Estimates from the linear regression model suggest deficits of 0.12 points over the entire range of child disability as indicated by the HUI2 score ($0.12 = \beta \times (1.0–0.09)$. Changes in preference weights greater than or equal to 0.03 points indicate clinically important differences in health states [28–31]. Inclusion of these impacts in economic evaluations would increase the benefits of all effective prevention strategies involving neural tube defects.

However, some caution should be exercised, as the methods for incorporating caregiver impact in economic evaluations are less clear. Similar to reference case rules for incorporating both QALY changes and income or productivity losses of patients, inclusion of caregiver QALY changes along with caregiver time costs may double-count productivity losses [32]. More research is required on methods for incorporating caregiver impacts in economic evaluations.

The study has several limitations and provides additional research issues. The use of caregivers as proxy informants of their child's health state, may introduce artificial correlation with their own

Table 6. Quality of well-being (QWB) preference scores for caregivers of children with spina bifida and controls by the domains of the health utilities index (HUI2)

HUI2 health domain	Case caregivers		Control caregivers	
	QWB score	N	QWB score	N
Child pain level ($p < 0.01$)				
Free of pain	0.788 (0.13)	27	0.812 (0.12)	20
Occasional pain	0.771 (0.09)	38	0.785 (0.07)	10
Frequent pain	0.698 (0.07)	15		
Child emotional state ($p = 0.01$)				
Happy	0.797 (0.12)	28	0.800 (0.12)	19
Fretful-some	0.707 (0.10)	43	0.787 (0.06)	10
Fretful, often – extreme	0.669 (0.05)	9	0.883 (0.17)	2
Child sensory level ($p = 0.02$)				
See, hear, speak normally	0.776 (0.10)	63	0.813 (0.10)	28
Requires equip. to see, hear, speak	0.707 (0.15)	11	0.687 (0.06)	3
Limited with equipment	0.738 (0.07)	6		
Child mobility level ($p = 0.02$)				
Normal for age	0.800 (0.08)	14	0.806 (0.10)	30
Limitations	0.745 (0.12)	12	0.651 –	1
Requires equipment	0.794 (0.11)	23		
Another person required/unable	0.731 (0.11)	31		
Child cognitive state ($p = 0.14$)				
Normal learner	0.779 (0.10)	33	0.799 (0.10)	27
Slower than peers	0.740 (0.08)	9	0.835 (0.14)	3
Very slow/unable	0.755 (0.13)	38	0.763 –	1
Child self care ability ($p = 0.16$)				
Normal	0.767 (0.11)	14	0.801 (0.11)	30
Some difficulty/requires equipment	0.775 (0.11)	14	0.814 (0.11)	1
Requires help of another person	0.759 (0.11)	52		

Notes: Child health domain scores from HUI2; caregiver preference scores measured by QWB scale; standard deviations in parentheses; statistical significance based on non-parametric trend test.

health state [33]. While this may be a potential problem, caregiver preference scores differed by lesion location suggesting real differences in caregiver health states due to the disability level of the child. In particular, this study suggests that the proxy informant factor may influence the magnitude, but not the overall slope of the relationship between child and caregiver health states.

Research on children has addressed the methodological issues associated with measuring preference scores across developmental stages [34]. Age of the child was not a central focus of our analyses. More research is needed on understanding the relationships between child and caregiver health states in populations of children with potentially severe disabilities across the age span.

Research also is needed on preference scores in very young children. No generic instruments have been validated for use below the age of 5. It is not known whether methods for determining preference scores generated from children above the age of 5 are relevant for children below the age of 5 [35].

The use of case families to recruit control families for research can produce samples that differ from population-based sampling schemes. Our interest in this study was not to generate a sample of population-based controls, but to create a control sample that differed in disability to the case families. By comparing case families that care for a disabled child with control families that have children with far fewer disabilities, we were able to demonstrate a relationship between disability in the child and the health state preference scores of caregivers. We believe future investigations will generate similar findings, but the overall estimates may differ in magnitude with larger samples and alternative sampling strategies.

Finally, it is not known how children with spina bifida in Arkansas compare to the rest of the country. Children with spina bifida in Arkansas have access to one multi-disciplinary specialty clinic that covers the entire state. However, our sampling strategy was population-based using one of the oldest birth defects registries in the country. This sampling strategy improves our ability to generalize the results as we did not have to rely on a selected sample based on clinic attendance or other criteria.

Conclusions

Previous research on caregivers has documented numerous physical and psychological impacts to the extent that caregivers have been called 'hidden patients' [36, 37]. Quantitative assessment of caregiver health using preference-weighted scores has the potential to illuminate these impacts across a spectrum of disabilities and determine whether such impacts should be considered in economic evaluations.

This study reports the first evidence of a relationship between disability in children and health preference scores of caregivers using a generic instrument. Caregiver health states and child health states differed across lesion locations – an objective measure of disease severity. The findings suggest the need for additional research on the measurement of caregiver health state preferences using generic instruments in other populations. Head-to-head comparisons between generic instruments, such as recent investigations into specific diseases [38, 39], would be particularly useful. Also, studies that have measured health-related quality of life in caregivers with the SF-36 [40], a widely used generic health status measure, can now generate preference scores using the methods developed by Brazier et al. [25, 41]. Preference scores of caregivers obtained from the SF-36 can be compared with the QWB scale or the HUI *Mark 3* [42, 43], in relation to patient stage of illness, illness severity, or health preference scores. Such studies would contribute to the debate over the value of generic instruments versus condition-specific caregiver measures. Moreover, research across disease settings and across populations such as adults with dementia or children with chronic or disabling conditions, could aid in assessing whether a general relationship exists between patient and caregiver preference scores.

The development of a general or condition-specific relationship between caregiver and patient preference scores potentially could guide economic evaluations of disease treatment and prevention. Such a relationship could inform cost-effectiveness evaluations of interventions aimed at minimizing the health impact on the caregiver from caring for persons with chronic or disabling conditions.

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