

Child health-related quality of life following neurocritical care for traumatic brain injury: an analysis of preference-weighted outcomes

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Abstract

Background Cost-effectiveness analysis relies on preference-weighted health outcome measures as they form the basis for quality adjusted life years. Studies of preference-weighted outcomes for children following traumatic brain injury are lacking.

Objective This study seeks to describe the preference-weighted health outcomes of children following a traumatic brain injury at 3- and 6-months following pediatric intensive care unit (ICU) discharge.

Setting/Patients Children aged 5–17 who required ICU admission and endotracheal intubation or mechanical ventilation.

Main Outcome Measures The Quality of Well-being (QWB) score was used to describe preference-weighted

outcomes. Clinical measures from the intensive care unit stay were used to estimate risk of mortality. Risk of mortality, Glasgow coma scores, patient length of stay in the intensive care unit, and parent-reported items from the Child Health Questionnaire (CHQ) were used to test construct validity.

Methods Subject data were obtained from nine pediatric intensive care units with consent procedures approved by representative institutional review boards. Medical records containing clinical information from the ICU stay were abstracted by the study coordinating center. Caregivers of children were contacted by telephone for follow-up interviews at 3- and 6-months following ICU discharge. All interviews were conducted by telephone with the primary caregiver of the injured child. Preference score statistics are presented overall and in relation to characteristics of the patient and their ICU admission.

Results A response rate of 59% was achieved for the 3-month interviews ($N = 56$) and 67% for the 6-month interviews ($N = 65$) for caregivers of children aged 5 years and above that consented to participate. Overall, QWB scores averaged 0.508 (95% CI: 0.454–0.562) at the 3-month interview and 0.582 (95% CI: 0.526–0.639) at the 6-month interview. For both interview periods, scores ranged from 0.093 to 1.0 on a 0–1 value scale, where 0 represents death and 1 represents perfect health. Specific acute and chronic health problems from the QWB scale were present more often in patients with higher injury severity. Mortality risk, ICU length of stay, Glasgow Coma Scales, and parental reported summary scores from the CHQ all correlated correctly with the QWB scores.

Conclusions The findings support the use of the QWB score with parental report to measure preference-weighted health outcomes of children following a traumatic brain injury. Information from the study can be used in economic

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61 evaluations of interventions to prevent or treat traumatic
62 brain injuries in children.

63 **Keywords** ■

64 **Introduction**

65 Cost-effectiveness analysis (CEA) is a method for evalu-
66 ating health outcomes from a health intervention in relation
67 to the costs of the intervention. For example, CEA could be
68 used to assess the cost per life year gained from the use of
69 decompressive craniectomy or other established or new
70 treatments for traumatic brain injury. CEA is most useful
71 when cost-effectiveness ratios can be compared across
72 different treatments such as the cost per life year saved
73 from decompressive craniectomy in children relative to the
74 cost per life year saved from more aggressive treatment for
75 heart failure in elderly adults. If a treatment has a high cost
76 per life year saved, especially relative to other treatments,
77 one could use this information in evaluating whether the
78 treatment appears warranted. Such comparisons, however,
79 are valid if and only if CEA is performed according to
80 standard methods, supported by valid economic principles.

81 In the early 1990s, the U.S. Public Health Service (PHS)
82 convened a panel of experts to provide guidelines for
83 conducting cost-effectiveness analysis of health interven-
84 tions in an attempt to standardize methods across studies
85 [1]. The resulting reference case analysis developed by the
86 panel embodied the set of standard procedures for con-
87 ducting CEA and included the recommendation to use
88 quality adjusted life years (QALYs) as the metric for
89 measuring health outcomes [2]. QALYs in CEA are formed
90 by combining life years gained from a health intervention
91 with preference-weighted health states. Preference weights
92 are typically measured on a 0–1 value scale, where 0
93 represents death and 1 represents perfect health [3]. Rec-
94 ognizing that most investigators do not have the resources
95 to collect original data on preference-weighted health
96 states, the PHS panel recommended the development of
97 preference scores for various conditions that might be used
98 “off-the-shelf” for CEA [4]. Further, the panel recom-
99 mended that preference scores be measured using generic
100 instruments, which rely on pre-scored multi-attribute health
101 status classification systems, as opposed to direct elicitation
102 methods that require respondents to value a given health
103 state using rating scales, time trade-off, or standard gamble
104 techniques.

105 A recent literature review identified a number of issues
106 associated with generic preference-weighted instruments as
107 they apply to quality of life measurement following trau-
108 matic brain injury, especially whether such instruments
109 were sensitive to outcome changes in TBI [5]. Importantly,

the review identified only a single study that has addressed
the valuation of health states following traumatic brain
injury with an instrument that provides preference-weight-
ed (or utility) scores. Although information on overall
scores was not reported, that study compared outcomes of
27 children in a randomized trial of decompressive
craniectomy [6] using the original Health Utilities Index
(HUI) [7].

Information on preference scores for a large cohort of
pediatric TBI survivors is needed. Preference score data for
this population could be invaluable for addressing a num-
ber of questions relevant to the treatment of TBI, especially
whether more aggressive treatment of TBI generates value
or benefits in excess of cost [8]. Surveys of critically ill
persons with traumatic brain injury have found large
variations in treatment patterns across different types of
institutions [9–11]. In addition, evidence indicates a trend
toward more aggressive treatment of pediatric TBI patients
and improved survival over time [12]. It is not known
whether different practice styles or whether more aggres-
sive treatment can be justified using CEA criteria because
of the dearth of information on preference-weighted
outcomes.

Addressing these questions, however, requires knowl-
edge as to whether health outcomes of children following a
traumatic brain injury can be measured using generic
preference-weighted instruments. The primary goals of this
study are (1) to report scores from the Quality of Well-
being (QWB) scale to provide information for conducting
CEA in this population and (2) to evaluate whether the
QWB scores correlate correctly with clinical characteristics
of the ICU admission and other outcome measures. Thus,
we report QWB scores describing the health-related quality
of life of children that survived a TBI following admission
to an intensive care unit at 3- and 6-month follow-up.
Scores are reported in relation to risk of mortality and other
patient characteristics associated with their ICU admission,
in addition to parent-reported items from the Child Health
Questionnaire (CHQ) [13, 14] and the Pediatric Overall
Performance Category (POPC) [15, 16] scale.

150 **Methods**

To illustrate the QALY metric and its use in CEA, Fig. 1
provides two different hypothetical outcome trajectories
for a child that suffered a TBI where outcomes are mea-
sured on the 0–1 value scale. In this bound, 0 represents
death and 1 perfect health, but it is possible (and probable)
that health states worse than death could be observed
following the TBI [17, 18]. With treatment, health can
improve over time and for some patients, may improve
more or faster with improved treatment regimes. In Fig. 1,



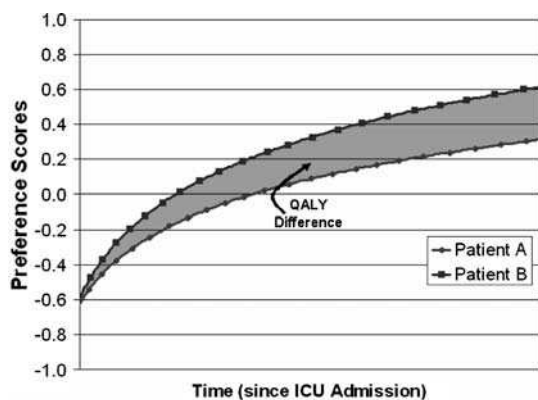


Fig. 1 Illustration of QALYs gained from improved treatment of traumatic brain injury

160 person B (or the average person in group B) is assumed to
 161 have a better health outcome from a more expensive
 162 treatment course relative to person A. The gain in prefer-
 163 ence-weighted health outcomes from improved treatment
 164 can be multiplied by the duration of time in a given health
 165 state to generate a quality adjusted life year. The shaded
 166 area in Fig. 1 illustrates the QALYs gained by person B
 167 relative to person A from better treatment or increased use
 168 of health services (the intervention). The gain in QALYs
 169 would be included in the denominator of an incremental
 170 cost-effectiveness ratio (ICER) [19] calculated as:

172 Data

173 Subjects for the study were recruited from 10 pediatric
 174 intensive care units (PICUs) across the United States. The
 175 PICUs were selected using convenience sampling in order
 176 to obtain a relatively large sample. Subject inclusion cri-
 177 teria required that the child be less than 18 years of age and
 178 admitted to the PICU with a CDC-defined traumatic brain
 179 injury [20] that required either endotracheal intubation or
 180 mechanical ventilation [21]. Patient selection criteria were
 181 chosen to correspond with prior work and to potentially
 182 provide information on “marginal” patients who survived
 183 a traumatic brain injury and who might have expired with
 184 less aggressive treatment [12].

185 Since the QWB scale asks questions about normal
 186 activities involving work, school, or housework, it typically
 187 is not used in persons less than 5 years of age. This study
 188 thus reports preference scores on children aged 5 and
 189 above. All subjects were recruited with an institutional
 190 review board-approved protocol for consent with the
 191 institutional review board of the University of Arkansas for
 192 Medical Sciences approving the overall study design and
 193 each of the participating institutions receiving study

194 approval from their designated IRB. Although the study
 195 was approved to recruit both Spanish- and English-speak-
 196 ing families, few Spanish-speaking households were
 197 recruited and only English-speaking families completed the
 198 study protocol.

199 Subjects who consented to participate in the study had
 200 their medical records abstracted by a research assistant at
 201 the study coordinating site. A single research assistant
 202 abstracted all of the medical records and entered the data
 203 into a customized Access software program. At 3- and
 204 6-months following ICU discharge, families that consented
 205 to participate were sent reminder letters and then
 206 telephoned repeatedly to schedule an interview using the
 207 approved protocol. Subjects that could not be contacted in
 208 the month following the reminder letter were dropped from
 209 the interview. All interviews were conducted by phone
 210 using trained research assistants. The primary caregiver
 211 answered questions about the child, the family, and their
 212 own health.

213 A total of 114 subjects consented to participate in the
 214 study from 10 participating hospitals. Interviews were
 215 completed on 67 (59%) caregivers at 3-month follow-up
 216 and 76 (67%) caregivers at 6-month follow-up. Of the 10
 217 participating hospitals, one hospital recruited only a single
 218 patient who was lost to follow-up. Of the remaining hos-
 219 pitals, follow-up rates ranged from 52% to 95%. A review
 220 of subject logs for telephone contact revealed that the
 221 primary reason subjects were lost to follow-up was due to
 222 an inability to schedule or conduct the interview by phone
 223 (no answer, left message on answering machine). Subjects
 224 that participated received \$25 for each interview.

225 The primary outcome measure for the study was the QWB
 226 scale [22, 23] as reported by the primary caregiver. The
 227 QWB scale has been widely used in different clinical settings
 228 to describe preference-weighted health outcomes for various
 229 conditions [24–29]. Respondents were asked to report on
 230 their health state across four subscales over a 3-day period.
 231 The subscales include a symptom/problem complex (CPX)
 232 subscale, and three functional subscales: physical activity
 233 (PAC), social activity (SAC), and mobility (MOB). Each of
 234 the subscale scores is determined by preference weights
 235 (scores) derived from a representative community sample by
 236 the QWB developers. The algorithm for preference-
 237 weighting health states uses a categorical rating scale method
 238 and a multi-attribute utility model. The preference-weighted
 239 subscale scores are then subtracted from 1.0 (perfect health)
 240 to determine the QWB score. The higher the subscale score,
 241 the greater the impairment associated with that subscale.
 242 Analyses presented below use total QWB scores and
 243 subscale scores based on subject responses averaged over the
 244 3-day period covering the interview.

245 We also captured information about the child using the
 246 parent report version of the Child Health Questionnaire

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(CHQ PF-50) [13]. The CHQ measures health over 14 domains, including general health perceptions, physical functioning, role/social functioning, parent impact-time, parent impact-emotional, self-esteem, mental health, behavior, family activities, family cohesion, and change in health. Two summary scores of physical and psychosocial health status can be calculated using 12 of the 14 domains. We use the summary scores to report correlations with the QWB subscale scores and the total score.

Injury severity was measured using a hospital risk of mortality score employed in previous studies [11, 30] and the Glasgow coma scale measured on admission to the ICU. The risk of mortality score captures six measures (low bicarbonate, low potassium, high glucose, fixed pupils, GCS less than or equal to eight, and vasoactive infusion) and translates findings to a risk of mortality using a previously published logit formula [11]. Other measures abstracted from the ICU stay included the use of intracranial pressure monitoring both on admission (first 24 h) and at any time during the stay, surgical openings of the skull, and ICU length of stay. Finally, we captured other subject characteristics such as gender, patient insurance status, race, and mechanism of injury. All of these measures were used to provide a better understanding of outcomes associated with ICU admission for traumatic brain injury and to demonstrate the feasibility of using the QWB scale to measure outcomes using parental report.

274 Statistical analysis

Findings from the QWB scale are presented as mean and 95% confidence intervals because mean values are used in the calculation of QALYs [31]. Linear regression analysis was performed on untransformed measures because other modeling strategies have not been shown to improve performance [32]. We used linear regression analysis to assess correlations with patient risk of mortality, GCS scores, ICU length of stay, and the summary scores from the parent-reported CHQ. Coefficients from the linear regression analysis indicate changes in QWB scores (or scale components) given a one-unit change in the independent variables. Our primary hypothesis was that the QWB scores would negatively correlate with increased risk of mortality and longer lengths of stay and positively correlate with higher GCS scores and higher CHQ summary scores.

290 Results

Table 1 provides characteristics of the patient population for subjects whose primary caregiver completed the 3-month and 6-month interviews. The sample is similar in many respects to our previous work that used nationally

Table 1 Sample characteristics

| Patient characteristics | 3-Month | 6-Month |
|----------------------------|--------------|--------------|
| Child age | 12.6 (3.7) | 12.3 (4.0) |
| Gender (%) | | |
| Male | 62.5 | 58.5 |
| Female | 37.5 | 41.5 |
| Child race (%) | | |
| Black | 23.2 | 24.6 |
| White | 67.9 | 67.7 |
| Hispanic | 3.6 | 3.1 |
| Other | 5.4 | 4.6 |
| Insurance (%) | | |
| Private | 60.7 | 58.5 |
| Medicaid | 8.9 | 7.7 |
| Uninsured | 19.6 | 20.0 |
| VOther/Unknown | 10.7 | 13.9 |
| Mechanism of injury (%) | | |
| ATV accident | 12.5 | 9.2 |
| Bicycle | 5.4 | 6.2 |
| Fall | 7.1 | 7.7 |
| Motor vehicle | 44.6 | 46.2 |
| Pedestrian/Motor vehicle | 16.1 | 16.9 |
| Other | 14.3 | 13.9 |
| Outcome measures | | |
| CHQ physical summary | 71.6 (27.2) | 78.8 (25.5) |
| CHQ psychosocial summary | 70.4 (28.2) | 69.5 (24.5) |
| POPC scale (%) | | |
| Normal | 21.1 | 34.9 |
| Mild | 45.6 | 28.6 |
| Moderate | 17.5 | 22.2 |
| Severe | 15.8 | 14.3 |
| ICU measures | | |
| ICU length of stay | 14.9 (9.3) | 13.8 (9.4) |
| ICP monitor (A) (%) | 18.2 | 18.8 |
| ICP monitor (S) (%) | 83.6 | 73.4 |
| Craniotomy/Craniectomy (%) | | |
| Yes | 20.0 | 18.5 |
| No | 80.0 | 81.5 |
| Risk of mortality | 0.229 (0.26) | 0.216 (0.26) |
| Glasgow coma scale | 5.1 (2.2) | 5.2 (2.37) |
| Pupil reactivity (%) | | |
| Yes | 64.2 | 67.7 |
| No | 35.9 | 32.3 |
| N | 56 | 65 |

Abbreviations: (A) Admission

(S) Stay

(ICU) Intensive Care Unit

(CHQ) Child Health Questionnaire

(ICP) Intracranial Pressure

(ATV) All-Terrain Vehicle

(POPC) Pediatric Overall Performance Category

295 representative longitudinal hospital administrative data and
 296 the same inclusion criteria. Both samples had similar mean
 297 age (12.5 years), percentage of patients of black race
 298 (23%), percentage of admissions due to pedestrian/motor
 299 vehicle injuries (16%) and falls (7%). The percentage of
 300 females (approximately 40%) and white respondents (68%)
 301 were elevated in the follow-up sample relative to the na-
 302 tional sample while the percentage of Hispanics (3–4%)
 303 was lower than the national sample. The percentage of
 304 subjects admitted to the ICU because of a motor vehicle
 305 crash (approximately 45%) is lower in this study while the
 306 percentage of ATV accidents (9–13%) is higher, possibly
 307 reflecting the trend of more ATV accidents with increasing
 308 ATV sales [33].

309 The percentage of children rated as normal on the POPC
 310 scale increased from 21% at the 3-month interview to 35%
 311 at the 6-month interview. The percentage of children in the
 312 moderate and severe categories stayed approximately the
 313 same for both interviews. There were no children in a
 314 vegetative state at the time of either interview.

315 Medical record data obtained from the ICU admission
 316 attests to the high severity of the patients in both the 3- and
 317 6-month samples. The average patient had a GCS score of
 318 5 with over 30% lacking pupil reactivity. The mortality rate
 319 in the national sample averaged approximately 22% in the
 320 most recent years available, which is similar to the mor-
 321 tality risk reported here. However, it is likely that the
 322 subjects in this sample have higher mortality risk on
 323 average, given that it consists solely of survivors who
 324 presumably had lower mortality risk than non-survivors.
 325 This finding is corroborated by the fact that more than 80%
 326 of the patients in the 3-month sample underwent ICP
 327 monitoring during their ICU admission. This rate is
 328 approximately three times higher than that found in hos-
 329 pital administrative data using the same selection criteria.

330 **Table 2** provides mean QWB scores by patient charac-
 331 teristics at the 3- and 6-month interviews. Data in **Table 2**
 332 can be used in economic evaluations of treatment and
 333 prevention interventions requiring estimates of QALYs
 334 gained or lost. Thus, we report mean QWB for patients
 335 responding in either period rather than for respondents
 336 captured in both sample periods. Overall, the mean QWB
 337 scores averaged 0.508 (95% CI: 0.454–0.562) at the
 338 3-month interview and 0.582 (95% CI: 0.526–0.639) at the
 339 6-month interview. Scores ranged between 0.093 and 1.0
 340 for both interview periods.

341 Examination of QWB scores by selected patient char-
 342 acteristics indicates fairly large confidence intervals due to
 343 the relatively small number of observations in a given cell.
 344 There is a marked similarity in scores by gender at both the
 345 3- and 6-month interview with mean score differences of
 346 approximately 0.01 points. All of the confidence intervals
 347 for the QWB scores overlap across different patient

348 demographic characteristics. There was no difference in
 349 outcomes according to insurance status, in contrast to our
 350 prior studies using clinical [11] and nationally representa-
 351 tive hospital data [12], which demonstrated an increased
 352 mortality risk for uninsured children.

353 Examination of QWB scores by the POPC scores indi-
 354 cates the expected trend. Children rated as normal at the
 355 time of the interview had the highest QWB scores and
 356 children rated as having severe a severe disability had the
 357 lowest scores. The mean QWB scores are similar at both
 358 the 3- and 6-month interview for children rated as normal
 359 and children rated as severe. The mean scores differ
 360 between periods for children rated as moderate or mild, but
 361 because of the large confidence intervals, the scores
 362 overlap for both interviews.

363 Selected clinical characteristics of the child are associ-
 364 ated with differences in outcome at the 6-month interview.
 365 For example, outcomes of children according to time of
 366 ICP monitor placement differed with non-monitored chil-
 367 dren having the best outcomes consistent with lower risk of
 368 mortality relative to children undergoing ICP monitoring.
 369 Children monitored later in the course of the admission had
 370 the worst outcomes. Children monitored on admission had
 371 higher mean risks of mortality and higher mean QWB
 372 scores than children monitored on the first day of admis-
 373 sion although the differences did not reach conventional
 374 levels of significance even after controlling for risk of
 375 mortality ($P = 0.104$). Children monitored late in the
 376 admission had the lowest mortality risk even when com-
 377 pared to non-monitored children (0.064 vs. 0.087;
 378 $P = 0.658$). Of the six children monitored late in the
 379 admission, four met criteria for ICP monitoring on
 380 admission [34] and two children deteriorated during the
 381 admission with one suffering a pulmonary contusion.

382 There were significant differences in scores for children
 383 requiring craniectomy or craniotomy. QWB scores also
 384 differed for children at lower risk of mortality relative to
 385 children at higher risk of mortality. Children with a GCS
 386 less than 5 had QWB scores that were 0.138 points lower
 387 than children with a GCS greater than or equal to 5
 388 ($P = 0.013$). Mean scores differed by more than 10 points
 389 for children who had reactive pupils on admission relative
 390 to children who did not, although the differences were not
 391 significant at conventional levels ($P = 0.09$).

392 To better illustrate the components of the QWB scale,
 393 **Table 3** provides the percent of respondents indicating the
 394 presence of a scale item both by overall respondents and by
 395 lower and higher severity subjects. For this analysis, we
 396 sought to create relatively equal numbers in the two
 397 severity groups with children having a GCS score less than
 398 5 on admission in one group and five and greater into the
 399 second group. For most questions, there was a higher
 400 percentage of symptoms in the more severe group

Table 2 Mean quality of well-being scores by patient characteristics (95% confidence intervals)

| Characteristic | QWB score 3 month | QWB score 6 month |
|------------------------|----------------------|---------------------|
| Overall | 0.508 (0.454–0.562) | 0.582 (0.526–0.639) |
| Child age | | |
| 5–12 | 0.498 (0.405–0.591) | 0.610 (0.520–0.700) |
| 13–18 | 0.514 (0.444–0.584) | 0.564 (0.489–0.639) |
| Gender | | |
| Male | 0.511 (0.437–0.585) | 0.587 (0.509–0.665) |
| Female | 0.504 (0.420–0.588) | 0.576 (0.491–0.660) |
| Child race | | |
| Black | 0.558 (0.406–0.710) | 0.643 (0.518–0.769) |
| White | 0.481 (0.418–0.544) | 0.559 (0.491–0.627) |
| Other | 0.585 (0.438–0.733) | 0.592 (0.308–0.875) |
| Insurance | | |
| Private | 0.509 (0.434–0.584) | 0.606 (0.525–0.688) |
| Medicaid | 0.494 (0.068–0.919) | 0.544 (0.335–0.753) |
| Uninsured | 0.508 (0.374–0.641) | 0.549 (0.398–0.699) |
| Other/Unknown | 0.523 (0.286–0.760) | 0.524 (0.437–0.612) |
| Mechanism of injury | | |
| ATV accident | 0.536 (0.342–0.730) | 0.672 (0.473–0.870) |
| Bicycle | 0.489 (–0.158–1.136) | 0.498 (0.067–0.929) |
| Fall | 0.687 (0.578 –0.796) | 0.675 (0.453–0.898) |
| Motor vehicle | 0.507 (0.434–0.581) | 0.545 (0.465–0.625) |
| Pedestrian/MV | 0.321 (0.234–0.407) | 0.539 (0.356–0.722) |
| Other | 0.614 (0.407–0.822) | 0.687 (0.511–0.863) |
| POPC scale | | |
| Normal | 0.734 (0.647–0.821) | 0.760 (0.681–0.838) |
| Mild | 0.519 (0.460–0.579) | 0.603 (0.506–0.700) |
| Moderate | 0.375 (0.282–0.468) | 0.458 (0.380–0.537) |
| Severe | 0.297 (0.172–0.421) | 0.293 (0.218–0.368) |
| Use of ICP monitoring | | |
| No | 0.661 (0.533–0.790) | 0.756 (0.657–0.854) |
| On admission | 0.490 (0.343–0.635) | 0.594 (0.464–0.723) |
| First day | 0.458 (0.386–0.530) | 0.504 (0.432–0.576) |
| Later than first day | 0.498 (0.316–0.679) | 0.418 (0.218–0.618) |
| Craniotomy/Craniectomy | | |
| No | 0.539 (0.479–0.599) | 0.613 (0.551–0.676) |
| Yes | 0.375 (0.250–0.500) | 0.429 (0.315–0.543) |
| Glasgow coma scale | | |
| ≥5 | 0.544 (0.453–0.636) | 0.650 (0.563–0.737) |
| <5 | 0.471 (0.404–0.538) | 0.515 (0.450–0.579) |
| Pupil reactivity (%) | | |
| Yes | 0.528 (0.453–0.602) | 0.610 (0.539–0.682) |
| No | 0.474 (0.393–0.555) | 0.509 (0.424–0.594) |
| <i>N</i> | 56 | 65 |

401 compared to the less severe group although the small
 402 sample size precluded the differences reaching statistical
 403 significance in many cases. For example, in items from the
 404 CPX scale, the more severe group was more likely to

experience “stuttering or unable to speak clearly” (35.3%
 vs. 15.2%; $P = 0.052$) and “fatigue or weakness” (47.1%
 vs. 27.3%; $P = 0.077$). Some of the more pronounced items
 included “joint pain, stiffness, weakness, numbness” with

405
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 407
 408

409 the lower severity group reporting 3% versus 32.4% for the
410 higher severity group ($P = 0.002$) and ‘‘frustration, irrita-
411 tion, losing temper’’ being reported by 39.4% of the lower
412 severity group and 82.4% of the higher severity group
413 ($P < 0.001$).

414 Additional differences occurred in the self care, physical
415 activity, and usual activity items with the same pattern of
416 results. Approximately 20% of the higher severity sample
417 reported spending the day in bed or chair due to health
418 compare to none of the lower severity group.

419 **Table 4** provides coefficients and the adjusted R^2 from
420 univariate regressions for the total QWB scores and their
421 subscales regressed on risk of mortality, GCS scores,
422 ICU length of stay, and the summary components from
423 the CHQ at the 3- and 6-month interview. All of the
424 coefficients have the expected signs with most of the
425 variables predicting total scores significant at the 0.05
426 level. At the 6-month interview, a change in mortality
427 risk from 0 to 1 is predicted to reduce total QWB scores
428 by over 25 points. Parent-reported child health, measured
429 by the POPC scale and the CHQ summary measures,
430 explain most of the variance in QWB scores. This
431 finding could be expected because the other measures are
432 captured at the time of ICU admission, while the POPC
433 scale and the CHQ are measured concurrently with the
434 QWB scale. ICU length of stay also explains more of the
435 variance in QWB scores as it captures more information
436 about the clinical course of the admission. ICU length of
437 stay and the QWB scores are negatively correlated while
438 the QWB scale components are positively correlated.
439 The POPC scale has the strongest correlation with the
440 QWB score explaining 48–50% of the variance in the
441 two samples.

442 Discussion

443 The primary goals of this study were to generate data on
444 preference-weighted health outcomes of children following
445 neurocritical care for a TBI and correlate this information
446 with clinical data obtained from the ICU stay. To our
447 knowledge, evidence on preference-weighted health out-
448 comes following traumatic brain injury is unavailable for
449 either children or adults [5]. The lack of preference-
450 weighted health outcome data for children with TBI is
451 typical of other conditions. Obtaining estimates can be
452 problematic for a number of reasons and can lead to an
453 inability to follow Public Health Service (PHS) guidelines
454 for conducting cost-effectiveness analysis [35, 36]. For
455 example, none of the generic instruments for measuring
456 preference-weighted health outcomes was designed to be
457 administered to children less than 5 years of age, even if
458 administered by proxy.

Subjects for the current study were chosen using the
same criteria as a prior study that used hospital adminis-
trative data. In that study, the sample consisted of children
with a CDC-defined TBI that required endotracheal intu-
bation or mechanical ventilation. The main findings in-
cluded evidence that survival probabilities for children
with TBI have improved over time consistent with
improvements in neurocritical care and that survival
probabilities are much worse for uninsured children than
for insured children. To ascertain the cost-effectiveness of
neurocritical care improvements or strategies to improve
survival outcomes for uninsured children with TBI, how-
ever, requires information on the preference scores of
children who survived a TBI following admission for
neurocritical care. In particular, it would be most useful
for CEA to have estimates of the preference scores of potential
‘‘marginal survivors,’’ or children who survived but would
have expired without a more aggressive treatment or some
other intervention that improves survival.

Using subjects from 9 pediatric ICUs, we generated a
relatively large sample of children who suffered a TBI and
required either mechanical ventilation or endotracheal
intubation. The specific scores provided in this study can be
used in CEA of prevention or treatment interventions that
prevent mortality in children from TBI following the PHS
guidelines. Findings from this study include poor outcomes
with QWB scores falling to a low of 0.093. However, in
general, the health outcomes of potentially marginal sur-
vivors are valuable and when used in a CEA, suggest that
the improved outcomes over the period 1988–1999 was
justified [37]. Without data on preference scores as de-
scribed in this study, CEA would have to rely on life years
gained, which may be an inadequate description of relative
value when comparing TBI survivors, for example, to
survivors of acute myocardial infarction [38].

Data from this study also can be used in evaluations of
potential trauma system changes that improve survival
outcomes. One trauma system change that appears worthy
of evaluation is whether reducing the time from injury to
placement of an ICP monitor results in improved survival
and is a cost-effective use of scarce neurosurgical re-
sources. It is well known that use of ICP monitoring is a
marker for more aggressive treatment of TBI with studies
frequently demonstrating that centers with higher rates of
monitoring have improved survival [39]. Data from an
observational study suggested a trend toward improved
survival in TBI patients who received an ICP monitor on
admission relative to later in the stay [11]. The current
study provides some data that also is suggestive of a trend
toward improved outcomes associated with placement of
an ICP monitor on admission. Trauma system changes to
permit more rapid assessment of TBI patients will cost
resources. Data from this study could be used with cost and

Table 3 Quality of well-being preference scores

| | | Injury severity | | | |
|--------------------------------------|--|-----------------|-------|--------|---------|
| | | Overall | Lower | Higher | P-value |
| <i>I. Acute and chronic symptoms</i> | | | | | |
| (1) | Health Symptoms (currently experienced) | | | | |
| a. | blindness/severely impaired vision (both eyes) | 3.1 | 3.0 | 3.2 | 0.738 |
| | blindness/severely impaired vision (one eye) | 6.3 | 6.1 | 6.5 | 0.669 |
| b. | stuttering/unable to speak clearly | 25.4 | 15.2 | 35.3 | 0.052 |
| c. | missing/paralyzed limbs | 10.6 | 6.1 | 15.2 | 0.213 |
| | missing/paralyzed digits | 3.0 | 0.0 | 6.1 | 0.246 |
| d. | any deformity | 4.6 | 0.0 | 9.1 | 0.119 |
| e. | fatigue/weakness | 37.3 | 27.3 | 47.1 | 0.077 |
| f. | weight gain/weight loss | 19.7 | 9.1 | 30.3 | 0.030 |
| g. | underweight/overweight | 16.7 | 9.1 | 24.2 | 0.093 |
| h. | problem chewing food | 4.6 | 0.0 | 9.1 | 0.119 |
| i. | hearing loss/deafness | 1.5 | 0.0 | 3.0 | 0.500 |
| j. | skin problems (acne, burns, scars) | 36.4 | 27.3 | 45.5 | 0.100 |
| k. | eczema/rash | 4.6 | 0.0 | 9.4 | 0.114 |
| Health Aides | | | | | |
| a. | Dentures | 0.0 | 0.0 | 0.0 | 1.000 |
| b. | Oxygen Tank | 0.0 | 0.0 | 0.0 | 1.000 |
| c. | Prosthesis | 3.0 | 3.0 | 3.0 | 0.754 |
| d. | Eye Glasses/Contacts | 33.3 | 39.4 | 27.3 | 0.217 |
| e. | Hearing Aide | 0.0 | 0.0 | 0.0 | 1.000 |
| f. | Magnifying Glass | 0.0 | 0.0 | 0.0 | 1.000 |
| g. | Brace (neck, back, leg) | 12.1 | 12.1 | 12.1 | 0.646 |
| (2) | Physical Problems (any time over 3 day period) | | | | |
| a. | vision not corrected by glasses/contacts | 9.0 | 9.1 | 8.8 | 0.969 |
| b. | eye pain/irritation/discharge/sensitivity to light | 3.0 | 3.0 | 2.9 | 0.983 |
| c. | headaches | 23.9 | 27.3 | 20.6 | 0.521 |
| d. | dizziness/earache/ringing ears | 6.0 | 6.1 | 5.9 | 0.975 |
| e. | difficulty hearing/discharge/bleeding f/ ear | 0.0 | 0.0 | 0.0 | 1.000 |
| f. | stuffy/runny nose/bleeding of nose | 16.4 | 9.1 | 23.5 | 0.111 |
| g. | sore throat/difficulty swallowing/hoarse voice | 7.5 | 3.0 | 11.8 | 0.174 |
| h. | tooth ache/jaw pain | 3.0 | 3.0 | 2.9 | 0.983 |
| i. | sore/bleeding lips/tongue/gums | 1.5 | 3.0 | 0.0 | 0.493 |
| j. | coughing/wheezing | 11.9 | 6.1 | 17.7 | 0.144 |
| k. | shortness of breath/difficulty breathing | 6.0 | 6.1 | 5.9 | 0.975 |
| l. | chest pain/palpitations/irregular heart beat | 1.5 | 0.0 | 2.9 | 0.507 |
| m. | abdominal pain/nausea/heartburn/vomiting | 17.9 | 15.2 | 20.6 | 0.562 |
| n. | pain/rectal area discomfort | 9.0 | 12.1 | 5.9 | 0.371 |
| o. | pain/burning/blood in urine | 1.5 | 3.0 | 0.0 | 0.493 |
| p. | loss of bladder control/frequency/difficulty | 10.5 | 6.1 | 14.7 | 0.247 |
| r. | broken bone (other than in the back) | 0 | 0.0 | 0.0 | 1.000 |
| s. | neck/back pain/stiffness/weakness/numbness | 4.5 | 3.0 | 5.9 | 0.573 |
| t. | hip/side pain/stiffness/weakness/numbness | 7.5 | 9.1 | 5.9 | 0.617 |
| u. | joint pain/stiffness/weakness/numbness | 17.9 | 3.0 | 32.4 | 0.002 |
| v. | swelling of ankles/hands/feet/abdomen | 7.5 | 3.0 | 11.8 | 0.174 |
| w. | fever/chills/sweats | 6.0 | 3.1 | 8.8 | 0.317 |
| x. | loss of consciousness/fainting/seizures | 0.0 | 0.0 | 0.0 | 1.000 |
| y. | difficulty w/ balance/standing/walking | 34.3 | 24.2 | 44.1 | 0.087 |



Table 3 continued

| | | Injury severity | | | (3) |
|---|---|-----------------|-------|--------|---------|
| | | Overall | Lower | Higher | p-value |
| <i>Behavioral Symptoms (any time over 3-day period)</i> | | | | | |
| a. | trouble falling asleep/staying asleep | 25.4 | 24.2 | 26.5 | 0.834 |
| b. | feeling nervous/shaky | 13.4 | 9.1 | 17.7 | 0.305 |
| c. | feeling upset/downhearted/blue | 29.9 | 21.2 | 38.2 | 0.128 |
| d. | excessive worry/anxiety | 17.9 | 9.1 | 26.5 | 0.064 |
| e. | loss of control of life | 28.4 | 24.2 | 32.4 | 0.462 |
| f. | feeling lonely/isolated | 19.4 | 15.2 | 23.5 | 0.386 |
| g. | frustration/irritation/losing temper | 61.2 | 39.4 | 82.4 | <0.001 |
| j. | confusion/memory loss | 25.4 | 23.5 | 27.3 | 0.725 |
| k. | recurring thoughts/images | 20.9 | 15.2 | 26.5 | 0.255 |
| l. | take any medication | 44.8 | 33.3 | 55.9 | 0.064 |
| m. | medically prescribed diet | 9.0 | 0.0 | 17.7 | 0.013 |
| n. | appetite loss/overeating | 4.5 | 0.0 | 8.8 | 0.125 |
| <i>II. Self care</i> | | | | | |
| (5) | (any time over 3-day period) | | | | |
| a. | patient in hospital/rehab center | 4.5 | 3.0 | 5.9 | 0.511 |
| b. | need help w/ personal care | 10.5 | 3.0 | 17.7 | 0.057 |
| <i>IV. Physical activity</i> | | | | | |
| (7) | (any time over 3-day period) | | | | |
| a. | trouble climbing stairs/inclines/walking off curb | 22.4 | 21.2 | 23.5 | 0.526 |
| b. | avoid walking/trouble walking/slow walking | 26.9 | 18.2 | 35.3 | 0.096 |
| c. | limp/uses cane/crutches/walker | 19.4 | 9.1 | 29.4 | 0.035 |
| d. | trouble bending/stooping/kneeling | 23.9 | 18.2 | 29.4 | 0.215 |
| e. | trouble lifting/carrying everyday objects | 23.9 | 15.2 | 32.4 | 0.086 |
| f. | limitations of physical movements | 14.9 | 9.1 | 20.6 | 0.165 |
| g. | spend day in bed/chair due to health | 10.5 | 0.0 | 20.6 | 0.006 |
| h. | spend day in wheelchair | 11.9 | 6.1 | 17.7 | 0.139 |
| <i>V. Usual activity</i> | | | | | |
| (8) | (any time over 3-day period) | | | | |
| a. | need help/avoid work/school/housework | 31.3 | 24.2 | 38.2 | 0.166 |
| b. | avoid recreational/religious activities | 29.9 | 21.2 | 38.2 | 0.104 |
| c. | change plans due to health | 19.4 | 12.1 | 26.5 | 0.119 |

512 effectiveness data to evaluate whether such resources are
513 warranted.

514 Our study confirmed the hypothesis that the QWB
515 scores of children at follow-up would correlate with ob-
516 served measures of injury severity and other health out-
517 come measures. Total QWB scores correlated negatively
518 with risk of mortality at the 3- and 6-month interview.
519 Scores also correlated positively with GCS scores and the
520 summary scales from the CHQ. Evidence on score corre-
521 lations is a necessary first step in establishing the construct
522 validity for measuring preference-weighted health out-
523 comes in children following TBI.

524 The study demonstrates the feasibility of obtaining
525 preference-weighted health outcomes for children

526 following a TBI using caregivers as proxy respondents.
527 There is some concern that proxy responses from primary
528 caregivers in order to rate their child's health will lead to a
529 bias where caregivers rate their child in a health state that is
530 worse than warranted [36, 40]. Systematic bias from
531 caregiver ratings should result in poor correlation between
532 the preference scores and clinical data.

533 The study has a number of limitations. Recruiting and
534 following-up TBI subjects and their families can be diffi-
535 cult and lead to selected samples. We were able to inter-
536 view more than 50% of the families who agreed to
537 participate, but when examined in relation to the number of
538 eligible families, our response rate almost certainly falls
539 below this threshold. It is possible that the families we

Table 4 Univariate linear regression coefficients for predictors of QWB score and subscales

| 6-Month interview | | | | | | | | | | |
|--------------------|---------------|-------|---------------|-------|----------------|-------|----------------|-------|----------------|-------|
| Predictor | QWB | R^2 | CPX | R^2 | MOB | R^2 | PAC | R^2 | SAC | R^2 |
| Risk of mortality | -0.257 | 0.07 | 0.131 | 0.02 | 0.004 | 0.00 | 0.077 | 0.12 | 0.045 | 0.10 |
| Glasgow coma scale | 0.029 | 0.08 | -0.016 | 0.04 | -0.0008 | 0.00 | -0.008 | 0.09 | -0.004 | 0.06 |
| CHQ physical | 0.005 | 0.26 | -0.003 | 0.22 | -0.0004 | 0.23 | -0.0006 | 0.07 | -0.0004 | 0.07 |
| CHQ mental | 0.002 | 0.04 | -0.002 | 0.05 | -0.0001 | 0.00 | -0.0002 | 0.00 | -0.0001 | 0.00 |
| POPC scale | -0.154 | 0.50 | 0.093 | 0.31 | 0.0067 | 0.12 | 0.0346 | 0.44 | 0.198 | 0.37 |
| ICU length of stay | -0.011 | 0.21 | 0.006 | 0.08 | 0.0009 | 0.17 | 0.003 | 0.25 | 0.002 | 0.24 |
| 3-Month interview | | | | | | | | | | |
| Predictor | QWB | R^2 | CPX | R^2 | MOB | R^2 | PAC | R^2 | SAC | R^2 |
| Risk of mortality | -0.202 | 0.05 | 0.076 | 0.00 | 0.002 | 0.00 | 0.082 | 0.11 | 0.041 | 0.07 |
| Glasgow coma scale | 0.025 | 0.06 | -0.016 | 0.05 | -0.001 | 0.00 | -0.004 | 0.00 | -0.004 | 0.04 |
| CHQ physical | 0.003 | 0.19 | -0.002 | 0.13 | -0.0004 | 0.20 | -0.0007 | 0.08 | -0.0004 | 0.06 |
| CHQ mental | 0.002 | 0.11 | -0.002 | 0.12 | -0.0002 | 0.03 | -0.0002 | 0.00 | -0.0003 | 0.06 |
| POPC scale | -0.145 | 0.48 | 0.078 | 0.31 | 0.0076 | 0.08 | 0.038 | 0.38 | 0.022 | 0.33 |
| ICU length of stay | -0.009 | 0.16 | 0.004 | 0.05 | 0.0004 | 0.01 | 0.004 | 0.35 | 0.001 | 0.08 |

Bold indicates coefficient significant at 0.05

QWB: Quality of Well-being total score

CPX: Symptom/complex subscale

MOB: Mobility subscale

PAC: Physical activity subscale

SAC: Social activity subscale

CHQ: Child Health Questionnaire

540 studied are not representative of the average family
 541 treated for severe TBI. Recruitment bias in studies of TBI
 542 indicate suggest specific factors associated with the
 543 admission can result in systematic bias [41, 42]. In par-
 544 ticular, our study appears to be limited in the number of
 545 respondents by public payer status and may be limited by
 546 injury severity. Prior studies suggest a bias toward more
 547 severe patients [42]. Such bias in the context of the
 548 current study appears less of an issue given our interest in
 549 marginal survivors for use in CEA. In addition, the data
 550 aligns to some extent with our prior data on national
 551 hospitalizations leading us to believe that the, scores we
 552 report are likely to be similar on average in larger and
 553 more representative populations.

554 Conclusions

555 Interest in studying the health-related quality of life of
 556 children following traumatic brain injury is increasing.
 557 Recent studies have examined outcome measures for
 558 children that can inform clinical decisions [43–46]. How-
 559 ever, outcome studies that can be used to assess the cost-
 560 effectiveness of interventions to treat or prevent TBI are
 561 lacking in both children and adults [5] despite a vast

562 literature describing preference-weighted outcomes of
 563 other conditions, especially those involving adult popula-
 564 tions. A number of issues have limited the application of
 565 preference-weighted instruments to study child outcomes
 566 [35, 36]. This study provides some of the first evidence
 567 describing preference-weighted outcomes following TBI in
 568 either children or adults. The study provides promising
 569 results for using the QWB scale to study outcomes of
 570 children following TBI.

571 Future research should consider comparing alternative
 572 instruments for measuring preference-weighted outcomes,
 573 as interest in such comparisons in other populations has
 574 burgeoned given that the outcomes are anchored on a 0–1
 575 value scale corresponding to death and perfect health [31,
 576 47–49]. It is possible that alternative instruments to mea-
 577 sure preference-weighted outcomes will return different
 578 scores for the same population. Recent work comparing the
 579 QWB scale to the HUI3 found similar scores in a study of
 580 children with hearing loss [50].

581 Future research should also obtain preference-weighted
 582 outcomes from longer follow-up periods and from studies
 583 using alternative designs. At a time where neurosurgical
 584 resources are limited, new data and new studies designed to
 585 assess the cost-effectiveness of trauma system changes
 586 appear especially warranted.



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