

Measuring the Cost-Effectiveness of Technologic Change in the Treatment of Pediatric Traumatic Brain Injury

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Substantial variation exists with respect to the management of traumatic brain injuries (TBI) in children. Centers that practice aggressive treatment of TBI may improve survival, but it is not clear that the outcomes can be justified using cost-effectiveness criteria. This study illustrates the use of cost-effectiveness analysis to assess interventions for improving outcomes in children by assessing the cost per quality-adjusted life year (QALY) gained from

technological change in the treatment of TBI. Cost and survival data associated with technological change in the treatment of pediatric TBI was based on nationally representative hospital administrative data for all children aged 0 to 21 years with a TBI who required endotracheal intubation or mechanical ventilation. With QALYs of pediatric TBI survivors based on life expectancies ranging between 5 and 30 years and on an estimated preference score of approx-

imately 0.5, the estimated incremental cost-effectiveness ratio ranges between \$19,000 and \$109,000 per QALY gained. Adding estimated rehabilitation costs increases the cost-effectiveness ratio to between \$57,000 and \$244,000 per QALY. Sensitivity analysis indicates that estimates of life year gained are critical to the estimated ratio. If TBI survivors live more than 5 years, then the estimated cost-effectiveness ratio seems favorable.

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Cost-effectiveness analysis (CEA) can be used to evaluate interventions for improving health outcomes in injured children in relation to the costs of the intervention. For example, a trauma system change (intervention) that ensures children are treated in the most appropriate setting likely will increase system costs, but may improve outcomes. A CEA evaluates the cost per life year gained or the cost per quality-adjusted life year (QALY) gained from the trauma system change. CEA is most useful when cost-effectiveness ratios can be compared across different interventions such as the cost per life year gained from treating children in pediatric facilities relative to the cost per life year gained from more aggressive treatment for heart failure in elderly adults. If a treatment has a high cost per life year saved, especially relative to other treatments, one could use this information in evaluating whether a given treatment or system change seems warranted. Such comparisons, however, are valid if and only if CEA is performed according to standard methods.

The US Public Health Service (USPHS) convened a panel of experts to provide guidelines for conducting CEA of health interventions.¹ The resulting reference case analysis developed by the panel embodied the set of standard procedures for conducting CEA. Tilford described issues associated with incorporating the USPHS guidelines in evaluations of emergency medical services for children,² especially the recommendation to use QALYs as the metric for measuring health outcomes.^{3,4} In particular, the USPHS panel recommended that QALYs be calculated using generic instruments so that health state values (variably referred to as preference weights or utilities) reflect community preferences. Pi-by-no instruments to measure QALYs, like other instruments to measure health-related quality of life, need to be age appropriate. Current instruments cannot be administered to young children and are not appropriate for children less than 5 years of age irrespective of whether a proxy is used to ascertain health states. Issues with the measurement of QALYs in children raised concerns as to whether the USPHS guidelines were appropriate for pediatric populations.⁵

QALYs are recommended for use in CEA because they combine gains in life years with a measure of health-related quality of life that can be scored to reflect preferences for health states.⁶ Most health state valuation techniques include a range from death (a preference weight of 0) to perfect health (a preference weight of 1).⁷ If QALY-based outcomes are used in CEA, then interventions used in the treatment of pediatric traumatic brain injuries (TBI) can be compared with interventions involving distinct patient groups such as elderly patients with acute myocardial infarction. In general, an incremental cost-effectiveness ratio (ICER) is calculated as $(Cost_b - Cost_a)/(QALY_b - QALY_a)$ ⁶ or the difference in costs divided by the difference in QALYs for patients in an intervention group (*b*) relative to a control group (*a*).

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Thus, generic instruments to preference-weight health outcomes are essential for calculating QALYs following the USPHS guidelines. To date, only two studies have measured preference-weighted health outcomes in children after a TBI with generic instruments. One study examined outcomes in children after decompressive craniotomy using the original Health Utilities Index.⁸ Recently, Tilford et al. reported TBI outcomes using the QWB scale.⁹ Given the lack of studies describing preference-weighted outcomes in children (or adults) after injuries, it is not surprising that only one economic evaluation provided information on traumatic injuries that followed the USPHS guidelines. Stein et al. examined indications for cranial computed tomography scanning after mild TBI using CEA.¹⁰ They used a decision-analytic model with outcome probabilities for the Glasgow Outcome Scale. The Glasgow Outcome Scale was assigned preference weights to permit a ranking of decisions based on the cost per QALY gained.

The primary goal of this study was to illustrate the issues involved in the measurement of ICERs associated with interventions to improve pediatric trauma outcomes that follows the USPHS guidelines. In particular, we focus on measuring the effectiveness of an intervention, the outcomes of the intervention, life expectancy for survivors of the intervention, and costs associated with the intervention. We illustrate these measurement issues in an evaluation of technological change in the treatment of pediatric TBI patients, which improved survival in this population over time. The study calculates costs based on changes in acute hospitalization costs and rehabilitation costs discounted to present value terms. QALY gains are based on recent descriptions of preference-weighted health outcomes in children after TBI. The findings provide an assessment of whether recent survival gains from technological change in the treatment of pediatric TBI are justified using cost-effectiveness criteria. Finally, the article provides a discussion of the critical issues that need to be addressed to assess the cost-effectiveness of interventions to provide optimal care to children such as a proposed study on the costs and outcomes of trauma for kids.

METHODS

The USPHS recommended that cost-effectiveness evaluations take a societal perspective in describing costs and outcomes. The measurement of ICERs from a societal perspective requires estimates for a number of key parameters. In this section, we describe critical parameters for calculating ICERs based on the cost per QALY gained.

Effectiveness

Our primary measure of effectiveness in this article is changes in survival probabilities associated with improved treatment for pediatric TBI. Our recent work indicates improved outcomes associated with hospitalizations for pediatric TBI possibly because of more aggressive treatment.¹¹ Thus, we used data from that study, which was based on the

Healthcare Cost and Utilization Project (HCUP), to obtain estimated gains in survival probabilities for children hospitalized with a TBI in this study. The HCUP is a federal/state partnership that produces a family of health care databases, including the Nationwide Inpatient Sample (NIS). The NIS contains hospital administrative data from a number of states covering the period 1988 to 2004. The data from the state inpatient databases is coded uniformly and then a 20% stratified random sample of all US community hospitals (defined as short-term, non-federal, general and specialty hospitals, excluding hospital units of other institutions) is drawn and weighted to produce national estimates.¹² The NIS includes 100% of discharges for all age groups and all payers from each sampled hospital. It contains data from approximately 1,000 hospitals and includes 7 million to 8 million hospital discharges annually.

All children aged 0 to 21 years with a Centers for Disease Control and Prevention-defined TBI¹³ that included a procedure code for endotracheal intubation or mechanical ventilation were identified from the NIS for the years 1988 to 1999 after our prior work. ICDMAP90 software was used to generate estimates of the injury severity scores.^{14–16} Survival probabilities for this study were estimated from the HCUP data using a logistic regression model with the injury severity scores and other covariates to generate risk-adjusted survival during the entire study period. The “adjust” command in Stata was then used to generate predicted mortality rates for the average patient in each study period. The resulting estimates provide gains in survival probabilities for the years 1989 to 1999 relative to the reference period (1988).

Outcomes

The study sought to follow the USPHS panel recommendation of using QALYs as the metric for the denominator in CEA. Indeed, the panel recommended the development of “off-the-shelf” preference scores for use in CEA, recognizing that most investigators do not have the resources to collect original data on preference-weighted health states.¹⁷ This study highlights this recommendation as we use preference scores developed from our prior study.⁹ Preference-weighted health outcomes in children who survived a TBI hospitalization were reported from a cohort of children admitted to 10 pediatric intensive care units (PICUs) that were located nationally. Subject inclusion criteria followed the inclusion criteria for estimating survival probabilities and required that the child be less than 18 years of age and admitted to the PICU with a Centers for Disease Control and Prevention-defined TBI¹³ that required either endotracheal intubation or mechanical ventilation. An initial description of these outcomes and construct validity has been reported elsewhere.⁹ Scores ranged from 0.09 to 1.00 at 3 and 6 months after discharge from the ICU, but mean scores increased from 0.51 to 0.58 between the two periods. Scores were correlated with clinical characteristics, injury severity, and other health-related quality of life measures.

Mean scores are typically used to describe preference-weighted health outcomes because of their use in QALY calculations.¹⁸ However, the use of average measures of preference-weighted health outcomes based on a cohort of survivors may overstate the true gain from technological advances. Ideally, information on “marginal” patients that survived a TBI who might have died with less aggressive treatment provides a better estimate for QALY estimation. The concept of the marginal patient does not imply that the child will have a marginal existence, but that the child is a survivor who would have died without the intervention. To reflect better the preference scores of marginal survivors, this study used weights based on children with higher risks of mortality than the average patient in the cohort and then conducted sensitivity analysis for different values. In particular, we used scores only for children that required intracranial pressure monitoring because this procedure typically is associated with more aggressive treatment.¹⁹ Finally, we used weights from the 6-month outcome data and did not alter them during the estimated gain in life years.

Life Expectancy

In this study, survivors are expected to live more than 1 year, but a number of issues need to be considered in calculating life expectancy. Some studies use life tables for calculating life expectancy based on the average age of the cohort and then adjust for increased risk of mortality caused by the illness or injury.¹⁰ For example, using life tables, a 10-year-old child could be expected to live an additional 68.2 years on average. However, the mortality experience of survivors of a TBI, especially marginal survivors, is likely to differ considerably from population averages. Recent work on life expectancies after TBI suggests that life expectancy will differ significantly depending on the functional outcome of the patient after hospital discharge.^{20,21} Patients with moderate disabilities were found to have a 4-year reduction in life expectancy, whereas patients rated as extremely severe were found to have a life expectancy only 50% of the population average.²² A study of children and adolescents after TBI also found substantial reductions in life expectancy when severe functional limitations were present.²³ For a child aged 15 years, life expectancy was an additional 14.9 years if the child was not mobile, 34.2 years if the child had poor mobility, and 54.8 years if mobility was fair or good.

Given the lack of precise data on life expectancy for pediatric populations, we calculated life expectancies during a wide range to account for uncertainty in actual estimates. QALYs were compared during a range including 5-year gains in life expectancy up to a maximum of 30 years. Survival gains beyond 30 years have little impact on estimated cost-effectiveness ratios in this example because of discounting where impacts that far into the future have little weight in present terms. With discounting of life expectancy and with all costs incurred in the first year, the ICER calculation

becomes $\frac{\Delta Cost}{\Delta p \sum_t \mu_t / (1+r)^t}$. In this calculation, δp is the change

in survival probability generated by the intervention, μ_t is the preference weight for calculating the QALY in year t , r is the discount rate and assumed to be 3%, and t is the expected life years gained for survivors affected by the intervention.

Costs

For this study, we captured data on two cost categories, the cost of inpatient hospitalizations and the cost of rehabilitation service use for survivors. To measure the cost of inpatient hospitalizations, we based the analysis on hospital charges in the NIS database and calculated the marginal change in charges during the study period using the same methods that were used to calculate survivor probabilities. Again, linear regression models were used to estimate hospital charges and expressed as the change in spending for the average patient during the course of the study period using the Stata adjust command. No attempt was made to generate costs from cost-to-charge ratios because the HCUP databases do not capture all of the relevant costs of the hospitalizations. Data on physician charges and emergency department charges are not captured. The approach is similar to that used in other studies where only Medicare Part A claims were used to capture changes in the cost of heart attack treatments.²⁴ All charges were converted to 2000 dollars using the US implicit price deflator.

Rehabilitation services were measured at the 3- and 6-month follow-up interviews from the cohort of children recruited from the network of PICUs. A reminder card was mailed to respondents before the interview asking them to record visits to medical providers after discharge from the hospital. Respondents indicated whether their child received a particular service and the number of services during the preceding 3-month period. Service utilization was converted into cost data using Medicare pricing schedules for the particular service. The resulting cost index was correlated with severity measures obtained during the PICU stay as a test of construct validity. Rehabilitation service costs were significantly associated with severity measures.²⁵ Following strategies used in the analysis of QALYs, only rehabilitation costs for children that received an ICP monitor were used in actual calculations.

RESULTS

Figure 1 provides estimated improvements in survival probabilities for pediatric TBI patients abstracted from the NIS during the period 1988 to 1999. By the end of the study period, survival probabilities increased 8.3% points or 8.3 per 100 TBI patients treated. This estimate is similar to estimated survival gains for elderly heart attack patients (9.8 per 100) during the period 1986 to 2002.²⁴

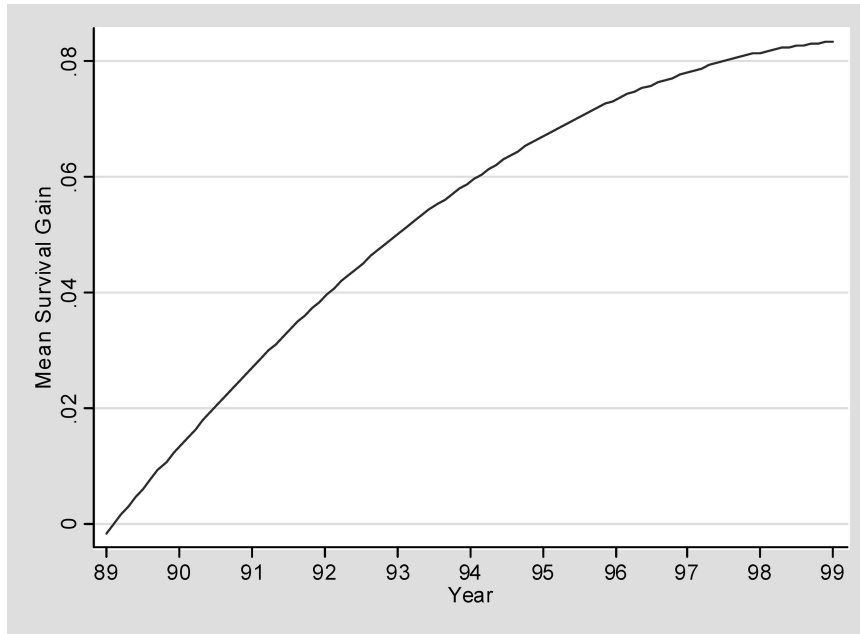


Fig. 1. Adjusted mean survival gain: 1989 to 1999.

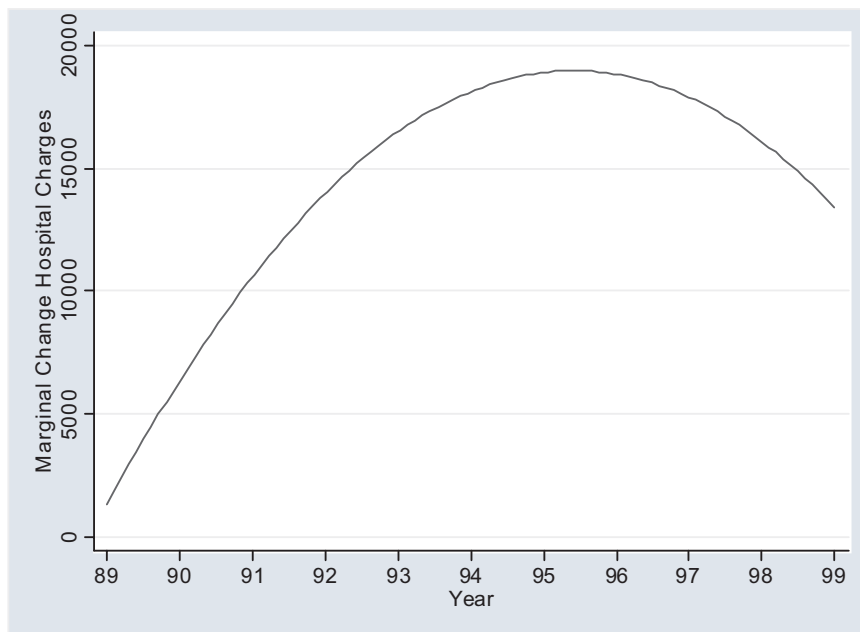


Fig. 2. Adjusted change in hospital charges: 1989 to 1999.

Figure 2 provides estimated increases in real hospital charges (in 2000 US dollars) during the same period. Hospital charges for pediatric TBI patients increased to a maximum of \$19,000 and then fell to approximately \$13,000. The estimates fall close to the increase in Medicare Part A claims associated with treating heart attacks in the elderly (\$12,399 in 2003 US dollars).²⁴

Table 1 reports post-acute care service utilization and costs for the first 3-month period and the period from 3 to 6 months postdischarge from the ICU using our cohort of children recruited from the 10 PICUs. The use of post-acute

care services was greater during the 3 months after discharge than at 6 months. On average, children who required an ICP monitor used approximately \$18,600 worth of services in the immediate period after discharge. Service costs decreased by approximately 50% between the 3-month follow-up interview and the 6-month follow-up interview. Assuming that service use declines linearly over time, the average cost per patient is approximately \$35,750 in the first year after discharge from the PICU.

Figures 3 and 4 summarize the ICERs, where the increment is defined for surviving children relative to nonsurviv-

F3-F4

Table 1 TBI Post-Acute Care Service Utilization

Rehabilitation Service	Probability of Service Use	Number of Visits/Day	Price per Visit/Day	Average Total Cost
3 mo				
Inpatient rehabilitation	0.313	43.6	\$739	\$10,085
Physical therapy	0.746	25.2	\$105	\$1,974
Occupational therapy	0.687	26.6	\$105	\$1,919
Speech or language therapy	0.627	24.4	\$114	\$1,744
Counseling	0.149	15.0	\$154	\$344
Visiting nurse	0.106	6.0	\$96	\$61
Home health aid	0.062	19.8	\$43	\$53
Special education	0.269	22.4	\$85	\$512
Tutors	0.209	24.4	\$85	\$433
Medications	0.507	90.0	\$2	\$91
6mo				
Inpatient rehabilitation	0.090	43.6	\$739	\$2,900
Physical therapy	0.430	25.8	\$105	\$1,165
Occupational therapy	0.392	25.8	\$105	\$1,062
Speech or language therapy	0.380	27.6	\$114	\$1,196
Counseling	0.180	8.0	\$154	\$222
Visiting nurse	0.040	6.0	\$96	\$23
Home health aid	0.000	0.0	\$43	\$0
Special education	0.256	50.5	\$85	\$1,099
Tutors	0.177	34.7	\$85	\$522
Medications	0.506	90.0	\$2	\$91

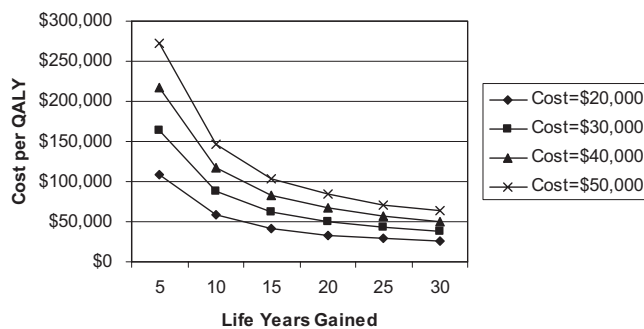


Fig. 3. Incremental cost-effectiveness ratios for pediatric TBI patients with utility = 0.47.

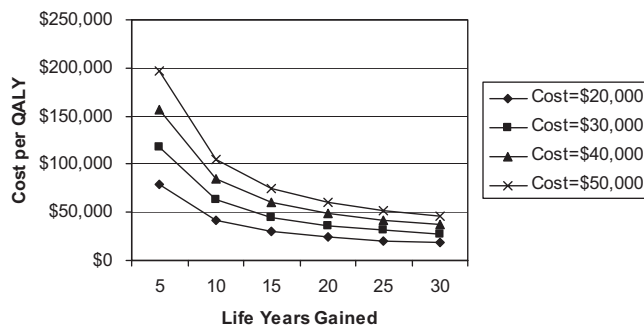


Fig. 4. Incremental cost-effectiveness ratios for pediatric TBI patients with utility = 0.65.

ing children. Sensitivity analysis is presented according to the cost of producing additional survival, the number of life years gained, and the preference score of the marginal survivor. In

Figure 3, a utility score of 0.47 is used with a survival gain of 0.083. Under these assumptions, the cost per QALY varies from a high of over \$250,000 to less than \$25,000. Estimated life expectancy of survivors has a large impact on estimated ICERs. If life expectancy approaches 15 years, which seems reasonable, then the estimated ICERs fall under or close to the \$100,000 per QALY acceptability threshold.²⁶ In Figure 4, the estimated utility value was increased to 0.65, which may be consistent with the view that TBI survivors have improving outcomes over time. Changing the utility value to 0.65 reduces the amount of life years gained necessary to achieve acceptable ranges of cost-effectiveness. With this utility gain, 10 years of additional life years produces ICERs in the acceptability range. Thus, under reasonable assumptions concerning the cost of technical change and the utility value attributed to the child's outcome, the ICERs seem favorable with life expectancies between 10 and 15 years.

If we calculate the costs per life year gained, following previous studies,²⁴ and ignore the issue of preference-weighting health outcomes, the estimated ICERs fall between \$38,000 and \$115,000 over the range of assumed costs. This range clearly falls in the acceptability range for cost-effectiveness ratios and indicates that technological change in the treatment of pediatric TBI in children, like the treatment of heart attacks in the elderly, is worth the cost.

DISCUSSION

Technological advances in medicine that produce effective interventions in the form of better drugs, devices, or

systems of care are generally thought to improve health care outcomes. Economists refer to these improvements as productivity changes.²⁷ Understanding productivity changes in health care is particularly important as new research on the value of life suggests that increased spending on health care may generate benefits well in excess of costs.²⁸ Prior research on productivity changes focused on improving survival with the majority of research addressing technological change in the treatment of heart attacks.²⁹ One study examined productivity improvement in child injury from advances in child safety.³⁰ Our prior research found evidence of productivity improvement in the treatment of pediatric TBI most likely because of more aggressive use of intracranial pressure monitoring over time.¹¹

Evidence of productivity improvement based on survival gains may not provide the most accurate evaluation because it ignores quality of life issues. The USPHS panel on cost-effectiveness recognized the need to incorporate both survival and quality of life changes in economic evaluations. Thus, the panel recommended the use of QALYs as the metric for conducting CEA.

This study follows the recommendations of the USPHS panel and provides an analysis of technological change in the treatment of pediatric TBI by evaluating the cost per QALY gained. The findings from this study suggest that the survival gain in children during the period 1988 to 1999 was likely cost-effective. ICERs for the cost per life year gained and QALY gained seemed acceptable under reasonable assumptions for the cost of improving outcomes. Costs were based on hospital charges and post-acute care service utilization in the year after discharge.

The findings can inform the management of pediatric TBI patients. Some clinicians may question whether more aggressive treatment of TBI provides benefit in excess of costs.³¹ This study, along with our findings on preference-weighted health outcomes in children with brain injuries, provides evidence that the outcomes of children who survive a brain injury are valuable in economic terms.

The study has a number of limitations, including the estimation of survival gains over time, the use of a small sample of children to estimate preference-weighted health outcomes and rehabilitation costs, and the lack of precise estimates to describe life expectancy for children that survive a TBI because of an intervention. Still, the study provides an excellent example of the challenges analysts need to overcome to conduct CEA from the societal perspective following the recommendations of the USPHS panel. In the remainder of this section, we describe these issues in detail to provide a framework for considering a prospective study to measure trauma costs and outcomes in a pediatric population.

Cost Estimation

The cost of technological change in the treatment of injuries and illness should include a number of components and rely on cost, not charges. The HCUP provides excellent

data for examining trends in hospital outcomes and hospital charges over time, but lacks a number of cost components that can be captured under a claims-based system such as Medicare. It is possible to convert charges to cost with average cost to charge ratios, but such calculations are unlikely to alter findings in longitudinal data if cost-to-charge ratios are approximately constant during the study period. Advances in the HCUP database that provide average cost-to-charge ratios according to institutional characteristics would greatly improve cost estimates.³² Cost-to-charge ratios likely differ considerably according to pediatric and nonpediatric hospitals or teaching and nonteaching hospitals.

In a prospective study of children, it will be possible to capture cost data at the department level if institutions have the necessary capabilities. Resource-based systems for cost accounting have been used in a number of studies. Such studies often use proprietary software for capturing cost data.

In this longitudinal analysis, we also did not consider productivity costs for the child or the caregiver. This exclusion was because of two factors. First, we captured the survival gains in terms of QALY. It is standard, although controversial, to exclude productivity differences in analyses using QALYs as it is assumed that the QALYs already capture productivity gains and including them constitutes double counting.³³ Second, we measured ICERs relative to children that die. It is not (currently) possible to capture incremental productivity differences for caregivers of surviving and dying children. Although it might be possible to relate caregiver productivity losses to QALYs of surviving children, such a procedure would capture differences between surviving children and healthy children, not surviving children and dying children.

Caregiver productivity costs could be considered in a prospective study of optimal treatment strategies for children after trauma. Strategies that improve outcomes in surviving children may impact caregiver work productivity, sleep, and leisure.³⁴ Cross-sectional estimates of these differences can be used to generate lifetime values.³⁵ Failure to incorporate important “family spillover effects” in CEA results in an underestimate of the full costs and benefits of effective interventions.³⁶

We also did not consider the issue of future costs that account for the difference in consumption and productivity.³⁷ Such calculations require estimates of future productivity for children after a severe TBI. If marginal survivors have consumption costs in excess of productivity, ICERs would be understated.

Preference-Weighted Health Outcomes

We used data on preference-weighted health outcomes from a cohort of children that survived a TBI.⁹ An analysis of the correlation in preference scores with clinical data obtained from the ICU admission suggested that such scores have construct validity. In theory, the scores can be used to consider acceptable ranges for conducting CEA as presented in this study. Still, the scores have limitations in that the

average score of the cohort may not reflect the score for the marginally surviving child where marginal implies a child who survived but would have died without the intervention. For this reason, we considered scores in the lower range of the cohort in the CEA. We also considered higher scores as little data describes preference scores associated with children after injury and that data relies on relatively short time periods. It is possible that children in the cohort, even marginally surviving children, will have higher scores in future periods with recovery from functional limitations.

The outcomes of the marginal survivor merit concerns in a longitudinal study of survival, but are unlikely to be an issue in a prospective study where outcomes can be compared across types of institutions. Such estimates represent marginal changes in outcomes. This issue also is less important in decision-analytic studies of treatment strategies as outcomes can be modeled in probability terms. Stein et al. used preference scores associated with the Glasgow Outcome Scale, but it is not clear how the scores were actually obtained.¹⁰

Consistent with recommendations from the US Panel on Cost-effectiveness, additional data on the preference scores of children captured at different time periods is needed to improve overall ICER estimates. Failure to use preference-weighted health outcomes in CEA reduces the ability to compare interventions and appropriately guide the allocation of resources.

Life Years Gained

Calculation of the ICER requires an estimate of life years gained for children that survived a TBI. As was the case with estimates of preference-weighted health outcomes, estimates of life years should be based on marginally surviving children (which again, does not imply a marginal existence in functional status terms). Data on the life expectancy of children after a TBI suggest that severe functional limitations can reduce life expectancy, but even children with severe limitations will survive 15 years or more.²³ It is probable that surviving children, even marginally surviving ones, might survive 30 years or more. This study calculated ICERs during a 30-year range and found that the evidence pointed to favorable ICERs if the average life expectancy exceeded 10 years or the cost of the intervention was in the lower end of the estimated range. Thus, how analysts address the issue of life expectancy can have a great influence on the estimated ICER.

Stein et al. used average life expectancy discounted to present value terms in their analysis adjusted for differences in life expectancy for TBI survivors.¹⁰ Such calculations were not possible in this study as current estimates are not available for young children. Still, it seems that remaining life expectancy of surviving children will exceed 15 years.

Effectiveness of Interventions to Improve Survival

In the case of elderly persons that suffered a heart attack, technological improvements in treatment brought about a large increase in survival during the period 1986 to 2003. Recent examination of outcome data, however, indicates a flattening of survival with increases in treatment costs. Data from this period do not suggest favorable ICERs. It is likely that survival gains are subject to the economic law of diminishing returns, especially in the relatively short run. Diminishing returns suggests that the cost of obtaining additional gains in survival will increase as productivity improves, given that gains are limited to 100% survival. The first intervention might be the least costly or most likely to improve outcomes. Subsequent gains in survival may be more difficult and/or costly to achieve. At the same time, it is possible that less-effective interventions to improving outcomes will cost less than interventions with large improvements in outcomes.

This study used longitudinal hospital data to estimate survival gains for children with a TBI. We relied on severity-adjusted estimates to obtain survival gains, but these estimates assume that admitting decisions at hospitals have not changed over time. A prospective study has the advantage of better control in selecting patient populations for making comparisons.

CONCLUSIONS

The US Panel on Cost-Effectiveness of Health Interventions suggested the use of QALYs as a metric in the calculation of ICERs. This study illustrates the calculation of ICERs based on QALYs to evaluate technological progress in the treatment of TBI in children. Over a range of reasonable assumptions, the ICERs are favorable and suggest that the improved outcomes that occurred during the period 1988 to 1999 were cost-effective. Estimated ICERs could be improved by better identification of marginal patients for cost and QALY calculations. The study provides a framework for considering the cost-effectiveness of other health interventions that lead to optimal care for injured children. Careful examination of the data indicates that assumptions concerning preference-weighted health outcomes and life expectancy of surviving children will have the most impact on estimated ICERs.

REFERENCES

1. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press; 1996:1–425.
2. Tilford JM. Cost-effectiveness analysis and emergency medical services for children: issues and applications. *Ambul Pediatr*. 2002; 2:330–336.
3. Gold MR, Patrick DL, Hadorn DC, et al. Identifying and valuing outcomes. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press; 1996:82–134.
4. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 1996;276:1253–1258.

5. Griebisch I, Coast J, Brown J. Quality-adjusted life-years lack quality in pediatric care: a critical review of published cost-utility studies in child health. *Pediatrics*. 2005;115:e600–e614.
6. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford: Oxford University Press; 1997.
7. Neumann PJ, Goldie SJ, Weinstein MC. Preference-based measures in economic evaluation in health care. *Annu Rev Public Health*. 2000;21:587–611.
8. Taylor A, Butt W, Rosenfeld J, et al. A randomized trial of very early decompressive craniectomy in children with traumatic brain injury and sustained intracranial hypertension. *Childs Nerv Syst*. 2001;17:154–162.
9. Tilford JM, Aitken ME, Goodman AC, et al. Child health-related quality of life following neurocritical care for traumatic brain injury: an analysis of preference-weighted health outcomes. *Neurocrit Care*. 2007;7:64–75.
10. Stein SC, Burnett MG, Glick HA. Indications for CT scanning in mild traumatic brain injury: a cost-effectiveness study. *J Trauma*. 2006;61:558–566.
11. Tilford JM, Aitken ME, Anand KJ, et al. Hospitalizations for critically ill children with traumatic brain injuries: a longitudinal analysis. *Crit Care Med*. 2005;33:2074–2081.
12. HCUP Databases. *Healthcare Cost and Utilization Project (HCUP)*. Rockville, MD: Agency for Healthcare Research and Quality; 2004.
13. Thurman D, Guerrero J. Trends in hospitalization associated with traumatic brain injury. *JAMA*. 1999;282:954–957.
14. Baker SP, O'Neill B, Haddon W, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma*. 1974;14:187–196.
15. Durbin DR, Localio AR, MacKenzie EJ. Validation of the ICD/AIS MAP for pediatric use. *Inj Prev*. 2001;7:96–99.
16. MacKenzie EJ. Injury severity scales: overview and directions for future research. *Am J Emerg Med*. 1984;2:537–549.
17. Bell C, Chapman RC, Sandberg EA, Stone PW, Neumann PJ. An off-the-shelf help list: a comprehensive catalog of preference weights from published cost-utility analyses. *Med Decis Mak*. 1999;19:519.
18. O'Brien BJ, Spath M, Blackhouse G, Severens JL, Dorian P, Brazier J. A view from the bridge: agreement between the SF-6D utility algorithm and the Health Utilities Index. *Health Econ*. 2003;12:975–981.
19. Bulger EM, Nathens AB, Rivara FP, et al. Management of severe head injury: institutional variations in care and effect on outcome. *Crit Care Med*. 2002;30:1870–1876.
20. Harrison-Felix C, Whiteneck G, DeVivo M, Hammond FM, Jha A. Mortality following rehabilitation in the Traumatic Brain Injury Model Systems of Care. *NeuroRehabilitation*. 2004;19:45–54.
21. Brown AW, Leibson CL, Malec JF, Perkins PK, Diehl NN, Larson DR. Long-term survival after traumatic brain injury: a population-based analysis. *NeuroRehabilitation*. 2004;19:37–43.
22. Strauss D, Shavelle RM, Devivo MJ, Harrison-Felix C, Whiteneck GG. Life expectancy after traumatic brain injury. *NeuroRehabilitation*. 2004;19:257–258.
23. Strauss DJ, Shavelle RM, Anderson TW. Long-term survival of children and adolescents after traumatic brain injury. *Arch Phys Med Rehabil*. 1998;79:1095–1100.
24. Skinner JS, Staiger DO, Fisher ES. Is technological change in medicine always worth it? The case of acute myocardial infarction. *Health Aff (Millwood)*. 2006;25:w34–w47.
25. Tilford JM. *Economic Evaluation of Intensive Care Services for Pediatric Traumatic Brain Injury Patients*. 2007. Final Report to the Health Resources and Services Administration.
26. Eichler HG, Kong SX, Gerth WC, Mavros P, Jonsson B. Use of cost-effectiveness analysis in health-care resource allocation decision-making: how are cost-effectiveness thresholds expected to emerge? *Value Health*. 2004;7:518–528.
27. Cutler DM, Huckman RS. Technological development and medical productivity: the diffusion of angioplasty in New York state. *J Health Econ*. 2003;22:187–217.
28. Murphy K, Topel R. Diminishing returns? The costs and benefits of improving health. *Perspect Biol Med*. 2003;46:S108–S128.
29. Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975–1995. *Am J Med*. 2001;110:165–174.
30. Glied S. The value of reductions in child injury mortality in the United States. In: Cutler DM, Berndt ER, eds. *Medical Care Output and Productivity*. Chicago, IL: The University of Chicago Press; 2001:511–534.
31. Kumar R, West C, Quirke C, et al. Do children with severe head injury benefit from intensive care? *Childs Nerv Syst*. 1991;7:299–304.
32. Friedman B, De La MJ, Andrews R, McKenzie DH. Practical options for estimating cost of hospital inpatient stays. *J Health Care Finance*. 2002;29:1–13.
33. Koopmanschap M, Burdorf A, Jacob K, Meerding WJ, Brouwer W, Severens H. Measuring productivity changes in economic evaluation: setting the research agenda. *Pharmacoeconomics*. 2005;23:47–54.
34. Grosse SD, Flores A, Robbins JM, Tilford JM. Impacts of spina bifida on parental caregivers: findings from a survey of Arkansas families. 2007.
35. Tilford JM, Grosse SD, Goodman AC, Li K. Time costs for caregivers of children with spina bifida: a population based analysis. 2004.
36. Basu A, Meltzer D. Implications of spillover effects within the family for medical cost-effectiveness analysis. *J Health Econ*. 2005;24:751–773.
37. Meltzer D. Accounting for future costs in medical cost-effectiveness analysis. *J Health Economics*. 1997;16:33–64.

DISCUSSION

Dr. Scheidt: A number of this morning's comments related to aspects of the National Children's Study, which is the largest long-term study of children's health and development that's ever been proposed. It proposes to follow 100,000 mother/child pairs from as early as possible in pregnancy until that child reaches adulthood, and to link a wide range of environmental exposures and genetic factors to children's health and development. It was proposed originally by a presidential task force and convened in the late 1990s, chaired by the Secretary of Health and Human Services and the Administrator of the Environmental Protection Agency with seven other cabinet officers charged to develop national strategies for reducing environmental effects on children's health and development. That task force very quickly came to the realization that there were not the data that would allow them to meet that charge and a program of research capable of defining the risks and guiding policy would be necessary. In the fall of 2000, Congress passed the Children's Health Act, which authorized NICHD and a consortium of federal agencies to go forward with the planning and implementation of this large study.

As conceived then and as planned now, the study will measure a wide range of environmental exposures, including various chemical exposures, factors of family, parenting, and neighborhood characteristics. It will examine multiple outcomes, neurocognitive development, growth, sexual matu-

ration, behavior, mental health conditions, such as autism, attention deficit, schizophrenia, aggression, and, of course, asthma and obesity because of the prevalence of those conditions in today's children.

What's the relationship of this study to the comments this morning about a large study of pediatric trauma? Certainly one could see the possibility of the opportunity for collecting prospective pretrauma data from a study like this. The NCS would enable measures of family, neighborhoods, nutritional status, and developmental status that could be important as determinants and predictors of outcomes of trauma. It offers the opportunity for long-term follow-up of development and function in the cohort as it progresses to adulthood.

Collecting detailed trauma care data are more problematic. As a matter of course in the study, we intend to collect healthcare data, but it would take some considerable enhancements to collect the trauma data that might be important for the kinds of studies that have been discussed here today.

Sample size is a bigger question. One hundred thousand seems like a lot of participants, but there would be still relatively few seriously injured children. By our estimates, hospitalized children for head trauma might be in the range of 1.5 to 2 per thousand, and that's the low end of the capability of this study to detect effects of alternatives in management and treatment for a relative risk of about two. Much more seriously and less frequently injured participants might be even less common and have less power.

Dr. Wilfond: Even if something occurs with an incidence as low as one in a thousand, that will still be a hundred

people for which you'll have such richly collected pre and post event data. That it still strikes me as being an incredible opportunity, even to do some sort of focused evaluation.

Male: There will be 17 years before he gets data on a 17-year-old, however.

Dr. Clark: We can predict that the environmental agent that will have the greatest effect on the health of these children will be the automobile. Will your study look at risk factors for that particular agent being deleterious in their health?

Dr. Scheidt: Clearly it will capture events related to automobile injuries, including distance of residence from motorways.

Male: It's going to look at neighborhood factors, parental supervision factors, socioeconomic factors, dynamics in the family, the developmental status of the child, and those factors that we see in our clinical practice as affecting risk of a motor vehicle injury. The limiting factor is going to be how many children in the first 5 years are going to be injured by motor vehicles.

Dr. Scheidt: If there are specific hypotheses that represent an opportunity to examine in more detail than would otherwise be collected as a matter of course, there's opportunity for enhancing the study or adding adjunct studies onto this platform. The Women's Health Initiative had more than 250 proposed and 98 funded ancillary studies in that large, longitudinal study. We anticipate that perhaps even the major contribution of this study will be the opportunity for those kinds of additional projects.

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES

1

AQ1— Please check whether the short title is OK as given.

AQ2— Is the expression 'children aged 0 to 21 years' valid?

AQ3— Please spell out 'QWB.'

AQ5— Kindly confirm update of Ref. 9.

AQ6— Please provide the publisher and location details for Ref. 25.

AQ7— Please provide the journal title, Vol. no., and page range details for Refs. 34 and 35.

AQ4— Please spell out 'NICHD' and 'NCS'.
