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ORIGINAL RESEARCH

# Long-Term Survival After Traumatic Brain Injury Part I: External Validity of Prognostic Models

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**Abstract**

**Objectives:** To develop prognostic models for long-term survival in adults with traumatic brain injury (TBI) and to assess their external validity in 2 independent populations.

**Design:** Survival analysis.

**Setting:** Post-discharge from rehabilitation units and long-term follow-up at regional centers.

**Participants:** Two cohorts of long-term survivors of TBI (N=12,481): the Traumatic Brain Injury Model Systems (TBIMS) cohort comprised 7365 persons who were admitted to a TBIMS facility and were assessed at ≥1 years postinjury, and the California Department of Developmental Services (CDDS) cohort comprised 5116 persons who sustained a TBI and received long-term services from the CDDS.

**Interventions:** Not applicable.

**Main Outcome Measures:** Survival/mortality.

**Results:** Older age, male sex, and severity of disability in walking and feeding were significant predictors of increased long-term mortality rates (all $P<.05$, both databases). The CDDS model predicted 623 deaths for persons in the TBIMS cohort, with an observed-to-expected ratio of .94 (95% confidence interval [CI], 0.87−1.02). The TBIMS model predicted a total of 525 deaths for persons in the CDDS cohort, with an observed-to-expected ratio of 1.08 (95% CI, 0.99−1.17). Regression calibration statistics were satisfactory, and both models ranked survival times well from shortest to longest (TBIMS: C index, .78; 95% CI, .76−.80; CDDS: C index, .80; 95% CI, .78−.82).

**Conclusions:** Long-term survival prognosis in TBI is related to age, sex, and severity of disability. When compared on the basis of these factors, the survival estimates derived from the TBIMS and CDDS cohorts are found to be similar. The close agreement between model predictions and actual mortality rates confirm the external validity of the prognostic models presented herein.

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Mortality rates of persons who have sustained a traumatic brain injury (TBI) with long-term disabilities are higher than those of the general population.[1-16] Because of this, individual prognosis for survival should be based on the mortality experience of persons with similar injuries and disabilities rather than on standard government tables. For example, Shavelle et al[7] found that life expectancies of persons with TBI who received services from the California Department of Developmental Services (CDDS) varied dramatically according to walking and feeding skills.

It is natural to ask whether prognostic estimates derived from a particular cohort apply equally well to persons with TBI from other states or countries where components of the health care system or population demographics may differ. In epidemiology, the ability of a prognostic model to make predictions for new cases outside the derivation cohort is known as external validity.[17]

A formal assessment of external validity is rarely reported in the research literature because it requires the collection of data from an independent validation cohort, which is often prohibitively expensive. When such assessments are carried out, the

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results may reveal the accuracy of a model to be lower on the validation cohort than on the derivation cohort. Potential reasons for this include (1) overfitting of the statistical model; (2) measurement errors associated with the interobserver variability of predictors; or (3) omission of important predictive variables.[17] Given this, clinicians and researchers are often skeptical of the applicability of prognostic models. Hence, validation studies are of utmost importance in the translation of research into practical tools.

In this article, we derive models for long-term mortality rates of persons with TBI from 2 independent cohorts and assess the external validity of these models by using a 2-sample cross-validation procedure. We derive the first model from an updated and expanded CDDS cohort that was studied previously by Shavelle.[7] Its external validity is tested against a validation cohort comprising persons with TBI who received care at the National Institute on Disability and Rehabilitation Research–funded Traumatic Brain Injury Model Systems (TBIMS) centers. Likewise, we derive a separate prognostic model from the TBIMS cohort and compare its predictions to actual outcomes in the CDDS cohort.

# Methods

This study was approved by the HCA-HealthONE Institutional Review Board at the TBIMS National Data and Statistical Center, Craig Hospital, Englewood, CO.

## Cohorts and comparison groups

The TBIMS and CDDS study cohorts are described in supplemental appendix S1 (available online only at http://www.archives-pmr.org/). In brief, the TBIMS cohort included persons who sustained a TBI at the age of ≥16, received comprehensive acute and rehabilitation care at a TBIMS center,[18] and provided follow-up information on functional skills assessed with the FIM instrument[19] ≥1 year postinjury. The CDDS cohort comprised persons with TBI who received services from the CDDS and provided long-term follow-up information on functional skills assessed with the Client Development Evaluation Report (CDER).[20-23] The vital status of TBIMS and CDDS cohorts was ascertained through the Social Security Death Index (SSDI) and the California Department of Public Health, respectively.

For simplicity, and to allow comparison with previous work, we chose to work with the 4 comparison groups considered in the 2007 study of Shavelle[7]: (1) does not walk, fed by others (CDER: walking = 1, feeding = 1; FIM: walking≤5, feeding≤3); (2) does not walk, self-feeds (CDER: walking = 1, feeding≥2; FIM: walking≤5, feeding≥4); (3) some walking with a handheld device or unsteadily alone (CDER: walking = 2 or 3; FIM: walking = 6); and (4) walks well alone (CDER: walking = 4; FIM: walking = 7).

***List of abbreviations:***

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| **CDDS** | **California Department of Developmental Services** |
| **CDER** | **Client Development Evaluation Report** |
| **CI** | **confidence interval** |
| **O/E** | **observed-to-expected** |
| **SSDI** | **Social Security Death Index** |
| **TBI** | **traumatic brain injury** |
| **TBIMS** | **Traumatic Brain Injury Model Systems** |

## Survival analysis and model validation

We computed empirical mortality rates of various subgroups by dividing the count of observed deaths by the total number of person-years of follow-up. We used multiplicative hazard regression[24] in each cohort to model mortality rates as a function of age, sex, and the 4 walking-feeding groups described above.

The regression model fitted to the CDDS cohort was used to predict mortality in the TBIMS cohort. Likewise, the TBIMS model was used to predict mortality in the CDDS cohort. That is, the TBIMS cohort served as the validation cohort for the CDDS model, and vice versa. We did not attempt to predict exactly when any particular individual would die. Instead, we computed a series of age-specific mortality rates and survival probabilities (ie, survival curves) for each individual. External validity was then assessed with measures of calibration and discrimination.[17,25]

Calibration of both models was assessed by comparing the number of deaths expected according to each model with the observed number in their respective validation cohorts. The expected numbers of deaths according to the models were computed by multiplying the mortality rates (which have units of deaths per person-year) by the number of person-years of follow-up. We calculated the observed-to-expected (O/E) ratios for various subgroups and computed 95% confidence intervals (CIs) based on the assumption that observed death counts followed a Poisson distribution. We also assessed calibration graphically by plotting the number of observed deaths versus the number of expected deaths by model-based risk deciles. This calibration plot allowed a visual assessment of whether the model systematically over- or underestimated mortality of low-, medium-, or high-risk groups.

We formally tested whether the prediction models required "recalibration in the large" or "shrinkage" by using regression methods. The recalibration in the large uses the original model predictions as a regression offset and tests whether a recalibration intercept indicates a significant over- or underestimation of mortality across the validation cohort as a whole. A well-calibrated model should have a recalibration intercept equal to 0. The recalibration through shrinkage uses the original model predictions as a covariate in a regression model, whose coefficient is the so-called recalibration slope. A well-calibrated model should have a recalibration slope coefficient equal to 1, which means that no shrinkage or expansion is required to adequately model the variability in the mortality of low- and high-risk groups.

Discrimination, that is, the ability of the model to rank survival times from shortest to longest, was assessed with the C index.

Data were analyzed with SAS version 9.2[a] and R version 3.0[b] software.

# Results

## Descriptions of the cohorts

The TBIMS cohort comprised 7365 persons (5400 men, 73% men), of whom 587 died over the course of 33,481 (collective) person-years of follow-up. The CDDS cohort included 5116 persons (3405 men, 67% men), of whom 568 died over the course of 54,306 person-years of follow-up. Thus, the empirical mortality rates were 17.5 (95% CI, 16.1–19.0) and 10.5 (95% CI, 9.6–11.4) deaths per 1000 person-years in TBIMS and CDDS cohorts, respectively.

Differences in the empirical mortality rates were partially explained by differences in the distributions of age and severity of