Published in final edited form as:
*Arch Phys Med Rehabil*. 2009 October ; 90(10): 1708–1715. doi:10.1016/j.apmr.2009.04.020.

# Risk of Mortality after Spinal Cord Injury: An 8-year Prospective Study

**James S. Krause, PhD**, **Yusheng Zhai, MSPH**, **Lee L. Saunders, PhD**, and **Rickey E. Carter, PhD**
College of Health Professions (Krause, Saunders), and the Department of Biostatistics, Bioinformatics, and Epidemiology (Zhai, Carter), Medical University of South Carolina, Charleston, SC

## Abstract

**Objective—**To evaluate a theoretical model for mortality after spinal cord injury (SCI) by sequentially analyzing 4 sets of risk factors in relation to mortality (i.e., adding 1 set of factors to the regression equation at a time).

**Design—**Prospective cohort study of data collected in late 1997 and early 1998 with mortality status ascertained in December 2005. We evaluated the significance of 4 successive sets of predictors (biographic and injury, psychologic and environmental, behavioral, health and secondary conditions) using Cox proportional hazards modeling and built a full model based on the optimal predictors.

**Setting—**A specialty hospital.

**Participants—**1,386 adults with traumatic SCI, at least 1 year post-injury, participated. There were 224 deaths. After eliminating cases with missing data, there were 1,209 participants, with 179 deceased at follow-up.

**Interventions—**N/A.

**Main Outcome Measures—**Mortality status was determined using the National Death Index and the Social Security Death Index.

**Results—**The final model included one environmental variable (poverty), 2 behavioral factors (prescription medication use, binge drinking), and 4 health factors or secondary conditions (hospitalizations, fractures/amputations, surgeries for pressure ulcers, probable major depression).

**Conclusions—**The results supported the major premise of the theoretical model that risk factors are more important the more proximal they are in a theoretical chain of events leading to mortality. According to this model, mortality results from declining health, precipitated by high-risk behaviors. These findings may be used to target individuals who are at high risk for early mortality as well as directing interventions to the particular risk factor.



Correspondence to James S. Krause, Ph.D, Department of Health Sciences and Research, College of Health Professions, Medical University of South Carolina, 77 President St, Suite 117, MSC 700, Charleston, SC 29425, krause@musc.edu.

Reprints are not available from the author.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

**Keywords**

Spinal cord injury; mortality; risk; health; life expectancy

Spinal cord injury (SCI) continues to be associated with elevated risk of premature mortality.[1–3] Because long-term mortality rates now appeared to have stabilized,[2] it is more important than ever to understand the broad range of factors that contribute to premature mortality after SCI, beyond those simply related to biographic or injury factors, such as age or injury severity. Identifying these factors is the key to intervention.

Krause[4] developed a theoretical risk model proposing 4 sequential stages of risk factors for mortality, beginning with basic biographic and injury factors. Although injury severity parameters are highly correlated with mortality, in the absence of consideration of age, recent research has suggested that they explain less than 2% of the variation in mortality and only raise concordance rates by about 6% percent above chance [50%].[5, 6] Injury factors are stable and must be accounted for in any prediction to statistically control for their effects.

After consideration of biographic and injury factors, there are 3 sets of additional levels of factors that serve as risk and protective factors for mortality, including: psychologic and environmental factors, behavioral factors, and health and secondary conditions. According to the model, these sets of factors are *not* of equal importance to mortality, but rather, there is a hierarchical predictive chain with the more proximal the factor to mortality, the stronger the predictive influence. Health factors and secondary conditions are the most immediate predictors of mortality, followed by health behaviors, and then psychologic and environmental factors. The model suggests at least partial causation, in that psychologic traits and environmental factors are believed to result in patterns of risk and protective behaviors, which, in turn, directly affect stability of health and the likelihood of secondary conditions. However, the model is not fully causal, in that, some variables may potentially have direct effects that are not mediated by other variables in the model.* Applied to prediction, the model suggests that health factors would be the most important predictors of mortality, followed by behaviors, and then psychologic and environmental factors.

Recent research has demonstrated relationships between a wider array of predictive factors and mortality. For instance, a violent etiology of injury was a significant predictor of mortality in a study utilizing data from the Model SCI Systems in the United States.[2] Two other studies using Model Systems data identified more diverse predictors of mortality. In the first study,[7] at least one variable from each level of the theoretical risk model was found to be predictive of mortality. Accounting for these variables led to substantial elevations in life expectancy under favorable circumstances. A more recent follow-up directly replicated this study,[8] suggesting that life expectancy estimates might have been inflated due to instability of a single variable (workers compensation) but providing insufficient detail to assess utility of the theoretical risk model or to identify the significance of other types of non-biographic and injury factors in relation to mortality.

Garshick and associates[9] identified 4 health risk factors for mortality, 3 being health status factors (diabetes, heart disease, reduced pulmonary function). They also found smoking, a behavioral factor, to be associated with mortality. Three risk factors were identified in a retrospective study of hospital records of all patients admitted to a Norwegian hospital

*Psychologic and environmental factors are distinct from each other but are introduced into the predictive model at the same point and are treated independent of each other in terms of prediction (i.e., they have mutual influence with relatively equal importance in the prediction of mortality).

between 1961 and 2002,[10] including cardiovascular disease, substance or alcohol abuse, and psychiatric disorders. The investigators emphasized the role of prevention in promoting longevity, as the 3 factors identified provide a basis for identification of those at high risk and targets for interventions.

In a series of prospective studies using the theoretical risk model, sets of variables were systematically evaluated in relation to mortality while controlling for biographic and injury factors. In contrast to the current study, where all sets of factors are evaluated simultaneously, each preliminary study focused on a single class of predictors (i.e., health, behavioral, psychologic, environmental). Separate analysis of each class of predictors identifies those most important for building a full model across all variables (the purpose of the current study).

In the first study focusing on health factors and secondary conditions as predictors of mortality,[6] 5 health factors were retained in the final model including: (a) surgeries for pressure ulcers, (b) depressive symptoms, (c) fractures/amputations, (d) symptoms of infections, and (e) hospitalizations. In an analysis of behavioral factors,[5] there were 4 behavioral predictors significantly related to mortality: (a) smoking, (b) binge drinking, (c) prescription medication use for pain, spasticity, sleep, or depression, and (d) time spent out of bed (a protective factor). Three psychologic factors were identified as significant predictors of mortality, including: (a) sensation seeking, (b) neuroticism-anxiety and (c) purpose in life (protective).[11] Lastly, 2 environmental variables were predictive of mortality – low income and social support (protective).[12]

### Purpose

Our purpose was to conduct a prospective cohort study to build a model of mortality after SCI that sequentially includes 4 sets of factors from the theoretical risk model of mortality.[4] Therefore, in contrast with earlier studies that were restricted to evaluating only one level of the overall theoretical risk model (i.e., psychologic, environmental, behavioral, or health), our purpose is to build a full model incorporating parameters from all levels. The sequential approach allows us to enter sets of predictors in the order in which they appear in the theoretical model. This is important because the model suggests that more distal predictors (those earlier in the predictive chain of factors) will become less important as additional factors are added. In other words, the strength of the association of psychologic and environmental factors should be diminished as behavioral factors are added, then have negligible effects after the addition of health status and secondary conditions as predictors.

The unique contribution of this study is the simultaneous evaluation of all factors from the theoretical risk model which will allow us to identify the most important predictors of mortality when considering all competing factors from each of the four general classes of predictors. Identifying the optimal predictors of mortality will allow us to more accurately predict individuals at risk for early mortality. From a conceptual standpoint, we can evaluate the utility of the theoretical risk model by determining whether the most proximal predictors of mortality are indeed those retained in the final model.

## METHODS

### Participants

Participants were identified from a large specialty hospital in the Southeastern United States using 3 types of records: (a) Model SCI Systems patient database, (b) Model SCI Systems registry, and (c) outpatient directory. All participants were adults with traumatic SCI of at least 1 year duration who had some residual neurologic impairment. Of the original cohort of 1929, 1386 participated (72%).

## Data Collection Procedures

Institutional Review Board approval was obtained prior to initiating the study. Letters were sent to all eligible participants describing the study and informing them that they would be receiving a questionnaire within the next few weeks. Two subsequent mailings were sent to non-respondents. Follow-up phone calls were also made and additional materials sent if requested. Participants received $20 remuneration and were entered for drawings totaling $1500. Data collection occurred between July 1997 and April 1998. Mortality status was assessed as of December 31, 2005, using the National Death Index of the National Center for Health Statistics[13] and the Social Security Death Index[14] of the Social Security Administration. Participants who were not found deceased by either method were presumed to be alive.

## Measures

All factors were measured using a mail-in health survey. For space considerations, we have only reported the essential information on these measures, although more detailed descriptions (including psychometric characteristics) are reported elsewhere.[5, 6, 11, 12]

**Biographic and Injury Characteristics—**Race was dichotomized as white and non-white. Age was measured at injury, and years lived with injury were calculated through the time of the survey. Injury level was categorized as cervical (C1–C4, C5–C8) and non-cervical, and injury function was dichotomized (ambulatory, non-ambulatory). This is a scheme that was used in the four preliminary studies.[5, 6, 11, 12] This is also similar to the scheme used from the Model SCI Systems,[15] except that we used ambulatory status as a proxy for ASIA D and broke down the ambulatory group by cervical and noncervical (they are combined in the Model Systems study).

**Environmental and Psychologic—**Income levels were presented in the categories utilized in the Behavioral Risk Factor Surveillance System (BRFSS),[16] a standardized instrument that is widely used by the Centers for Disease Control. Because income was highly skewed, an indicator variable was created to represent low income (< $20,000). Income was based on all sources from all members of the *household*, rather than the individual's earnings alone.

The Reciprocal Social Support Scale[17] was used to measure social support. Participants answered 8 questions on a 7-point scale (1 = never; 7 = always) rating type of support received from their families, friends, and community. They were also asked the frequency with which upsetting things happened between them and their family, friends, or community. We used the total social support scale and the upsets score.

The Zuckerman Kuhlman Personality Questionnaire[18] is a 99-item measure of personality, which generates information on five scales. These scales include: Impulsive Sensation Seeking, Neuroticism-Anxiety, Aggression-Hostility, Sociability, and Activity. We used 2 of these scales (Impulsive Sensation Seeking and Neuroticism-Anxiety). *Impulsive Sensation Seeking* was designed to measure a lack of planning and the tendency to act impulsively and served as a proxy for reckless and dangerous behavior. *Neuroticism-Anxiety* measures tension, worry, and fearfulness.

The Purpose in Life Scale[19] was developed from a humanistic perspective by measuring the degree to which an individual perceives himself/herself as finding meaning in life. It consists of 20 statements rated on a 7-point scale. Scores range from 20 to 140.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

**Behavioral—**We used core portions of the BRFSS to measure *alcohol behaviors* and *smoking behaviors.* Binge drinking was defined as the number of occasions in the past month the participant reported consuming five or more drinks. In contrast, a composite score was developed for three smoking items that assessed a participant's *smoking behaviors.* The first 2 items assessed if the participant had ever smoked on a regular basis or if the participant currently smokes in bed using either "no" (1) or "yes" (2) as the response categories. The number of cigarettes a day currently smoked was assessed as none at all (1), 1 to 9 (less than half a pack) (2), 10 to 19 (<1 pack) (3), 20 to 40 (1–2 packs) (4), or more than 41 (more than 2 packs) (5). The sum of these items was used to indicate higher smoking risk behaviors (standardized Cronbach $\alpha$ =.76).[5]

The Spinal Cord Injury Health Survey[20] measures *prescription medication usage* – how frequently participants use prescription medications that may have psychotropic effects. Participants were asked how frequently they used medications for pain, spasticity, depression, and sleep. Each item had 4 response categories: never, sometimes, weekly, and daily. A composite score was constructed as simple summated rating scales of the 4 items (standardized Cronbach's alpha=0.68), and a higher score indicated a higher use of medications. Lastly, a single item reflecting the number of hours out of bed during the day was used as a general activity indicator. This is a widely used indicator of activity and is in the Craig Handicap Assessment and Reporting Technique.[21]

**Health—**Several instruments were used to measure the health factors and secondary conditions, including items from the Life Situation Questionnaire-Revised (LSQ-R)[22, 23] and The Older Adult Health and Mood Questionnaire (OAHMQ).[24] Selected items were also developed for the study. Chronic diseases, such as heart disease, diabetes, and pulmonary function, are important factors to consider in relation to mortality, as they are both preventable and have been identified in previous research. However, we did not assess these conditions in the current study as they require a diagnosis by a physician, and we were concerned that they would not be reported accurately. There are similar restrictions in measuring conditions such as urinary tract infections. Therefore, our assessment focused on conditions that are more accurately reported in self-assessment, such as hospitalizations and injuries, as well as symptoms that may result from a condition (e.g., amputations may relate to diabetes; fractures may relate to osteoporosis; sweats, chills and fevers may relate to urinary tract infections).

The number of days hospitalized over the previous 12 months was used from the LSQ-R.[22, 23] Several types of secondary conditions were assessed, including the number of symptoms of infection including fevers, sweats and chills, and UTIs (number of occurrences of each of these in the past year using ordinal rankings: 0, 1–2, 3–6, 7–12, ≥13). A summary measure (summated score) was created. Another item reflected whether participants had ever had either an amputation or extremity fracture. Pressure ulcers were defined as "*open sores* in pressure areas, such as your tailbone, ischium, heel, elbows." Participants were asked to indicate the number of surgeries to heal pressure ulcers since SCI onset.[20]

The 22-item OAHMQ[24] was used to measure depressive symptoms. Scores of 11 or higher were considered to indicate probable major depression.

### Statistical Considerations

A 3-stage hierarchical model building strategy was employed to identify the association of psychologic, environmental, behavioral, and health factors with mortality and determine an optimal set of predictors of mortality. Independent variables within each factor were selected based on results from the previous studies.[5, 6, 11, 12] Cox proportional hazards modeling was used with the number of days between the survey and event (i.e., mortality) as the dependent variable.

During the first stage of analysis, a base model consisting of biographic (sex, race, age at injury, and years lived since injury) and injury characteristics (functional injury classification) was specified.

The second stage of the analysis focused on adding single variables to the base model as a means of "screening" potential predictors for the final stage model. All variables significant at the alpha=0.15 level were considered for subsequent modeling. Variables that passed through the initial screening process were then put together to assess for multicollinearity. No variance inflation factor (VIF) was larger than 10, and no tolerance was smaller than 1 for all variables, indicating no multicollinearity.[25]

In proceeding to the final model, variables retained from the second stage screening were added to the base model sequentially as a group by factor. Three intervening models were generated based on the theoretical risk model.[4] The first intervening model added the psychologic and environmental factors simultaneously to the base model. The second intervening model added the behavioral factors to the first intervening model. The health factors were added to the second intervening model to create the third intervening model. At each intervening model, backwards elimination, with alpha=0.15 as the significance level, was employed to select the optimal set of predictors.

The final stage of the analysis formulated a model that consisted of all variables retained from the third intervening model with significance at 0.05. Once the final model was established, all pair-wise interaction terms were included to further assess goodness of fit. A Wald linear contrast indicated no interaction item was needed (p =0.4), therefore all interaction items were removed. The proportional-hazards assumption of the final model was tested using the Schoenfeld residuals[26] and found to be tenable (Global test p=0.75). The fit of the model was assessed using Nagelkerke's pseudo-$R^2$ [27] and the C-statistic.[28–30] The former is a comparative fit index that can be used to assess the strength of the model fit, and the latter is interpretable as the probability that the cases (ie, deaths) have higher risks as measured by the linear component of the regression model. Accordingly, a value of 0.5 is used for chance prediction, and the discrimination of the model is improved as the C-value approaches 1.0; however, both indices, like most comparative fit indices, have limited generalizability beyond the dataset at hand.

Model building and calculation of VIF, tolerance, and Nagelkerke's pseudo-$R^2$ were conducted using SAS System version 9.1.3.[31] Validation of the proportional hazards assumption and estimation of the C-statistic were performed using STATA version 10.0.[32]

# RESULTS

## Participant Characteristics

There were 1,209 participants included in the final statistical model, of which 179 (14.8%) died. Participants' mean age at injury was 31.8 (s.d.=14.0), with an average of 8.9 (s.d.=6.9) years since their injury (Table 1). Overall, 54.4% had cervical injuries, and 21.1% of participants were ambulatory. The majority of participants were white (74.8%) and were men (74.0%).

Comparison of those with and without missing data (Table 2) indicated that deceased cases were disproportionately represented among those with missing data (25.1% of the deceased had missing data compared with 14.8% for the survivors; p<.001). Significant differences were also observed for race, as 69.3% of those with missing data were white compared with 75.8% of those with complete data (p<.05). Similarly for sex, 66.7% of those with missing data were men compared with 74.9% of those with complete data (p<.05). The average age of onset of those with missing data was 35.4 compared with 31.3 for those without missing data (p<.001). There were no differences as a function of injury severity or duration of SCI.

### Modeling

Variables were entered in accordance with the theoretical risk model (Table 3). The base model represents only biographic and injury characteristics. When adding the psychologic and environmental factors (Intervening 1), biographic and injury characteristics, which were significant in the base model, remained significant. Low income was the only statistically significant environmental factor and sensation seeking and purpose in life were significant psychologic factor.

Behavioral factors were added next in the Intervening 2 model. The addition of behavioral factors did not impact the previously entered factors, and all 4 behavioral predictors were significant in addition to those variables already in the equation.

Health factors, added in Intervening model 3, had the greatest effect on other factors. Previously significant biographic and injury characteristics remained, as did low income (environmental); however, as expected in the theoretical risk model, all psychologic variables lost significance. Two behavioral factors also became non-significant (out-of-bed hours, smoking composite score), with binge drinking and prescription medication use remaining significant.

### Final Model

In the final model, injury classification remained significantly associated with mortality, where the hazard of mortality increased for each increase in injury level among persons who were not able to ambulate (Table 4). Age at injury (hazard ratio [HR] =1.06, p<.0001) and years since injury (HR=1.05, p<.0001) were the only biographic factors related to mortality. One environmental factor was significant, as persons with low income had a 41% increased hazard of mortality (HR=1.41, p=0.04). Two behavioral factors were retained – prescription medications and number of binge drinking days. Lastly, all health factors except one (number of infectious symptoms) were significantly associated with mortality. Having a fracture or amputation was most strongly associated with mortality (HR=2.89, p=0.0006). Also, persons with probable major depression had a 78% increased hazard of mortality (HR=1.78, p=0.0003). A standardized HR was reported for the number of surgeries to repair ulcers, and for 1.0 s.d. increase, the hazard of mortality increased 21%. Also, for 1.0 s.d. (8.7) increase in days spent in the hospital, the hazard of mortality increased 16%.

With the addition of each set of factors, both the pseudo-$R^2$ and the C-statistic increased (Table 5). The pseudo-$R^2$ increased from 0.121 to 0.179 from the base to the final model, with the largest increase after the addition of behavioral factors (from 0.136 to 0.161). The C-statistic changed from 0.730 in the base model to 0.784 in the final model.

## DISCUSSION

These results provide relatively strong support for the theoretical risk model and the need to consider multiple sets of risk and protective factors in relation to mortality. First, as each set of risk factors was entered into the equation, those factors more distal to mortality were most likely to become non-significant. For example, when health factors were introduced, psychologic factors were no longer significant. This is consistent with the basic mediating hypothesis that each successive set of factors mediates the relationship between the previous factors and subsequent factors, ultimately ending in mortality.

Second, the model fit improved with the addition of each set of factors, including health factors that were entered last. The fact that several health predictors were retained in the final model and the model improved after their inclusion is a testament to their importance in mediating the relationship between other predictors and mortality.

There were some inconsistencies however. Specifically, low income, binge drinking, and prescription medication use were retained in the final model. This suggests that these are very powerful predictors of the model that were not mediated by health conditions in the current study. This may be because they have an independent effect or contribution to mortality (contrary to the model) or may reflect the limited scope of measurement of health conditions. In other words, had additional health factors been included, these variables *may* no longer have been significant.

## Implications

Ultimately, the importance of any study can be gauged by the extent to which it helps to lead to actual changes in outcomes (in this case – increased longevity). In contrast with biographic and injury factors that are not modifiable, the risk and protective factors identified in the current study present opportunities for identification of individuals at high risk for premature mortality and targets for interventions. Because the theoretical risk model is sequential in nature, with a series of mediating relationships, interventions targeted at the earliest sets of variables (psychologic and environmental) factors may have the greatest promise for early prevention. Intervening at later stages of risk (e.g., after the development of specific health conditions) is less likely to be successful. Just as the strength of prediction is greater the more proximal the risk factor to mortality, the more difficult it will be to intervene to extend longevity.

There are many ways the current findings can be translated into clinical practices to reduce early mortality. First, although it is not surprising that any of these particular risk factors are associated with early mortality, the identification of the *optimal set of predictors* will allow clinicians from multiple disciplines to assess risk for mortality quickly and efficiently. A minimum intervention for any clinician is to share with the individual who has SCI what factors increase or decrease the risk for mortality. This alone will empower the individual.

Second, clinicians may utilize the information on the specific risk factors to develop interventions in their own area of expertise. For instance, the finding that a depressive disorder was significantly related to mortality is an indicator of the importance of routinely assessing for depressive disorders and treating wherever possible. Rehabilitation psychologists should be intricately involved with this process to ensure that assessments are routine, including at outpatient visits, and that those at high risk for depression are identified and appropriate follow-up is implemented. Although our findings do not indicate causality, physicians need to be aware of the relationship between psychotropic prescription medication use and mortality and be cautious when prescribing these medications, particularly multiple medications for different symptoms (i.e., pain, spasticity, sleep, depression).

A third way to utilize these findings is to develop a systems approach to treatment for SCI that includes high-risk areas, such as alcohol abuse. Factors including tobacco use and sensation seeking were not significant in the final model, indicating that they did not contribute in a *unique* variance to the predictive model, but each has been previously identified as a risk factor for mortality. Despite the importance of behavioral factors on mortality and other important health outcomes,[20, 33] rehabilitation programs rarely implement any types of intervention for tobacco or substance misuse. If we are to successfully intervene to reduce early mortality and increase longevity, we must aggressively promote healthier behaviors and improvement of overall health.

## Study Limitations

The primary limitations include: (a) left censoring of the data (sample is drawn from some point after inception - the time of the SCI), (b) absence of participants who experienced mortality within the first year after injury when mortality is highest, (c) potential influence of missing data on estimating life expectancy and the strength of predictors, (d) time between prospective data collection and determination of mortality, (e) use of self-report data, (f) utilization of proxy variables for classification of injury severity, (g) inclusion of only a subset of risk and protective factors, and (h) nature of the statistics.

Whereas the first three limitations (a–c) applied broadly to the study and have been discussed elsewhere,[5, 6] the other methodological limitations are important to discuss. First, the 8-year interval between collection of the prospective data and determination of mortality limits the power of the study, as some of the predictor variables may change over time. Conversely, although increasing the window may weaken predictors, extending the prediction beyond 8 years would also be of great value. Second, we use self-report measures of health outcomes, whereas collecting this data through clinical assessments would have been preferable. However, it simply is not economically feasible to perform the number of clinical assessments necessary in epidemiologic studies of mortality, so utilization of self-report is a necessary trade-off. Similarly, injury status was determined by self-report, rather than clinical examination, so ambulatory status essentially serves as a proxy variable for neurologically incomplete injury with motor sparing (i.e., ASIA D). Although this study included very diverse predictors from each component of the theoretical risk model, the specific risk and protective factors used represent only a subset of all possible variables. This could, but does not necessarily, account for the finding that 1 environmental and 2 behavioral variables remained significant after the addition of health factors. Granting agencies and institutional review boards attempt to minimize participant burden in self-report studies, and this places constraints on the number and diversity of variables that can be included in any study. Finally, the interpretation of the model fit indices (pseudo $R^2$ and C-statistic) has limited generalizability beyond this data.

## Future Research

Ongoing research is needed to incorporate *more frequent assessments* of risk and protective factors and *incorporate additional parameters*, including biomarkers of stress, age, and vascular health. These assessments should take place over intervals longer than 8 years. Quality-of-life indicators also need to be incorporated into the model, as they were among the first factors to be identified in association with mortality.[34–36] Additional research is needed to identify the underlying mechanisms for the observed findings, such as the heightened risk of mortality related to fractures and amputations. We currently do not know whether these factors were significant by virtue of being indicators of overall health, or whether the physiologic processes related to fractures or amputations actually contribute to the early mortality. Lastly, investigation of an expanded set of risk and protective factors in association with causes of death would dramatically enhance our understanding of premature mortality and guide intervention strategies to promote greater longevity.

## CONCLUSIONS

Using a prospective cohort design guided by a theoretical risk model, we identified an optimal set of predictors of mortality that included 1 environmental factor (income), 2 behavioral factors (binge drinking, psychotropic prescription medication use), and 4 health factors (hospitalizations, fractures/amputations, surgeries for pressure ulcers, and probable major depression). Assessing these constructs in clinical settings will identify individuals at high risk for premature mortality, as well as provide targets for prevention strategies.

## Acknowledgments

This research was supported by a field initiated grant from the National Institute for Disability and Rehabilitation Research (H133G030117), the Model Spinal Cord Injury Systems Grant (H133N000005), and funding from the National Institutes of Health (1R01 NS 48117). The opinions here are those of the grantee and do not necessarily reflect those of the funding agencies.

## List of Abbreviations

| | |
|---|---|
| **BRFSS** | Behavioral Risk Factor Surveillance System |
| **HR** | Hazard Ratio |
| **LSQ-R** | Life Situation Questionnaire-Revised |
| **OAHMQ** | Older Adult Health and Mood Questionnaire |
| **SCI** | Spinal Cord Injury |
| **VIF** | Variance Inflation Factor |

## References

1. National Spinal Cord Injury Statistical Center (NSCISC). Annual Statistical Report. Birmingham, AL: University of Alabama; 2006 June.
2. DeVivo MJ, Krause JS, Lammertse DP. Recent trends in mortality and causes of death among persons with spinal cord injury. Arch Phys Med Rehabil. 1999; 80(11):1411–9. [PubMed: 10569435]
3. Strauss DJ, DeVivo MJ, Paculdo DR, Shavelle RM. Trends in life expectancy after spinal cord injury. Arch Phys Med Rehabil. 2006; 87:1079–85. [PubMed: 16876553]
4. Krause JS. Secondary conditions and spinal cord injury: A model for prediction and prevention. Topics SCI Rehab. 1996; 2(2):217–27.
5. Krause JS, Carter RE, Pickelsimer E. Behavioral risk factors for mortality after spinal cord injury. Arch Phys Med Rehabil. 2009; 90(1):95–101. [PubMed: 19154835]
6. Krause JS, Carter RE, Pickelsimer E, Wilson D. A prospective study of health and risk of mortality after spinal cord injury. Arch Phys Med Rehabil. 2008; 89:1482–91. [PubMed: 18674984]
7. Krause J, Devivo M, Jackson A. Risk factors for mortality after spinal cord injury. Arch Phys Med Rehabil. 2004; 85:1764–73. [PubMed: 15520971]
8. Strauss D, DeVivo M, Shavelle R, Brooks J, Paculdo D. Economic factors and longevity in spinal cord injury: a reappraisal. Arch Phys Med Rehabil. 2008; 89(3):572–4. [PubMed: 18295640]
9. Garshick E, Kelley A, Cohen SA, Garrison A, Tun CG, Gagnon D, et al. A prospective assessment of mortality in chronic spinal cord injury. Spinal Cord. 2005; 43(7):408–16. [PubMed: 15711609]
10. Lidal I, Snekkevik H, Aamodt G, Hjeltnes N, Biering-Sorensen F, Stanghelle J. Mortality after spinal cord injury in Norway. J Rehab Med. 2007; 39(2):145–51.
11. Krause JS, Carter RE, Zhai Y, Reed KS. Psychological factors and risk of mortality after spinal cord injury. Arch Phys Med Rehabil. in press.
12. Krause JS, Carter RE. Risk of mortality after spinal cord injury: Relationship with social support, education, and income. Spinal Cord. in press.

13. National Death Index. [cited 2007 September 28]. Available from: URL: http://www.cdc.gov/nchs/ndi.htm
14. Social Security Death Index. [cited 2007 September 28]. Available from: URL: http://www.ancestry.com
15. DeVivo, MJ.; Stover, SL. Long term survival and causes of death. In: Stover, SL.; DeLisa, JA.; Whiteneck, GG., editors. Spinal cord injury: clinical outcomes from the model systems. Gaithersburg, MD: Aspen; 1995. p. 289-316.
16. Powell-Griner E, Anderson JE, Murphy W. State-and sex-specific prevalence of selected characteristics--behavioral risk factor surveillance system, 1994 and 1995. Morbity and Mortality Weekly Report CDC Surveill Summ. 1997; 46(3):1–31.
17. Anson CA, Stanwyck DJ, Krause JS. Social support and health status in spinal cord injury. Paraplegia. 1993; 31(10):632–8. [PubMed: 8259325]
18. Zuckerman M, Kuhlman DM, Joireman J, Teta P, Kraft M. A comparison of three structural models for personality, The Big Three, The Big Five and The Alternate Five. J Pers Soc Psychol. 1993; 65:757–68.
19. Crumbaugh JC. Cross-validation of Purpose-In-Life test based on Frankl's concepts. J Ind Psychol. 1968; 24:74–81.
20. Krause JS. Factors associated with risk for subsequent injuries after the onset of traumatic spinal cord injury. Arch Phys Med Rehabil. 2004; 85:1503–8. [PubMed: 15375825]
21. Whiteneck, GG.; Charlifue, SW.; Gerhart, KA.; Overholser, JC.; Richardson, GN. The Craig Handicap Assessment and Reporting Technique. Englewood, CO: Craig Hospital; 1992.
22. Krause JS. Intercorrelations between secondary conditions and life adjustment among people with spinal cord injuries. SCI Psychosocial Process. 1998; 11:3–7.
23. Krause JS. Dimensions of subjective well-being after spinal cord injury: an empirical analysis by gender and race/ethnicity. Arch Phys Med Rehabil. 1998; 79(8):900–9. [PubMed: 9710160]
24. Kemp BJ, Adams BM. The Older Adult Health and Mood Questionnaire: A measure of geriatric depressive disorder. J Ger Psyc Neuro. 1995; 8(3):162–7.
25. Belsley, DA.; Edwin, K.; Roy, EW. Regression diagnostics: Identifying influential data and sources of collinearity. New York: John Wiley and Sons; 1982.
26. Schoenfield D. Chi-squared goodness-of-fit tests for the proportional hazards regression model. Biometrika. 1980; 67:145–53.
27. Nagelkerke N. A note on general definition of the coefficient of determination. Biometrika. 1991; 78:691–2.
28. Harrell FEJ, Lee KL, DBM. Multivariate prognostic models: Issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996; 15:361–87. [PubMed: 8668867]
29. Harrell, FEJ. Regression modeling strategies with applications to linear models, logistic regression, and survival analysis. New York, New York: Springer-Verlag New York Inc; 2001.
30. Harrell FEJ. Evaluating the yield of medical tests. JAMA. 1982; 247:2543–6. [PubMed: 7069920]
31. SAS System for Windows. Version 9.2. Cary, NC: SAS Institute; 2008.
32. STATA for Windows. Version 10.0. College Station, TX: STATA Corp; 2009.
33. Krause JS, Broderick L. Patterns of recurrent pressure ulcers after spinal cord injury: Identification of risk and protective factors 5 or more years after onset. Arch Phys Med Rehabil. 2004; 85:1257–64. [PubMed: 15295750]
34. Krause JS, Crewe NM. Prediction of long-term survival of persons with spinal cord injury: An 11 year prospective study. Rehabil Psychol. 1987; 32:205–13.
35. Krause JS, Saari JM, Dykstra D. Quality of life and survival after spinal cord injury. SCI Psychosocial Process. 1990; 3:4–8.
36. Krause JS. Survival following spinal cord injury: A fifteen-year prospective study. Rehabil Psychol. 1991; 36(2):89–98.

## Table 1

Sample Description

| Variable | Raw dataset N | % |
|---|---|---|
| **Injury Classification** | | |
| C1–C4, non-ambulatory | 175 | 13.16 |
| C5–C8, non-ambulatory | 406 | 30.53 |
| Non-cervical, non-ambulatory | 468 | 35.19 |
| Cervical, ambulatory | 142 | 10.68 |
| Non-cervical, ambulatory | 139 | 10.45 |
| **Biographic** | | |
| White | 1032 | 74.84 |
| Men | 1026 | 74.03 |
| Age at injury (Mean±SD) | 31.83 ± 13.99 | |
| Years since injury (Mean±SD) | 8.86 ± 6.86 | |
| **Psychologic Factors** | | |
| Sensation Seeking | 4.35 ± 2.75 | |
| Neuroticism-Anxiety | 3.56 ± 2.41 | |
| Purpose in Life | 99.02 ± 21.29 | |
| **Environmental Factors** | | |
| Low income (<$20,000) | 684 | 51.47 |
| Social support | 17.54 ± 3.89 | |
| Social upset | 7.50 ± 3.61 | |
| **Behavioral Factors** | | |
| Prescription medication use | 7.61 ± 3.38 | |
| Number of binge drinking days | 1.24 ± 3.87 | |
| Out-of-bed hours | 12.73 ± 3.89 | |
| Smoking composite score | 4.27 ± 1.69 | |
| **Health Factors** | | |
| Days in the hospital | 4.34 ± 8.66 | |
| Number of infection symptoms | 9.80 ± 9.64 | |
| Fracture/amputation | 31 | 2.24 |
| Surgeries to repair ulcers | 0.55 ± 1.54 | |
| Probable major depression | 339 | 24.53 |

NIH-PA Author Manuscript
NIH-PA Author Manuscript

## Table 2

Comparison of those with and without missing data.

| Variable | Participants | Complete Data N =1209 | Complete Data % | Missing Data N=177 | Missing Data % | p -value of $\chi^2$ |
|---|---|---|---|---|---|---|
| Number of Deaths | | 179 | 14.8 | 45 | 25.1 | 0.0003 |
| Injury Classification | | | | | | |
| C1–C4, non-ambulatory | | 160 | 13.2 | 15 | 13.2 | 0.80 |
| C5–C8, non-ambulatory | | 368 | 30.4 | 36 | 31.6 | 0.83 |
| Non-cervical, non-ambulatory | | 423 | 35 | 41 | 36 | 0.63 |
| Cervical, ambulatory | | 131 | 10.8 | 10 | 8.77 | 0.55 |
| Non-cervical, ambulatory | | 127 | 10.5 | 12 | 10.5 | 0.12 |
| Biographic | | | | | | |
| | White | 917 | 75.8 | 79 | 69.3 | 0.02 |
| | Men | 906 | 74.9 | 76 | 66.7 | 0.04 |
| Age at injury (Mean±SD) | | 31.34 ± 13.33 | | 35.41 ± 17.76 | | 0.0005* |
| Years since injury (Mean±SD) | | 8.90 ± 6.96 | | 8.54 ± 6.15 | | 0.52* |

* t-test comparing 2 means

NIH-PA Author Manuscript
NIH-PA Author Manuscript

**Table 3**

Intervening Models.

| Variable | Base | | Intervening 1 | | Intervening 2 | | Intervening 3 | |
|---|---|---|---|---|---|---|---|---|
| | HR | p-value | HR | p-value | HR | p-value | HR | p-value |
| **Injury Classification** | | | | | | | | |
| C1–C4, non-ambulatory | 4.83 | <.0001 | 5.04 | <.0001 | 3.20 | 0.004 | 3.41 | 0.001 |
| C5–C8, non-ambulatory | 3.13 | 0.002 | 2.73 | 0.01 | 2.10 | 0.06 | 2.22 | 0.03 |
| Non-cervical, non-ambulatory | 3.41 | 0.001 | 2.89 | 0.01 | 2.22 | 0.04 | 2.05 | 0.05 |
| Cervical, ambulatory | 1.16 | 0.74 | 0.95 | 0.91 | 0.85 | 0.74 | 1.03 | 0.94 |
| Non-cervical, ambulatory (referent) | 1.00 | -- | 1.00 | -- | 1.00 | -- | 1.00 | -- |
| **Biographic** | | | | | | | | |
| White | 0.91 | 0.57 | 1.23 | 0.29 | 1.31 | 0.20 | 1.13 | 0.50 |
| Men | 1.12 | 0.51 | 1.12 | 0.55 | 1.14 | 0.51 | 1.18 | 0.37 |
| Age at injury | 1.06 | <.0001 | 1.06 | <.0001 | 1.06 | <.0001 | 1.06 | <.0001 |
| Years since injury | 1.05 | <.0001 | 1.06 | <.0001 | 1.06 | <.0001 | 1.05 | <.0001 |
| **Psychologic Factors** | | | | | | | | |
| Sensation Seeking | | | 1.05 | 0.08 | 1.05 | 0.10 | -- | -- |
| Neuroticism-Anxiety | | | 1.06 | 0.11 | -- | -- | -- | -- |
| Purpose in Life | | | 0.99 | 0.01 | 0.99 | 0.05 | -- | -- |
| **Environmental Factors** | | | | | | | | |
| Low income (<$20,000) | | | 1.64 | 0.01 | 1.44 | 0.05 | 1.41 | 0.04 |
| Social support | | | -- | -- | -- | -- | -- | -- |
| Social upset | | | -- | -- | -- | -- | -- | -- |
| **Behavioral Factors** | | | | | | | | |
| Prescription medication use | | | | | 1.08 | 0.001 | 1.06 | 0.004 |
| Number of binge drinking days | | | | | 1.04 | 0.01 | 1.04 | 0.02 |
| Out-of-bed hours | | | | | 0.94 | 0.004 | -- | -- |
| Smoking composite score | | | | | 1.08 | 0.10 | -- | -- |
| **Health Factors** | | | | | | | | |
| Days in the hospital | | | | | | | 1.02 | 0.03 |
| Number of infection symptoms | | | | | | | -- | -- |

NIH-PA Author Manuscript
NIH-PA Author Manuscript

| | Base | | Intervening 1 | | Intervening 2 | | Intervening 3 | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **HR** | **p-value** | **HR** | **p-value** | **HR** | **p-value** | **HR** | **p-value** |
| Fracture/amputation | | | | | | | 2.89 | 0.0006 |
| Surgeries to repair ulcers | | | | | | | 1.13 | 0.0003 |
| Probable major depression | | | | | | | 1.78 | 0.0003 |

*[a]* Injury and biographic variables only, 203 deaths over 1312 subjects

*[b]* Added psychologic and environmental models to model [a], 161 deaths over 1123 subjects

*[c]* Added behaviors to model[b], 155 deaths over 1090 subjects

*[d]* Added Health Factors to model[c], 179 deaths over 1209 subjects

-- Variable not significant and removed from the model

**Table 4**

Final Cox proportional hazards model for predicting mortality after SCI.

| | Adjusted Model [a] | | Final Model* | | | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **HR** | **p-value** | **HR [b]** | **95% CI** | | **p-value** | **Std HR [c]** |
| **Injury Classification** | | | | | | | |
| C1–C4, non-ambulatory | NA | | 3.41 | 1.62 | 7.18 | 0.001 | -- |
| C5–C8, non-ambulatory | NA | | 2.22 | 1.08 | 4.54 | 0.03 | -- |
| Non-cervical, non-ambulatory | NA | | 2.05 | 1.01 | 4.18 | 0.05 | -- |
| Cervical, ambulatory | NA | | 1.03 | 0.43 | 2.47 | 0.94 | -- |
| Non-cervical, ambulatory (referent) | | | 1.00 | 1.00 | -- | -- | -- |
| **Biographic** | | | | | | | |
| White | NA | | 1.13 | 0.79 | 1.61 | 0.50 | -- |
| Men | NA | | 1.18 | 0.82 | 1.69 | 0.37 | -- |
| Age at injury | NA | | 1.06 | 1.05 | 1.07 | <.0001 | 2.20 |
| Years since injury | NA | | 1.05 | 1.03 | 1.07 | <.0001 | 1.38 |
| **Psychologic Factors** | | | | | | | |
| Sensation Seeking | 1.12 | <.0001 | -- | -- | -- | -- | -- |
| Neuroticism-Anxiety | 1.05 | 0.10 | -- | -- | -- | -- | -- |
| Purpose in Life | 0.99 | <.0001 | -- | -- | -- | -- | -- |
| **Environmental Factors** | | | | | | | |
| Low income (<$20,000) | 1.93 | <.0001 | 1.41 | 1.01 | 1.97 | 0.04 | -- |
| Social support | 0.95 | 0.003 | -- | -- | -- | -- | -- |
| Social upset | 1.02 | 0.22 | -- | -- | -- | -- | -- |
| **Behavioral Factors** | | | | | | | |
| Prescription medication use | 1.10 | <.0001 | 1.06 | 1.02 | 1.11 | 0.004 | 1.23 |
| Number of binge drinking days | 1.04 | 0.005 | 1.04 | 1.01 | 1.07 | 0.02 | 1.15 |
| Out-of-bed hours | 0.92 | <.0001 | -- | -- | -- | -- | -- |
| Smoking composite score | 1.19 | <.0001 | -- | -- | -- | -- | -- |
| **Health Factors** | | | | | | | |
| Days in the hospital | 1.03 | <.0001 | 1.02 | 1.00 | 1.03 | 0.03 | 1.16 |

| Variable | Adjusted Model [a] | | Final Model* | | | | |
|---|---|---|---|---|---|---|---|
| | HR | p-value | HR [b] | 95% CI | | p-value | Std HR [c] |
| Number of infection symptoms | 1.03 | <.0001 | -- | -- | -- | -- | -- |
| Fracture/amputation | 3.69 | <.0001 | 2.89 | 1.57 | 5.29 | 0.0006 | -- |
| Surgeries to repair ulcers | 1.20 | <.0001 | 1.13 | 1.06 | 1.21 | 0.0003 | 1.21 |
| Probable major depression | 2.21 | <.0001 | 1.78 | 1.30 | 2.45 | 0.0003 | -- |

*179 deaths over 1209 subjects in the final model

[a]Estimated HR for variables separately adjusted for injury and biographic variables only

[b]Hazard ratios are adjusted for all variables that have estimates provided.

[c]The standardized HR are reported for 1 Std change in continuous variables

-- Variable not significant and removed from the model

NIH-PA Author Manuscript
NIH-PA Author Manuscript

## Table 5

Model fit statistics.

| Model | Description | Pseudo-$R^2$ | Change | C-statistics | Change |
|---|---|---|---|---|---|
| 1 | Injury severity only | 0.016 | ND | 0.578 | ND |
| 2 | Base model | 0.121 | 0.105 | 0.730 | 0.152 |
| 3 | Intervening model [1] | 0.136 | 0.120 | 0.760 | 0.182 |
| 4 | Intervening model [2] | 0.161 | 0.144 | 0.776 | 0.198 |
| 5 | Final model | 0.179 | 0.163 | 0.784 | 0.206 |
| 6 | Maximum model | 0.178 | 0.162 | 0.788 | 0.210 |

Abbreviation: ND, no data to enter into cell.

1. Five category breakdown (C1–C4, C5-8, non-cervical, and so forth)

2. Add core biographic variables includes white, men, age at injury, and years since injury

3. Add psychologic and environmental factors to the base model

4. Add behavior factors to Intervening model [1]

5. The final model as identified on Table 3

6. The maximum model consisted all variables of interest in addition to the base model