2008

# Gender Difference in Traumatic Brain Injury Outcomes: Survival, Functional Independence, and Employment Status

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# GENDER DIFFERENCES IN TRAUMATIC BRAIN INJURY OUTCOMES: SURVIVAL, FUNCTIONAL INDEPENDENCE, AND EMPLOYMENT STATUS

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A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2008

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EPIDEMIOLOGY

ABSTRACT

Medical and rehabilitative care of women living with traumatic brain injury (TBI) is based on information drawn from research conducted primarily on men. Care for men may be adequate for women, but all of the body's organs have the capability to respond differently based on gender, and research should examine the genders separately. This dissertation examines the survival to 24 months post-TBI and the functional independence and employment status at 12 and 24 months post-TBI of men and women. Participants were drawn from a longitudinal study of injured persons and include those diagnosed only with a TBI. Variables used in these analyses were abstracted from medical records, self-reported, or obtained through the National Death Index. Mortality was documented with the National Death Index. Functional independence and employment status were self or proxy reported during the 12 and 24 month follow-up interviews. Functional independence was measured with the Functional Independence Measure (FIM). Between 24 hours and 24 months post-injury, gender was not associated with mortality after adjusting for age, head injury severity and type of head injury. The functional independence analyses were stratified by respondent (participant or

proxy). Gender was not associated with post-injury functional independence when the participant responded to the follow-up questionnaire at 12 or 24 months post-injury after adjusting for injury and demographic factors. When a proxy responded to the follow-up questionnaire, female gender was associated with a 13% decrease in average FIM score at 12 months post-injury (p=0.0198), but not at 24 months post-injury after adjusting for other relevant variables. Gender was not associated with employment status 12 or 24 months post-injury. Gender's only role in the TBI outcomes examined was in level functional independence at 12 months, but only with a proxy response.

ACKNOWLEDGEMENT

This research was supported in part by Grant No. R49-CE000191 from the Centers for Disease Control and Prevention, National Center for Injury Prevention and Control to the UAB Injury Control Research Center

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### TWENTY FOUR MONTH SURVIVAL OF MEN AND WOMEN AFTER TRAUMATIC BRAIN INJURY

LIST OF ABBREVIATIONS

| | |
|---|---|
| AIS | Abbreviated Injury Scale |
| CI | confidence interval |
| FAM | Functional Assessment Measure |
| FIM | Functional Independence Measure |
| GCS | Glasgow Coma Score |
| GOS | Glasgow Outcome Score |
| HR | hazard ratio |
| ICD-9 | International Classification of Diseases, 9th edition |
| ICRC | Injury Control Research Center |
| NDI | National Death Index |
| OR | odds ratio |
| RR | risk ratio |
| TBI | traumatic brain injury |
| UAB | University of Alabama at Birmingham |

# INTRODUCTION

## Physiological and Psychological Gender Differences

The belief that gender plays some role in effect of or recovery from traumatic brain injury (TBI) emanates from awareness of the fundamental physiological and psychological differences between men and women. One such difference lies in brain structure. The brains of men and women show differences in weight, neuronal density, and brain structures. [1-7] In particular, women's brains have more cortical gray matter, greater volume in regions associated with language function, greater volume of the hippocampus, and greater volume of white matter associated with inter-hemispheric connectivity.[8] Men, on the other hand, have a larger volume of overall white matter, a larger volume of the hypothalamus, and more cerebrospinal fluid.[8] The brains of men appear to have greater functional asymmetry than brains of women. [9] That is, brain processing in women is more equally distributed between the two hemispheres of the brain while men process in either one hemisphere or the other. While there do seem to be gender-related differences in adult brains, the etiology, importance, and implications of these differences are unknown.

Another important, albeit controversial, difference between men and women is in psychological functioning. Psychological functioning refers to the mental health, or the intellectual, emotional, behavioral, or social role functioning of the person.[10] It has been a long-held belief that psychological functioning of men and women is different (i.e., inherently, men and women have different mental health problems, different intellectual abilities, different emotional and behavioral reactions to given situations, etc.). Recently, however, this theory has drawn fire. New research has suggested that the apparent psychological differences between men and women are not truly differences, but artifacts of gender bias and cultural norms. [11]

Whether true differences exist in the psychological functioning of men and women (i.e., whether gender is a risk factor for certain psychological disorders), it is evident there are gender differences in the reporting and diagnosis of mental, emotional, or behavioral problems. Physicians more readily prescribe mood altering psychotropic drugs to women, and women are more likely to disclose mental problems and seek help than are men. Conversely, men are more likely to disclose alcohol problems than are women. [12]

## Gender's Role in Traumatic Brain Injury Outcome Research – Overview

Historically, gender's relationship with outcomes in traumatic brain injury research has not been examined, and the outcomes for men and women have not been explored separately. The exclusion of gender in this line of research is rationalized because men are twice as likely to experience a traumatic brain injury as are women.[13] However, this relative risk is somewhat misleading. These incidence differences between men and women are seen mainly between puberty and middle age.[14] During childhood (pre-puberty) and post-middle age adulthood (45 to 75 years of age), TBI incidence in men and women is approximately equal.[14] Regardless of age, there are approximately 2 million women living with TBI,[15] and their post-injury recovery is an important public health issue.

The medical and rehabilitative care of women living with TBI is based on information drawn from research conducted primarily on men. This rehabilitative care may be adequate for women, but, according to the Institute of Medicine, all of the body's organs have the capability to respond differently based on gender, and research should be designed to examine the genders separately.[16] Since studies have shown that men and women differ in their development of and response to chronic and infectious diseases,[17] it seems reasonable to hypothesize that men and women may differ in their response to and recovery from TBI, and that the best choices for their post-TBI care may differ. Therefore, it is important to determine if gender plays a role in TBI survival and recovery, and if it does, how strong a role.

Specific examples of the growing body of research examining gender differences after TBI for both humans and animals are discussed more fully in the papers that follow. Research to date covers a wide variety of topics, from mortality to post-injury psychological outcomes, and both the methodology and results are quite varied. There is some evidence that gender does plays a role in at least some post-TBI outcomes, but the nature and mechanism of that role is not yet understood.

## Gender's Role in Trauma Outcomes Research

A related area of study examines gender's role in trauma outcomes. Research in this area is more extensive than that of gender differences in TBI-specific outcomes. There is the suggestion that gender does play some role post-injury, but research in this area, like research in the area of gender's role in post-TBI outcomes, has been unable to determine the mechanism of gender's influence and raises many questions. [18]

A recent, large study by Magnotti, et al., of gender differences after blunt injury showed that after adjusting for factors related to injury severity and age, gender was not associated with post-injury mortality but was associated with the development of ventilator-associated pneumonia, bacteremia, or acute respiratory distress syndrome after injury. [19] These results complement those of Sperry and colleagues who found that gender played no role in post-trauma mortality, but did impact post-trauma multiple organ failure and development of nosocomial infections after adjustment for many relevant injury-related factors.[20]

Other work has found gender's influence on post-trauma outcomes to be intertwined with age. This relationship implies that hormones are responsible for the gender differences in post-injury outcomes. Much research supports the notion that female hormones protect against the negative effects of injury. [21, 22, 23] For example, Mostfa, Huynh, et al., found that male gender was associated with higher post-trauma mortality, but only for those under age 45. When older (over age 45) age groups were examined, gender was not related to mortality. [24] Similarly, George and colleagues found that in the case of blunt trauma, male gender increased the risk of death in those under 50 years of age, but not for those over 50 years of age. In the case of penetrating trauma, male gender decreased the risk of death, but only in those over 50 years old. There was no significant association between gender and mortality after penetrating injury for those under 50 years.[25] Conversely, George and colleagues performed a similar, but larger, study using data from the National Trauma Data Bank and found that male gender was associated with increased risk of death after blunt trauma, but only in those over 50 years of age. No statistically significant association between gender and mortality was found after blunt trauma in those less than 50 years of age. After penetrating trauma, male gender was associated with a decreased risk of death in only the 40-49 year old age group. There was no association between gender and mortality after penetrating trauma in the other age groups.[26]

Post-trauma gender differences research has examined outcomes after hospital discharge. Holbrook, Hoyt, and Anderson found that, after adjusting for injury severity, demographic factors and age, women displayed lower quality of well-being 6 months, 12 months and 18 months post-trauma. Additionally, women were more likely than men to be depressed at discharge, 6, 12, and 18 months post-trauma and were more likely to have symptoms of acute stress reaction at time of discharge.[27, 28] In other research, Holbrook and colleagues found that after trauma, women were at increased risk for post-traumatic stress disorder through 18 months post-injury. [29]

## Importance of Current Research

The role of gender in TBI outcomes is uncertain. Differences in brain structure and possible differences in psychological functioning between men and women combined with anecdotal evidence of different post-injury outcomes for men and women led researchers to hypothesize that TBI and recovery from TBI may be experienced differently by men and women. The research literature is still exploratory. Theories are arising from animal model research, but their direct application to humans is unclear. To date, the research has suggested post-injury differences between men and women exist, but the nature of those differences is not established.

This research adds to the literature examining the relationship between gender and traumatic brain injury outcome. As the body of evidence grows, alternative strategies for treating men and women could be developed and implemented, if future research results show that differing strategies are warranted. Specifically, the three analyses that follow examine (1) survival to 24 months post-injury, (2) functional independence at 12 and 24 months post-injury, and (3) employment status at 12 and 24 months post-injury of both men and women.

It is hypothesized that (1) Women will be more likely than men to survive from 24 hours to 24 months post-TBI; (2) Women will display greater post-TBI functional independence than men at both 12 and 24 months post-TBI; (3) Women will be more likely than men to be employed at both 12 and 24 months post-TBI.

TWENTY FOUR MONTH SURVIVAL OF MEN AND WOMEN AFTER TRAUMATIC BRAIN INJURY

by

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In preparation for *Archives of Physical Medicine and Rehabilitation*

Format adapted for dissertation

ABSTRACT

Objective: To investigate the influence of gender on survival after traumatic brain injury (TBI) from 24-hours post-injury to 24 months post-injury.

Design: Retrospective follow-up study

Setting: General community

Participants: Participants were drawn from the database of potential participants whose medical records were abstracted to identify those eligible for a larger, longitudinal study, and include patients at least age 18 years diagnosed only with a TBI. Those diagnosed with injuries other than TBI or with injuries in addition to a TBI were not eligible. TBI is defined as International Classification of Diseases, Ninth Revision (ICD9) codes 800-803, 851-854. There are 1221 participants available (884 men, 337 women).

Main Outcome Measure: Mortality as recorded by the National Death Index

Results: During the time period specified, 24 hours post-injury to 24 months post-injury, gender was not associated with mortality (women vs. men: HR 1.02, 95%

CI 0.71 – 1.48), nor was type of head injury (open vs. closed: HR 0.66, 95% CI 0.37 – 1.18). The variables in the model that significantly influenced mortality were higher age at time of injury (HR 1.83, 95% CI 1.46 – 2.29) and higher head AIS score (HR 2.24, 95% CI 1.88 - 2.67).

Conclusion: There is no statistically significant evidence that survival following TBI is different for women and men based solely on gender.

Key Words: Gender, Sex, Traumatic Brain Injury, Survival, National Death Index, Mortality

INTRODUCTION

Historically, traumatic brain injury (TBI) research has focused primarily on men, and it has been assumed that the best course of medical treatment for women is the same as that for men. However, the Institute of Medicine states that all of the body's organs have the capability to respond differently based on gender, and that research should be designed to examine the genders separately.[1] The primary outcome of interest immediately following TBI is survival. The body of literature examining post-TBI gender differences in survival is growing, but producing mixed results.

Davis, Douglas, and colleagues examined post-TBI mortality differences in pre- and post-menopausal women versus men. They found that after adjusting for injury severity, age, type of injury, blood pressure, and Glasgow Coma Score (GCS), there was no difference in survival from incidence of injury to hospital discharge between pre-menopausal women and men. Post-menopausal women, however, were more likely to survive to hospital discharge than were men. This finding suggests that female hormones (a suspected cause of post-TBI gender differences) play no role in short-term survival.[2] If female hormones did play a role, one would expect to see different outcomes for men and pre-menopausal women. Conversely, Ponsford, Myles, Cooper, et al., found that women were less likely to survive to 6 months post-injury than were men after adjusting for GCS, mechanism of injury, and age. [3]

Kraus, Peek-Asa, and McArthur, examining self-reported or family-reported survival up to 18 months post-TBI, found no gender difference in mortality after adjusting for GCS, type of injury, and presence of multiple trauma.[4] Studying people who sustained a TBI through a motor vehicle crash, Slewa-Younan, Green, and colleagues matched men and women on age, education, mode, type, and speed of crash. In their analysis, the resulting injuries of men were more severe than the injuries of women (severity determined by GCS and duration of post-traumatic amnesia). Despite differences in severity, these researchers found no differences in functional ability, GCS, or mortality after rehabilitation.[5]

In a related area of research, gender differences have been seen in post-TBI secondary brain injuries, changes that occur over a period of time after the primary brain injury. Secondary injuries result in further cellular damage and include edema, intracranial infection, systemic hypoxia and hypotension. Among a group of people with severe TBI, women had less oxidative damage after a given injury than did men. Men, however, responded more favorably to treatment intended to reduce this damage.[6] Other research has found that gender is associated with post-TBI lactate and glutamate levels (higher levels cause neuronal swelling) with women having lower post-injury levels of lactate and glutamate; however, men responded more favorably to the treatment to ameliorate these secondary injuries.[7]

Gender has been found to play a role in TBI severity in animal models. Research has shown that after controlled, experimental head injury, the resulting cortical contusion experienced by intact female rats was smaller than that experienced by their male counterparts. Furthermore, the resulting contusion experienced by ovariectomized female rats did not differ from that of males.[8-9]

The body of literature examining gender differences in TBI survival is small and methodologically varied making it difficult to draw an informed conclusion about the role of gender in survival from TBI, particularly long-term survival. The purpose of this study is to investigate the influence of gender on survival after TBI from 24-hours post-injury to 24 months post-injury. It is hypothesized that women will be more likely to survive than men.

# METHODS

Participants in this retrospective follow-up study are people diagnosed with TBI drawn from a large, prospective cohort study (*A Longitudinal Study of Rehabilitation Outcomes*, as described below).

## A Longitudinal Study of Rehabilitation Outcomes

In 1989, the University of Alabama at Birmingham's Injury Control Research Center (UAB ICRC) received approval from the UAB Institutional Review Board to initiate a prospective, longitudinal study of persons with one or more of the following injuries: spinal cord injury, traumatic brain injury, intra-articular fractures of the lower extremities, or severe burns. Medical record information was abstracted for all patients admitted to any of eight participating hospitals in the central and northern Alabama area with one or more of these injuries. From this database of potential participants, those who met the inclusion criteria were asked to participate in the longitudinal study. The inclusion criteria were: (a) having sustained one or more of the aforementioned injuries between 1989 and 1992; (b) having a documented acute care hospital stay of 3 or more days due to that injury; (c) residing and having been injured in Alabama; (d) being at least 18 years of age when injured; and (e) agreement to participate in regularly scheduled telephone follow-up interviews conducted by UAB ICRC personnel.

Within one year of injury, potential participants who met the inclusion criteria were sent a letter that described the study in detail. A UAB ICRC representative then contacted each person, explained the study in greater detail and obtained the person's informed consent. Telephone follow-up interviews began as close as possible to the 12 month anniversary of the participants' initial discharge from the acute care setting. Subsequent telephone follow-up interviews continued approximately annually, with the exceptions of 36 and 84 months, and recently ended after 15 years of follow-up.

## Participants in This Research

Subjects were drawn from the database of potential participants whose medical records were abstracted to identify those eligible for *A Longitudinal Study of Rehabilitation Outcomes*, and include only those at least age 18 and diagnosed with a traumatic brain injury. Patients diagnosed with injuries other than or in addition to TBI were not eligible for this study. For the purposes of this study, TBI is defined as International Classification of Diseases, Ninth Revision (ICD9) codes 800-803, 851-854. There are 1221 participants available (884 men, 337 women).

## Variables

With the exception of mortality status and underlying cause of death, all variables included in these analyses (age, gender, injury severity, open versus closed head injury, race, marital status, and injury etiology) were abstracted from medical records. Injury severity was documented using the Abbreviated Injury Scale (AIS).[10] The AIS is a widely used anatomical scoring system that ranks injuries on a scale from 1 (minor injury) to 6 (unsurvivable injury). The Head AIS reflects injury to the head only, with the same ranking categories. The Head AIS is the injury severity measure used in the analyses. Age at time of injury was categorized as 18-30 years, 31-50 years, and 51+ years. Race is dichotomized to white or black. Martial status is categorized as married or not married. Injury etiology is categorized as transportation related, fall related, intentional injury or other.

## National Death Index

Mortality was assessed using the National Death Index (NDI). Information on those patients whose data were abstracted to find the potential study participants was submitted to the NDI to determine if and when they died, as well as underlying cause of death. If they died between 24 hours post-injury and 24 months post-injury, they were classified as “dead” for purposes of the gender-specific survival analysis. If the person was still alive or died more than 24 months post-injury, he/she was classified as “alive” for the survival analysis. Those patients who died within 24 hours of their injury were excluded from the analysis. This exclusion removes those patients so severely injured that they had little chance of survival, leaving a population likely to have a meaningful survival time. The ICD death codes from the NDI results were obtained to classify cause of death. These codes were classified according to the likelihood of relation to the injury.

The National Death Index was established by the National Center for Health Statistics as a resource for ascertainment of mortality status. It is available only for medical and health research purposes. This central computerized listing compiles death record information from individual State vital statistics offices. Death record information is recorded annually, and information is available for deaths occurring from 1979 to present.[11]

The accuracy of the NDI's ability to document mortality has been demonstrated. Research has shown the NDI's sensitivity to range between 87% and 97.9%. In cases when the social security number is available, the sensitivity generally exceeds 95%.[12-19] The NDI's specificity has also been shown to be high, 99-100%.[12, 16, 18] The accuracy of the cause of death recorded for NDI has also been examined. In a study comparing the NDI cause of death with ICD-9 codes independently assigned by trained nosologists, Sathiakumar and colleagues found a discrepancy of only 4%.[20]

## Statistical Analysis

Differences in demographic characteristics between men and women were evaluated using either a chi-square or t-test. The survival analysis was performed via Cox Proportional Hazards.

Besides gender, other variables in the model are those believed most likely related to post-injury survival and used in previous research: head injury severity, age at time of injury, and type of head injury (open vs. closed). Twenty four hours post-injury was defined as the date of injury plus 1 day. Survival time in days for each participant was calculated from 1 day post-injury until the day of death, as determined by NDI, or until 730 days post-injury, whichever came first. The proportional hazard assumption was checked in two ways for the variables in the Cox model. First, the assumption was checked visually by plotting the log[-log S(t)] versus survival time. Then, the assumption was checked by adding the interaction of *variable**time to the model to check for statistical significance. All alphas were set at 0.05.

# RESULTS

Of the 1,221 participants submitted to the National Death Index, 112 died within the first 24 hours after injury. These 112 were excluded from further analysis. The analyses were performed using 1,109 subjects (799 men, 310 women).

Both the men and the women in this study were mostly single and had sustained a closed head injury. However, the women were older at time of injury than the men (average age 43 years, SD 22 vs average age 36, SD 17), were less likely to have a head AIS score of 3 (25% vs 33%), were more likely to have been white (75% versus 67%), and were less likely to have sustained an intentional injury (10% vs 17%). (Table 1)

Overall, 134 participants - 89 men (11%) and 45 women (15%) - died between 24 hours and 24 months post-injury. For the Cox Model, missing data for some variables included in the model prohibited use of all 1,109 participants, resulting in data from only 1,090 participants. Of these participants with complete data, 132 died (44 women, 88 men) and 958 were censored (lived at least 24 months post injury).

With the exception of gender, any non-proportionality of hazards of the variables in the model occurred very early in the time frame. Hazards were proportional after approximately 30 days. In the case of gender, the hazards generated were equal, with the hazards diverting late within the time frame. As the purpose of this research is to characterize differences in mortality over a long (24-month) time period, all variables are considered proportional for purposes of the model. Figure 1 portrays a graphic evaluation of proportional hazards assumption for gender.

During the time period 24 hours post-injury to 24 months post-injury, gender was not associated with mortality (HR 1.02, 95% CI 0.71 – 1.48), nor was type of head injury (HR 0.66, 95% CI 0.37 – 1.18). The variables in the model were associated with mortality were age category at time of injury (HR 1.83, 95% CI 1.46 – 2.29) and head AIS score (HR 2.24, 95% CI 1.88 - 2.67). (Table 2)

Table 3 lists causes of death and percentage of persons who died from each cause for the 134 men and women who died between 24 hours and 24 months post-injury. Cause of death was categorized as "likely related to TBI" and "not likely related to TBI." Causes likely related to TBI were (1) motor vehicle crashes, (2) all other injury producing events and adverse effects, (3) homicide and legal intervention, (4) suicide, (5) intracerebral and other intracranial hemorrhage. During this time period, 21% of men and 40% of women died from a cause "not likely related to TBI". This difference was statistically significant ($p=0.02$).

If the time period in question is shortened to 30 days in an attempt to examine those deaths more temporally related to injury, we find 86 participants (26 women and 60 men) died during this period (between 24 hours and 30 days post-injury). The causes of death were classified as "likely related to TBI" and “not likely related to TBI.” With this shorter time frame, 7% of men and 19% of women died from causes of death classified as “not likely related to TBI”. This difference is not statistically significant.

## DISCUSSION

Gender was not associated with survival after TBI between 24 hours and 24 months post injury in these data. However, the risk of death was shown to increase 2.2 times for each increase in the head AIS score and increase 1.8 times for each increase in age category in the presence of the other variables in the model. Older, more seriously injured participants were more likely to die. While the hypothesis that women would be more likely than men to survive to 24 months post-TBI was not supported by the results herein, these results do agree with those of previous research. Kraus, Peek-Asa, and McArthur [4] as well as Slewa-Younan, Green and colleagues [5] found no difference in the survival of men and women post-TBI. Davis, Douglas, and colleagues [2] found no difference in post-TBI survival between pre-menopausal women and men.

The examination of cause of death during this time period revealed that the survival analysis performed was survival after TBI as opposed to survival of (or from) TBI. Between 24 hours and 24 months post-injury, 21% of men and 40% of women died from causes unlikely related to TBI. When the time period was shortened to 24 hours to 30 days post-injury, 7% of men and 19% of women died from causes unlikely related to TBI. During this shorter time period, the difference was not statistically significant, but this is likely due to small cell count.

Much of the mortality experienced in this cohort, especially late in the time frame, does not appear related to the sequelae of traumatic brain injury received.

The current research extends the time period examined in the survival analysis to 24 months post-injury. Past research has examined mortality at time of hospital discharge,[2] at 6 months post-TBI,[3] at 18 months post-TBI,[4] or at time of discharge from rehabilitation.[5] This extension allowed a fuller exploration the role of gender in post-TBI survival, and showed that, long-term, gender plays no statistically significant role in survival after TBI.

Using the National Death Index to ascertain vital status is an improvement in methodology compared to a previous study that relied on contacting participants or family members.[4] Self-report and family-report is not as reliable as the National Death Index. When relying on family members to report mortality, the family of the participant must be contacted to document the death. Deaths could easily be missed by inability to find the participant or speak with the family to confirm vital status. The National Death Index is considered the gold standard for ascertaining vital status with high sensitivity and specificity.[12-19] Online sources frequently used in mortality studies to ascertain vital status, such as the Social Security Death Index, do a poor job identifying deaths among younger persons, women, and those whose identifying information is incomplete, possibly resulting in an under-ascertainment of mortality.[21-24]

Although the current research offers several advantages over past research, it is not without limitations. This research is secondary data analysis and therefore is subject to the inherent limitations of that type of research. The parent study was not designed to evaluate the influence gender has upon post-injury mortality.  If it had been, different information may have been collected about the participants or different instruments may have been used to collect information. Additionally, no information was available concerning pre-existing conditions or medical conditions arising between 24 hours and 24 months post-TBI.

# CONCLUSIONS

There is no evidence that gender plays a statistically significant role in survival after traumatic brain injury between 24 hours and 24 months post-injury. Having a more severe head injury and older age at time of injury are the factors that most strongly influence death in this time period among these participants. Gender may play a role in survival in the first 24 hours post-TBI.

The role of gender in post-TBI survival is unclear, as research provides conflicting results. Some of the conflict could arise because when measuring gender's influence on post-injury outcomes, it is difficult to segregate the effects of biology, the effects of hormones, and the effects of social role functioning. Future research should be cognizant of these subtleties and work to isolate the individual effects.

ACKNOWLEDGEMENT

This research was supported in part by Grant No. R49-CE000191 from the Centers for Disease Control and Prevention, National Center for Injury Prevention and Control to the UAB Injury Control Research Center

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Table 1: Participant characteristics

| Characteristic | Men (N=799) | Women (N=310) | *p*-value |
|---|---|---|---|
| **Average age** at time of injury (years) | 36 (SD 17) | 43 (SD 22) | $p < 0.0001$ |
| **Age** at time of injury (Categories) | | | |
| 18-30 years | 352 (44%) | 96 (31%) | $p < 0.0001$ |
| 31-50 years | 279 (35%) | 97 (31%) | |
| 51+ years | 168 (21%) | 117 (38%) | |
| **Race** | | | |
| Black | 258 (33%) | 78 (25%) | $p$=0.021 |
| White | 535 (67%) | 229 (75%) | |
| **Marital Status** | | | |
| Married | 287 (39%) | 112 (38%) | $p$=0.83 |
| Single | 445 (61%) | 179 (62%) | |
| **Type of head injury** | | | |
| Open | 89 (11%) | 26 (8%) | $p$=0.17 |
| Closed | 708 (89%) | 284 (92%) | |
| **Injury Severity (Head)** | | | |
| Head AIS 2 – Moderate | 295 (38%) | 134 (44%) | $p$=0.08 |
| Head AIS 3 – Serious | 256 (33%) | 78 (25%) | |
| Head AIS 4 – Severe | 165 (21%) | 61 (20%) | |
| Head AIS 5 – Critical | 70 (9%) | 33 (11%) | |
| **Injury Etiology** | | | |
| Transportation Related | 477 (60%) | 198 (64%) | $p$=0.0011 |
| Falls | 116 (15%) | 64 (21%) | |
| Intentional | 138 (17%) | 32 (10%) | |
| Other | 68 (9%) | 16 (5%) | |

Table 2: Hazard Ratios: Risk of death between 24 hours and 24 months post-injury

| Variable | Hazard Ratio | 95% CI |
|---|---|---|
| Gender (women vs. men) | 1.02 | 0.71 – 1.48 |
| Head AIS† | 2.24 | 1.88 – 2.67 |
| Age at time of injury† | 1.83 | 1.46 – 2.29 |
| Type of head injury (open vs closed) | 0.66 | 0.37 – 1.18 |

†Statistically significant
Head AIS rankings: Moderate, Serious, Severe, Critical; Age categories: 18-30 years, 31-50 years, 51+ years

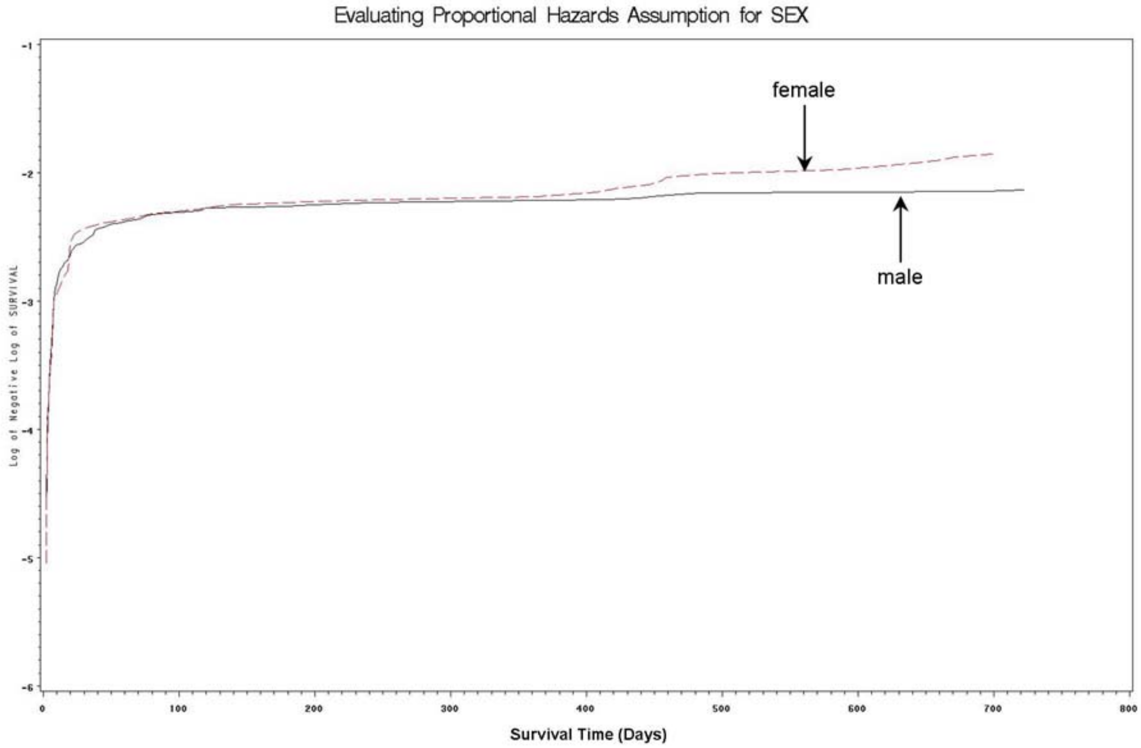
Table 3: Cause of death 24 hours through 24 months post-injury

| | | % of Deaths | |
|---|---|---|---|
| | **Cause of Death** | **Men (n=89)** | **Women (n=45)** |
| Cause of Death Likely Related to TBI | Motor vehicle crashes | 39% | 32% |
| | All other injury producing events and adverse effects | 25% | 18% |
| | Homicide and legal intervention | 6% | 4% |
| | Suicide | 5% | 4% |
| | Intracerebral and other intracranial hemorrhage | 5% | 2% |
| Cause of Death Unlikely Related to TBI | All other forms of heart disease | 8% | 13% |
| | All other diseases (residual) | 1% | 7% |
| | Acute myocardial infarction | 1% | 7% |
| | Septicemia | - | 4% |
| | All other and late effects of cerebrovascular disease | 3% | 2% |
| | Malignant neoplasm of breast | - | 2% |
| | Other diseases of the endocardium | - | 2% |
| | Ulcer of stomach and duodenum | - | 2% |
| | Old myocardial infarction and other forms of chronic ischemic heart disease | 2% | - |
| | Symptoms, signs, and ill-defined conditions | 2% | - |
| | Hernia of abdominal cavity and intestinal obstruction without mention of hernia | 1% | - |
| | Diabetes mellitus | 1% | - |
| | Other chronic obstructive pulmonary diseases and allied conditions | 1% | - |

Table 4: Cause of death 24 hours through 30 days post-injury

| | | % of Death | |
|---|---|---|---|
| | **Cause of Death** | **Men (n=60)** | **Women (n=26)** |
| Cause of Death Likely Related to TBI | Motor vehicle crashes | 45% | 46% |
| | All other injury producing events and adverse effects | 30% | 27% |
| | Suicide | 7% | 8% |
| | Homicide and legal intervention | 7% | - |
| | Intracerebral and other intracranial hemorrhage | 5% | - |
| Cause of Death Unlikely Related to TBI | All other forms of heart disease | 5% | 8% |
| | All other diseases (residual) | - | 4% |
| | Septicemia | - | 4% |
| | Other diseases of the endocardium | - | 4% |
| | All other and late effects of cerebrovascular disease | 2% | - |

Figure 1: Evaluating proportional hazards for gender



# FUNCTIONAL INDEPENDENCE AND EMPLOYMENT STATUS OF MEN AND WOMEN TWELVE AND TWENTY FOUR MONTHS AFTER TRAUMATIC BRAIN INJURY

by

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In preparation for *Archives of Physical Medicine and Rehabilitation*

Format adapted for dissertation

ABSTRACT

Objective: To investigate the influence of gender on functional independence and employment status after traumatic brain injury (TBI) at 12 and 24 months post-injury.

Design: Retrospective follow-up study

Setting: General community

Participants: Participants were drawn from a longitudinal study of survivors of catastrophic injury and include only those diagnosed with a traumatic brain injury. TBI is defined as International Classification of Diseases, Ninth Revision (ICD9) codes 800-803, 851-854. There are 580 participants (163 women, 417 men) available at the 12 month post-injury follow-up interview and 489 participants (137 women, 352 men) available at the 24 month post-injury follow-up interview.

Interventions: None

Main Outcome Measure: The Functional Independence Measure (FIM) and self-reported employment status

Results: Gender was not associated with post-injury functional independence at 12 or 24 months post-injury when the participant responded to the follow-up questionnaire. When a proxy responded, the unadjusted analysis showed that female gender was associated with lower levels of functional independence at both 12 and 24 months post-injury ($p<0.05$). After adjusting for other factors, female gender was associated with a 13% decrease in average FIM score at 12 months post-injury ($p=0.0198$), but not at 24 months post-injury. Gender was not associated with employment status at either 12 or 24 months post-injury.

Conclusion: Functional independence varied across respondent categories. When a proxy responded, female gender was associated with lower average FIM scores at 12 months post-injury, but not at 24 months post-injury. The role of gender in post-TBI employment status did not differ across respondent categories. Gender played no important role in employment status post-injury.

Key Words: Gender, Sex, Traumatic Brain Injury, Functional Independence, Employment Status, Functional Independence Measure, Proxy

# INTRODUCTION

Historically, traumatic brain injury (TBI) research has focused primarily on men, and it has been assumed that the best course of medical treatment for women is the same as that for men. However, the Institute of Medicine states that all of the body's organs have the capability to respond differently based on gender, and research should be designed to examine the genders separately.[1] The differences seen in the structure of male and female brains brings up questions of how those differences could influence the brain's response to injury.[2-11]

Gender differences in post-TBI outcomes could be the result of a variety of factors. Variation in brain structure could cause dissimilar brain responses to and recovery from traumatic brain injury for women compared to men. Hormonal levels could play a role, resulting in gender differences being seen in some age groups but not others. Finally, the disparities could be the result of different psychological reactions to TBI.

Functional independence is one's ability to perform activities of daily living, such as self-care, locomotion, communication, and social cognition. The primary goal after TBI is survival, but once the person has survived, attention turns to other outcomes such as reintegration into his/her former life. The extent to which this reintegration is successful depends on the person's post-injury level of functional independence. Related to functional independence, and an important post-TBI milestone, is return to work. Previous work examining gender's influence on post-injury functional independence and return to work has produced mixed results.

Slewa-Younan, Green, and colleagues found that TBIs sustained by men were more severe than those of women, but found no differences in functional ability, Glasgow Outcome Scale, or mortality after rehabilitation. [12] These results concur with those of Brown and colleagues who found that gender was not predictive of post-injury disability, independent living, or productivity,[13] and with those of Ponsford, Miles, et al., who found no gender differences in Extended Glasgow Outcome Scale score between men and women 6 months after severe TBI. [14]

Research examining gender differences in post-injury employment status has produced mixed results. Some research has shown that men are more likely than women to return to work upon hospital discharge [15] while other research has shown that men were less likely to be employed than women 12 months post-TBI. [16] A recent study by Corrigan, et al. found women to be more likely to stop working post-TBI. This study also found interactions between gender and age as well as between gender and marital status. [17] Conversely, a meta-analysis of studies examining both genders found that women were more likely than men to return to work after TBI. [18]

Research examining gender differences on a variety of factors related to functional independence and the ability to be employed post-TBI has also produced mixed results. Post-TBI women have been found to have better executive functioning (one's ability to interpret surrounding events, formulate appropriate reactions to situations, and process feedback),[19] attention, memory and language skills, [20] to display less cognitive decline,[21] to have fewer interpersonal problems, less aggressiveness,[22] less emotional distress,[23] less bipolar affective disorder,[24] and less difficulty in social integration after a TBI [25] than do men. Other research has found that after TBI, women, more often than men, experience psychological difficulties,[23] major depression,[23, 26] have more difficulty with physical independence,[15, 25] are less likely to return to school,[27] experience post-concussive syndrome, [28] have more days of post-traumatic amnesia, and experience dizziness, irritability, insomnia, and headache. [18]

Mixed methodology, differing definitions of functional ability and return to work, and different time periods examined could have produced the mixed results seen in previous gender studies of post-TBI outcomes. A literature review uncovered no previous work specifically documenting gender differences in post-TBI functional independence using the Functional Independence Measure (FIM). The FIM allows for assessment of the level of independence the person has with a variety of everyday tasks, both physical and cognitive, thereby providing a more complete depiction of that person's post-injury status. The other studies explored post-TBI gender differences in similar, but narrower, constructs such as physical independence, post-injury disability, and independent living using individual questions or other measurement scales.[12, 13, 15, 25] The use of the FIM provides a more comprehensive assessment of functional independence. Additionally, the current research has the ability to document not only whether the person returned to work, but whether he/she returned to his/her pre-injury work location, and, if unemployed post-injury, to document whether the person is looking for a job or is unemployed due to injury. Previous research has focused more strictly on return to work vs. failure to return to work.

The purpose of this research is to investigate the possible influence of gender upon functional independence and employment status 12 and 24 months post-injury. It is hypothesized that women will display greater functional independence and will be more likely to be employed than men at both 12 and 24 months post-injury.

# METHODS

Participants in this retrospective follow-up study were participants diagnosed with TBI drawn from a large, prospective cohort study (*A Longitudinal Study of Rehabilitation Outcomes*, as described below).

## A Longitudinal Study of Rehabilitation Outcomes

In 1989, the University of Alabama at Birmingham's Injury Control Research Center (UAB ICRC) received approval from the UAB Institutional Review Board to initiate a prospective, longitudinal study of persons with one or more of the following injuries: spinal cord injury, traumatic brain injury, intra-articular fractures of the lower extremities, or severe burns. Medical record information was abstracted for all patients admitted to any of eight participating hospitals in the central and northern Alabama area with one or more of these injuries. From this database of potential participants, those who met the inclusion criteria were asked to participate in the longitudinal study. The inclusion criteria were: (a) having sustained one or more of the aforementioned injuries between 1989 and 1992; (b) having a documented acute care stay of 3 or more days due to that injury; (c) residing and having been injured in Alabama; (d) being at least 18 years of age when injured; and (e) agreement to participate in regularly scheduled telephone follow-up interviews conducted by UAB ICRC personnel.

Within one year of injury, potential participants who met the inclusion criteria were sent a letter that described the study in detail. A UAB ICRC representative then contacted each person, explained the study in greater detail and obtained the person's informed consent. Telephone follow-up interviews began as close as possible to the 12 month anniversary of the participants' initial discharge from the acute care setting. Subsequent telephone follow-up interviews continued approximately annually, with the exceptions of 36 and 84 months, and recently ended after 15 years of follow-up.

## Participants in This Research

Participants in this research are drawn from *A Longitudinal Study of Rehabilitation Outcomes*, and include only those diagnosed with a traumatic brain injury. Those diagnosed with injuries other than TBI or with injuries in addition to a TBI are not eligible for this study. For the purposes of this study, TBI is defined as International Classification of Diseases, Ninth Revision (ICD9) codes 800-803, 851-854. At the 12-month follow-up interview, there are 580 participants available (163 women, 417 men). At the 24-month follow-up, there are 489 participants available (137 women, 352 men). Between the 12 month and 24 month follow-up, 6 participants died (3 women, 3 men) and 87 were lost to follow-up (24 women, 63 men). Comparison of those participants lost with those in the 12 month follow-up revealed the two groups to be similar in gender, race, type of head injury, marital status (pre-injury and at 12 months post-injury), employment status (pre-injury and at 12 months post-injury), and education. Those that were lost were less severely injured than those retained in the study.

## Variables

Variables were either abstracted from medical records or collected during the telephone follow-up interviews. Response to the telephone interviews could be given by either the participant or a proxy. Specifically, age at time of injury, gender, type of head injury, and injury severity were abstracted from medical records. Injury severity was documented using the Abbreviated Injury Scale (AIS). [29] The AIS is a widely used anatomical scoring system that ranks injuries on a scale from 1 (minor injury) to 6 (unsurvivable injury). The Head AIS is the AIS reflecting injury to the head only, with the same ranking categories. The Head AIS is the injury severity measure used in the analyses.

## The Functional Independence Measure (FIM)

The Functional Independence Measure (FIM) [30] (Appendix 1) was used to assess functional independence for participants in *A Longitudinal Study of Rehabilitation Outcomes*. The FIM is a widely accepted functional assessment tool used in the rehabilitation community. It measures independent performance in self-care, sphincter control, transfers, locomotion, communication, and social cognition. The FIM is an 18-item ordinal scale. Scores on each item range from one to seven, with higher scores indicating greater independence. A total score is calculated by adding the item scores. Possible total scores range from 18 to 126 (with 126 indicating the highest level of independence). The FIM has cognitive and motor subscales. The cognitive subscale consists of 5 items characterizing the patient's cognitive ability with a score ranging from 5 to 35 (higher scores indicating greater cognitive ability). The motor subscale consists of 13 items characterizing the patient's motor ability with a score ranging from 13 to 91 (higher scores indicating greater motor ability). The FIM is an instrument of demonstrated reliability and validity for use with people with a variety of disabilities, including traumatic brain injury. [31-38] Traditionally, the FIM has been completed by a clinician, but this study uses the FIM as a self-report instrument. Completing the FIM in this manner has been demonstrated to yield results comparable to what is found when a clinician completes the scale. [39-40]

## Employment Status

Employment status was determined through self-report during the 12 month and 24 month follow-up interviews. Employment status at time of injury and at 12 months post-injury was assessed with a series of questions in the first follow-up interview (12 months post-injury). Employment status at 24 months post-injury was assessed with a series of questions in the second follow-up interview (24 months post-injury). In the 12 and 24 month follow-up interviews, the participants were asked whether they were employed full-time, employed part-time, self-employed, unemployed, a student, retired, or not working due to their TBI. If the participant was unemployed, he/she was asked whether he/she was looking for a job. If the participant was employed, he/she was asked whether he/she was working in the same location as before the TBI.  During the 12 month follow-up interview, pre-injury employment status was ascertained by asking if, prior to injury, the participant was employed full-time, employed part-time, self-employed, unemployed, a student, retired, or not working due to a previous injury. (Appendix 2)

For the employment status analyses, only those participants who were employed (full-time, part-time, self-employed, student) prior to injury are considered. Those unemployed, not working due to a prior injury, or retired before their TBI are not expected to be employed post-injury and were excluded from the analyses. This criterion excluded 108 men (62 unemployed, 27 retired and 19 unemployed due to a previous injury) and 65 women (31 unemployed, 27 retired and 7 unemployed due to a previous injury). Post-TBI employment was categorized as employed (combining those employed full-time, part-time, self-employed or a student) and unemployed (combining those unemployed, unemployed due to injury and retired).

## Statistical Analysis

Differences in demographic characteristics between men and women were evaluated using either a chi-square or t-test. The functional independence analysis was performed via negative binomial regression. The employment status analysis was performed via logistic regression, but risk ratios were reported by mathematically converting the odds ratios produced by the logistic regression procedure.

Negative binomial regression was chosen for the functional independence analysis because the outcome variables (the FIM scores) are count data (ordinal) and not normally distributed, but clustered around a smaller number of values. Data from such a distribution are typically analyzed using Poisson regression. However, the Poisson distribution requires that the mean and the variance of the data are equal, and this assumption does not hold for these data where the variance is greater than the mean. The overdispersion of these data makes the negative binomial distribution a more appropriate choice. The negative binomial regression was performed using SAS software, Version 9.1.3 *proc genmod* with the negative binomial distribution specified in the option statement (*dist=negbin)*. Model fit was assessed using the ratio of deviance to degrees of freedom. If this ratio is close to 1, then the model fits the data. A large ratio (or a small ratio) suggests that the model is either misspecified or that the response variable is over-dispersed (or under-dispersed). Over- or under-dispersion results in an incorrect estimation of the standard errors of the parameter estimates.

The measure of association reported from the negative binomial regression model was the percent difference in the average FIM score of one group compared to another group. This percent difference is calculated by the formula $100*[\exp(\beta) - 1]$, where $\beta$ is the regression coefficient for a particular variable. For example, a $\beta$ of -0.105 indicates a 10% decrease in the average score on the FIM for (1) the exposed compared to the unexposed (women compared to men, or those with an open head injury compared to a closed head injury); (2) each increase in head injury severity category; or (3) each one year increase in age.

For the employment status analyses, logistic regression was chosen. The model fit for the logistic regression model was assessed using the Hosmer-Lemeshow (HL) goodness-of-fit statistic. This statistic compares, in groups, the observed outcomes with the outcomes determined by the model using a Pearson chi-square statistic. A non-statistically significant p-value indicates that the actual and model-derived outcomes were similar and the model is a good fit for the data. The outcome of interest (unemployment) was common so the odds ratio was not the most appropriate measure of association. In situations where the outcome is common, the odds ratio will overestimate the more preferable measure of association, the risk ratio. Since logistic regression provides an odds ratio, each odds ratio was converted to a risk ratio through a simple formula $RR = OR/((1-P_0)+(P_0*OR)$. [41] In this situation RR = risk ratio, OR=odds ratio, and $P_0$ = incidence of the outcome in the unexposed group. The risk ratio produced describes the risk of unemployed post-injury. For example, a risk ratio of 0.90 indicates a 10% decrease in the risk unemployment for (1) the exposed compared to the unexposed (women compared to men, the unmarried compared to the married); (2) each increase in head injury severity category; or (3) each one year increase in age.

Besides gender, other variables included in the model are those hypothesized to be related to outcome in question and that were used in similar research:  age at time of injury (years), severity of head injury (head AIS score), education level (less than high school, high school, greater than high school), level of functional independence (total FIM score), marital status (unmarried vs. married), and type of head injury (open vs. closed). Specifically, in the FIM negative binomial models, total FIM score or FIM subscale score were the dependent variables and gender, age, injury severity and type of head injury were included as independent variables. For the employment status logistic regression models, employment status (unemployed or employed) was the dependent variable and gender, age, total FIM score, education level and injury severity were the independent variables.

# RESULTS

Characteristics of men and women were similar at both the 12 and 24 month follow-up interviews. Participants were primarily white, not married, and had sustained a moderate-to-serious, closed head injury. Overall, women were older when injured and more likely to be unemployed at 12 and 24 months post-injury ($p<0.05$). At both 12 and 24 months post-injury, women were more likely to respond to the follow-up interview themselves, rather than have a proxy respond for them ($p<0.05$). (Table 1)

## Functional Independence

It was already noted that women are more likely to respond to the follow-up survey for themselves. Further analysis showed that higher total FIM scores were associated with participant response as compared to proxy response. The unadjusted association between gender and FIM score was not statistically significant when all respondents were considered together. When the unadjusted analysis was stratified by respondent, female gender was associated with a 15% decrease in average FIM score at 12 months ($p= 0.0075$) and with a 12% decrease in average FIM score at 24 months ($p= 0.0181$), but only under the proxy response condition. Because of these discrepancies, further FIM analyses were stratified by respondent (participant or proxy).

*Participant and Proxy Response to the FIM at 12 Months Post-Injury*

When participants responded for themselves, the median FIM score was 125 for men and 124 for women at 12 months post-injury. The median cognitive FIM subscale score for men and women was 35 and the median motor FIM subscale score was 91 for men and 90 for women. These scores indicate a high level of functional independence, and gender differences in functional independence were minimal when the participants responded for themselves. When a proxy responded for the participants, the median FIM scores at 12 months post injury was 122 for men and 108 for women. The median cognitive FIM subscale score was 33 for men and 27 for women, and the median motor FIM subscale score was 91 for men and 84 for women. These scores indicate a higher level of functional independence for men than for women. Gender's unadjusted role in FIM total and subscale scores was statistically significant in all instances. (Table 2)

When participants responded for themselves at 12 months post-injury, the negative binomial regression revealed gender was not associated with FIM score. Having an open head injury was associated with a 3% lower average FIM score after adjusting for gender, age, and head injury severity (p=0.0396). When a proxy responded for the participant at 12 months post-injury, the negative binomial regression revealed female gender to be associated with a 13% decrease in average FIM score (p= 0.0198) and greater head injury severity to be associated with a 10% decrease in average FIM score (p= 0.0001), after adjustment for other factors. The other variables in the model (age, type of head injury) were not associated with FIM score. (Table 3) Model fit statistics indicated that the participant response and proxy response models fit the data. The ratio of the deviance to the degrees of freedom was 1.16 and 1.09, respectively, indicating appropriate model specification.

Analysis of the FIM subscales revealed gender not associated with the FIM cognitive or motor subscales scores at 12 months post-injury when the participant was the respondent. Greater head injury severity was associated with a 2% decrease in average FIM cognitive subscale score ($p=0.0395$) and having an open head injury was associated with a 3% lower average FIM motor subscale score ($p=0.0329$) after adjusting for other factors at this time point. When a proxy was the respondent, analysis of the FIM subscales revealed gender not associated with the FIM cognitive subscale after adjusting for age, injury severity and type of head injury. Greater head injury severity was associated with an 11% decrease in average FIM cognitive subscale score ($p<0.0001$). Females had a 14% lower FIM motor subscale score ($p=0.0128$) and greater head injury severity was associated a 9% decrease ($p=0.0004$) in average FIM motor subscale after adjusting for age and type of head injury. (Table 4)

*Participant and Proxy Response to the FIM at 24 Months Post-Injury*

When the participant was the respondent at 24 months post-injury, the median FIM score was 124 for men and 123 for women. The median cognitive

FIM subscale score was 34 for men and 35 for women, and the median motor FIM subscale scores was 91 for men and 90 for women. These scores indicated a high level of functional independence. When a proxy was the respondent, the median FIM score was 123 for men and 114 for women at 24 months post-injury. These scores indicate a higher level of functional independence for men than for women. The median cognitive FIM subscale score was 34 for men and 27.5 for women, and the median cognitive FIM subscale score was 91 for men and 88 for women. Gender's unadjusted role in FIM total and subscale scores was statistically significant in all instances. (Table 2)

When the participant was the respondent at 24 months post-injury, having an open head injury decreased the average FIM score by 4% (p=0.0002). None of the other variables in the 24 month model (gender, age, head injury severity) were associated with the FIM score. When a proxy was the respondent at 24 months post-injury, greater head injury severity was associated with an 8% decrease in FIM score (p=0.0015) after adjustment for other factors. None of the other variables in the model (gender, age, type of head injury) were associated with the FIM score. (Table 3) Model fit statistics indicated that both the participant and proxy models fit the data. The ratios of the deviance to the degrees of freedom were 1.09 and 1.14, respectively, indicating appropriate model specification.

Under participant response at 24 months post-injury, having an open head injury decreased average scores on the FIM cognitive subscale by 10% (p=0.0002) and female gender decreased the average FIM motor subscale score by 2% (p<0.0001), both after adjustment for other factors. When a proxy was the respondent at 24 months post-injury, analysis of the FIM subscales adjusting for other factors revealed the average FIM cognitive subscale was decreased 1% for every year increase in age (p<0.0001) and 9% for every increase in head injury severity (p=0.0002) after adjusting for gender and type of head injury. Gender was not associated with the FIM motor subscale score. Greater head injury severity lowered average FIM motor subscale scores by 7% (p=0.0055) at this time point, after adjusting for gender, age and type of head injury. (Table 4)

## Employment Status

The employment status analyses restricted the dataset to just those employed prior to injury. In this subset of the data, women were more likely to respond to the survey themselves rather than have a proxy respond for them. Further analysis showed that participants who responded for themselves were more likely to be employed at 12 months post injury. This association did not hold for the 24 month follow-up interview. However, although the point estimates for gender's association with employment status did vary somewhat by respondent category, none of those point estimates were statistically significant.

There were 300 men (172 employed, 128 unemployed) and 95 women (54 employed, 71 unemployed) available at the 12 month follow-up and 260 men (166 employed, 94 unemployed) and 81 women (44 employed, 37 unemployed) available at the 24 month follow-up. Women were older at time of injury and less severely injured (p<0.05, Table 5). The unadjusted associations between employment status and gender at 12 and 24 months post-TBI were not statistically significant. (Table 6)

Of those employed 12 months post-injury, 116 men (67%) and 39 women (72%) worked in the same location as prior to injury. Of those unemployed 12 months post-injury, 34 men (27%) and 8 women (11%) were looking for a job. Additionally, 97 men (76%) and 29 women (41%) were unemployed due to their TBI. Among those employed 24 months post-injury, 63 men (40%) and 19 women (43%) were working in the same location prior to injury. Of those unemployed 24 months post injury, 22 men (23%) and 5 women (14%) were looking for a job. Additionally, 65 men (70%) and 27 women (72%) were unemployed due to their TBI. None of these differences were statistically significant, but there were small numbers of participants in some categories. (Table 6).

After adjusting for education, FIM score, injury severity, age, and marital status, gender was not associated with employment status at either 12 or 24 months post-injury. At 12 months post-injury lower levels of education (RR 0.72, 95% CI 0.57 – 0.90), lower overall FIM scores (RR 0.87, 95% CI 0.83 – 0.90), and being unmarried (RR 1.37, 95% CI 1.04 – 1.67) increased the risk of unemployment after adjustment for other factors. At 24 months post-injury, only lower levels of functional independence increased the risk of unemployment (RR 0.87, 95% CI 0.84 – 0.91) after adjustment for other factors. (Table 7) The 12 and 24 month models both fit the data well. For the 12 month model, the Hosmer-Lemeshow chi-square was 6.74 (p=0.056), and for the 24 month model, the Hosmer-Lemeshow chi-square was 6.99 (p= 0.54). The non-significant p-value indicated the models were a good fit for the data.

# DISCUSSION

Gender's relationship to functional independence differed across respondent category (participant or proxy), while gender's relationship with employment status did not differ across respondent category. Analyses of the FIM data, but not the employment status data, were stratified by respondent.

Median total FIM scores as well as FIM cognitive and motor subscale scores were very high at both 12 and 24 months when the participant responded to the interview, indicating a high level of functional independence for both men and women. In situations when a proxy responded, women had lower median FIM total scores as well as lower FIM cognitive and motor subscale scores at 12 and 24 months. However, women did show an improvement in scores between 12 and 24 months post-TBI under proxy response, but their 24 month median scores were still lower than those of men. Men's scores were stable between the two time periods. This improvement over time could suggest that women, while less functionally independent after injury, continue to improve in their functional abilities over a longer period of time than do men.

When considering the differences in FIM scores between participant and proxy response, those who respond for themselves are the people with the highest levels of functional independence, so finding no gender differences under self-report situations is reasonable. The discrepancy between FIM scores of men and women under proxy response could be because men are more likely than women to have a proxy respond for them, so women who use proxies are more severely injured than men who use proxies. It is worth noting, however, the proxy response was not related to head injury severity as measured by the AIS. Another possibility is that the proxies for the women underestimated the women's abilities, but the proxies for the men showed no such bias. Alternatively, although self-report has been found comparable to clinician report of the FIM, [39-40] the women in this data may have over-estimated their functional abilities in self-report situations, and the more objective assessment given by the proxy could result in lower, but more accurate, FIM scores.

In self-report situations, gender was found to have no association with functional independence at 12 or 24 months post-injury after adjusting for age, head injury severity, and type of head injury. When a proxy responded to the interview at 12 months post-injury, female gender lowered the average FIM score by 13% after adjusting for age, head injury severity and type of head injury. At 24 months post-injury when a proxy responded to the interview, gender was not associated with functional independence, after adjusting for age, head injury severity, and type of head injury.

When the participant responded, gender was not associated with the cognitive FIM subscale at 12 or 24 months or with the FIM cognitive subscale at 24 months after adjustment for relevant factors. Female gender was minimally associated with the average FIM motor subscale score at 24 months, decreasing it by 2% after adjustment for relevant factors. When a proxy responded, female gender lowered the average FIM motor subscale score by 14% at 12 months post-injury adjusting for age, head injury severity and type of head injury. Such a relationship was not seen at 24 months post-injury.

The reasons for the differences between participant and proxy response are those mentioned previously. The women with proxy response could have been more severely injured and therefore truly more functionally dependent. Alternatively, the proxies for the women could have under-estimated the motor abilities of those women, or the women who responded for themselves could have over-estimated their abilities.

Regardless of the explanation, the results found herein do not support the study's hypothesis that women would display greater functional independence at both 12 and 24 months post-TBI. The results of the participant stratum agree with those of similar research that found gender not to be associated with post injury functional ability.[12-14] The results of the proxy stratum agree with similar research finding women to have less functional ability post injury.[15, 18, 23, 25, 27]

Over half of men and women were employed at 12 and 24 months post-TBI. At 12 month post-injury, 67% of men and 72% of women who were employed were working at the same location as prior to injury. That percentage drops at 24 months post-injury, but is still similar between men and women. Of those unemployed at 12 months post-injury, more men than women are looking for a job and more men than women indicated that their unemployment was due to their TBI. By 24 months post-injury, the number of men and women looking for a job has evened somewhat, and the percentages of men and women who indicate that their unemployment is due to their TBI are approximately equal. This job seeking gender difference could be explained by the desire to keep the household income level steady if the men held the higher paying jobs in the household. When considering the designation of unemployment due to injury, could be less accepting of their disability at 12 months post-injury and therefore reluctant to attribute their unemployment to their injury at that time.

It is worth clarifying that when considering all participants, regardless of their pre-injury employment status, women were less likely than men to be employed at both 12 and 24 months post-injury. This result is driven by women's being less likely to be employed prior to injury. However, when analyses are restricted to just those participants employed prior to injury, there was no difference in the unadjusted comparison of gender and employment status.

In the unadjusted analysis, gender was not associated with employment status at 12 or 24 months post-injury. After adjusting for education, FIM score, injury severity, age, and marital status, gender was not associated with employment status at either 12 or 24 months post-injury. At 12 months post-injury the risk of unemployment decreases 18% as education level, decreases 13% as FIM scores increase, and increases 37% for those who are unmarried, after adjustment for other relevant factors. At 24 months post-injury as total FIM score decreased, the risk of unemployed increased by 13% after adjustment for other factors. It is reasonable that those who are more physically and mentally independent would be better able to return to work post-injury. Similarly, those who are married being more likely to return to work could be explained by family obligations and incentive to keep the household income steady.

The results herein do not support the study's hypothesis that women would be more likely than men to be employed 12 and 24 months post-injury. Previous studies had found that gender played a role in post-injury employment status, but those studies disagreed about the nature of that role. [16, 20-22]

None of the previous gender-based research has examined post-TBI functional independence using the Functional Independence Measure. The FIM allows for the different dimensions of functional independence to each be measured, providing a comprehensive view of functional independence. Other studies have used the GOS [12, 14] which provides less comprehensive, gross overview functional independence, or the Functional Assessment Measure (FAM),[12] which was designed to be used in conjunction with the FIM as a supplement for measuring cognitive abilities, not independently. Other researchers examined predicted functional outcome based on return to work at time of hospital discharge.[15] The current research examined functional independence at both 12 and 24 months post-injury, extending the period examined by previous work, and using a multi-dimensional instrument of demonstrated reliability and validity. [12, 13, 15, 18, 31-40]

Previous TBI outcome studies have examined gender differences in return to work at time of hospital discharge[15] and at 12 months post-injury.[16] The extended time examined by this study (24 months) allows for rehabilitation or additional at-home recovery that may have precluded return to work immediately upon hospital discharge, and thus provides a more meaningful assessment of post-injury return to work. Additionally, the data used in current research allow for comment on not only gender differences in post-injury employment, but for gender comparisons of those employed in the same location pre and post-injury, as well as on gender comparisons among the unemployed who are seeking employment and the unemployed who are unemployed due to injury.

The role telephone interview respondent played in the current study highlights the need to closely examine differences in responses given by the respondent and a proxy when documenting gender differences in post-TBI outcomes. Gender's relationship with functional independence differed by respondent category. This relationship led to the stratification of all FIM analyses by respondent, and gender differences in TBI outcomes were only seen when a proxy responded to the interview. Had the analyses not been stratified, no gender differences would have been found.

Although the current research offers advantages over that performed by others, it does have limitations. For the functional independence analysis, it would have been informative to have a FIM score sooner after injury than 12 months as well as a pre-injury measure of functional ability. However, there is no reason to believe that the preponderance of the participants were functionally impaired prior to disability. For the employment status analysis, knowing when the participant returned to work would have resulted in a more meaningful analysis. Although approximately equal numbers of men and women were employed post-injury, the rate at which they returned to work is unknown. The women could have returned to work more quickly than the men (or vice versa), but a gender difference such as this is not detectable in this data. Finally, the employment status and, to some extent, the level of functional independence of the participant may have been influenced more by social role expectations than by their biologic sex. Information about their role within their household could have shed more light on their post-injury employment decisions and functional abilities.

# CONCLUSION

In these data, gender played no role in level of functional independence after adjustment for other factors at 12 months or 24 months post-injury when the participant provided the information used in analysis, with the exception of female gender's minimal association with a lower FIM motor subscale score at 24 months post-injury. When a proxy provided the information for the analysis, female gender was associated with lower average FIM score at 12 months post-injury and with lower average scores on the FIM motor subscale at 12 months post-injury after adjustment for other factors. Gender played no role in employment status at 12 or 24 months post-TBI.

Much work is needed before the implications of gender upon response to and recovery from traumatic brain injury can be fully realized. Although work in this area is growing, results are still conflicting. One problem lies in that there are both physical and psychological responses to and recoveries from TBI. Strictly speaking, sex and gender refer to different constructs. Sex refers to the biologic manifestation of male and female while gender is defined through social roles.[1, 42] The role of sex could be different from the role of gender in the response to and recovery from TBI. The conflicting results of research in this area of research could be because these studies are quantifying the influence of two different constructs on injury outcomes. The word "gender" is used throughout this study but the construct actually measured is some amalgamation of sex and gender, as little or no information was available concerning the participants genetic, hormonal, or social role conditions. Future research should focus on isolating sex from gender when examining TBI outcome differences between men and women.

ACKNOWLEDGEMENT

This research was supported in part by Grant No. R49-CE000191 from the Centers for Disease Control and Prevention, National Center for Injury Prevention and Control to the UAB Injury Control Research Center

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Table 1: Overall participant characteristics

| Characteristic | 12 months | | 24 months | |
|---|---|---|---|---|
| | Men (n=417) | Women (n=163) | Men (n=352) | Women (n=137) |
| Average age at time of injury (years)† | 35 (SD 16) | 43 (SD 20) | 34 (SD 15) | 44 (SD 19) |
| Race | | | | |
| Black | 121 (29%) | 39 (24%) | 97 (28%) | 33 (24%) |
| White | 294 (71%) | 121 (76%) | 253 (72%) | 102 (76%) |
| Type of head injury | | | | |
| Open | 39 (9%) | 14 (9%) | 12 (9%) | 33 (9%) |
| Closed | 377 (91%) | 149 (91%) | 125 (91%) | 318 (91%) |
| Injury Severity (Head) | | | | |
| Moderate | 165 (40%) | 79 (49%) | 134 (39%) | 68 (50%) |
| Serious | 137 (34%) | 39 (24%) | 118 (34%) | 31 (23%) |
| Severe | 87 (21%) | 36 (22%) | 73 (21%) | 30 (22%) |
| Critical | 19 (5%) | 8 (5%) | 18 (5%) | 7 (5%) |
| Marital Status | | | | |
| Married | 157 (38%) | 56 (35%) | 157 (45%) | 56 (41%) |
| Not married | 257 (62%) | 106 (65%) | 195 (55%) | 81 (59%) |
| Employment Status† | | | | |
| Employed | 182 (45%) | 56 (36%) | 178 (52%) | 45 (34%) |
| Unemployed | 58 (14%) | 27 (17%) | 46 (13%) | 21 (16%) |
| Retired | 29 (7%) | 27 (17%) | 19 (6%) | 18 (13%) |
| Unemployed Due to Injury | 139 (34%) | 46 (30%) | 101 (29%) | 50 (37%) |
| Education | | | | |
| Less than HS | 154 (38%) | 56 (35%) | 134 (38%) | 53 (39%) |
| High School | 140 (34%) | 45 (28%) | 102 (29%) | 34 (25%) |
| More than HS | 116 (28%) | 58 (36%) | 113 (32%) | 49 (36%) |
| Survey Respondent† | | | | |
| Proxy | 226 (54%) | 51 (31%) | 209 (60%) | 50 (37%) |
| Participant | 191 (46%) | 112 (69%) | 142 (40%) | 86 (63%) |

†p<0.05 at both 12 and 24 months post-injury; Employment status considers all participants, not just those employed prior to injury

Table 2: Median FIM total and subscale scores for men and women at 12 and 24 months post-injury stratified by respondent

| | Participant Response | | Proxy Response | |
|---|---|---|---|---|
| | **Men** | **Women** | **Men** | **Women** |
| **12 Months Post-Injury** | | | | |
| FIM Total‡ | 125 | 124 | 122 | 108 |
| FIM Cognitive Subscale‡ | 35 | 35 | 33 | 27 |
| FIM Motor Subscale‡ | 91 | 90 | 91 | 84 |
| **24 Months Post-Injury** | | | | |
| FIM Total‡ | 124 | 123 | 123 | 114 |
| FIM Cognitive Subscale‡ | 34 | 35 | 34 | 27.5 |
| FIM Motor Subscale†‡ | 91 | 89 | 91 | 88 |

†Statistically significant with participant response
‡Statistically significant with proxy response
Negative binomial regression was used to determine differences by gender without adjusting for other factors.

Table 3: Percent difference in average FIM score at 12 and 24 months post-injury stratified by respondent

| | Participant Response | | Proxy Response | |
|---|---|---|---|---|
| **Variable** | **Percent Difference** | **p-value** | **Percent Difference** | **p-value** |
| **12 Months Post-Injury** | | | | |
| Gender (Women vs. Men) ‡ | 0 | 0.6454 | -13 | 0.0198 |
| Age | 0 | 0.1888 | 0 | 0.0001 |
| Head AIS Score‡ | -1 | 0.1531 | -10 | 0.0001 |
| Head Injury Type† (Open vs. Closed) | -3 | 0.0396 | 9 | 0.2611 |
| **24 Months Post-Injury** | | | | |
| Gender (Women vs. Men) | -1 | 0.1058 | -9 | 0.0907 |
| Age | 0 | 0.0446 | 0 | < 0.0001 |
| Head AIS Score‡ | 0 | 0.7130 | -8 | 0.0015 |
| Head Injury Type† (Open vs. Closed) | -4 | 0.0022 | 2 | 0.8100 |

†Statistically significant with participant response; ‡Statistically significant with proxy response; Head AIS rankings: Moderate, Serious, Severe, Critical

Table 4: Percent difference in average FIM motor and cognitive subscale scores at 12 and 24 months post-injury stratified by respondent

| | Participant Response | | Proxy Response | |
|---|---|---|---|---|
| **Variable** | **Percent Difference** | **p-value** | **Percent Difference** | **p-value** |
| **12 Months Post-Injury** | | | | |
| **FIM Cognitive Subscale** | | | | |
| Gender (Women vs. Men) | 1 | 0.5336 | -10 | 0.1151 |
| Age | 0 | 0.6309 | 0 | 0.0005 |
| Head AIS Score†‡ | -2 | 0.0395 | -11 | <0.0001 |
| Head Injury Type (Open vs. Closed) | -4 | 0.1431 | 1 | 0.9217 |
| **FIM Motor Subscale** | | | | |
| Gender (Women vs. Men) ‡ | 0 | 0.3212 | -14 | 0.0128 |
| Age | 0 | 0.0286 | 0 | 0.0002 |
| Head AIS Score‡ | 0 | 0.3675 | -9 | 0.0004 |
| Head Injury Type† (Open vs. Closed) | -3 | 0.0329 | 12 | 0.1600 |
| **24 Months Post-Injury** | | | | |
| **FIM Cognitive Subscale** | | | | |
| Gender (Women vs. Men) | 2 | 0.3148 | -6 | 0.2312 |
| Age‡ | 0 | 0.4045 | -1 | <0.0001 |
| Head AIS Score‡ | 0 | 0.9341 | -9 | 0.0002 |
| Head Injury Type † (Open vs. Closed) | -10 | 0.0002 | -3 | 0.6968 |
| **FIM Motor Subscale** | | | | |
| Gender (Women vs. Men) † | -2 | <0.0001 | -10 | 0.0805 |
| Age | 0 | 0.0055 | 0 | 0.0003 |
| Head AIS Score‡ | 0 | 0.5976 | -7 | 0.0055 |
| Head Injury Type (Open vs. Closed) | -1 | 0.1294 | 3 | 0.6768 |

†Statistically significant with participant response; ‡Statistically significant with proxy response; Head AIS rankings: Moderate, Serious, Severe, Critical

Table 5: Participant characteristics of those employed prior to injury

| Characteristic | 12 months Men (n=300) | 12 months Women (n=95) | 24 months Men (n=260) | 24 months Women (n=81) |
|---|---|---|---|---|
| Average age at time of injury (years)† | 32 (SD 13) | 35 (SD 14) | 32 (SD 13) | 36 (SD 14) |
| Median FIM score | 125 | 123 | 124 | 123 |
| Race | | | | |
| Black | 71 (24%) | 21 (22%) | 60 (23%) | 17 (21%) |
| White | 228 (76%) | 73 (78%) | 200 (77%) | 63 (79%) |
| Type of head injury | | | | |
| Open | 28 (9%) | 8 (8%) | 23 (9%) | 6 (7%) |
| Closed | 262 (91%) | 87 (92%) | 237 (91%) | 75 (93%) |
| Injury Severity (Head) † | | | | |
| Moderate | 112 (38%) | 55 (59%) | 98 (39%) | 46 (58%) |
| Serious | 104 (36%) | 22 (23%) | 88 (35%) | 19 (24%) |
| Severe | 60 (21%) | 15 (16%) | 54 (21%) | 13 (16%) |
| Critical | 16 (5%) | 2 (2%) | 14 (6%) | 2 (3%) |
| Marital Status | | | | |
| Married | 122 (41%) | 36 (38%) | 125 (48%) | 36 (44%) |
| Not married | 176 (59%) | 58 (61%) | 135 (52%) | 45 (56%) |
| Education | | | | |
| Less than HS | 89 (30%) | 20 (21%) | 81 (31%) | 21 (26%) |
| High School | 109 (37%) | 30 (23%) | 83 (31%) | 22 (27%) |
| More than HS | 99 (33%) | 44 (47%) | 97 (38%) | 38 (47%) |
| Survey Respondent† | | | | |
| Proxy | 150 (50%) | 28 (29%) | 144 (55%) | 29 (36%) |
| Participant | 150 (50%) | 67 (71%) | 116 (45%) | 52 (64%) |

†$p<0.05$ at both 12 and 24 months post-injury

Table 6: Post-injury employment characteristics of those employed prior to injury

| | 12 months | | 24 months | |
|---|---|---|---|---|
| **Characteristic** | **Men (n=300)** | **Women (n=95)** | **Men (n=260)** | **Women (n=81)** |
| Employed | 172 (57%) | 54 (57%) | 166 (64%) | 44 (54%) |
| Employed In Same Location Prior to Injury | 116 (67%) | 39 (72%) | 63 (40%) | 19 (43%) |
| Unemployed | 128 (43%) | 71 (43%) | 94 (36%) | 37 (46%) |
| Looking for a Job | 34 (27%) | 8 (11%) | 22 (23%) | 5 (14%) |
| Unemployed due to TBI | 97 (76%) | 29 (41%) | 65 (70%) | 27 (72%) |

Differences between men and women were not statistically significant

Table 7: Factors associated with increased likelihood of unemployment at 12 or 24 months post-TBI

| | 12 Months Post-Injury | | 24 Months Post-Injury | |
|---|---|---|---|---|
| **Variable** | **Risk Ratio** | **95% Confidence Interval** | **Risk Ratio** | **95% Confidence Interval** |
| Gender (women vs. men) | 1.00 | 0.67 – 1.35 | 1.25 | 0.84 – 1.68 |
| Education† | 0.72 | 0.57 – 0.90 | 0.80 | 0.62 – 1.00 |
| FIM Score†‡ | 0.87 | 0.83 – 0.90 | 0.87 | 0.84 – 0.91 |
| Head Injury Severity | 1.07 | 0.90 – 1.25 | 0.97 | 0.77 – 1.19 |
| Age | 1.00 | 0.99 – 1.01 | 1.02 | 1.00 – 1.03 |
| Marital Status† (not married vs. married) | 1.37 | 1.04 – 1.67 | 1.41 | 1.00 – 1.80 |

†Statistically significant at 12 months post-injury
‡Statistically significant at 24 months post-injury
Education categories: less than high school, high school, greater than high school; Head Injury Severity: Moderate, Serious, Severe, Critical

## Appendix 1 – Functional Independence Measure

<table>
<tr><td rowspan="9">Levels</td><td>7 – Complete Independence (Timely, Safely)</td><td rowspan="2">No Helper</td></tr>
<tr><td>6 – Modified Independence (Device)</td></tr>
<tr><td>Modified Dependence</td><td rowspan="7">Helper</td></tr>
<tr><td>5 – Supervision</td></tr>
<tr><td>4 – Minimal Assist (Subject = 75%+)</td></tr>
<tr><td>3 – Moderate Assist (subject = 50%+)</td></tr>
<tr><td>Complete Dependence</td></tr>
<tr><td>2 – Maximal Assist (Subject = 25%+)</td></tr>
<tr><td>1 – Total Assist (Subject = 0%+)</td></tr>
</table>

| **Task** | **Score** |
|---|---|
| | |
| Self-Care | |
| A. Eating | |
| B. Grooming | |
| C. Bathing | |
| D. Dressing – Upper body | |
| E. Dressing – Lower body | |
| F. Toileting | |
| Sphincter Control | |
| G. Bladder Management | |
| H. Bowel Management | |
| Transfers | |
| I. Bed, Chair, Wheelchair | |
| J. Toilet | |
| K. Tub, Shower | |
| Locomotion | |
| L. Walk/Wheelchair | |
| Circle One: *Walk* *Wheelchair* *Both* | |
| M. Stairs | |
| **Motor Subtotal Score** | |
| Communication | |
| N. Comprehension | |
| O. Expression | |
| Social Cognition | |
| P. Social Interaction | |
| Q. Problem Solving | |
| R. Memory | |
| **Cognitive Subtotal Score** | |
| | |
| **Total FIM** | |

Appendix 2 – Work status questions 12 and 24 months post-injury

1. At the time of your injury, were you…[Asked at 12 months post-injury only]

    a. Employed – part time
    b. Self-employed
    c. Unemployed
    d. Student
    e. Retired
    f. Not working because of a previous disability
    g. Other (__________)
    h. Unknown

2. At the present time, are you…
    a. Employed – full time
    b. Employed – part time
    c. Self-employed
    d. Unemployed
    e. Student
    f. Retired
    g. Not working because of your injury
    h. Other (__________)
    i. Unknown

3. IF NOT EMPLOYED, Are you looking for a job?
    a. Yes
    b. No
    c. Other
    d. Unknown

4. IF CURRENTLY WORKING, Are you working now at the same place as you were when you were injured?
    a. Yes
    b. No
    c. Unknown

<u>IF *YES* TO ITEM 4</u>

4a. Do you have the same job as when you were injured?
    a. Yes
    b. No

4b. Do you have more, less or the same job duties/responsibilities?
   a. More
   b. Less
   c. Same
   d. Unknown

IF *MORE* OR *LESS* TO ITEM 4B

4b.1 Was the change in job duties/responsibilities due to your injury?
   a. Yes
   b. No
   c. Unknown

4b.2 Would you describe your job duties/responsibilities as better, worse, or the same as your old job duties/responsibilities?
   a. Better
   b. Worse
   c. Same
   d. Unknown

IF *NO* TO ITEM 4

4c. Was the change in your job due to your injury?
   a. Yes
   b. No
   c. Unknown

4d. Would you describe your new job as better, worse, or the same as your old job?
   a. Better
   b. Worse
   c. Same
   d. Unknown

# CONCLUSIONS

All of the body's organs are capable of responding differently based on gender.[16] Men and women develop, respond to, and recover from chronic and infectious disease differently, so it is reasonable to believe that men and women may respond to and recover from traumatic brain injury differently, as well.[16] Historically, most TBI research has been performed without regard to gender using mostly male participants. These male driven outcomes have guided post-injury care and rehabilitation for both men and women. This care may be adequate for women, but it may not.

A growing body of research is examining the relationships between gender and traumatic brain injury outcomes. Traumatic brain injury outcome is a broad classification covering a wide variety of topics from length of unconsciousness after injury to mortality to psychological adjustment post-injury. The research in this area is methodologically varied and the results often conflict across studies. There is some evidence that gender plays a role in post-TBI outcomes, but the nature and extent of that role is still unknown.

The purpose of the current research was to determine whether differences existed between men and women on survival from 24 hours to 24 months post-injury, and for those who did survive, to determine whether differences existed between men and women in level of functional independence and in employment status at both 12 and 24 months post-injury. It was hypothesized that women would be more likely than men to survive to 24 months post-TBI, to be more functionally independent at both 12 and 24 months post-injury, and to be more likely employed at 12 and 24 months post-injury.

During the time period examined, 24 hours post-injury to 24 months post-injury, gender (women versus men) was not associated with mortality (HR 1.02, 95% CI 0.71 – 1.48) after adjusting for type of head injury, injury severity and age at time of injury. Age category at time of injury (HR 1.83, 95% CI 1.46 – 2.29) and head AIS score (HR 2.24, 95% CI 1.88 - 2.67) were the factors significantly associated with mortality post-TBI. Those who were older and more severely injured were more likely to die, regardless of gender, within the time-interval being studied. Gender may play a role in post-TBI survival, but that role is likely to be seen soon after injury, as many of the participants in these data died from events unlikely related to their TBI.

The functional independence analyses were stratified by respondent (participant or proxy) since the stratum specific results differed. Gender was not associated with post-injury functional independence (FIM total score) in either the adjusted or the unadjusted analyses when the participant responded to the follow-up questionnaire at 12 or 24 months post-injury. When a proxy responded, the unadjusted analysis showed that female gender was associated with lower levels of functional independence at both 12 and 24 months post-injury ($p<0.05$). After adjusting for age, head injury severity and type of head injury, female gender was associated with a 13% reduction ($p=0.0198$ ) in FIM total score at 12 months post-injury, but no relationship between gender and functional independence was seen at 24 months post-injury.

When examining the participant response to the FIM subscales, the unadjusted analysis showed that gender was associated only with the FIM motor subscale score at 24 months post-injury. After adjusting for age, head injury severity, and type of head injury, female gender as minimally associated with lower FIM motor subscale scores at 24 months, reducing the average score by 2%. When examining proxy response to the FIM subscales, the unadjusted analysis showed gender to play a role in both the cognitive and motor subscale scores at 12 and 24 months post-injury. After adjustment for age, head injury severity and type of head injury, the analysis showed female gender to be associated with a 14% decrease (p=0.0128) in the average FIM motor subscale score at 12 months, but not associated with the other subscale scores at either time period.

The employment status analyses were not stratified by respondent (participant or proxy) since the stratum specific results did not differ. The unadjusted analysis revealed gender was not associated with employment status post-TBI of those who had been employed prior to injury. After adjusting for education, FIM score, head injury severity, age and marital status, gender was not associated with employment status 12 or 24 months post-injury. At 12 months post-TBI, higher levels of education decreased the risk of unemployment by 28% (RR 0.72, 95% CI 0.57 – 0.90), higher FIM scores decreased the risk of unemployment by 13% (RR 0.87, 95% CI 0.83 – 0.90), and being unmarried increased the risk of unemployment by 37 (RR 1.37, 95% CI 1.04 – 1.67) after adjustment for the other factors. At 24 months post-TBI, lower FIM scores increased the risk of unemployment by 13% (RR 0.87, 95% CI 0.84 – 0.91).

There is no evidence in this data that suggests gender has a major role in the outcomes examined from 24 hours through 24 months post-injury. Gender was not associated with post-injury mortality or post-injury employment status before or after adjustment for other factors. When a proxy provided the response, female gender did increase the risk of lower levels of functional independence (lower total FIM score) at 12 months post-injury after adjusting for age head injury severity, and type of head injury, but this relationship was not present at 24 month post injury, and no relationship existed at either time point between gender and functional independence when the participant provided the response. This data suggests that women may take longer to recover their functional abilities than men, but why the relationship existed only with proxy response is unknown.

When considering the gender differences in FIM scores between participant and proxy response, the discrepancy could be because men are more likely than women to have a proxy respond for them, so women who use proxies are more severely injured than men who use proxies. It is worth noting, however, the proxy response was not related to head injury severity as measured by the AIS. Another possibility is that the proxies for the women underestimated the women's abilities, but the proxies for the men showed no such bias. Alternatively, the women in this data may have over-estimated their functional abilities in self-report situations, and the more objective assessment given by the proxy could result in lower, but more accurate, FIM scores. Future research should be cognizant of who provides the response to study items, and should not take for granted that the proxy and participant response is equal.

Quantifying the role of gender in TBI outcomes is a multi-faceted task and not as straightforward as it first appears. Although frequently used interchangeably sex and gender are not always the same. Sex refers to a biologic classification while gender is defined by self-representation and social role expectations. [16-17] What is thought of as a “sex” or “gender” difference could be the result of chromosomal differences, hormonal differences, or social role expectations. These varying interpretations of gender are difficult to measure and oftentimes overlooked in research. The conflicting results seen in this body of literature may be the result of unintentionally having different definitions of gender. Furthermore, gender’s impact on post-TBI outcomes may depend on whether the outcome in question is physical or psychological or may depend on whether the outcomes is measured sooner or later after injury.

Although the word gender was used in this study, the construct measured was some amalgamation of sex and gender. No detailed information was available on the participants’ genetic, hormonal, social role or self-representation status. Future research specifically designed to examine post-injury gender differences should make efforts to explore the topic from both the biologic and social role points of view, or should designate which aspect of gender is being investigated.

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# APPENDIX

# IRB APPROVAL

OMB No. 0990-0263
Approved for use through 11/30/2008

# Protection of Human Subjects
## Assurance Identification/IRB Certification/Declaration of Exemption
### (Common Rule)

*Policy*: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the Common Rule. See section 101(b) of the Common Rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the Common Rule.

Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

| 1. Request Type | 2. Type of Mechanism | 3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No. |
|---|---|---|
| [ ] ORIGINAL<br>[✓] CONTINUATION<br>[ ] EXEMPTION | [ ] GRANT [ ] CONTRACT [ ] FELLOWSHIP<br>[ ] COOPERATIVE AGREEMENT<br>[ ] OTHER:______ | |

| 4. Title of Application or Activity | 5. Name of Principal Investigator, Program Director, Fellow, or Other |
|---|---|
| A Longitudinal Study of Rehabilitation Outcomes (UAB Injury Control Research Center) | LOBELLO, STEVEN G |

6. Assurance Status of this Project *(Respond to one of the following)*

[X] This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance Identification No. FWA00005960, the expiration date 10/26/2010 IRB Registration No. IRB00000196

[ ] This Assurance, on file with *(agency/dept)*__________, covers this activity.
Assurance No.__________, the expiration date__________ IRB Registration/Identification No.__________ *(if applicable)*

[ ] No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

[ ] Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph__________.

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)

[X] This activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations.
by: [ ] Full IRB Review on (date of IRB meeting)__________ or [X] Expedited Review on (date) 5-6-08
[ ] If less than one year approval, provide expiration date __________

[ ] This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments
Protocol subject to Annual continuing review.
HIPAA Waiver Approved?: No

Title X960215015
A Longitudinal Study of Rehabilitation Outcomes (UAB Injury Control Research Center)

IRB Approval Issued: 5-6-08

| 9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided. | 10. Name and Address of Institution |
|---|---|
| 11. Phone No. *(with area code)* (205) 934-3789<br>12. Fax No. *(with area code)* (205) 934-1301<br>13. Email: smoore@uab.edu | University of Alabama at Birmingham<br>701 20th Street South<br>Birmingham, AL 35294 |
| 14. Name of Official<br>Marilyn Doss, M.A. | 15. Title<br>Vice Chair, IRB |
| 16. Signature Marilyn Doss | 17. Date 5-6-08 |

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# Project Revision/Amendment Form

*(PLEASE TYPE: In MS Word, highlight the shaded, underlined box and replace with your text; double-click checkboxes to check/uncheck.)*

9/24/08 Hhw

- Federal regulations require IRB approval before implementing proposed changes.
- Change means any change, in content or form, to the protocol, consent form, or any supportive materials (such as the Investigator's Brochure, questionnaires, surveys, advertisements, etc.).
- Complete this form and attach the changed research documents.

Today's Date: *September 23, 2008*

**1. Contact Information**

Principal Investigator's Name: *Steven G. LoBello* BlazerID: *psyepi* E-mail: *slobello@aum.edu*
Contact Person's Name: *Andrea Underhill* BlazerID: *moonpie* E-mail: *Andrea.Underhill@ccc.uab.edu*
Telephone: *4-2862* Fax: *5-8143*
Campus Address: *CH-19 401 ZIP 2041*

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**2. Protocol Identification**

Protocol Title: *A Longitudinal Study of Rehabilitation Outcomes*
IRB Protocol Number: *X960215015*

**Current Status of Project (check only one):**

☐ Currently in Progress (Number of participants entered:_____)
☐ Study has not yet begun (No participants entered)
☒ Closed to participant enrollment (remains active)—
Number of participants on therapy/intervention:_____
Number of participants in long-term follow-up only: *804*
☐ Closed to participant enrollment (data analysis only)—
Total number of participants enrolled:_____

**This submission changes the status of this study in the following manner (check all that apply):**

☐ Protocol Revision
☐ Protocol Amendment
☐ Study Closed to participant entry
☐ Study Closure
☐ Revised Consent Form
☐ Addendum (new) consent form
☐ Enrollment temporarily suspended by sponsor
☐ Change in protocol personnel
☒ Other, (specify) *Add Andrea Underhill to the current IRB approval form as a student using data from this project for dissertation research*

**3. Reason for change**

Briefly describe, and explain the reason for, the change. If normal, healthy controls are included, describe in detail how this change will affect those participants.
*Include a copy of the protocol and any other documents affected by this change (e.g., consent form, questionnaire) with all the changes highlighted.*

**Andrea Underhill, MS, MPH came to work with *A Longitudinal Study of Rehabilitation Outcomes* (described below) in January 2002 as a graduate student assistant, became the full-time administrator for the project in March 2003, and was listed as a co-investigator on the project's (successful) grant application to the funding agency (National Center for Injury Prevention and Control, Centers for Disease Control and Prevention) in November 2003.**

**Mrs. Underhill maintains current IRB certification and is listed on the study's IRB protocol as a person "involved in the design, conduct, and reporting of the research" (item 6 of the IRB progress report). She became a part-time doctoral student in Epidemiology in August 2003 while maintaining her full-time position at UAB.**

**In May 2007, Mrs. Underhill proposed using data from *A Longitudinal Study of Rehabilitation Outcomes* for her doctoral dissertation. We are filing this amendment to request that Mrs. Underhill's name be added to the current IRB approval form as a student using data from this**

Amendment 092308

**study for her dissertation research project. We did not file this amendment last May because (a) Mrs. Underhill already had IRB certification, (b) *A Longitudinal Study of Rehabilitation Outcomes* already had IRB approval, (c) Mrs. Underhill was already involved with said project, and (d) Mrs. Underhill's dissertation is such that it would have been done in her professional capacity as an investigator if not being done in her capacity as a student. Mrs. Underhill's dissertation project is not a side project of *A Longitudinal Study of Rehabilitation Outcomes*; it is work that fulfills the project's primary purpose.**

**The analyses she proposes would have been performed in her professional capacity as co-investigator on the project, even if not proposed for doctoral dissertation purposes. A series of 3 analyses are proposed. These analyses are of existing data and do not require additional contact with the participants. Mrs. Underhill seeks to document gender differences in traumatic brain injury outcomes through 24 months post-injury by performing a survival analysis, an analysis of functional independence, and an analysis of employment status. These analyses directly correspond to 2 specific research questions outlined in *A Longitudinal Study of Rehabilitation Outcomes'* protocol: (1) What is the mortality experience of the study participants? and (2) What are factors related to changes in functional independence? Additionally, the dissertation analyses address two of the project's specific goals: (1) systematically analyze and compare the physical, psychological, and social impact of disability, and (2) quantitatively assess the relationships among physical, psychological, and social factors that may interact to enhance or detract from personal autonomy, satisfaction with life, and general psychological health.**

**<u>Synopsis of *A Longitudinal Study of Rehabilitation Outcomes*</u>: *A Longitudinal Study of Rehabilitation Outcomes* is a telephone follow-up survey of individuals with one of four types of injuries (traumatic brain injury, spinal cord injury, severe burn, or intra-articular fracture of the lower extremity). The study documents and describes the long term physical, psychological, and social status of injured individuals, and determines the physical, psychological, and social factors that contribute to persistent limitations and disability in injured persons.**

**4. Does this change revise or add a genetic or storage of samples component?**
☐Yes ☒No

If yes, please see the Guidebook to assist you in revising or preparing your submission, or call the IRB office at 934-3789.

**5. Does the change affect subject participation (e.g. procedures, risks, costs, etc.)?**
☐Yes ☒No

**6. Does the change affect the consent document(s)?** ☐Yes ☒No

If yes, briefly discuss the changes. _____

*Include the revised consent document with the changes highlighted.*

Will any participants need to be reconsented as a result of the changes? ☐Yes ☒No

If yes, when will participants be reconsented?_____

Signature of Principal Investigator [signature] Date 09.23.08

QOCA 5-6-08

signature verifying Andrea P. Underhill has been listed with the IRB as an investigator on this project since 2003.

APPROVED
[signature] 9-24-08
MARILYN DOSS, M.A.
Vice Chair – IRB

Amendment 092308