A. COVER PAGE

Project Title: All-Cause and Cause-Specific Mortality Resulting from Non-Fatal Occupational Injuries	
Grant Number: 5R01OH011511-04	**Project/Grant Period:** 09/30/2018 - 09/29/2022
Reporting Period: 09/30/2021 - 09/29/2022	**Requested Budget Period:** 09/30/2021 - 09/29/2022
Report Term Frequency: Final	**Date Submitted:** 12/01/2023
Program Director/Principal Investigator Information: LESLIE I BODEN , PHD **Phone Number:** 6173582651 **Email:** lboden@bu.edu	**Recipient Organization:** BOSTON UNIVERSITY MEDICAL CAMPUS BOSTON UNIVERSITY MEDICAL CAMPUS 85 East Newton Street, M-921 BOSTON, MA 021182340 **DUNS:** 604483045 **UEI:** FBYMGMHW4X95 **EIN:** 1042103547A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: DIANE BALDWIN 25 Buick Street, Suite 200 Boston, MA 022151300 **Phone number:** 6173534365 **Email:** ospera@bu.edu	**Signing Official:** DIANE BALDWIN 25 Buick Street, Suite 200 Boston, MA 022151300 **Phone number:** 6173534365 **Email:** ospera@bu.edu
Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Many injured workers suffer chronic health impacts and long-term declines in earnings. In our earlier study of workers in New Mexico (1), we found that non-fatal occupational injuries substantially increase mortality hazard over the 20 years after injury. We propose to deepen the prior analysis of the mortality consequences of non-fatal occupational injuries using data from a state with a much larger working population, the State of Washington.

By comparing the injury-mortality relationship in Washington State with that in New Mexico, we can determine whether these relationships are stable across two states that have different workers' compensation systems and different labor market conditions. In addition, using a larger state with more injuries, we can now estimate the relationship between specific injury characteristics and mortality outcomes. We can also analyze which causes of death are most elevated. Studies have shown that occupational injuries are associated with diminished earnings (2), anxiety and depression (3-7), chronic pain (3, 8), and opioid use (9-13). This leads us to hypothesize that mortality of injured workers is elevated for back injuries when compared with injuries at other sites and for suicide and drug overdose.

To accomplish these goals, we propose the following steps:

Specific Aim 1: Construct a database to test the study hypotheses.

Using an existing research dataset from Washington State, we will define a population consisting of about 269,000 workers with non-fatal lost-time workers' compensation injuries or illnesses occurring between 1994 and 2001 and 579,000 comparison group workers with medical-only injuries during the same period. Lost-time injuries have payments for lost earnings, while medical-only injuries have payments for medical bills but not for lost earnings. We will link this cohort with Social Security Administration (SSA) mortality data from the Death Master File (DMF) for follow-up from 1994 through 2018. This cohort will consist of injured workers with the maximum mortality follow-up of 25 years and approximately 17,000,000 person-years. We will then link National Center for Health Statistics (NCHS) data on mortality from the National Death Index (NDI) to (a) validate all deaths identified by SSA and (b) identify cause of death.

Specific Aim 2: Test whether all-cause mortality is elevated among workers with lost-time injuries.

2. a. We will derive Kaplan-Meier curves separately for workers with lost-time and medical-only injuries within sex and age groups. Using separate Cox proportional hazards regressions for men and women, both for workers with lost-time injuries and for comparison workers, we will estimate the impact of lost-time injuries on the all-cause hazard of mortality, controlling for age, industry, and pre-injury earnings.

2. b. We will conduct a quantitative bias analysis to assess the impact of unmeasured confounders on the injury-mortality relationship, using injury and confounder data from the Panel Study of Income Dynamics (14) and estimates of the confounder-mortality relationships from the scientific literature.

Specific Aim 3: Test hypotheses that mortality is elevated for specific causes of death and specific injury sites.

3. a. Use competing risks Cox proportional hazards regression to determine subhazard ratios and cumulative incidence functions for major causes of death, comparing injured and comparison workers.

3. b. Use Cox proportional hazards to estimate overall mortality hazard ratios and cumulative incidence functions for specific injury sites (for example, back injuries or lower extremity injuries).

3. c. Conduct quantitative bias analysis to determine the extent to which the mortality hazards estimated in Specific Aims 3.a and 3.b may have been biased by unobserved or unmeasured confounders.

Some hypotheses to be tested:

1. Work-related non-fatal lost-time injuries increase the hazard of mortality. We have published this result using New Mexico data and will test it again in Washington State.

2. Specific causes of death have elevated subhazard ratios and cumulative incidence, including mortality due to drugs and suicide among women and men.

3. Back injuries result in elevated overall mortality hazard ratios and cumulative incidence for men and women, with other factors held constant.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Mortality2 RPPR Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have been in regular contact with the Washington State Department of Labor and Industries (LNI) about our findings. The Principal Investigator has also been working with LNI to help them conduct their own mortality analysis using a very large employment and injury database that they have developed. He will continue to work with them after the completion of the current grant.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

ACCOMPLISHMENTS

1. **Major activities**

    a. We created our research database. The Washington State Department of Labor and Industries provided workers' compensation data, including worker gender, employer industry, disability type and duration, and benefit characteristics. Our study population consisted of people who received workers' compensation benefits for injuries and illnesses occurring from 1994 through 2000. Among injured workers, those who received cash benefits because they lost more than three days from work or had a permanent injury-related disability are the exposed group, which we refer to as the "lost-time" injured. The comparison group was "medical-only" injured workers who had at most three days lost from work and received benefits for medical expenses but not to replace lost earnings. We linked the workers' compensation data to Social Security Administration (SSA) earnings and mortality data based on name, date of birth, sex, and Social Security Number, successfully linking more than 95% of cases. We then linked a stratified sample of cases that we classified as dead by SSA to the National Death Index (NDI).

    b. Using Cox proportional hazard survival analysis, we estimated the all-cause mortality hazard ratio for lost-time injured compared with medical-only cases.

    c. We then used estimates of pre-injury smoking and obesity among the treated and comparison groups to do a quantitative bias analysis (QBA) to estimate all-cause mortality hazard ratios accounting for these important unobserved confounders. We returned to our New Mexico data, did a QBA for this state as well. We published a paper with results from both states.

    d. We were not able to do a parallel analysis comparing back injuries with other injuries because the medical-only (comparison group) cases did not have an indicator for part of body injured.

    e. We did cause-specific mortality competing risks hazard estimation and QBA for suicide mortality and for opioid-related mortality. We will shortly be submitting these results for publication.

2. **Specific objectives**

    Specific Aim 1: Construct a database to test the study hypotheses.

    Using an existing research dataset from Washington State, we will define a population consisting of about 269,000 workers with non-fatal lost-time workers' compensation injuries or illnesses occurring between 1994 and 2001 and 579,000 comparison group workers with medical-only injuries during the same period. Lost-time injuries have payments for lost earnings, while medical-only injuries have payments for medical bills but not for lost earnings. We will link this cohort with Social Security Administration (SSA) mortality data from the Death Master File (DMF) for follow-up from 1994 through 2018. This cohort will consist of injured workers with the maximum mortality follow-up of 25 years and approximately 17,000,000 person-years. We will then link National Center for Health Statistics (NCHS) data on mortality from the National Death Index (NDI) to (a) validate all deaths identified by SSA and (b) identify cause of death.

    Specific Aim 2: Test whether all-cause mortality is elevated among workers with lost-time injuries.

1

2. a. We will derive Kaplan-Meier curves separately for workers with lost-time and medical-only injuries within sex and age groups. Using separate Cox proportional hazards regressions for men and women, both for workers with lost-time injuries and for comparison workers, we will estimate the impact of lost-time injuries on the all-cause hazard of mortality, controlling for age, industry, and pre-injury earnings.

2. b. We will conduct a quantitative bias analysis to assess the impact of unmeasured confounders on the injury-mortality relationship, using injury and confounder data from the Panel Study of Income Dynamics (14) and estimates of the confounder-mortality relationships from the scientific literature.

Specific Aim 3: Test hypotheses that mortality is elevated for specific causes of death and specific injury sites.

a. Use competing risks Cox proportional hazards regression to determine subhazard ratios and cumulative incidence functions for major causes of death, comparing injured and comparison workers.

b. Use Cox proportional hazards to estimate overall mortality hazard ratios and cumulative incidence functionus for specific injury sites (for example, back injuries or lower extremity injuries).

c. Conduct quantitative bias analysis to determine the extent to which the mortality hazards estimated in Specific Aims 3.a and 3.b may have been biased by unobserved or unmeasured confounders.

Some hypotheses to be tested:

a.   Work-related non-fatal lost-time injuries increase the hazard of mortality. We have published this result using New Mexico data and will test it again in Washington State.

b.   Specific causes of death have elevated subhazard ratios and cumulative incidence, including mortality due to drugs and suicide among women and men.

3. **Significant results (including) major findings, developments, or conclusions (both positive and negative)**

   a. All-cause mortality for Washington State workers with lost-time injuries was higher than for those with medical-only injuries. The estimated mortality HR was 1.24 for women (95% CI 1.21 to 1.28) and 1.22 for men (95% CI 1.20 to 1.24). After adjusting for unmeasured pre-injury smoking and obesity, the estimated HR for women was 1.10, 95% simulation interval (SI) 1.00 to 1.21; for men, it was 1.15, 95% SI 1.04 to 1.27. .Estimated HRs were reduced by accounting for unobserved confounding but remained significantly greater than 1.0. Estimated HRs for Washington were consistent with those previously estimated for New Mexico, a less populous state with lower median wages and a different workers' compensation insurance mechanism. This suggests that the relationship between workplace injury and long-term mortality may be generalizable to other US states. This association should be examined in additional locations, with different study conditions, or using additional data on pre-injury risk factors.
   b. Opioid mortality was higher for Washington State workers with lost-time injuries than for those with medical-only injuries. The estimated hazard ratio for a lost-

2

time injury was 1.31, 95% CI: (1.16-1.48) for women and 1.51, 95% CI: (1.39-1.64) for men. After accounting for confounding by pre-injury extramedical opioid use, the estimated hazard ratio for a lost-time injury was 1.235, 95% CI: (1.04-1.45) for women and 1.45, 95% CI: (1.34-1.57) for men. This study found substantial excess opioid-related mortality among workers in Washington State with lost-time occupational injuries. This excess was reduced, but not eliminated, by a quantitative bias analysis that accounted for confounding by pre-injury extramedical opioid use. This supports and extends the findings of earlier studies.

c.   Suicide mortality was higher for Washington State workers with lost-time injuries than for those with medical-only injuries. The estimated hazard ratio for a lost-time injury was 1.31, 95% CI: (1.16-1.48) for women and 1.51, 95% CI: (1.39-1.64) for men. After accounting for confounding by pre-injury major depression, the estimated hazard ratio for a lost-time injury was 1.13, 95% SI: (0.88-1.45) for women and 1.33, 95% SI: (1.15-1.49) for men. This study supports previous analysis of drug-related mortality by the authors and other researchers.

4.   **Key outcomes or other achievements**

a.   This research continued and broadened nascent research on the mortality impacts of work-related injuries and illnesses. It provided evidence that the hazard of all-cause mortality rose following lost-time occupational injuries. It also provided parallel evidence for increased cause-specific suicide mortality and opioid-related mortality.

b.   The studies conducted with this CDC/NIOSH funding are the first and only studies to date to account for potentially important unobserved confounding using quantitative bias analysis (QBA). The application of QBA reduced the estimated effect sizes. Except for the estimated suicide hazard ratio for women, lower simulation intervals remained above 1.0.

3

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes
Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Applebaum KM, Asfaw A, O'Leary PK, Busey A, Tripodis Y, Boden LI. Suicide and drug-related mortality following occupational injury. American journal of industrial medicine. 2019 September;62(9):733-741. PubMed PMID: 31298756; PubMed Central PMCID: PMC7485601; DOI: 10.1002/ajim.23021.
N/A: Not NIH Funded	Busey A, Asfaw A, Applebaum KM, O'Leary PK, Tripodis Y, Fox MP, Stokes AC, Boden LI. Mortality following workplace injury: Quantitative bias analysis. Annals of epidemiology. 2021 December;64:155-160. PubMed PMID: 34607011; PubMed Central PMCID: PMC10026009; DOI: 10.1016/j.annepidem.2021.09.015.
N/A: Not NIH Funded	Boden LI, Asfaw A, Busey A, Tripodis Y, O'Leary PK, Applebaum KM, Stokes AC, Fox MP. Increased all-cause mortality following occupational injury: a comparison of two states. Occupational and environmental medicine. 2022 December;79(12):816-823. PubMed PMID: 36253089; PubMed Central PMCID: PMC10124819; DOI: 10.1136/oemed-2022-108481.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
LBODEN@BU.EDU	Y	BODEN, LESLIE I.	PHD	PD/PI	7.2	0.0	0.0			NA
KAPPLEBAUM	N	Applebaum, Katie M.	MOTH,AB,SCD	Co-Investigator	1.8	0.0	0.0			NA
MFOX@BU.EDU	N	Fox, Matthew Alexander Pease	MPH,DSC	Co-Investigator	0.7	0.0	0.0			NA
YORGHOS@BU.EDU	N	Tripodis, Yorghos	MS,BA,MS,PHD	Co-Investigator	1.3	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RS - Reentry Supplement
DS - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

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G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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I. OUTCOMES

I.1 What were the outcomes of the award?

Studies have shown that work-related injuries and illnesses have long-term health, disability, and economic consequences. In specific, work-related injuries have been shown to be associated with opioid use and depression . This raises the concern that these injuries increase the risk of death from opioid poisoning and suicide, two causes of death that have been rising for more than a decade. This study examined whether people injured at work die prematurely from any cause. It also looked to see whether deaths related to opioid overdose and suicide were especially elevated.

There is evidence that smoking and obesity increase the risk of injury, and we know that they also increase the risk of premature death. This could make it appear that the impact on mortality of work-related injuries is larger than it actually is. This study took this concern into account when estimating the impact of work-related injury on premature death. For opioid overdose deaths, there is a similar concern: extramedical opioid use may increase both the probability of injury and the risk of opioid overdose mortality. In parallel, major depression may increase the probability of work-related injury and of suicide death respectively. In examining the relationship between work-related injury and opioid poisoning mortality, this study took into account the potential impact of pre-injury extramedical opioid use; and when estimating the relationship between work-related injury and suicide death, the study accounted for pre-injury major depression. Accounting for these additional factors did not qualitatively change the conclusions: work-related injury causes an increase in overall mortality as well as in mortality from suicide and opioid poisoning.