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Mortality following workplace injury: Quantitative bias analysis

Andrew Busey, B.S.[a], **Abay Asfaw, Ph.D**[b], **Katie M. Applebaum, Sc.D**[c], **Paul K. O'Leary, Ph.D.**[d], **Yorghos Tripodis, Ph.D.**[e], **Matthew P. Fox, D.Sc.**[f], **Andrew C. Stokes, Ph.D.**[g], **Leslie I. Boden, PhD**[h,*]

[a]NERA Economic Consulting, Boston, MA, USA

[b]Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Washington, DC, USA

[c]Department of Environmental and Occupational Health, Milken Institute School of Public Health, George Washington University, Washington, DC, USA

[d]U.S. Social Security Administration, Office of Retirement and Disability Policy, Washington, DC, USA

[e]Department of Biostatistics, Boston University School of Public Health, 715 Albany St., Boston, MA 02118, USA

[f]Departments of Epidemiology and Global Health, Boston University School of Public Health, 715 Albany St., Boston, MA 02118, USA

[g]Department of Global Health, Boston University School of Public Health, 715 Albany St., Boston, MA 02118, USA

[h]Department of Environmental Health, Boston University School of Public Health, 715 Albany St., Boston, MA 02118, USA

Abstract

Purpose: Recent studies have shown increased all-cause mortality among workers following disabling workplace injury. These studies did not account for 2 potentially important confounders, smoking and obesity. We estimated injury-related mortality accounting for these factors.

Methods: We followed workers receiving New Mexico workers' compensation benefits (1994–2000) through 2013. Using data from the Panel Study of Income Dynamics, we derived the joint distribution of smoking status and obesity for workers with and without lost-time injuries. We

[*]Corresponding Author: Leslie I. Boden, Department of Environmental Health, Boston University School of Public Health, 715 Albany Street, Boston, MA 02118, lboden@bu.edu (L.I. Boden).

QBA annals credit author statement
Andrew Busey: Software, Data Curation, Formal Analysis, Writing – Original Draft, Review and Editing
Abay Asfaw: Software, Data Curation, Formal Analysis, Writing – Review and Editing
Katie M. Applebaum: Conceptualization, Formal Analysis, Writing – Review and Editing
Paul O'Leary: Software, Data Curation, Formal Analysis, Writing – Review and Editing
Yorghos Tripodis: Conceptualization, Formal Analysis, Validation, Writing – Review and Editing
Matthew P. Fox: Conceptualization, Formal Analysis, Validation, Writing – Original Draft, Review and Editing
Andrew Stokes: Software, Formal Analysis, Writing – Review and Editing
Leslie I. Boden: Conceptualization, Funding Acquisition, Project Administration, Supervision, Formal Analysis, Validation, Writing – Original Draft, Review and Editing

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conducted a quantitative bias analysis (QBA) to determine the adjusted relationship of injury and mortality.

Results: We observed hazard ratios after adjusting for smoking and obesity of 1.13 for women (95% simulation interval (SI) 0.97 to 1.31) and 1.12 for men (95% SI 1.00 to 1.27). The estimated fully adjusted excess hazard was about half the estimates not adjusted for these factors.

Conclusions: Using QBA to adjust for smoking and obesity reduced the estimated mortality hazard from lost-time injuries and widened the simulation interval. The adjusted estimate still showed more than a 10 percent increase for both women and men. The change in estimates reveals the importance of accounting for these confounders. Of course, the results depend on the methods and assumptions used.

Keywords

Epidemiological bias; Quantitative bias analysis; Confounding; Excess mortality; Occupational Safety

Introduction

Recent studies have found that people injured at work have long-term increases in all-cause mortality. A study conducted of injured workers in New Mexico estimated that experiencing a work injury involving more than a week lost from work increased all-cause mortality approximately 20% in women and about the same amount in men [1]. A similar study focused on back injuries in West Virginia estimated that mortality increased 40% for men and women combined [2]. A third study observed that both men and women in Ontario who received permanent partial disability benefits for work-related injuries experienced an increase in mortality that was over 20% [3].

Substantial lost earnings, only a small portion of which is replaced by workers' compensation benefits, also exemplify the long-term impact of occupational injuries [4–7]. Occupational injuries also lead to elevated long-term permanent disability [8, 9]. In addition, studies have indicated that occupational injuries can lead to depression [10, 11] and opioid morbidity [12, 13]. These sequelae of occupational injuries may increase mortality.

The mortality studies have added a new dimension to the recognized harms caused by work-related injuries. Still, the recent mortality studies may be subject to confounding when the source data lack individual-level information on factors that increase both risk of injury and mortality. Chief among the causes of uncontrolled confounding are smoking and obesity, both of which are major risk factors for occupational injury [14–17] and major contributors to mortality [18, 19]. In the New Mexico study population, over half the deaths had an underlying cause of cancer, circulatory system disease, or respiratory disease. The same is true for the U.S. population as a whole [20]. Smoking and obesity are primary contributors to excess mortality from these causes. In fact, they contribute to the risk of death from the 5 leading causes of death [21–23].

The problem of missing confounder information in epidemiologic research is a common one. Quantitative bias analysis (QBA) is an approach to this problem that simulates what

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the data would have looked like had a bias been absent. For an unmeasured confounder problem, we simulate what the data would look like had we measured the missing covariates and been able to adjust for them, contingent on assumptions we make about these variables. Simple QBA methods have been proposed for estimating the impact of a single unmeasured confounder on study results [24,25], but far less work has been done in understanding how to deal with multiple, potentially correlated unmeasured categorical variables, particularly when those variables have more than two levels.

In this study, we apply a QBA method to extend a prior study of occupational injuries on long-term mortality in New Mexico [1]. The original study had data on the exposure and outcome and a number of covariates but lacked obesity and smoking information. To address this, we extend previous bias analysis methods to allow simulation of more than 1 confounder, identifying key bias parameters from external data. In order to simulate missing information on obesity and smoking, we infer the joint distribution of those covariates and injury and the strength of their association with all-cause mortality using national datasets. We then estimate the association between injury and long-term mortality, adjusting for smoking and obesity.

Materials and methods

Primary analysis without bias analysis

We have previously described methods of identifying injured workers and assessing mortality follow-up, which we explain here in brief. The State of New Mexico provided workers' compensation data, including worker, employer, injury, and benefit characteristics. Our study population consisted of people who received workers' compensation benefits for injuries occurring from 1994 through 2000.

Among injured workers, those who received cash benefits as a result of losing more than 7 days from work or were deemed to have a permanent injury-related disability serve as our exposed group, which we refer to as the "lost-time" injured. The comparison group was "medical-only" injured workers who experienced 7 or fewer days lost from work. Workers with medical-only injuries received benefits for medical expenses but no benefits to cover lost earnings. For workers with more than one lost-time injury in the study period, we chose the first lost-time injury as the index injury. For workers with only medical-only injuries, we chose the first as the index injury. For workers with both kinds of injury, the first lost-time injury was the index injury. We excluded workers with a lost-time injury in 1992 or 1993 because they had a lost-time injury before the study period. We restricted the data to workers aged 15 to 80.

We linked the workers' compensation data to Social Security earnings and mortality data based on name, date of birth, sex, and Social Security Number, successfully linking more than 95% of cases. In addition, we used the Social Security Administration's (SSA's) Numerical Identification System and Vital Status System to categorize vital status as dead, alive, and unknown and to determine date of death. We validated the SSA's vital status determination by linking random samples stratified by SSA vital status, lost-time vs. medical-only, and sex with the National Death Index (NDI). We previously reported high

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concordance between the SSA and NDI vital status (over 99%), and as a result, we used the New Mexico data with mortality determined by SSA as our primary data.

Our primary analysis used Cox proportional hazards separately for men and women, adjusting the association between lost-time injuries and mortality for age, pre-injury earnings, and industry. However, as noted, we did not have data on two key confounders, smoking and obesity, for which we conducted a quantitative bias analysis. For both this hazard analysis and the QBA, we used StataMP© Version 16.

The Institutional Review Board at Boston University approved this study. It waived informed consent based on the criteria under 45 CFR 46.116(d). We signed confidentiality agreements with the State of New Mexico for use of the workers' compensation data, and the SSA signed a confidentiality agreement with the National Center for Health Statistics for use of the NDI data.

Confounding and quantitative bias analysis

For the QBA we simulated smoking as a three-level variable (never, former, or current) and obesity as a dichotomous variable where those with a body mass index (BMI) greater than or equal to 30 kg/m^2 are considered obese. We provide details of the method we used to conduct the QBA in the online appendix at https://www.bu.edu/sph/files/2021/08/QBA_Methodology-Injury-and-Mortality.pdf. We provide an intuitive overview next, along with a flowchart (Fig. 1).

To simulate the missing covariates, we needed to estimate bias parameters. These included data on the probability of being in each of the 6 categories of smoking-obesity among those with and without lost-time injury. We also needed information on the strength of the effect of each category of the smoking-obesity variable on the outcome (mortality). Estimating the parameters required two steps. First, we determined the likely joint distribution of pre-injury smoking and obesity status for those with and without lost-time injury using secondary data from the Panel Study of Income Dynamics (PSID) [26]. We used this information to simulate imputed smoking and obesity categories for our primary data.

The PSID is a publicly available longitudinal interview study of a stratified random sample of U.S. individuals and their families designed to be representative of the population as a whole [26]. It focuses on economic behavior, but includes measures of health status and health behaviors. Beginning with the 1999 wave, the PSID has consistently obtained wave-to-wave response rates of 95%–97% and has averaged about 17,000 sample persons since the 1999 wave. In the PSID, we know the temporality of the relationship between lost-time work injury and potential confounders. This is an important advantage, as we are interested in the values of these potential confounders before injury.

From the PSID waves in 2003–2010, we obtained the national distribution of BMI and smoking categories for two groups of employed individuals: those who received workers' compensation cash benefits (lost-time) and those who did not. For each lost-time worker, we selected 20 randomly sampled workers from the group without workers' compensation

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cash benefits. This latter group is primarily uninjured workers, who we use as a stand-in for workers with medical-only injuries.

We drew this 20:1 matched sample of uninjured workers from the PSID, stratifying by sex, age group (less than 25, 25–34, 35–44, 45–54, 55–64, 65+ years), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Other), and education (less than high school, high school graduate, college graduate). For men and women separately, we calculated percentages in the six joint smoking and obesity categories reported in the wave of the PSID survey before the injury (for lost-time injured: survey wave before injury; for the sampled uninjured, survey wave before the injury of the matched injured worker). We weighted all measures derived from the PSID by sample weights provided by the PSID. A limitation of the PSID is the small number of lost-time injured workers surveyed in this period (131 men and 117 women). Although the PSID is a national sample and our sample is from New Mexico, the distributions of smoking and BMI categories for all New Mexico adults and U.S. adults were similar. Using the Behavioral Risk Factor Surveillance System (BRFSS) for the year 2000, we used the median percentage of characteristic across states. The median percent across states of current smokers (23.2%) and percent obese (20.1%) were within 1 percentage point of New Mexico’s (23.6% and 19.3% respectively). The smoking percentages remained close for other study years, although obesity was less prevalent in New Mexico. For example, for 1996, the median state’s percent of current smokers was 23.4% and in New Mexico 22.8%. For obesity, these numbers were 16.8% and 14.1% [27]. This suggests the PSID data can be used to approximate the distribution of smoking and obesity in our study population.

The PSID had virtually no deaths among injured workers. Therefore, we turned to the National Health and Nutrition Examination Survey (NHANES) to estimate mortality for BMI-smoking categories. We drew a sample from NHANES III (1988 – 1994) and Continuous NHANES waves (1999 – 2014), including people ages 35–79 at the time of the survey and employed in the private sector or state and local government. We did not include self-employed individuals or Federal workers, as the New Mexico and other state workers’ compensation systems do not cover them.

To derive the association of each smoking-obesity category with mortality, we applied Cox proportional hazards regressions with age as the underlying timescale to the NHANES data [28]. We constructed independent variables to account for 6 joint categories of smoking and obesity at survey. We adjusted for sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other), and educational attainment (less than high school, high school or equivalent, some college or greater).

Next, we applied methods described by Lash, Fink and Fox [24] to estimate what the strength of the relationship between mortality and lost-time injury would have been in the New Mexico data if we had data on smoking and obesity. We first used the unconditional relationships between lost-time injury and mortality in the New Mexico data together with the estimated hazard ratios from the NHANES regressions to estimate mortality probabilities for PSID observations based on their injury, obesity, and smoking status, controlling for sex, race, and education. This in turn yielded a probability distribution of smoking and obesity

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status for each sex-injury-mortality group. To account for uncertainty from the NHANES regression estimation, we sampled 100 iterations of random smoking/obesity effects on mortality from normal distributions around the regression coefficients using the standard errors from the regressions.

We then used the PSID probability distributions for smoking and obesity, stratified by sex, injury and mortality status, to simulate smoking and obesity values for observations in the primary New Mexico dataset. For each person in the New Mexico data, we imputed a value for them of being in 1 of the 6 smoking/obesity categories using the values derived above. We used the imputed value in the proportional hazards regression of the association between lost-time injury and mortality, adjusted for this new covariate (and other measured covariates). Because the proportions in the six categories are themselves estimates, subject to uncertainty, we repeated this process such that in each iteration a person could change their value of the smoking/obesity variable, and therefore each time leading to a different result from the proportional hazards regression.

Because these probability distributions are also estimated with uncertainty about the relationship between lost-time injury and smoking/obesity in the PSID dataset (separate from the uncertainty in the relationship between smoking/obesity and mortality in the NHANES dataset), we sampled 100 iterations of smoking/obesity values from normal distributions around the logit transformations for each of the 100 iterations of probability distributions calculated in the previous step. Thus, we had 100 × 100 = 10,000 simulations of smoking and obesity values. We used each probabilistic simulation of the confounders in the Cox proportional hazards regressions of worker mortality on lost-time injury, also controlling for age, pre-injury earnings and industry. We then added random error to each adjusted estimate by sampling from a standard random normal distribution, multiplying by the estimated standard error, and subtracting the result from the estimate adjusted for the systematic error. The betas from each model represent a single possible corrected result, which we then summarized using the median of the distribution as a point estimate and the 2.5th to the 97.5th percentile of the distribution as an interval accounting for systematic error. We compared this to the conventional analysis to see the impact of the bias on the magnitude, direction and uncertainty of the results due to the unmeasured confounding.

Results

Table 1 presents the baseline characteristics of the New Mexico workers' compensation data. The numbers in the table are weighted to reflect the sampling of deaths before submission to the NDI. Women comprised 38% of the study population, and more than half of participants were between the ages of 25 and 44. Workers with lost-time injuries were relatively older (median age was 39 and 35 years for women and men, respectively) than workers with medical-only injuries (median age was 36 for women and 32 years for men).

Among women, the median follow-up time was 16.0 years (range, 0.1 –19.5) among those with lost-time injuries and 16.8 years (range, 0.1 – 19.5) among those with medical-only injuries. For men, the median follow-up time was 16.0 years (range, 0.1 – 19.5) for those with lost-time injuries and 16.9 years (range, 0.1 – 19.5) for those with medical-only

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injuries. Table 2 presents characteristics of the PSID stratified random sample used to develop probability distributions on the smoking and obesity confounders. For both men and women, the proportion of those who were never-smoker, non-obese was much lower for those with lost-time injuries. For women, the proportion of current smokers was higher for those with lost-time injuries, while for men, the proportion of former smokers was elevated for this group. Online Appendix Table A3 presents the results of the NHANES mortality analysis. As might be expected, this analysis reflects current smoking and obesity as substantial mortality risk factors.

Table 3 presents estimates for the hazard ratio for lost-time injuries with and without adjustment for potential bias from confounding smoking and obesity. The adjusted hazard ratios remain elevated for both women and men after adjustment (1.13 and 1.12, respectively), though they are smaller than the unadjusted hazard ratios. For the adjusted estimates, the lower bound of the 95% SI for men is 1.0 and for women is a little below 1.0.

Discussion and conclusions

This QBA strongly suggests that the original unadjusted all-cause mortality hazard ratio reflected an upward bias because the analysis lacked information on smoking and obesity, 2 strong predictors of both lost-time injury and mortality. Adjusting for these confounders reduced the estimates of excess hazard by about one half and decreased their precision. This reinforces the importance of taking such biases into account in future studies. Still, we note that this bias analysis employs a method of estimating bias that has limitations, is based on data from imperfect secondary sources, and uses only 2 bias variables.

We based our approach to adjusting estimates for the unmeasured confounding on a method used for binary outcomes that does not account for time to event. As such, it makes assumptions that the unmeasured confounder effects can be approximated by a model that does not account for person time. This is not an ideal solution, which should be considered when interpreting our results. However, we lacked data to parameterize a model on how the unmeasured confounder would affect time to event for our outcome measure. Speculating on the exact ways in which the confounders affected person time could easily lead to a poorly specified model. Given this, we consider our approach prudent. We have used it to provide improved estimates of the outcome of interest.

We also note that the PSID data had a relatively small number of lost-time injured workers (131 men and 117 women), so estimates of smoking-obesity categories lacked precision. This led to a substantial decrease in the precision of the estimates of the lost-time injury hazard ratio compared with the earlier, partially corrected estimates.

The PSID smoking and obesity data compared uninjured workers with those with lost-time injuries. Ideally, we would have compared smoking and obesity among lost-time injured workers with medical-only cases. However, the medical-only category was not present in the PSID, and we could not find another dataset with the required health and labor-market variables. We note that studies found little difference between post-injury earnings of uninjured workers and medical-only workers [29, 30]. Smoking and obesity rates among medical-only workers may not be the same as those of uninjured workers and may well fall between the rates for uninjured workers and those with lost-time injuries. In that case, our QBA-adjusted hazard ratios would be biased toward the null.

This QBA used only smoking and obesity as unobserved covariates. Other unobserved worker characteristics might affect both the probability of injury and mortality. However, smoking and obesity are very likely predominant concerns because they differ substantially between the lost-time injured and uninjured and are major mortality risk factors. Given the limited number of lost-time injured workers in the PSID, adding additional potential confounders would lead to even smaller cell sizes for injured workers in the PSID data, and are likely to be correlated with variables we have now adjusted for. Such correlation may already be present in our model, as smoking and obesity have been shown to have a negative relationship with earnings [31–33]. Because we have accounted for earnings in our model, adjusting our estimates for smoking and obesity may have overcorrected our bias-adjusted hazard ratios.

Still, this analysis has overcome two challenges. First, we identified appropriate information needed to adjust for multiple missing confounders (bias parameters). This is difficult, as there is rarely information in the literature to describe the joint distribution of those unmeasured variables within levels of the exposure and outcome. There is also rarely information on the strength of the effect of those confounders on the outcome (including any interactions between them as well as with the exposure). Second, we identified methods to simulate the confounders in our primary dataset that we would expect had the information been collected. (See more detail here.) We have taken a step toward addressing potentially strong confounders of this relationship and have shown the importance in this case of accounting for these missing confounders. Even after adjusting for bias from smoking and obesity, the median mortality hazard shows a likely increase of more than 10 percent for both women and men. Although the 95% simulation interval for women includes 1.0, long-term excess mortality following lost-time occupational injury remains a concern [34].

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Abbreviations:

SSA	Social Security Administration
NDI	National Death Index
QBA	Quantitative bias analysis
BMI	Body Mass Index
PSID	Panel Study of Income Dynamics

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NHANE	National Health and Nutrition Examination Survey

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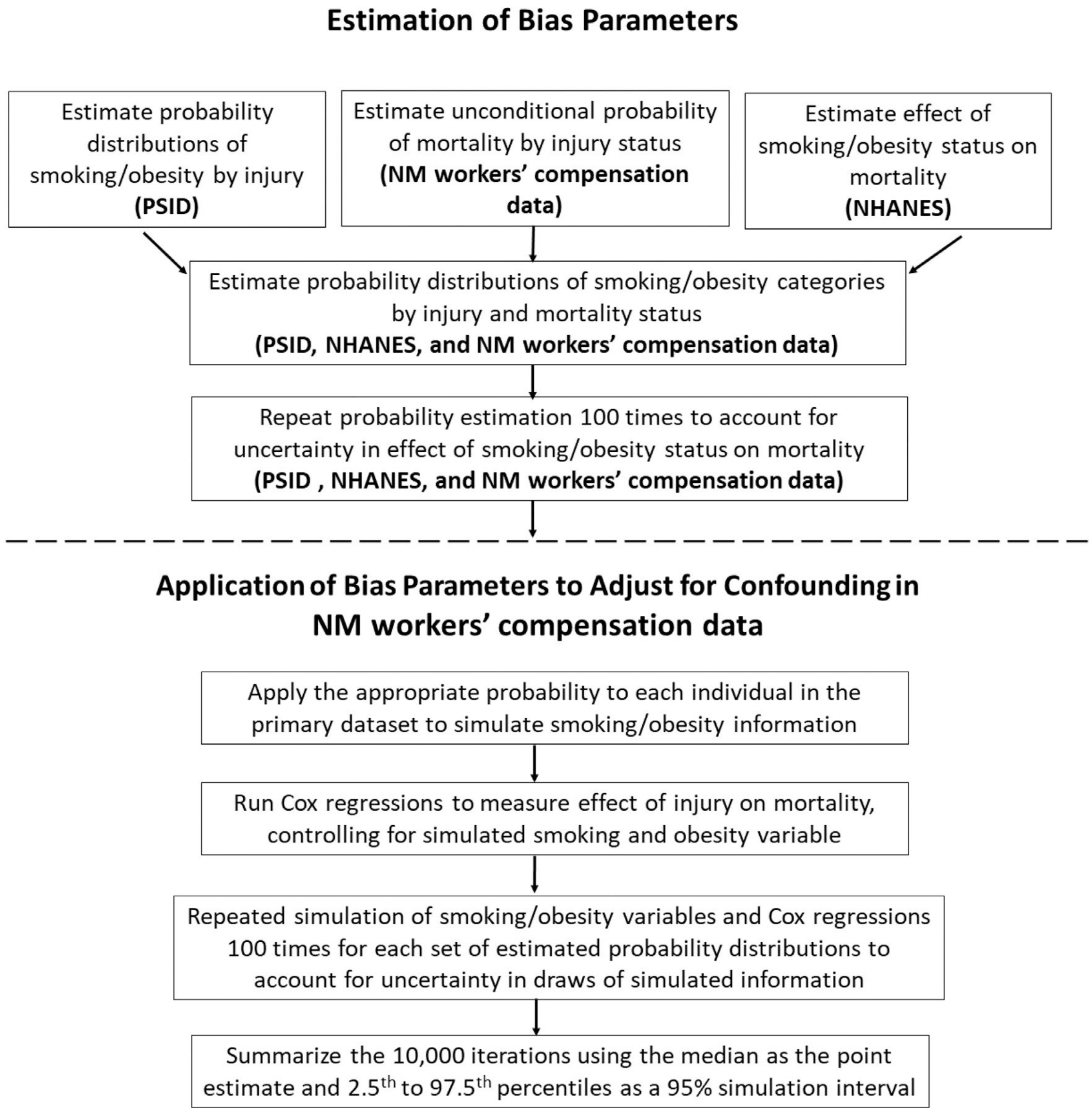

Fig. 1.

Steps in conducting a quantitative bias analysis to adjust for confounders in a study of injury and long-term mortality. Note: The dashed line in the figure distinguishes between two phases of the QBA, starting with the estimation of bias parameters using external datasets and then the application of the parameters to adjust for smoking and obesity in the primary study dataset (New Mexico workers' compensation data). Two external datasets provided information on the distribution of joint categories of smoking and obesity among the injured and non-injured (PSID) and mortality within categories of smoking and obesity (NHANES). Abbreviations: NM, New Mexico; PSID, Panel Study of Income Dynamics; NHANES, National Health and Nutrition Examination Survey.

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Table 1

Summary statistics, New Mexico workers' compensation cases, 1994 through 2000*

	Women		Men	
	Lost-time injury *N* = 12,357	**Medical-only injury *N* = 25,980**	**Lost-time injury *N* = 23,726**	**Medical-only injury *N* = 38,793**
Baseline characteristics				
Age, y,%				
< 25	12.1	18.9	16.4	24.8
25–34	24.2	26.6	29.5	31.7
35–44	31.1	28.1	29.0	24.5
45–54	21.6	18.7	16.6	13.0
55–64	9.2	6.7	7.3	5.3
65+	1.8	0.9	1.2	0.7
Annual pre-injury earnings, 2007$,%				
Less than $10,000	34.2	29.9	24.2	24.4
$10,000 – $19,999	31.9	28	23.2	21.8
$20,000 – $29,999	18.3	19.7	21.0	20.0
$30,000 – $39,999	8.2	11.2	14	13.6
$40,000–$49,999	4.0	5.9	8.1	8.5
$50,000 +	3.4	5.4	9.5	11.6
Industry,%				
Agriculture, Forestry, & Fishing	1.5	1.4	10.7	7.0
Mining & Construction	2.0	3.2	22.8	18.8
Manufacturing	6.5	6.7	9.4	10.6
Transportation	6.3	7.7	10.2	7.3
Wholesale & Retail Trade	30.3	23.1	20.2	23.6
Finance, Insurance, & Real Estate	2.6	3.2	1.4	1.2
Services	12.0	10.2	10.5	11.4
Health	16.0	15.0	2.0	2.7
Government	5.1	7.2	5.9	9.0
Law, Education, & Social	17.6	22.6	7.0	8.6
Characteristics, end of follow-up				

	Women		Men	
	Lost-time injury *N* = 12,357	**Medical-only injury *N* = 25,980**	**Lost-time injury *N* = 23,726**	**Medical-only injury *N* = 38,793**
Years follow-up, median	16.0	16.8	16.0	16.9
Total deaths**	936	1,265	2,601	2,953

* Weighted to account for sampling of deaths.

** Unweighted.

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Table 2

PSID sample characteristics*

	Women			Men		
	N	**Lost-time injury**	**Uninjured**	***N***	**Lost-time injury**	**Uninjured**
Sample	2457	100.0%	100.0%	2751	100.0%	100.0%
Non-obese, never smoker	1101	32.0%	48.2%	1075	24.9%	40.7%
Non-obese, former smoker	165	6.2%	8.2%	221	13.3%	8.0%
Non-obese, current smoker	442	26.6%	19.1%	633	22.1%	22.4%
Obese, never smoker	504	24.8%	15.4%	517	23.2%	18.8%
Obese, former smoker	82	4.3%	3.8%	119	8.9%	4.3%
Obese, current smoker	163	6.1%	5.4%	186	7.6%	5.8%

* Percentages in table use PSID sampling weights.

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Table 3

Association between lost-time injury in New Mexico worker's compensation 1994–2000 and mortality through 2013

	Partially Adjusted*		Also adjusted for Smoking and Obesity*		
	HR	**95% CI**	**Median HR**	**2.5th percentile**	**97.5th percentile**
Women	1.26	(1.16–1.37)	1.13	0.97	1.31
Men	1.21	(1.15–1.27)	1.12	1.00	1.27

* Adjusted for age, pre-injury earnings, and industry.