# A marginal structural model approach to analyse work-related injuries: an example using data from the health and retirement study

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## ABSTRACT

**Background** Biases may exist in the limited longitudinal data focusing on work-related injuries among the ageing workforce. Standard statistical techniques may not provide valid estimates when the data are time-varying and when prior exposures and outcomes may influence future outcomes. This research effort uses marginal structural models (MSMs), a class of causal models rarely applied for injury epidemiology research to analyse work-related injuries.

**Methods** 7212 working US adults aged ≥50 years, obtained from the Health and Retirement Study sample in the year 2004 formed the study cohort that was followed until 2014. The analyses compared estimates measuring the associations between physical work requirements and work-related injuries using MSMs and a traditional regression model. The weights used in the MSMs, besides accounting for time-varying exposures, also accounted for the recurrent nature of injuries.

**Results** The results were consistent with regard to directionality between the two models. However, the effect estimate was greater when the same data were analysed using MSMs, built without the restriction for complete case analyses.

**Conclusions** MSMs can be particularly useful for observational data, especially with the inclusion of recurrent outcomes as these can be incorporated in the weights themselves.

## INTRODUCTION

US workers, aged ≥55 years are estimated to account for 25% of the workforce by 2020.[1] This ageing workforce not only experiences a high risk for injuries but, compared with younger workers, are at an even higher risk for experiencing more severe outcomes as a result of such injuries.[2–4] However, there is limited research pertaining to work-related injuries among ageing workers using a longitudinal study design.[5] Additionally, the existing efforts may be limited from several biases. Common biases include information bias related to self-reported information, recall and misclassification. Other sources include those associated with confounding and loss to follow-up.[6–10] With the exception of randomised controlled trials, causal associations between relevant exposures and outcomes may be difficult to establish as the associations may be affected by existing biases.[11 12]

While several injury epidemiology researchers have used strategies to assess and manage information bias,[13–15] few have appropriately accounted for confounding and censoring in longitudinal research efforts. This is because longitudinal studies contain time-varying covariates which may simultaneously be confounders and intermediates; analysis techniques that condition on past exposure and confounder history fail to account for such joint effects.[16–18] Although some longitudinal injury epidemiology studies have discussed selection bias resulting from loss to follow-up, researchers have primarily based their conclusions from comparisons between those who were retained in the study and those who were censored in terms of exposures of interest.[6 9] There appears to be a dearth of injury epidemiology research that has accounted for such censoring, using statistical models.

Relevant to confounding, most research efforts have used strategies that control for such variables. However, a marginal approach enables the creation of weights that balance each substratum of covariates.[12 16 17] Through a weighting technique and projection, causal inferences can then be drawn from data in which both the exposures and the censoring may depend on exposure history, other covariates and the outcome itself.[19] The marginal structural models (MSMs) are a class of causal models that use this weighting technique (inverse probability-of-treatment or exposure weights (IPW)) to provide valid estimates of the effect of time-varying exposures on the outcome of interest.[12 16 18 20 21] These IPW estimators are known to be more efficient than the naive estimators.[16 17 20–24] It is important to note that IPW can appropriately adjust both for confounding and selection bias, resulting from time-varying exposures—given the assumptions of consistency, exchangeability, positivity and no misspecification of the model used to estimate the weights.[20]

While MSMs have been used in traditional epidemiological research for modelling health outcomes for several years,[17 25] they have been rarely used for analysing work-related injuries. Only one previous study[26] could be identified that examined the association between work-related injuries and job loss. However, the authors did not compare estimates between MSMs and traditional models. The current study, therefore, appears to be among the first that demonstrates the use of MSMs for analysing work-related injuries as the outcome.

Injuries, which are recurrent in nature, are among outcomes that could also be risk factors for future injuries, exposures and other covariates, as well. The aim of this research effort was to demonstrate how MSMs can be used to analyse data pertaining to work-related injuries among the ageing US workforce. This research also demonstrates how previous outcomes, that is, work-related injuries, that may occur at multiple time points or are recurrent,[13] can be used to generate final weights. Additionally, this research effort demonstrates an approach in which the final analysis is not restricted to complete cases, as that used when dealing with chronic outcomes.[18]

## Methods

### Sample and study design

The baseline study cohort consisted of ageing US workers, aged 50 years and above, who responded by self-report to the Health and Retirement Study (HRS) survey in the year 2004, a survey replenishment year. The HRS is a publicly available, biennial and nationally representative, multistage area probability sample of US households that has been active since 1992.[27 28] There were a total of 20 129 primary HRS respondents in the year 2004 (wave 7), from which this study selected a cohort of 7212 ageing adults who, in the year 2004, were aged ≥50 years and were working for pay. This cohort of 7212 adults was then followed prospectively until the year 2014, the most recent HRS interview wave for which data had been made available at the time of the analyses. At each study wave, following the baseline, persons who were no longer working for pay were excluded from the main analyses. Note that the probability of being censored due to other reasons, for example, dropping was accounted for using the weights.

### Study variables

Outcome: *Work-related injury*: HRS defines work-related injuries as 'any injuries at work that required special medical attention or treatment or interfered with your work activities'. Those who reported having a work-related injury were further asked about the number or counts of such events.

Exposures: *Demographic factors*: information was obtained about the respondents' age, gender, race, ethnicity, education, marital/partner status, whether born in the USA or not, and household income and assets. *Health-related factors*: information pertaining to alcohol consumption (number of drinks consumed per week), smoking behaviour, presence of diagnosed chronic physical and mental health conditions (high blood pressure, diabetes, heart problems, lung disease, stroke, arthritis and psychiatric problems), and presence of depression-related symptoms (acute depression) in the 2 weeks prior to the interview was obtained.

*Work-related characteristics*: during each interview wave, these included: work category (US Census-based masked categories); total hours worked in primary and second jobs, if any; work status assessed as full-time, part-time, and partly-retired; having a second job; tenure in the current workplace; and any previous history of work-related injuries. Physical work requirement, ascertained as, 'does your current job require high physical effort?' was the primary exposure of interest. This was measured on a Likert scale, ranging from all/almost all of the time to none/almost none of the time. The associations between physical work requirement and injuries[3 29 30] were then estimated using MSMs and a traditional regression model, that is, generalised estimating equations (GEEs).[31] The physical work requirement variable was re-categorised as a binary variable. Those who reported that their workplaces entailed physical effort requirements all/almost all, most, and some of the time were identified as being employed in workplaces with high physical work requirements. Conversely, workplaces identified as having low physical requirements were those that identified such requirements as none/almost none of the time.

Missing exposure information was imputed by carrying information from the last wave forward.

### Analyses

MSMs were fit to estimate the effect of physical work requirements on work-related injuries. To accomplish this, person-specific and wave-specific exposure and censoring weights were first estimated.[16 17] A directed acyclic graph (DAG)[11] was developed *a priori* to facilitate the process (figure 1). DAGs have previously been used for occupational safety and health research[8 32] and also in the case of time-varying covariates.[18]

In the figure, the exposure of interest, that is, physical work requirement (outcome for the person and wave-specific weight models), is denoted by the letter 'A' and the integers 0 (representing the year 2004), and 1 (year 2006) are examples of two survey time points. Note that, this is just for illustration and the actual data consisted of four more survey waves, that is, years 2008–2014. Next, A0 represents physical work requirements at time point 0 and A1 at time point 1. Job category (Z0 and Z1) is shown separately for demonstration purposes to guide the reader, whereas all other variables, including injuries, are indicated by variables L0 and L1. Note that in the DAG, the outcome, that is, work-related injuries, is a time-varying variable itself and is represented along with variables in cluster L (L0, and L1). Separate censoring weights were also obtained and the

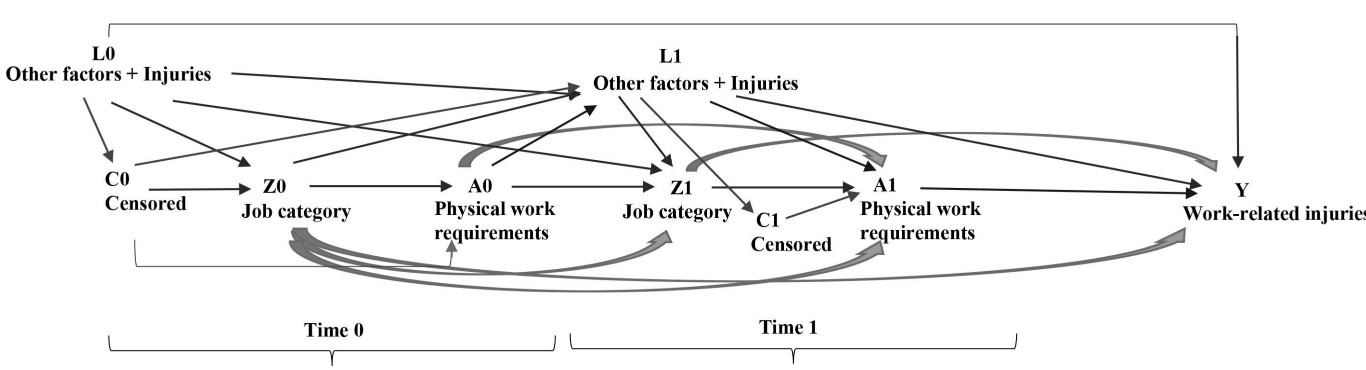


**Figure 1** Directed acyclic graph representing the association between exposure of interest, the outcome and other variables with two time points as an example.

variables, C0 and C1, denote wave-specific censoring variables. As shown, all the variables presented in the DAG demonstrate temporality from left to right; those that come earlier, in time, are presented on the left in the DAG.

At each survey wave, physical work requirements and censoring were regressed on a fixed baseline and time-varying covariate history, using logistic regression models to estimate predicted probabilities.[18] For each study participant, at each survey wave, both an inverse probability person-specific and wave-specific exposure ($W^{x}_{ij}$) and censoring weight ($W^{c}_{ij}$), accounting for those who dropped out or died, were estimated. Respectively, these weights accounted for the measured confounders and selection bias that may have been created by the participants' exposures[20 22] and the outcome, that is, work-related injuries.

Stabilised exposure ($SW^{x}_{ij}$) and censoring weights ($SW^{c}_{ij}$) were then achieved by inclusion of a numerator while creating weights, which maintained the original sample size in the weighted data and reduced the variance.[12 16 22 33 34] The numerator used was the probability of a participant receiving his or her own exposure, irrespective of other exposures.[17 22] As there were extremes, the stabilised weights were progressively truncated by resetting the values that were greater than p (100 p) percentile to the value of p (100 p) percentile. The decision to use truncated or original weights was made based on the bias–variance tradeoff.[22]

The final step was, to run a weighted repeated measures regression model, that is, weighted GEEs,[31] using the above-mentioned stabilised weights. Previous researchers[21 22 25 35] had estimated the final weight ($SW_{ij}$) to be used in the weighted GEE model by obtaining a product of the individual wave-specific weights, that is, $SW_{ij}=SW^{x}_{ij}\,x\,SW^{c}_{ij}$. However, these studies modelled a chronic outcome and, thus, were interested in estimating the effect that the cumulative exposure history had on these outcomes. Injuries, however, can be recurrent and previous injuries may not only affect future injury experiences but may also affect other exposures. Therefore, the original person-and wave-stabilised weights were used; a product of the weights was not obtained. Accordingly, if a final product of weights was used in this case, the estimates could only be calculated for the last wave because injury information for all other waves would already be incorporated in the final product of weights. Table 1 is a dummy table representing final wave-specific weights for one person. As noted, in the table, the person with ID 1 will not have a weight in the year 2012 because the exposure information was missing. If the final weight used was a product of the wave-specific weights for this person, the person shown in the dummy table would have had a missing weight. Accordingly, the final weight would be 0.99*0.92*0.93*0.93*.*1.08='.'. Therefore, there would have been a final weight only for those who had an observation at each time point. In other words, the final analyses would only be a complete case analysis.[18] However, retaining each of the individual person-specific and wave-specific weights does not require the analyses to be limited to complete cases.

**Table 1** Dummy table representing the wave-specific weights for one person

| ID | year | Physical effort | Injury events | Final stabilised weight ($SW_{ij}$) |
|---|---|---|---|---|
| 1 | 2004 | 0 | 0 | 0.99 |
| 1 | 2006 | 0 | 1 | 0.92 |
| 1 | 2008 | 0 | 0 | 0.93 |
| 1 | 2010 | 0 | 0 | 0.93 |
| 1 | 2012 | . | 0 | . |
| 1 | 2014 | 1 | 0 | 1.08 |

ID, Person identifier.

Finally, the results from traditional GEEs were compared with those from MSMs and conclusions were drawn. In both models, injury counts (number of injury-related events) were the outcome of interest and a negative binomial error distribution was used. Incident rate ratios (IRRs) and corresponding 95% CIs were accordingly estimated.

## Results

At baseline, that is, in the year 2004 from the total sample of 7212 ageing adults in the study, 5% (n=397) sustained at least one work-related injury; 53% of those injured were women, 77% were White/Caucasian and 89% were Non-Hispanic. The characteristics of the study cohort are presented in table 2. Further details on the study cohort have been published, previously.[35]

The mean unstabilised weight was 2.07 (median=1.15, SD=3.73, range=189.59), whereas the mean stabilised weight was 1.00 (median=0.99, SD=0.21, range=13.13). To assess the amount of confounding, unstabilised and stabilised weights were visually compared. As shown in table 3, the stabilised weight distribution included extreme weights; therefore, progressive weight truncation was considered.

Extreme weights were then progressively truncated and evaluated with regard to the bias that may be created by truncation and the precision that could be increased by doing the same (table 4). The mean weight, the minimum and maximum weights, and the change in the point estimate affected by the truncation were also evaluated to select the final set of weights to be used in the model. Table 4 shows that truncation had little, if any, effect on the point estimates and the 95% CI. Therefore, the original weights were retained, without truncation.

The adjusted MSM (table 4) demonstrated that the risk of experiencing a work-related injury, among those whose jobs had high, compared with low, physical work requirements, was almost three times greater (incidence rate ratios (IRR): 2.62, 95% CI 2.14 to 3.20). In comparison, the estimates obtained from the GEEs were similar in size (strength) and precision (95% CI) (adjusted IRR: 2.09, 95% CI 1.67 to 2.62 (data not shown)). For these analyses, the traditional (unweighted) GEEs were adjusted for the same variables as the MSMs and both accounted for within-person and within-household correlations.

## DISCUSSION

This research effort applied MSMs for repeated-measures data to estimate the potential causal association between exposures of physical work requirements and work-related injuries. It is important to note that, while this research effort characterised the exposure of interest, that is, physical work requirement as a binary or dichotomous variable, MSMs can also be used for ordinal or continuous exposures.[36]

MSMs were used because traditional statistical (unweighted) regression models like the GEEs may be inappropriate in the presence of time-varying covariates that are affected by previous exposure levels and other covariates.[21] The observed estimates from both the GEEs and MSMs were similar in terms of strength and direction. However, the MSMs, which take the time-varying nature of the covariates into account, produced a larger estimate of the injury risk compared with the GEEs. Unlike the results obtained in this study, previous research efforts[21 37] have shown that the effect estimates could be considerably different between

**Table 2** Baseline demographic, other personal and work-related characteristics among the uninjured and injured sample at the baseline (n=7212)

| Exposures | Uninjured n (%) | Injured n (%) |
|---|---|---|
| Age categories (years) | | |
| 50–60 | 3892 (56.9) | 226 (63.3) |
| 60–70 | 2255 (33.0) | 107 (30.0) |
| ≥70 years and above | 612 (9.0) | 21 (5.9) |
| Gender | | |
| Men | 3375 (49.3) | 168 (47.1) |
| Women | 3465 (50.7) | 189 (52.9) |
| Race | | |
| White/Caucasian | 5490 (80.3) | 275 (77.0) |
| Black/African American | 945 (13.8) | 54 (15.1) |
| Other | 403 (5.9) | 28 (7.8) |
| Ethnicity | | |
| Hispanic | 594 (8.7) | 38 (10.6) |
| Non-Hispanic | 6245 (91.3) | 319 (89.4) |
| Birthplace | | |
| US born | 6097 (89.1) | 322 (90.2) |
| Born elsewhere | 722 (10.6) | 34 (9.5) |
| Education | | |
| Left high school/GED | 1166 (17.0) | 77 (21.6) |
| High-school graduate | 1954 (28.6) | 115 (32.2) |
| Some college | 1698 (24.8) | 95 (26.6) |
| College and above | 2020 (29.5) | 70 (19.6) |
| Marital status | | |
| Married/partnered | 5165 (75.5) | 245 (68.6) |
| Separated/divorced/ widowed | 1439 (21.0) | 98 (27.4) |
| Never married | 232 (3.4) | 14 (3.9) |
| Total household assets ($) | | |
| ≤63 500 | 3731 (54.6) | 239 (67.0) |
| >63 500 | 3109 (45.5) | 118 (33.1) |
| Alcohol consumption (drinks/week) | | |
| None | 4031 (58.9) | 226 (63.3) |
| 1–5 | 2715 (39.7) | 122 (34.2) |
| ≥6 | 79 (1.2) | 6 (1.7) |
| Chronic physical health conditions | | |
| 0 | 2216 (32.4) | 90 (25.2) |
| 1 | 2305 (33.7) | 124 (34.7) |
| ≥2 | 2319 (34.0) | 143 (40.1) |
| Acute depression | | |
| No | 3437 (50.2) | 134 (37.5) |
| Yes | 3117 (45.6) | 207 (58.0) |
| Work category | | |
| Managerial | 1016 (14.8) | 38 (10.6) |
| Professional/technical | 1314 (19.2) | 52 (14.6) |
| Sales | 718 (10.5) | 27 (7.6) |
| Clerical/administrative | 1105 (16.1) | 40 (11.2) |
| Healthcare | 174 (2.5) | 27 (7.6) |
| Protection service | 121 (1.8) | 11 (3.1) |
| Household/building cleaning service and food preparation service | 271 (4.0) | 16 (4.5) |
| Personal service | 438 (6.4) | 26 (7.3) |
| Mechanical/repair | 202 (2.9) | 12 (3.4) |
| Farming/forestry/fishing | 200 (2.9) | 18 (5.0) |
| Construction/extraction | 222 (3.2) | 20 (5.6) |
| Precision production | 184 (2.7) | 9 (2.5) |
| Operators: machine, transportation | 815 (11.9) | 57 (16.0) |
| Work status | | |
| Full-time | 4391 (64.2) | 270 (75.6) |
| Part-time | 966 (14.1) | 45 (12.6) |
| Partly retired | 1483 (21.7) | 42 (11.8) |
| Work tenure (years) | | |
| ≤5 | 2966 (43.4) | 128 (35.8) |
| >5 | 3486 (56.2) | 229 (64.1) |
| Work-requirement factors: does your job require… | | |
| Excessive physical effort | | |
| All/almost all the time | 1136 (16.6) | 98 (27.4) |
| Most of the time | 822 (12.0) | 64 (17.9) |
| Some of the time | 1799 (26.3) | 95 (26.6) |
| None/almost none of the time | 2255 (33.0) | 64 (17.9) |

Missing values are not shown.

MSMs and alternative traditional techniques and could also be in the opposite direction. It is possible that such a difference was not observed between the two models because ageing compared with younger workers may be less likely to change jobs and may be engaged in jobs with the same physical work requirements over the study period. However, future researchers who may use this methodology for different occupational settings and populations may see results similar to those shown in the literature.

This study used a 'repeated measures' MSMs approach, suggested by previous researchers.[18] This approach ultimately enabled estimating the overall risk for injuries over the entire study period as the individual person-specific and wave-specific weights were used in their original state without estimating a final product. The use of a final product of weights for each person may be more meaningful when the outcome is non-recurrent, like AIDS.[17]

The interpretation of the study findings should be done in light of the assumptions including that information on the self-reported physical effort requirements were accurate, and that the measured covariates were sufficient to adjust for confounding and selection bias due to censoring. Unfortunately, these assumptions cannot be tested.[21] Specifically, the assumption that the baseline and time-varying covariates are sufficient to control for confounding at each survey wave is important to make causal inferences from the estimates.[18]

**Table 3** Percentiles (quantiles) for unstabilised and stabilised weights

| Level | Unstabilised weight | Stabilised weight |
|---|---|---|
| 100% Max | 190.59 | 13.27 |
| 99% | 17.95 | 1.72 |
| 95% | 7.69 | 1.19 |
| 90% | 3.41 | 1.11 |
| 75% Q3 | 1.27 | 1.04 |
| 50% Median | 1.15 | 0.99 |
| 25% Q1 | 1.08 | 0.95 |
| 10% | 1.05 | 0.90 |
| 5% | 1.03 | 0.76 |
| 1% | 1.02 | 0.46 |
| 0% Min | 1.00 | 0.14 |

**Table 4** Bias–variance tradeoff in Marginal Structural Models: truncation percentiles, relative mean estimated weights, and incident rate ratios with 95% CIs

| | Estimated weights | | *Risk of experiencing a work-related injury event among those in jobs with high, compared with low, physical work requirements |
|---|---|---|---|
| Truncation percentiles | Mean (SD) | Minimum/ Maximum | IRR (95% CI) |
| 0, 100 | 1.00 (0.21) | 0.20/13.27 | 2.62 (2.14 to 3.20) |
| 1, 99 | 1.00 (0.15) | 0.46/1.72 | 2.62 (2.15 to 3.20) |
| 5, 95 | 0.99 (0.09) | 0.76/1.19 | 2.57 (2.10 to 3.14) |
| 10, 90 | 0.99 (0.06) | 0.90/1.11 | 2.52 (2.05 to 3.10) |

*Adjustment for fixed baseline (age, gender, race, education) and time-varying covariates (work category, previous physical effort requirements, chronic physical health conditions, acute depression and previous injury experiences) is done by weighting.
IRR, incidence rate ratio.

However, extensive consideration included a wide range of covariates that could have affected the association between physical work requirements and injuries (figure 1). The positivity assumption was not violated in this research effort as the study cohort involved only working adults. The probability of receiving the exposure, that is, physical work requirements was non-zero for all levels of time-varying covariates. The last assumption was that the exposure and censoring models were correctly specified. However, it is important to note that similar assumptions are required by traditional statistical models, as well and, when time-varying data are present, MSMs are less restrictive than the traditional models. Even in point-exposure studies, the stated assumptions are required to make causal interpretations.[17]

The major advantage of using MSMs is that they enable causal inferences in situations where conventional randomisation and censoring assumptions are violated. In other words, the MSMs are useful when previous exposures and other variables affect future exposures and censoring.[19] Therefore, in the present study, controlling for the time-varying covariates using the traditional GEEs could not be causally interpreted as the overall effect of physical work-requirement factors on injury events.

Other alternative techniques like time-varying Cox models and Propensity Score models may also condition on time-varying covariates that may be intermediates between the exposures of interest and the outcome. Additionally, in situations where time-varying covariates may be affected by unmeasured confounders, the former techniques may also induce collider-stratification bias. On the other hand, IPW estimators control for time-varying confounding without risk of collider-stratification bias and, also, account for bias due to informative censoring.[38] MSMs however are less useful when the exposure varies dynamically and not at discrete time points. In such situations, other models like the structural nested models may be more appropriate. Yet, MSMs are easier to implement and are computationally more straightforward because they are structurally similar to traditional regression models.[20]

## CONCLUSIONS

MSMs are an intuitively useful tool for analysing complex epidemiological data, especially time-varying data that are not dynamically varying. A major advantage of using these models is their resemblance to standard regression models.[36] MSMs can be particularly useful when dealing with recurrent outcomes like injuries as these can be incorporated in the wave-specific weights themselves. This research effort importantly also demonstrates the use of MSMs, without restriction of complete case analyses to analyse recurrent outcomes like injuries by structuring the data using a long format and retaining each of the person-specific and wave-specific weights that were ultimately used in the final weighted GEE model.

### What is already known about his subject?

- Limited research efforts focusing on work-related injuries among the ageing workforce have included longitudinal analyses.
- The existing analytical techniques that have addressed time-varying injury-related data may have several biases.
- Marginal structural models (MSMs) can provide valid estimates of the effect of time-varying exposures on the outcome of interest. However, these have been rarely used in injury epidemiology research.

### What this study adds?

- When analysing recurring outcomes such as injuries, MSMs can be used to account for the *time-varying nature of the outcome*.
- This research effort further demonstrates the importance of structuring data to avoid limitations associated with complete case analysis.

### How might this impact on policy or clinical practice in the foreseeable future?

- Researchers conducting analyses involving recurrent outcomes, not limited to injuries, can benefit from the approach discussed in this research effort.

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