UAW-GM Cohort Study

Online-only Content

# eAppendix: The full cohort and other sensitivity analyses

## Cohort description and exploratory analyses

A directed acyclic graph (DAG) showing our working hypothetical causal structure is presented in eFigure 1. Under our working assumptions, reducing the risk of worker exit prior to retirement would reduce the risk of suicide and fatal overdose. Note that underlying depression was unmeasured. By conditioning on calendar time and plant, the causal parents of plant closure, we partially reduced the magnitude of confounding bias through that path.1

eFigures 4a and 4b show the person-time contribution of suicide and fatal overdose cases, respectively, arranged by date of worker exit. There does not appear to be clear temporal clustering of worker exit dates among cases. Worker exit became more frequent over calendar time, and there was significantly more follow-up time before worker exit than after.

## Sensitivity analyses

Employment status was determined using worker exit dates from company job records. If a case occurred after worker exit, their exit date should precede their date of death. If a case occurred while employed, their exit date should equal their death date. However, we expect the exit dates to be imperfectly recorded, given the administrative nature of the data. We attempted to characterize the extent of possible misclassification by examining the distribution of difference between the dates of death and exit.

The left-side panel of eFigure 3 presents a histogram of the difference between death and exit dates for suicide cases. The distribution had a strong right-skew and a striking mode in the third bin representing cases whose death date was later than their exit date and less than or equal to one year after exit. Among cases that occurred within a year of job exit, the distribution still showed a strong right skew, but with two local modes centered approximately around 0 and 33 days. The observed times centered around 0 were roughly bounded by a radius of 14 days (eFigure 3b).

In the main analysis, we assumed that cases occurred while employed if the death date preceded or equaled the exit date. In the sensitivity analysis we assumed that a case occurred while employed if the death date was within a week of the exit date. That is, we assumed that all the cases whose exit dates preceded their death dates by no more than one week were misclassified as not employed at death when they were in fact employed (see eTable 1).

To estimate the hazard ratio associated with a more temporally-proximate outcome, we restricted follow-up to more than five years after worker exit. The right side of eTable 1 presents hazard ratio estimates for suicide within after worker exit; once again, cases that occurred within a week after worker exit were assumed to have occurred while employed. Sensitivity analyses complementing Table 3 with follow-up was restricted to five years after worker exit are presented in eTable 2. The point estimates and overall shape of the associations remained approximately the same.

To better understand the shape of the exposure-outcome relationship, we fitted models which included a restricted penalized spline function (*df*= 4) of continuous age at exit.2 To fit these splines and compute hazard ratio estimates, we assumed that the hazard associated with age at exit was constant for those who left work at 55 or older, conditioning on all other covariates. To complement the analyses for categorical age at exit presented in the main body, we fitted these models for suicide and for the combined outcome (eFigure 5).

## Competing risks

A competing risks analysis of age at leaving work on suicide was performed to account for the increasing risk of mortality due to other causes in an aging cohort. As in the categorical models presented in the main body, subjects entered follow-up upon leaving work and were followed until they experienced the event of interest (suicide, n = 158 or suicide and fatal overdose combined, n = 190), the competing risk (mortality due to other causes, n = 10,906 or n = 10,874), or the end of/loss to follow-up (n = 8,214).

Using both parametric and non-parametric methods of analysis,3,4 cumulative incidence and subdistribution hazard ratios of were estimated at different points during follow-up. Across all estimators, employees who left work before the age of 55 had higher cumulative incidence of both suicide and the combined outcome than employees who left work after the age of 55. The difference did not diminish when accounting for baseline factors such as sex, type of work, the total amount of time spent away from work during employment, or the plant where the worker was employed. A targeted maximum likelihood analysis utilizing bounds to account for the rare event of interest produced slightly diminished, though concordant estimates.

Subdistribution hazard ratios complementing Table 3 and eTable 2 are presented in eTables 3 and 4, respectively. The subdistribution hazard ratio estimates followed the same shape as did the cause-specific hazard ratios, with the risk of suicide or the combined outcome of suicide and overdose attaining a maximum for those who left work between the ages of 20 and 39 years. The effect of competing risks appears to be greater among those who leave work at a younger age and when follow-up is unrestricted.

**References**

1. Greenland, S. & Pearl, J. Adjustments and their consequences—collapsibility analysis using graphical models. *Int. Stat. Rev.* **79**, 401–26 (2011).

2. Eilers, P. & Marx, B. Flexible smoothing with B-splines and penalties. *Stat. Sci.* 89–102 (1996).

3. Kalbfleisch, J. & Prentice, R. *The statistical analysis of failure time data.* (John Wiley & Sons. Inc., 2002).

4. Fine, J. P. & Gray, R. J. A proportional hazards model for the subdistribution of a competing risk. *J. Am. Stat. Assoc.* **94**, 496–509 (1999).