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Letter to the Editor

Re: Adjustment for duration of employment in occupational epidemiology

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Dear editors,

In regards to the recent manuscript by Ko et al., we are writing to express concerns with their conclusions regarding control of healthy worker survivor bias (HWSB) [1], namely that HWSB should be addressed, when estimating associations between cumulative occupational exposure and mortality, either by adjustment for duration of employment as a confounder in Cox proportional hazards models or by inverse probability weighting (IPW) in Cox marginal structural models. We support this effort to identify simple approaches in this area. However, we assert that their results should not be used for general recommendations, in part because one of the main findings resulted from an analytic error.

An important complexity of HWSB arises when an occupational exposure affects employment status as well as disease occurrence, and employment status also affects further exposure. These "components" of HWSB are illustrated in their Figure 2. When these components are all present, neither of the approaches recommended by Ko et al. (pg 40) are appropriate. Their suggested approaches do not fully address HWSB and they may induce further bias in estimates. Given that the authors' approach runs counter to advice in much of the literature on HWSB in the last 30 years, further scrutiny is warranted.

The result they use to support their conclusions comes from a simulation in which workers are assigned a duration of employment *first*, exposure is then simulated for employed person-years, and mortality is simulated last. Because exposure does not impact employment in the simulation, unlike their Figure 2, the success of their approach that adjusts for duration of employment is not surprising. If employment is not affected by prior exposure, employment duration is a standard time-varying confounder, which permits standard regression methods of adjustment [2,3].

The success of the IPW approach was surprising because the type of occupational exposure-mortality studies discussed by Ko et al. inherently violate the positivity assumption, as noted by Robins et al. in the first epidemiologic paper on marginal structural models [4]. Ko et al. counter this established claim, stating "the individual can still receive at least one level of cumulative annualized radiation dose given the stratum for duration of employment. Therefore, the positivity assumption is not automatically violated" (pg 36). However, positivity must hold for all levels of exposure assessed and not just one. Still, the results are compelling, and the authors generously provided their code for further study.

The apparent success of this method is due to offsetting biases, rather than bias control. In their simulation code, the authors collapsed all person-time after an employee left work into a single observation (i.e. collapsed multiple person-time units) and pooled these observations with all employed person-time (with one time-unit per record). Thus, the estimated propensity scores do not validly estimate exposure probabilities, a necessary condition for the validity of IPW. To assess why the authors found no bias, we repeated their first simulation scenario ($\psi = -0.3$) using their method and achieved an average weight of 0.96, which does not signal severe issues with positivity because the average stabilized weight should be close to 1.0 [5]. However, when we repeated their simulations without pooling any person-time, we estimated an average weight of 942 and a bias of ~260 %, which signals a serious non-positivity issue. Additionally, Ko et al. truncated the weights at the 99th percentile (a standard default). When we repeated their simulation exactly except for truncating at the 99.5th or the 98.5th percentiles, IPW was again biased (~ −30 % bias and ~ 30 % bias, respectively). Weight truncation typically increases bias and reduces variance [5]. Thus, the lack of bias in their IPW approach appears to result from offsetting biases from weight-miscalculation and weight truncation, rather than valid control of HWSB.

If exposure does not affect employment (as in the simulations of Ko et al. [1]), then adjustment for employment as a time-dependent variable via adjustment or stratification is a valid approach to reducing bias. However, if exposure affects employment (e.g. by causing illness that leads to employment changes), an important aspect to HWSB, then g-methods (IPW, g-estimation, and g-computation) are needed. We have observed a number settings in which exposure is associated with the subsequent hazard of leaving work, so we would generally advocate in favor of g-methods (e.g. [6–13]). However, IPW, as implemented by Ko et al., is not an appropriate method for reducing healthy worker survivor bias in any setting that violates the positivity assumption.

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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

Declaration of Competing Interest

All authors declare they have no actual or potential competing financial interest.

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