Dear SJWEH,

Thank you for your careful attention to our paper. Please find our point-by-point responses to your comments and concerns below.

E.1) Please fix the citations in the text. There should be a space before the citation and the period should come after and not before: "...ambient air pollution standards.(1)" should be "...ambient air pollution standards (1)." "...NIOSH Criteria Document.(4,6–9)" should be "...NIOSH Criteria Document (4, 6–9)." Etc

In text citations were corrected to reflect SJWEH guidelines.

E.2) The references need tidying up. Please see [https://www.sjweh.fi/index.php?page=for-authors#preparation](https://www.sjweh.fi/index.php?page=for-authors" \l "preparation" \t "_blank) for instructions. Remove punctuation around abbreviated journal titles and unnecessary information, there are also several typos.  
For example:  
Betenia N, Costello S, Eisen E a. Risk of cervical cancer among female autoworkers exposed to metalworking fluids. Scand. J. Work. Environ. Health [Internet] . 2012 Jan [cited 2013 May 31];38(1):78–83. Available from: [http://www.ncbi.nlm.nih.gov/pubmed/21901243](http://www.ncbi.nlm.nih.gov/pubmed/21901243" \t "_blank)  
should be  
Betenia N, Costello S, Eisen EA. Risk of cervical cancer among female autoworkers exposed to metalworking fluids. Scand J Work Environ Health. 2012;38(1):78–83.

References were tidied: punctuation in abbreviated journals removed, typos corrected, and capitalization standardized (technical documents and textbooks in Title Case, journal article titles in Start case).

E.3) Table 1, do not place Mean (SD) and N (%) in the same columns. You can use either 4 columns (N, %, Median, Q1, Q3) or 2 [N (%) and Median (Q1, Q3)]

Table 1 has been re-shaped to avoid confusion between statistic types.

E.4) Table 2: CIs are presented as 0.89–0.92 and not 0.89,0.92 etc

All confidence interval endpoints were delimited using the en-dash (–) and not the comma.  
  
R1.1) There is significant potential misclassification of exposure within MWF types because the specific MWF components not only varied across time but also across process applications regarding corrosion control, cooling, lubricity and other requirements, e.g., grinding vs. milling;  
aluminum vs. steel. The 21 yr lag choice should be explained and may be confounded; it  
is quite long for lymphopoietic cancers like leukemias.

1.1) We have added a short section to our discussion section which addresses the impact of exposure misclassification and the 21 year lag. The section says “Due to the quantitative exposure assessment of MWF, this UAW-GM cohort study has contributed substantially to our understanding of the health effects of MWF. However, any exposure assessment based on a Job Exposure Matrix will result in some non-differential exposure misclassification which would likely result in attenuation of results. Additionally, the necessary use of a 21 year lag may also lead to attenuation, especially for cancers with shorter latency.” As we explain in the Exposure subsection of the Methods section, work records are available only through 1995, thus the 21 year lag was necessitated by the available employment data.

R1.2) The 3 yr requirement for population inclusion is problematic if workers with the highest exposures leave employment relatively soon, as with respiratory impairment.

1.2) We agree and brought this up in our discussion of healthy worker bias when we wrote “We expect that those who survived the first 3 years of work may be different from those that left earlier and therefore note that there is built-in left truncation bias by study design.” The 3 year eligibility restriction was a feature of Richard Monson’s original study design and we do not have the data necessary to include shorter term workers in our analyses.

R1.3) Poisson regression with expected-rate offset has the advantage: the intercept shows HWE and/or possible exposure-misclassification (if RR > 1.0).

1.3) Indeed, using a Poisson regression with an expected-rate offset would have been an alternative analytic choice. We chose survival methods to be more consistent with the majority of research from this, and other, occupational cohorts.

R1.4) Confounding non-MWF exposures are a significant source of negative confounding for several outcomes: welding, heat treat, forging, assembly materials: polymerizing adhesives, painting, parts washers.

1.4) We have added this point to our discussion of overall attenuation due to negative confounding. The Discussion section now includes “If assembly workers were more likely to be exposed to other occupational chemicals, smoke cigarettes, or have less favorable socio-economic status than machine operators or machinists, our results could be globally attenuated due to confounding.”

R1.5) For COPD, where the expected SMR for healthy workers would be  
0.6-0.8, there appear to have been 130 – 300 attributable deaths (1 – 1.7% of all deaths), indicating widespread threats to respiratory health. Similarly, taking HWE into account (often dismissed for malignancies despite abundant contrary evidence), there appears to be  
about 15% excess of lung cancer, or another 1.5% of all deaths.

1.5) The reviewer’s point is well taken and we certainly agree that HWE (both HH and HWSE) can bias cancer studies as well as studies of chronic disease. However, given the inherent limitations (biases) in SMRs, along with the strengths of our quantitative exposure assessment, we elected to emphasize results of the internal analyses.

R1.6) Skilled trades status is a worker attribute which would affect exposure assignments. “Machinist” is a skilled trade, not a production worker. Machinists make tooling and other machine repairs; they make up a small proportion of workers <1% while metalworking  
production workers (sometimes classified as “machine operator”) are a majority.

1.6) We thank the reviewer for pointing out the distinction between machinist and machine operator. We agree that most of the workers in this cohort with direct exposed to MWF were working in machining or grinding operations as operators. We also agree that highly skilled machinists may have had the highest concentrations of MWF exposure. However, we do not have information on the skill level associated with specific machining jobs.

R1.7) HWSE would occur even with uniform susceptibility if incident cases terminate exposure as a result; this problem is somewhat diminished by lagging.

1.7) We have added the following sentence to our discussion of HWSE to reflect this point “The use of a 21 year lagged exposure metric diminishes the problem, but does not account for any self-selection out of the work force that occurred prior to 21 years before cancer mortality.”  
  
R1.8) The text implies that SMRs were calculated using LTAS; it should be  
so stated.

1.8) Kevin – not sure what more you could add, seems pretty explicit already to me…

Perhaps we could state that *all* analyses were performed using R version 3.6.1?

Mendeley Reference here: (R Core Team 2019)

R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

R1.9) The reference group specified for soluble MWF (lower 5%) was chosen  
because that was the most prevalent MWF (fewest unexposed)?

1.9) Yes, that’s correct. We have updated our analytic methods section to make this more explicit. We now say “For soluble exposures, a more ubiquitous exposure in this cohort, the upper bound of the reference group was set to 0.05 mg/m3 to avoid extremely small numbers of cancer cases in the reference group and thereby increase stability of the HR estimates.”

R1.10) Exposure stratification: in quartiles or tertiles

1.10) The exposure categorization is described in the analytic methods section. We used a pre-specified reference group (zero for straight and synthetic fluids and 0.05 mg/m^3 for soluble fluid) and then defined as many categories as we could using the number of cases of each cancer as our guide.

R1.11) What does “natural causes” in Table 2 exclude (crime? drug  
OD,..)

The causes excluded in “natural causes” are the so-called “external causes” shown in the last row of Table A1.1. NIOSH identifies these causes as groups 24–26 (in their list of 92 cause grouping).

The “external causes” are

* Transportation accidents: “any accident involving a device designed primarily for, or being used at the time primarily for, conveying persons or goods from one place to another”
* Accidental poisonings: “accidental overdose of drug, wrong drug given or taken in error, and drug taken inadvertently” OR “accidents in the use of drugs and biologicals in medical and surgical procedure”
* Late effects of accidental injury: “indicate accidental injury as the cause of death or disability from late effects, which are themselves classifiable elsewhere. The ‘late effects’ include conditions reported as such, or occurring as sequelae one year or more after accidental injury.”
* Drugs, medicinal, and biologics causing adverse effects in therapeutic use: “correct drug properly administered in therapeutic or prophylactic dosage, as the cause of any adverse effect”
* Suicide and self-inflicted injury
* Homicide and injury purposely inflicted by other persons
* Legal intervention, both as punishment, and in the course of law-enforcement or military action.
* Injury of undetermined intent: “when it is stated that an investigation by a medical or legal authority has not determined whether the injuries are accidental, suicidal, or homicidal. They include self-inflicted injuries, but not poisoning, when not specified whether accidental or with intent to harm.”
* Injury resulting from war operations

Note that cause groupings differ slightly between the ICD-9 and ICD-10 revisions.  
  
  
R2.1) Abstract, Conclusion: It is a bit strange to start Conclusions with “However”. I suggest to delete this word.

2.1: We have deleted the word “However”.

R2.2) Introduction, Page 3, line 5: The abbreviation UAW should be interpreted here. Also, it could be made more clear that this is the labor organization, and GM the employer, especially with regard to the role UAW plays on page 4

2.2 We have interpreted UAW and clarified that it is a labor union.

R2.3) Results, Page 8, line 4: The last word “the” should be deleted.

2.3 We have removed this unnecessary word.

R2.4) Discussion, Page 11, line 15: “smoking for stomach cancer”. It is now well established that the main cause of stomach cancer is Helicobacter Pylori infection, and that diet and smoking (among others) are possible contributing factors.

2.4) We have modified our text to indicate that H. Pylori infection is the primary known risk factor for stomach cancer.