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Author Response: Risk of Cancer in a Community Exposure to Per- and Poly-Fluoroalkyl Substances

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Dear Editor,

We are grateful that our hypothesis-generating cross-sectional ecological study conducted in response to ongoing community concerns has captured the attention of scientists in New Hampshire. In our abstract, we clearly state that further research is warranted to elucidate if residents experience increased cancer risk due to exposure to PFAS contamination in southern New Hampshire. We eagerly hope that the letter writers will leverage their institutional resources to access and/or collect the necessary data. It has been 6 years since the public recognition of the widespread PFAS pollution in southern New Hampshire (specifically Merrimack) and decades after it began. Countless times, the community has expressed their concerns with the approach used to assess the levels of cancer and chronic disease in Merrimack during public and statutory commission meetings.

Most of the letter writers' comments seem to reiterate issues that are transparently described in our publication. We stated in our publication that we were denied access to granular data by the states of New Hampshire and Vermont, other than what we cited in our paper.¹ This includes, but is not limited to, socio-economic data related to the cases in Merrimack and cancer incidence rates in other NH towns.

Yet once again, in December of 2021, before our paper was published, the state released another study using the same approach which compared the cancer incidence in Merrimack to the rest of NH for the following 10-year period. Their study concluded that Merrimack citizens experience significantly higher kidney cancer incidence, but other cancers were nearly statistically significant, as well. The state is using those results to inform further studies. However, the details of the state dataset like those referenced by the commenters, or sensitivity calculations have never been made available to the public, despite multiple requests.

We hope the commenters will eagerly pursue further research on hypotheses we generated. We would welcome collaboration on the project.

Below are more detailed responses to the stated concerns in their letter.

- Standardization for age: The analyses presented do not adjust for the distribution of age. Age-standardization or

adjustment is essential in most cancer studies because cancer is strongly related to age. Without adjustment for the difference in the distribution of age in the populations being compared, it is impossible to interpret the data/ odds ratios presented.

We completely agree age adjustment is needed in cancer studies, but the states of New Hampshire and Vermont would not provide the granularity for information necessary to complete this kind of analysis. This was explained on page 4 of our paper. We presented age-adjusted thyroid cancer incidences at the county level that were publicly accessible (see Figure 5).

As stated above, our study was published 6 years since the discovery of widespread PFAS contamination in the water system in Merrimack. Community members, legislators, and the authors made numerous requests for additional epidemiological studies.

Our work is intended to generate hypotheses and encourage future studies. More research on the relationship between cancer and exposure in Merrimack and other communities in New Hampshire is desperately needed, and hope our study inspires additional research by larger institutions such as Dartmouth.

- Choice of comparator towns: The control or comparison towns to which Messmer compares Merrimack cancer numbers, were chosen as being similar to Merrimack other than being unexposed to PFAS. A quick look at Table 1 doesn't support this: Merrimack residents are older than South Portland and Auburn; are more likely to have health insurance than all comparators except Colchester; have far higher median income, higher educational attainment, and are far more likely to own their homes. The Maine Department of Environmental Protection is currently investigating areas near all 3 of the comparison towns for potential PFAS contamination issues.² Therefore, the comparison with these towns, quite apart from the lack of age standardization, is not likely to be meaningful. According to the protocol published by the Centers for Disease Control and Prevention,³ "the reference



population could be the surrounding census tracts, other counties in the state, or the state as a whole (not including the community under study).” A more appropriate analysis would compare Merrimack with the rest of NH outside the immediate PFAS-affected region taking into account differences in age.

Without the associated demographic and cancer data for Merrimack or other towns in NH, we selected a descriptive analysis approach to compare similar towns in other New England states with publicly available cancer data (“comparator towns”) to Merrimack. While not ideal, the comparator towns we selected were quite appropriate because as the letter writers point out—Merrimack residents have higher rates of health insurance, are more highly educated, and are wealthier (owning their own homes and median income). Therefore, Merrimack residents should experience lower incidences of cancer than our comparator towns based on these socioeconomic indicators, but in fact, they experience higher rates.

We pooled the data for the 4 comparator towns, where available, to overcome limitations to demographic factors and strengthen our analysis. Our analysis indicates that Merrimack citizens experience a higher incidence of cancer very strongly suggests environmental factors are contributors.

In addition, as stated on page 4 of our publication, since the area of southern New Hampshire and the seacoast are population-dense portions of the state, these areas are likely significant drivers of the overall cancer incidence in the state. Therefore, considering the previously described limitations we faced, a comparison of US National incidences, and similar New England towns separately and pooled are more appropriate comparators to assess whether cancer incidences are elevated.

Further, we performed a sensitivity analysis that showed Merrimack cancer rates were more like Bennington, VT, a town also impacted by PFAS. We also found that incidences of several cancers in Merrimack were similar to Auburn, ME, a town that the state of Maine considers to be a priority town for PFAS investigation as discussed on page 13 of our publication.

While there may be other factors affecting cancer rates in Merrimack, the only way to know for sure is additional research that we hope the team from Dartmouth or other institutions will actively pursue.

- Comparison with whole of US: We agree with Messmer et al that there are challenges in selecting “unexposed” comparator communities when PFAS exposure is ubiquitous in the US. However, comparison with the whole of the US without adjustment for age and stratification for race/ethnicity is very problematic due to the known

age-, race-, ethnicity-, and regional differences in cancer incidence. A further complexity arises due to likely confounding by arsenic exposure, and by other industrial pollution in the Northeast and elsewhere, which raises serious doubts over the value of a simple comparison of Merrimack with the US to make inferences about the effects of PFAS.

Again, as mentioned in the paper and this response, detailed demographic data on cancer cases in NH is not publicly available and we hope the attention this paper receives will reform that policy that so that multiple scientists can perform the analyses suggested by Dartmouth’s team. On page 12, we clearly mentioned arsenic as a potential confounder as well as other industrial sources in the Discussion section starting on page 10. We note though, that since about half of the people in Merrimack are public water system customers and the public water systems were generally in compliance with the state’s drinking water criteria for arsenic levels, it’s unlikely arsenic is a confounder for the public water users.

However, most residents of Merrimack have been on the public water supply that was found to contain high levels of PFAS. Further, bladder cancer rates for Merrimack were not significantly different than for Bennington, VT citizens where arsenic is not naturally occurring in the geologic substrata. Therefore, PFAS contamination of the water supply may be at least in part contributing to the elevated levels of bladder cancer for Merrimack citizens and warrants further investigation.

In closing, we are grateful that our work has attracted attention and are hopeful that with all the resources available to the scientists who signed the letter, studies will be conducted by other researchers who can gain access to additional information that we could not access. We are also hopeful that future studies will be designed that are responsive to concerns raised by exposed communities.

We are hopeful that our cross-sectional ecological study raised awareness of the need to conduct cancer evaluations that are responsive to concerns raised by the exposed communities in the region that have been impacted by PFAS emissions. Further, we hope that those studies will encompass cancer and chronic diseases that are of concern to the community rather than limiting those studies to kidney cancer.

With the recent US Environmental Protection Agency decision to significantly reduce the health advisories for PFAS, we are confident that concerns raised by exposed communities are well-founded. Communities have a right to understand

their exposure so they can make informed personal healthcare decisions.

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