

Assessment of occupational exposure to pesticides in a pooled analysis of agricultural cohorts within the AGRICOH consortium: authors' response

In his letter, Tomenson¹ provides his opinion on the development and use of crop-exposure matrices (CEMs) in a pooling project within the AGRICOH consortium.² Although overall his concerns repeat acknowledged limitations of the developed CEMs, discussed in detail in our paper, we disagree with his conclusion.

Tomenson concludes that "it is difficult to see how the pooling project can be worthwhile unless the exposure measures are greatly improved." Part of this conclusion is based on his interpretation of low agreement between self-reported pesticide use in the Agricultural Health Study (AHS) and exposure assigned to this population using two CEM approaches approximating methods developed for the two European cohorts. We refer readers to the original paper² for a detailed discussion of important differences between the AHS and the European cohorts, that will impact exposure prevalence and agreement between the different exposure assessment methods used. This comparison was limited to 1 year, and despite that we consider self-reported data in the AHS to be of high quality, it is not a gold standard and may underestimate exposure.³

As alternative exposure data were not available to compare CEM estimates with, Tomenson's related statement that "the CEM approaches also appear to greatly overestimate exposure when applied in their own cohorts," cannot be quantitatively validated. Indeed, the CEMs are highly sensitive. They assign all farmers cultivating a crop (CNAP), or performing pesticide treatment tasks on a crop (AGRICAN), exposure to individual pesticides registered for use on that crop and sold in the respective countries. This results in high positive correlations between pesticides registered for the same crop(s); this must be considered when interpreting epidemiological results based on exposure data from these CEMs. We do not agree, however, that high

sensitivity makes the CEMs unsuitable for application in epidemiological studies in agricultural occupational populations. Highly specific methods, which avoid misclassifying unexposed as exposed, are warranted for exposures with low prevalence. However, for highly prevalent exposures, the reverse is true.⁴ All studies included in our project are agricultural occupational cohorts, in which pesticide use is common (63% of the population across cohorts). For pesticides commonly used, sensitivity of the exposure assessment becomes more important, while for rarely used pesticides, highly sensitive CEMs may produce more substantial misclassification.

We agree that more work on improving the exposure assessment for pesticides is necessary, particularly for regions with diverse crop production. Several promising methods have been published using additional data sources, which provide a more comprehensive picture of pesticides used by agricultural workers: for example, farmer treatment calendars, input from industry and crop protection experts.^{5, 6} Within AGRICOH, we plan to extend the exposure assessment for specific pesticides, within time periods for which this is possible. This would be facilitated by more publicly accessible data on pesticide sales and use by farmers, from pesticide industry and regulatory agencies.

Despite acknowledged limitations, our work represents the first opportunity to investigate associations of specific pesticide exposures with rare cancer outcomes in agricultural occupational populations across multiple countries.

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