

POPULATION VARIATION IN BIOMONITORING DATA FOR PERSISTENT ANALYTES: AN EXAMINATION OF MULTIPLE DATASETS

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Introduction

National biomonitoring efforts designed to characterize the levels and distribution of pollutants in populations have typically relied upon a resource-intensive sampling strategy and analysis of hundreds or thousands of individual biological samples. In Australia, a series of studies relying on pooled serum samples, a less resource-intensive approach, has been employed to characterize central tendencies of concentrations of selected persistent analytes, but this approach does not provide estimates of typical upper bound concentrations.

This analysis assesses the feasibility of an empirical approach to estimating population upper bound reference values based on the examination of population variation from available nationally representative biomonitoring datasets from the US, Canada, Germany, and the Catalan region of Spain, with the results tested against data from the Flemish population of Belgium.

Arithmetic mean (AM) concentrations and the ratio of the 95th percentile to the mean (P95:AM) were assessed in each survey for defined age subgroups for three polychlorinated biphenyls (PCBs 138, 153, and 180), hexachlorobenzene (HCB), and p,p-dichlorodiphenyl-dichloroethylene (DDE).

Materials and methods

Biomonitoring data for PCBs 138, 153, and 180, HCB, and DDE were obtained from nationally representative biomonitoring datasets with nearly 10,000 individual samples:

- US National Health and Nutrition Examination Survey (NHANES, 2003-2004)
- German Environmental Survey (GerES) III (1998) and IV (2003-2006) ^{1,2}
- Canadian Health Measures Survey (CHMS, 2007-2009) ³
- Catalan Health Interview Survey (CHIS, 2001-2002) ⁴
- Flemish Environment and Health Survey II (FLEHS II, 2008-2011) ⁵

Results from biomonitoring of age-specific pooled samples in Australia, representing estimates of the age-specific arithmetic means for the Australian population, were also collected. Age-specific AMs, 95th percentiles (P95s), and the P95:AM ratio were calculated for each dataset except the FLEHS II. P95:AM ratios were compared across datasets for consistency, and a unified estimate with confidence intervals was made for each analyte based on the underlying multiple datasets.

The results of the variation analysis were validated using the FLEHS II data. We calculated age-specific AMs from the dataset and predicted the age-specific P95 values using the P95:AM ratios derived from the other datasets. These were compared to the actual P95s.

Results and discussion

Age-specific arithmetic mean concentrations for the included analytes varied widely among surveys, by more than a factor of 10 in many cases. However, the P95:AM ratios for each analyte were similar, with no clear pattern by age group or consistent differences among surveys (Figures 1 and 2). 95:AM ratios for PCBs 138, 153, and 180 and for HCB were similar (approximately 2.1 to 2.3). The average of the across-age-group P95:AM ratios for DDE was higher, approximately 3.0.

We combined the P95:AM estimates across age groups and surveys to construct a unified P95:AM ratio for each analyte. We applied that ratio to the calculated AMs from the FLEHS II dataset to predict the 95th percentiles by age group and analyte. This method accurately predicted P95 values for the FLEHS II based on arithmetic means from that survey (Figure 3).

These results suggest that factors controlling variation (interindividual variation in elimination efficiency and variation in long term exposure rates due to variation in dietary patterns) may for chemicals like those investigated in this study be similar across populations, even when absolute exposure levels are different.

Population upper bound reference level estimates are useful for assessing individual biomarker results to detect “unusual” levels of exposure and for examining population exposure levels compared to health-relevant guidelines.⁶ Comprehensive national sampling programs relying on analysis of hundreds or thousands of individual biological samples are resource intensive. Pooled sampling approaches are more efficient but provide direct measure only of arithmetic means, and do not provide information on population variation or allow identification of upper bound reference values. The degree of variation of biomarker concentrations for each of the 5 POPs presented here was similar across populations and age groups. These results suggest that population upper bound reference concentrations can be estimated with some confidence based on pooled sampling strategies, which allow improved detection limits and reduced analytical costs for population monitoring. These results also suggest the cautious application of the P95:AM ratio observed in the NHANES and other cross-sectional datasets to estimate P95s for other persistent analytes based on pooled samples. Future efforts may include assessing possible temporal changes in observed AM:P95 ratios should be investigated on the basis of future measurements in individual samples.

Full results from this analysis have been recently published.⁷

Acknowledgements

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References:

- 1 Schulz C, Conrad A, Becker K, Kolossa-Gehring M, Seiwert M & Seifert B. (2007) *Int. J. Hyg Environ Health* 210: 271-297.
- 2 Schulz C, Seiwert M, Babisch W, Becker K, Conrad A, Szewzyk R et al. (2012) *Int. J. Hyg Environ Health* 215: 435-448.
- 3 Statistics Canada. (2011). http://www.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.pdf.
- 4 Porta M, Gasull M, Puigdomenech E, Gari M, Bosch de Basea M, Guillen M *et al.* (2010) *Environ Int* 36: 655-664.
- 5 Schoeters G, Colles A, Den Hond E, Croes K, Vrijens J, Baeyens W *et al.* (2011). CHAPTER 2F in *Issues in Toxicology No. 9. Biomarkers and Human Biomonitoring, Volume 1: Ongoing Programs and Exposures*. L.E. Knudsen and D.F. Merlo. Royal Society of Chemistry.
- 6 Angerer J, Aylward LL, Hays SM, Heinzow B & Wilhelm M. (2011) *Int. J. Hyg Environ Health* 214: 348-360.
- 7 Aylward LL, Green E, Porta M, Toms LM, Den Hond E, Schulz C *et al.* (2014) *Environ Int* 68: 127-138.

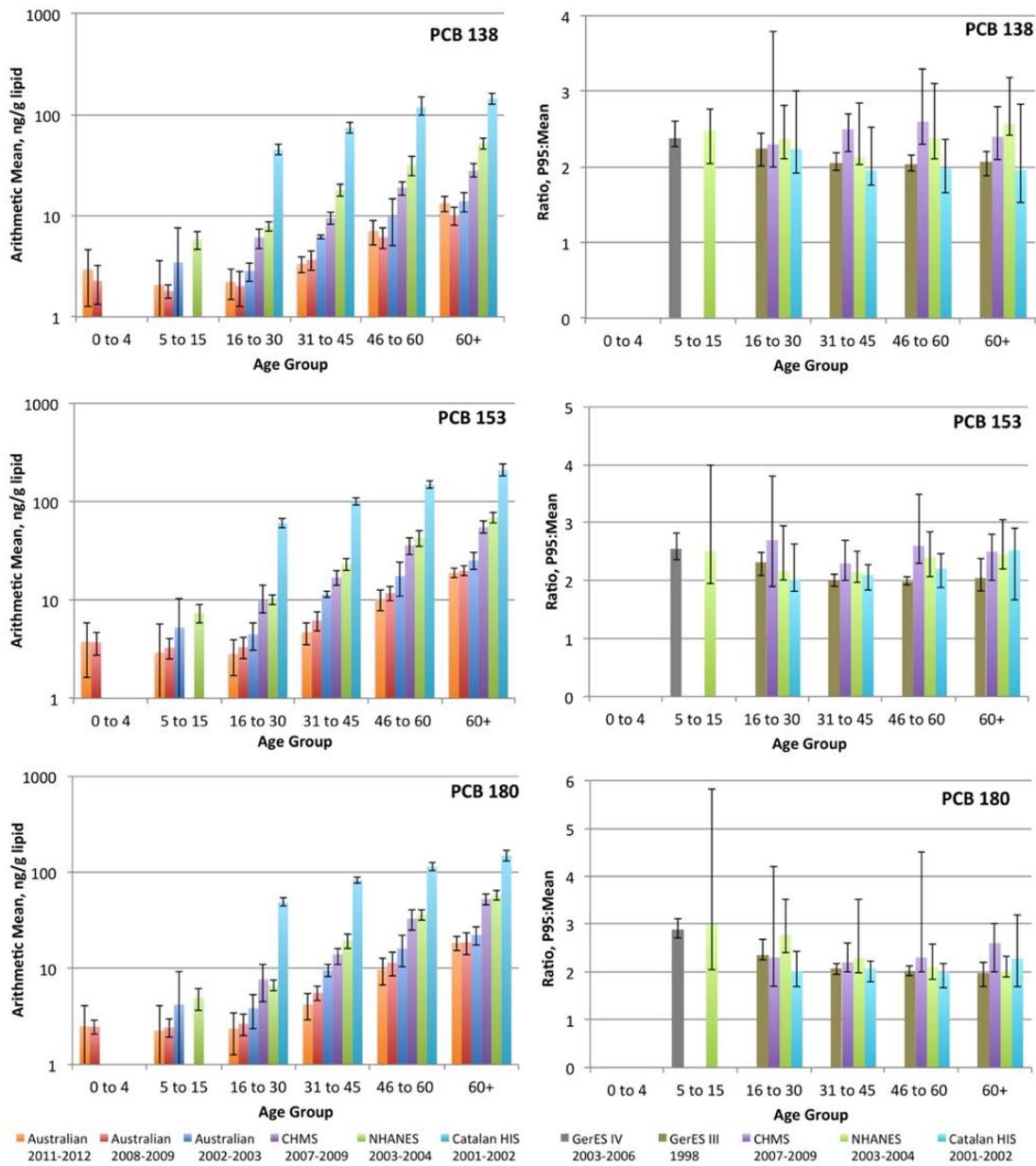


Figure 1: Arithmetic means and P95:AM ratios for PCBs 138, 153, and 180 (Aylward et al., 2014).⁷

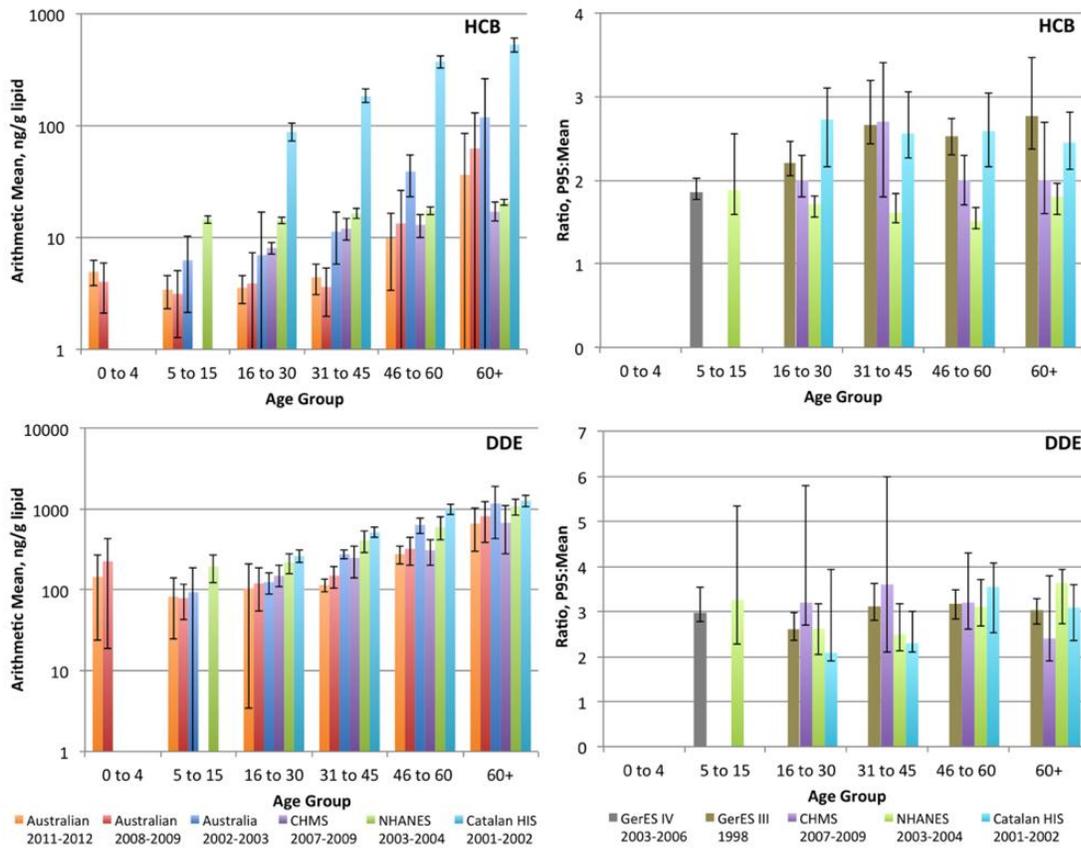


Figure 2: Arithmetic means and P95:AM ratios for HCB and DDE. Figure from Aylward et al. (2014).⁷

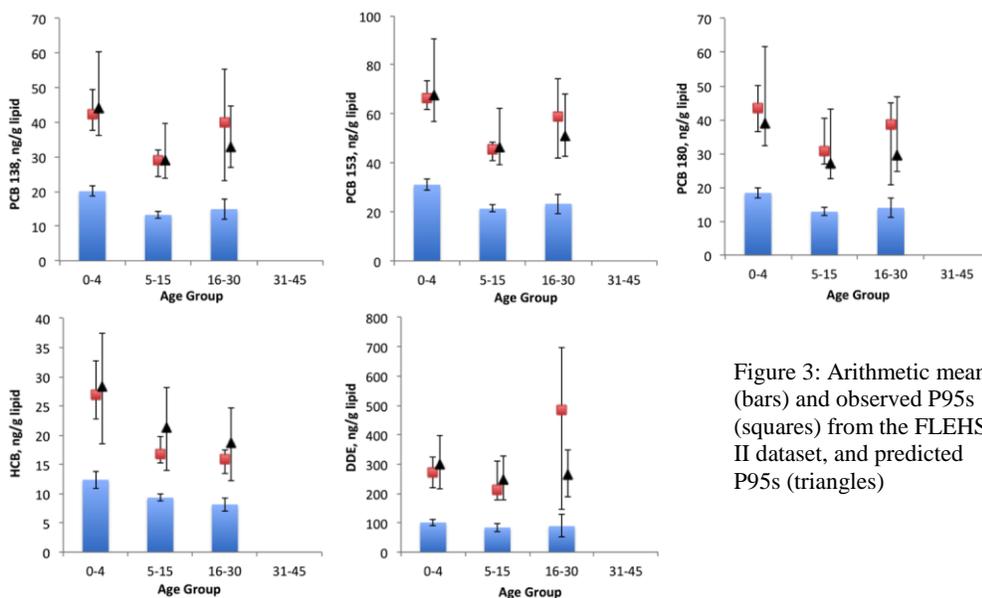


Figure 3: Arithmetic means (bars) and observed P95s (squares) from the FLEHS II dataset, and predicted P95s (triangles)