Longitudinal Studies of Diabetes in Environmental Epidemiology: Is Incident Diabetes the Right Outcome?

Charles J. Everett*†

*Master of Environmental Studies Program, College of Charleston, Charleston, SC, USA

While numerous cross-sectional studies have shown associations between environmental pollutants and diabetes, the results of longitudinal studies have been mixed [1]. The question remains, why do some longitudinal studies of incident diabetes and environmental pollutants have negative results?

A case-control study assessed the effects of spraying 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-contaminated herbicides in Vietnam. Veterans exposed to more TCDD than the background concentration, whose service was in 1969 or earlier, and/or consisted of ≥90 days of spraying, were more likely to develop diabetes than the reference group [2]. A Taiwanese study with 24 years of follow-up evaluated persons accidentally exposed to high levels of polychlorinated biphenyls (PCBs) and furans by consumption of contaminated rice-bran oil. In logistic regressions, women in the exposed group, but not men, had an increased risk of developing diabetes [3]. A cohort study of Great Lakes sport fish consumers followed subjects from 1994-1995 to 2004-2005. The sum of PCBs and PCB 118 were not associated with incident diabetes [4]. Data from the Coronary Artery Risk Development in Young Adults (CARDIA) cohort were used to examine the association of 22 PCB congeners and nine other persistent organic pollutants, and incident diabetes. Five dioxin-like PCBs were not associated with incident diabetes [5].

The longitudinal studies listed above all used incident diabetes as an outcome. In cross-sectional studies, persons who have had diabetes for some time are included. These subjects may have complications of diabetes, such as retinopathy (disorders of the retina), neuropathy (nerve damage), peripheral arterial disease (leg pain), hypertension and nephropathy (kidney disease). Among various disorders, diabetic nephropathy is the most common cause of end-stage renal disease, which could account for disability and high mortality rates in patients with diabetes [6].

In a cross-sectional study of dioxin and dioxin-like compounds, and diabetes, Everett and Thompson [7] found toxic equivalency (TEQ) ≥81.58 TEQ fg/g was associated with total diabetes (diagnosed and undiagnosed) when compared to <13.82 TEQ fg/g. The odds ratio for total diabetes with ≥81.58 TEQ fg/g was 3.08 (95% CI 1.21-7.90). We have also done some additional cross-sectional analyses of diabetic nephropathy and dioxin TEQ. In this case, nephropathy was defined as urinary albumin to creatinine ratio ≥30 mg/g, representing microalbuminuria or macroalbuminuria [8]. Of the persons in our sample, with total diabetes, 30.4% had nephropathy. The odds ratio for total diabetes with ≥81.58 TEQ fg/g, among persons who did not have nephropathy, was 2.20 (95% CI 0.84-5.80). The odds ratio for total diabetes with ≥81.58 TEQ fg/g, among persons who had nephropathy, was 19.73 (95% CI 1.34-289.89). While this point estimate is unstable, it is significant, and does indicate that the subjects with nephropathy were largely responsible for the significant result in the original analysis reported in Everett and Thompson [7].

Our analysis of diabetic nephropathy and dioxin TEQ provides strong evidence that complications of diabetes should be considered as outcomes in longitudinal studies of diabetes and environmental pollution. It is possible that multiple complications of diabetes could be used as an outcome in a longitudinal study of environmental pollution. For example, diabetic nephropathy and/or diabetes with hypertension, as an outcome in a longitudinal environmental epidemiology study. Exploratory analyses are needed to determine the most appropriate combination. This approach may prove fruitful when environmental epidemiology studies of incident diabetes do not.

References


*Corresponding author: Charles J. Everett, Master of Environmental Studies Program, College of Charleston, Charleston, SC, USA. Email: everettc@cofc.edu

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