COMPARING WAYS TO MODEL HISTORICAL DIOXIN EXPOSURE IN FOOD AS A PREDICTOR OF CURRENT SERUM DIOXIN CONCENTRATION

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INTRODUCTION & OBJECTIVES

The effect of specific food consumption on human serum dioxin levels is often of interest. We consider two methods for modeling serum levels of 2,3,7,8-TCDD as a function of covariates based on quantity of food consumed and yearly lifetime history of consumption. Given a questionnaire with yearly responses on food consumption, we compare two overall strategies for testing food covariates: (1) including meals per year and years of consumption as separate variables in the model, and (2) summarizing the consumption history in terms of an estimated current serum dioxin contribution, given each year's residual concentration based on congener-, age- and body mass index (BMI)-specific half-life values. Although the PK-based calculation requires greater programming effort, the simplicity of a PK model interpretation in terms of 2005-equivalent serum TCDD level is worthwhile.

METHODS

- This investigation was carried out using data from the University of Michigan Dioxin Exposure Study (UMDES). The UMDES was carried out in Midland, Saginaw and parts of Bay Counties (potentially exposed areas) and Jackson and Calhoun Counties (control areas) of Michigan, USA.
- The UMDES questionnaire asked several hundred questions including demographics, smoking and pregnancy history, occupational exposure, activities in the contaminated area, food consumption, and other questions possibly related to serum levels. The specific information pertaining to diet included: (1) Food consumption amounts (meals per year) in the previous five years for each of dozens of specific foods, and (2) Specific years over the lifetime in which broad categories of foods were consumed, such as "chicken, turkey, duck or goose".
- Linear regression, with $\log_{10}$ serum TCDD concentrations as the outcome variable, was performed with two different methods of formulating covariates to evaluate the effects of historical food consumption. We compared the two strategies for testing such covariates: (1) including meals per year and years of consumption as separate variables in the model ('ordinary covariates'), and (2) summarizing the entire consumption history in terms of the estimated of 2005 serum TCDD contribution, given each year's estimated residual concentration based on congener-, age- and body mass index (BMI)-specific half-life values ('PK-based covariates').

RESULTS

Over 1300 subjects were interviewed as part of the UMDES study, and 946 provided serum samples. We first illustrate the 'ordinary covariates' (Figure 1a and 1b) and the 'PK-based covariates' (Figure 2) that were used in the regression models.

Figure 1a below gives a typical plot of food consumption (meals/yr) versus age for poultry. For example, eating poultry every day would correspond to 365 meals/yr. The plot indicates that most participants ate poultry less than once a day, but many ate it at least once per week (52 meals/yr), with evident rounding patterns.

Figure 1b shows a scatterplot of the number of years eating fish between 1960-1979 versus the number of years eating fish between 1980 and 2005. Note the strong patterns as a function of age, and the fact that most people either did not eat fish, or ate fish, their whole lives (right-hand bar of points).

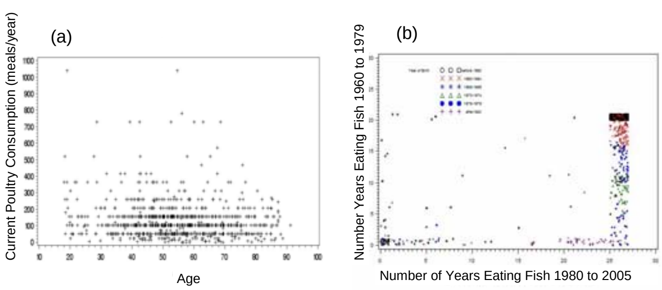

***Figure 1**. (a) Plot of food consumption (meals/yr) versus age for poultry. (b) Plot of Years eating fish 1960-1979 versus 1980-2005.*

Figure 2 (above right) plots the PK-based variable for the estimated contribution to 2005 serum TCDD concentration versus age. As has been observed in both exposed and background populations, the serum concentration rises with age, reflecting a combination of a cumulating burden over time and high environmental levels in past years.

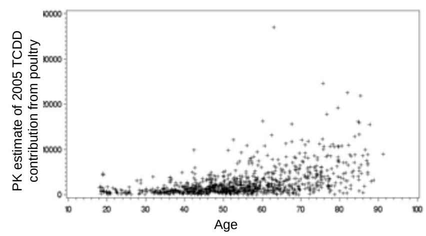

Figure 2. Plot of PK-based estimates of the 2005 serum TCDD contribution from past consumption of poultry by age.

Table 1 below gives selected regressions results for meat, game meat, and hunting using 'ordinary' and 'PK-based" covariates. The adjusted R^2 values are very similar in the two models. However, the covariate interpretations are easier in the 'PK-based' model.

***Table 1**. Regression results for 'ordinary' and 'PK-based' covariates (blue), modeling serum $\log_{10}$ TCDD.*

	'Ordinary Covariates'		*'PK-based Covariates'*	
Adjusted R^2 for whole model	69.7		68.0	
Selected Variables	***Estimate***	***p-value***	***Estimate***	***p-value***
Yrs eating game meat 1960-79	-0.0107	0.0002		
Meals/yr of deer (Sag* R area)	-0.1549	0.0024		
Meals/yr of squirrel/rabbit (elsewhere)	0.1069	0.0098		
PK _squirrel/rabbit (elsewhere)			0.0018	0.0000
PK _squirrel/rabbit (Tittab R* area)			0.0029	0.0018
Yrs hunting near Tittab R* 1960-79 (high)	0.3785	0.0005		
(med)	-0.0331	0.6671		
Meals/yr beef/poultry/lamb/veal elsewhere (high, vs low)	0.1017	0.0056		
(med, vs low)	0.0170	0.7655		
PK: beef/poultry/lamb/veal (Sag R*)			0.0000	0.0000
PK: chicken/turkey/duck/goose (bought)			0.0000	0.0041
PK: chicken/turkey/duck/goose (Tittab R)			0.0002	0.0176

Tittab R =Tittabawassee River; Sag R = Saginaw River

CONCLUSIONS

Interpreting regression coefficients in the presence of covariate collinearity is difficult. Food variables in multiple forms (meals/yr and numbers of years during two time periods) suffer from problems of collinearity with each other and with age. The resulting regression coefficients can have 'wrong signs', such as the strangely protective effects of eating game meat and deer on serum TCDD concentration, seen in Table 1 above. The difficulty of interpreting these 'ordinary covariates' is at least partially solved by the use of 'PK-based covariates'. Although the PK-based calculation requires greater programming effort, the simplicity of a PK model interpretation in terms of 2005-equivalent serum TCDD level is helpful. The assumptions of both model formulations need careful attention.

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