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## Fruit and vegetable intake, as reflected by serum carotenoid concentrations, predicts reduced probability of polychlorinated biphenyl–associated risk for type 2 diabetes: National Health and Nutrition Examination Survey 2003-2004



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#### ABSTRACT

Type 2 diabetes has been shown to occur in response to environmental and genetic influences, among them nutrition; food intake patterns; sedentary lifestyle; body mass index; and exposure to persistent organic pollutants, such as polychlorinated biphenyls (PCBs). Nutrition is essential in the prevention and management of type 2 diabetes and has been shown to modulate the toxicity of PCBs. Serum carotenoid concentrations, considered a reliable biomarker of fruit and vegetable intake, are associated with the reduced probability of chronic diseases, such as type 2 diabetes and cardiovascular disease. Our hypothesis is that fruit and vegetable intake, reflected by serum carotenoid concentrations, is associated with the reduced probability of developing type 2 diabetes in US adults with elevated serum concentrations of PCBs 118, 126, and 153. This cross-sectional study used the Center for Disease Control and Prevention database, National Health and Nutrition Examination Survey 2003-2004, in logistic regression analyses. Overall prevalence of type 2 diabetes was approximately 11.6% depending on the specific PCB. All 3 PCBs were positively associated with the probability of type 2 diabetes. For participants at higher PCB percentiles (eg, 75th and 90th) for PCB 118 and 126, increasing serum carotenoid concentrations were associated with a smaller probability of type 2 diabetes. Fruit and vegetable intake, as reflected by serum carotenoid concentrations, predicted notably reduced probability of dioxin-like PCB-associated risk for type 2 diabetes.

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Abbreviations: A1C, glycosylated hemoglobin; AhR, Aryl hydrocarbon receptor; BMI, body mass index; CVD, cardiovascular disease; LOD, limit of detection; NAFLD, nonalcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey; NIH, National Institutes of Health; PCB, polychlorinated biphenyl; PIR, poverty income ratio; POP, persistent organic pollutant.

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#### 1. Introduction

Recent decades have seen increased rates of type 2 diabetes, and it is now estimated to affect 25.8 million Americans and 346 million people worldwide [1,2]. Type 2 diabetes has been shown to occur in response to environmental and genetic influences [3-9], among them food intake patterns; sedentary lifestyle; body mass index (BMI); and exposure to persistent organic pollutants (POPs), such as polychlorinated biphenyls (PCBs) [10-15]. Although not produced in the United States since 1977, PCBs persist in the environment and concentrate in adipose tissue of organisms. They remain detectable in soil, air, water, and sediment, where they enter the food chain [16]. The primary route of PCB exposure today is through dietary intake of contaminated foods and through inhalation of airborne pollutants [17]. Increasing evidence from animal [10-12,18,19] and epidemiological research suggests that background exposure to PCBs is associated with type 2 diabetes, including studies examining National Health and Nutrition Examination Survey (NHANES) data [13]; low-dose PCB exposure [14,15]; 5-year prospective data from an elderly population in Sweden [20]; the PCB-exposed population of Anniston, AL [21]; a review of epidemiological studies from a National Toxicology Program Workshop [22]; and prospective data from the Nurses' Health Study as part of a meta-analysis [23].

Nutrition is essential in the prevention and management of type 2 diabetes [6-9] and has been shown to modulate the toxicity of PCBs [19,24-29]. Consistent intake of fruits and vegetables has been associated with a healthy weight, positive antioxidant status, and a reduced risk of chronic diseases. Dietary antioxidants, such as vitamin C and the carotenoids, when consumed at adequate levels, can provide a balanced defense against the harmful effects of reactive oxygen species [30]. Serum carotenoids, a family of lipophilic plant pigments with potent antioxidant activity, are considered a reliable biomarker of fruit and vegetable intake [31]. Serum responses to carotenoids have been reported to depend on a variety of factors, including the amount consumed, food matrix, and half-life variability of individual carotenoids [32]. The predominant carotenoids in human sera are  $\alpha$ -carotene,  $\beta$ -carotene,  $\beta$ -cryptoxanthin, lycopene, lutein, and zeaxanthin [33]. Observational studies of carotenoids reveal inverse associations with type 2 diabetes [34], cardiovascular disease (CVD) [35,36], and all-cause mortality [37,38], although individual carotenoid effects have been inconsistent.

In the present study, we tested the hypothesis that fruit and vegetable intake, reflected by serum carotenoid concentrations, is associated with the reduced probability of developing type 2 diabetes in US adults with elevated serum concentrations of PCBs 118, 126, and 153. The objective was to use the Center for Disease Control and Prevention database, NHANES 2003-2004, to establish whether serum carotenoid concentrations are associated with a reduced risk of developing type 2 diabetes in adult participants with elevated serum concentrations of PCBs 118, 126, and 153.

#### 2. Methods and materials

#### 2.1. Procedure and study population

National Health and Nutrition Examination Survey is a series of nationally representative, cross-sectional surveys of the civilian, noninstitutionalized US population. National Health and Nutrition Examination Survey 2003-2004 survey procedures, laboratory assays, and ethics review board approval are published in detail [39]. Approval for our analysis of the NHANES data was granted by the University of Kentucky Institutional Review Board.

In NHANES 2003-2004, a random, ½ subsample was selected for fasting plasma glucose measurements, and a separate random, but overlapping, 1/3 subsample was selected for serum PCB measurements. Measurement of serum carotenoids was a fixed component of the mobile examination center examination without dedicated subsample status.

For our study, we used the following inclusion criteria for a larger subpopulation (n = 5041; Table 1): adults 20 years or older examined at the mobile examination center, having measurements for serum carotenoid concentrations and either a fasting glycosylated hemoglobin (A1C) value or history of type 2 diabetes diagnosis. A prototype individual represents this group. Mean values were drawn from this larger subpopulation. The prototype was a 50-year-old non-Hispanic, white male, at the 50th percentile of poverty income ratio (PIR) (2.23), the 50th percentile of BMI (27), and the 50th percentile serum carotenoid concentrations (1.7  $\mu$ mol/L). Approximately 1200 of these subjects had at least 1 PCB concentration measured.

The BMI of the prototype individual was varied to help understand the changing relationship between the variables in our models. The National Institutes of Health (NIH), National Heart, Lung, and Blood Institute defines BMI, as weight (kilograms) divided by height squared (square meters) and its use, as a measure of body fat based on height and weight in adults [40]. The Center for Disease Control and Prevention interprets BMI using standard weight status categories: less than 18.5, underweight; 18.5 to 24.9, normal weight; 25.0 to 29.9, overweight; 30.0 to 39.9, obese; 40.0 or higher, extremely obese [41].

Sociodemographic covariates included sex, age, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other ethnicities), PIR, and BMI. Poverty income ratio was determined by the ratio of total family income to poverty, as determined by the US Department of Health and Human Services annual poverty guidelines. Women and non-Hispanic whites comprised more than 50% of the sample (Table 1). Approximately 22% of participants reported being current cigarette smokers, although 79% to 81% had serum cotinine levels of 0.015 ng/mL or higher, considered a positive indicator of passive or active smoking; thus, we did not include smoking in our models.

#### 2.2. Exposure variables

#### 2.2.1. Serum carotenoids

Individual carotenoids were pooled and assessed as total carotenoids. The carotenoids of interest in this study were  $\alpha$ -carotene,  $\beta$ -carotene,  $\alpha$ -cryptoxanthin,  $\beta$ -cryptoxanthin, lycopene, lutein, and zeaxanthin. Lutein and zeaxanthin

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