

Name: Carine Sakr, MD MPH ¹
Robin Leonard, PhD ²
Mark Cullen, MD ¹

Program Affiliation: ¹Yale Occupational and Environmental Medicine Program
²Epidemiology Program at DuPont Haskell Laboratory for
Health and Environmental Sciences

Address: 135 College Street, 3rd floor
New Haven, CT 06510

Phone: 856-816-1539

Fax: 203-785-7391

Email: carine.sakr@yale.edu

TITLE Twenty-five year longitudinal study of serum total cholesterol related to a serum biomarker of exposure (serum perfluorooctanoate or PFOA) in a polymer production plant.

BACKGROUND

- Perfluorooctanoate (PFOA, $C_7F_{15}COO^-$) is a perfluorinated carboxylate, primarily used as a surfactant in the production of fluoropolymer high-performance materials. Fluoropolymers are used in architectural fabrics; chemical processing piping and vessels; automotive fuel systems; telecommunications and electronic wiring insulation; and computer chip processing equipment and systems- in addition to consumer products such as cookware and apparel.
- PFOA has been found in the serum of production workers with occupational exposure (1-3). Lower levels of PFOA have been reported in serum samples of non-occupationally exposed men and women in the USA as well as in other countries, which suggests a widespread, albeit low, exposure to the general population (4-8).
- Animal studies suggested that the liver is the primary target organ for PFOA-induced toxicity in rats and monkeys. PFOA produced hypolipemia in rodents (9, 10) and increased liver weight as a result of mitochondrial proliferation in monkeys (11). PFOA exposure also increased incidence of adenomas of the liver, pancreas, and testes in rats (12).
- Previous studies in exposed workers evaluating the association between PFOA and total cholesterol have yielded conflicting results (13,14).

METHODS

- The relationship between total cholesterol and serum PFOA was examined in a 25-year longitudinal study (1979-2004) with repeated measurements using a mixed effects model in a cohort of 454 workers with occupational exposure to PFOA.
- The serum PFOA levels used were part of an industrial hygiene surveillance program. The blood cholesterol levels and other covariates were abstracted from the medical surveillance program at the plant. There were no available data on use of lipid lowering medications. Unless cholesterol was measured in the same year as PFOA, the cholesterol level corresponding to a PFOA test was interpolated from the values of the 2 nearest before and after dates.
- Univariate analyses were utilized to determine the distributions of PFOA and cholesterol.
- All analyses were conducted using a 95% level of confidence ($\alpha = 0.05$) in SAS version 9.01.

RESULTS

- The cohort included 334 males and 120 females.
- At the end of the study, 49.3% of the subjects were still employed; the rest were either terminated (43.4%) or dead (7.3%).
- For those still employed, the mean age was 51.3 years.
- The mean serum PFOA for the entire cohort was 1.69 ppm (SD 3.24). Serum PFOA seemed to decrease with calendar time (Figure 1).
- All the people in the cohort had at least 2 measurements of serum PFOA (median: 3; range 2-17).
- Total cholesterol increased with age for both men and women (Figure 2) and had a close to normal distribution in the cohort (Figure 3).
- After adjusting for age, BMI, and gender, there was a statistically significant positive association between serum PFOA and total cholesterol (Table 1).

CONCLUSIONS

- Serum PFOA is positively associated ($p = 0.007$) with total cholesterol in a longitudinal analysis of exposed workers. The parameter estimate is 1.152 mg/dl/ppm PFOA. However, this result is not adjusted for use of lipid lowering medications. The true relationship might be in fact stronger.
- Further studies should be considered to further understand the relationship between exposure to PFOA and total cholesterol.

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Figure 1 Blood PFOA (ppm) versus calendar time

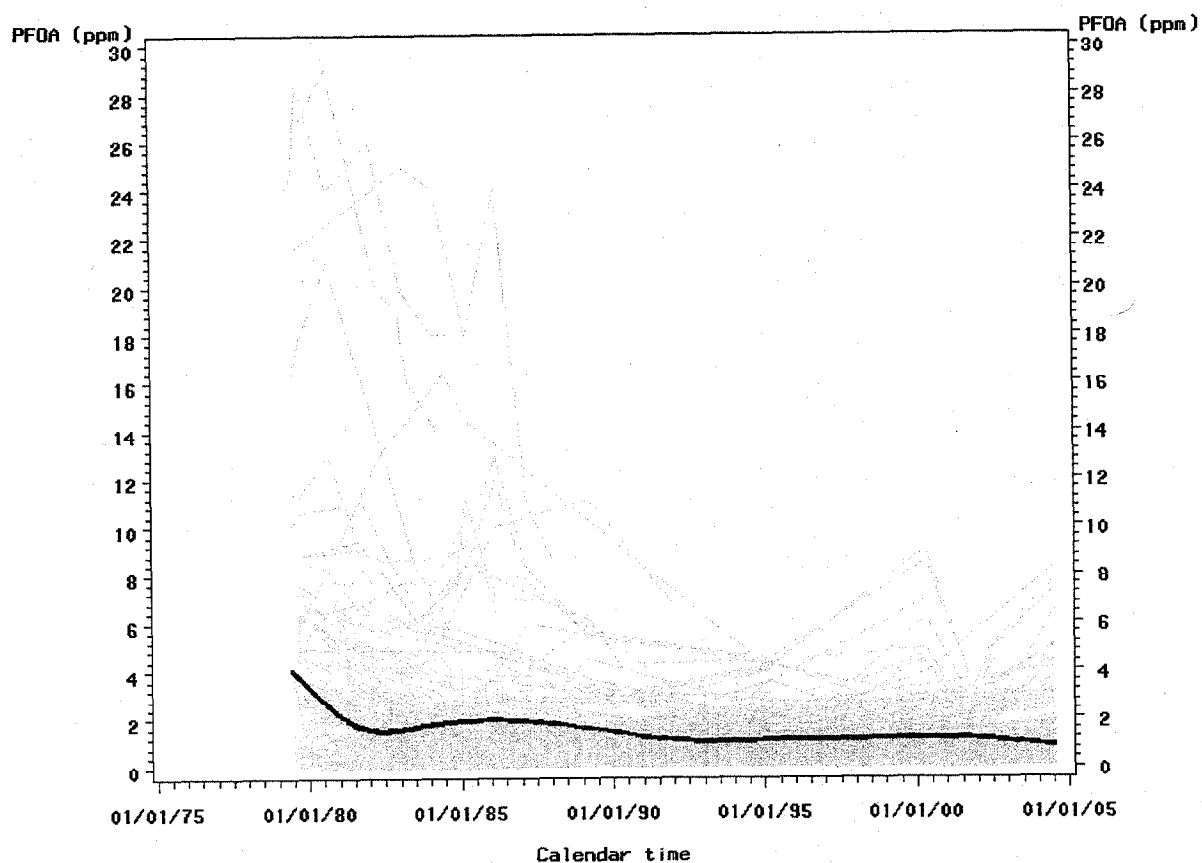


Figure 2 Total cholesterol (mg/dl) versus age stratified by gender

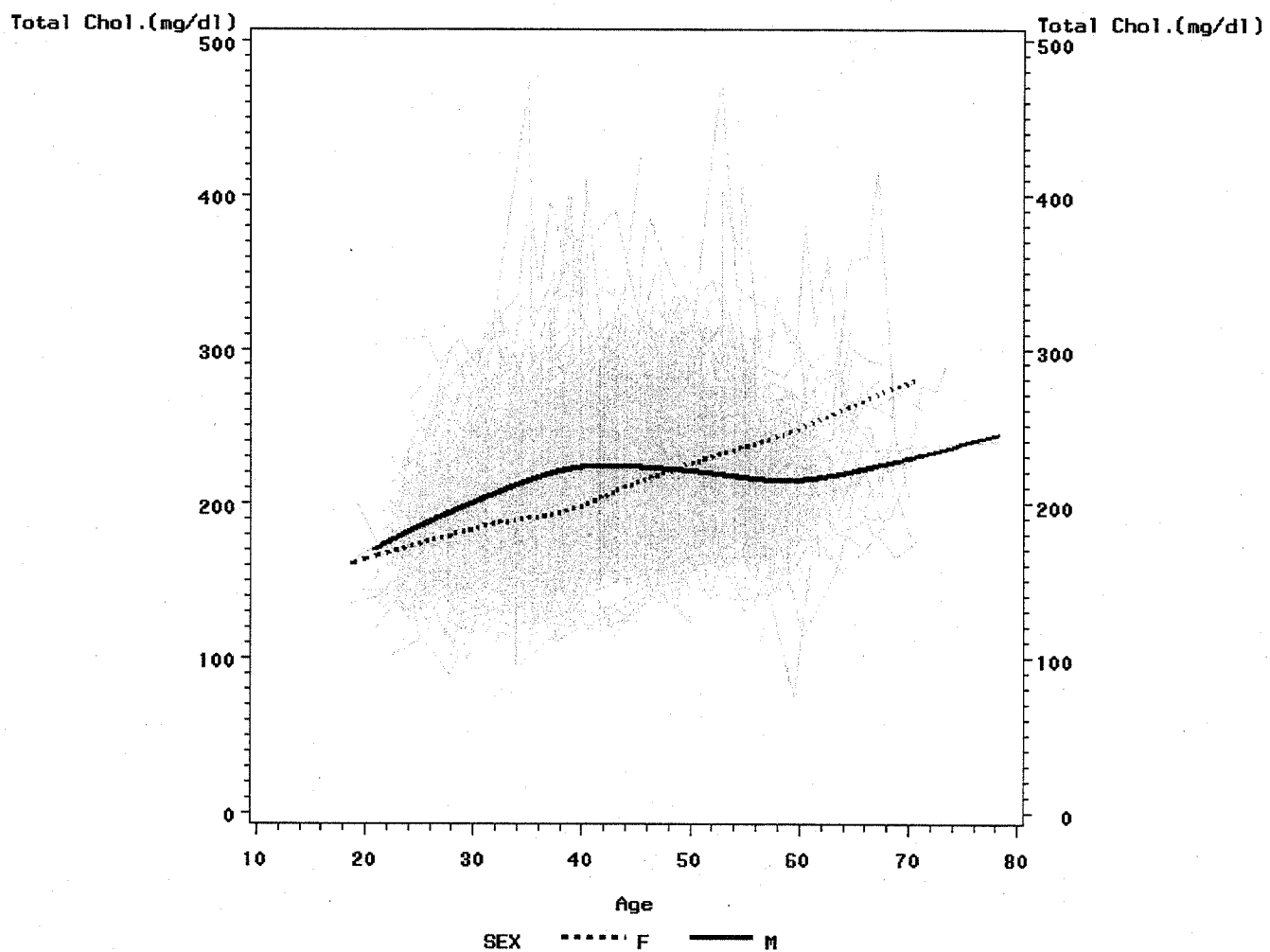


Figure 3 Distribution of total cholesterol (mg/dl)

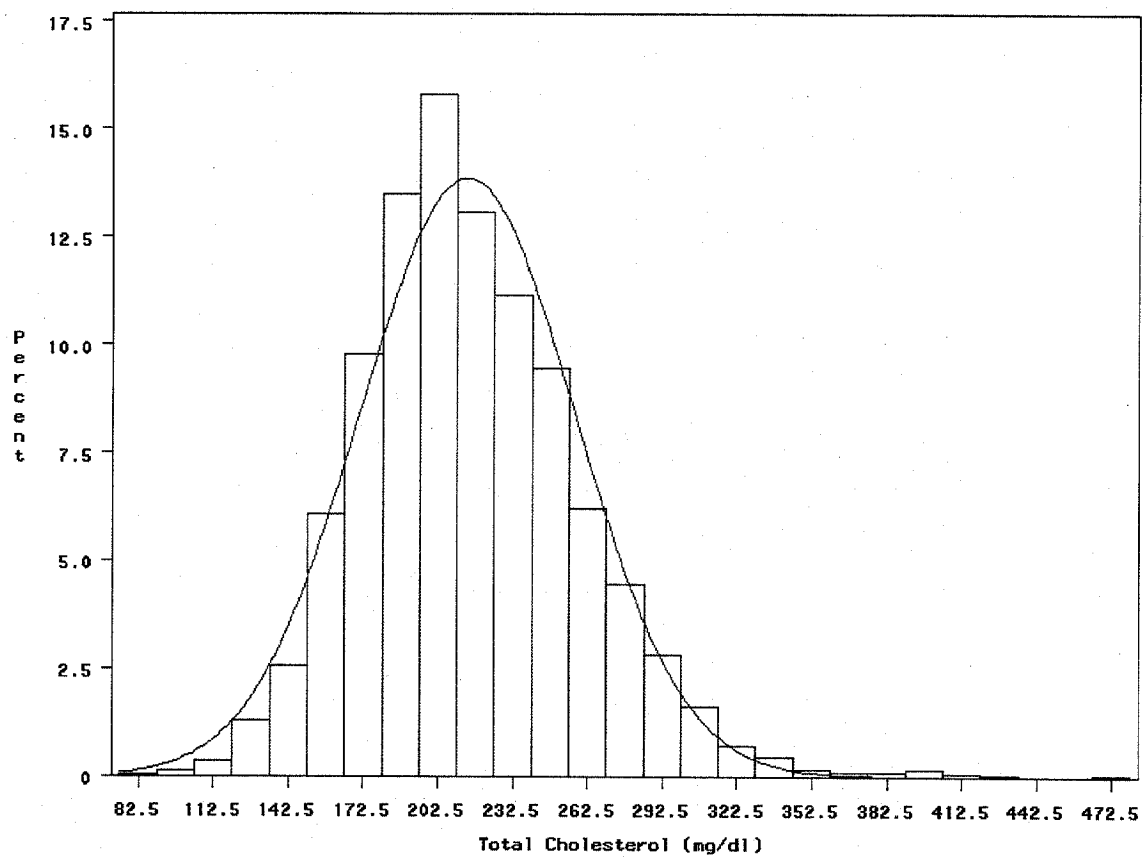


Table 1 Longitudinal analysis of total cholesterol (mg/dl) by blood PFOA (ppm) and other covariates

Effect	Parameter Estimate	Pr> t
Blood PFOA	1.152	0.007
BMI	1.14	0.008
Age	-0.33	0.037
Gender (female)	-71.69	<0.001
Age*gender (female)	1.63	<0.001
Hiredecade	-4.58	0.008

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