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Self-Reported Medical Conditions in Perfluorooctanesulfonyl Fluoride Manufacturing Workers

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Learning Objectives

- Summarize relevant characteristics of perfluorooctane sulfonate (PFOS) and other perfluorinated chemicals, and the findings in animals exposed to high levels of these materials.
- Identify any associations found in 1,400 employees completing a questionnaire between levels of occupational exposure to PFOS on the one hand and, on the other, the risk of various malignant and benign disorders and adverse pregnancy outcomes.
- Compare the PFOS exposure levels experienced by employees in this study to those in the general population.

Abstract

Objective: *To evaluate whether some cancers, other conditions, and pregnancy outcomes were related to occupational perfluorooctane sulfonate (PFOS) exposure.* ***Methods:*** *We surveyed current and former employees of a perfluorooctanesulfonyl fluoride production facility, using a self-administered questionnaire to ascertain several cancers and health conditions. Female cohort members also completed a brief pregnancy history. We requested medical records to validate reported melanoma, breast, prostate, and colon cancers. PFOS exposure was estimated based on a job exposure matrix up to the year of the diagnosis of the condition.* ***Results:*** *Of the 1895 eligible participants, 1400 questionnaires were returned. No association was observed between working in a PFOS-exposed job and the risk of any of the surveyed conditions.* ***Conclusion:*** *We observed no association between working in a PFOS-exposed job and several cancers, common health conditions, and birth weight.* (J Occup Environ Med. *2007;49:722–729*)

A manufacturing facility in Decatur, Alabama, was one of two major production sites of perfluorooctanesulfonyl fluoride (POSF; $C_8F_{17}SO_2F$)-based specialty chemicals. These specialty chemicals have a wide range of applications, including surface treatments, paper and packaging protectants, and performance chemicals.[1] POSF-based chemicals can degrade or be metabolized to perfluorooctane sulfonate (PFOS; $C_8F_{17}SO_3^-$), which also is used as a primary component in a limited number of specialty chemical applications.

PFOS and other perfluorinated chemicals are pervasive pollutants that persist in the environment and can accumulate in wildlife.[1–4] PFOS has been quantified at serum concentrations of 30 to 40 ng/mL in the general population,[5–10] and has a long serum elimination half-life of several years in humans,[11] which may be due to saturable renal resorption.[12] The presence of PFOS in nonoccupationally exposed populations and wildlife has raised concerns about the environmental and health effects of PFOS and prompted the phase-out of the production of POSF-based chemicals by the major producer.[1]

Toxicological studies of rats and cynomolgus primates have shown that high doses of PFOS induced enlargement of liver and apparent alterations in metabolic processes, including reduced serum cholesterol levels.[13,14] Although not found to be a developmental toxicant in rats or rabbits,[15] higher maternal doses of

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PFOS increased neonatal mortality, absorptions, resorptions, and reduced weight gain in rat pups.[16–19] Multigeneration studies did not indicate effects on postnatal neurological development, or fertility and estrous cycling in offspring. The mechanism of toxicity, though not fully understood, may be due to an effect on fatty acid transport and metabolism, membrane function, peroxisome proliferation, or mitochondrial bioenergetics.[20–22]

Human health effects of PFOS exposure have been studied in occupationally exposed populations with average serum concentrations ranging from 500 to 2000 ng/mL.[23] Standard clinical blood and urine chemistry analyses did not vary by PFOS exposure.[9] Indirect measures of health-related events, as measured by frequency of health insurance claims filed by workers, found more frequent claims among exposed workers for the a priori conditions, biliary tract disorders, and cystitis recurrence as well as benign colon polyps, malignant colorectal tumors, and malignant melanoma.[24] A cohort mortality study of employees of a POSF manufacturing facility did not find associations with a priori conditions, but reported an excess risk of death from bladder cancer; although, the result was based on three cases.[25] A case-finding effort to ascertain incident, nonfatal bladder cancer cases in that population did not show evidence of a high risk of bladder cancer in relation to PFOS exposure.[26] As part of the bladder cancer investigation, several additional health outcomes, based on prior toxicological and human health studies, were ascertained to further investigate potential health effects of exposure to these chemicals. Herein we report the results of this investigation.

Materials and Methods

Study Population

The study population included employees of a facility that manufactures POSF-based chemicals and specialty films. The plant is divided in two major sections, chemical and film, which are approximately 300 yards apart. The study population was that of the original cohort mortality study and included all current, retired, and former employees with a cumulative employment of at least 1 year. A roster of all known addresses and telephone numbers were obtained through company personnel or retiree records. The address information and vital status were updated through a variety of tracing resources available to the University of Minnesota, including TransUnion, Lorton Data, and National Change of Address. If a cohort member was noted to have died since the end of the mortality study, a copy of the death certificate was obtained from the state of record.

Recruitment

The University of Minnesota Institutional Review Board approved the study protocol. Before recruitment, a series of meetings was held with current employees and retirees to inform them of the upcoming study and allow them to ask questions about the study. Recruitment of presumed living cohort members was initiated with a letter and brochure detailing the study scope and procedures, and assurances of confidentiality. A questionnaire, with cover letter and postage-paid return envelope, followed the recruitment letter by approximately 1 week. Nonrespondents received reminder post cards followed by a second questionnaire. Undeliverable addresses identified on returned mail were re-entered into the search engines to identify possible alternate addresses to re-send the questionnaire. Cohort members who did not respond to the second questionnaire mailing after 1 month were contacted by telephone to verify receipt of the questionnaire and inquire about intent to participate. At that time, the respondent was offered the opportunity to complete the questionnaire by telephone if they preferred.

Questionnaires

A self-administered questionnaire was developed to enumerate the occurrence of diseases and conditions selected based on the toxicological studies of PFOS, the cohort mortality analysis, and the study of episodes of care. The questionnaire ascertained diagnoses of cancers, including melanoma, liver, prostate (men only), breast (women only), colon, or rectal cancer, and noncancerous conditions, including liver disease (cirrhosis and hepatitis), cholelithiasis, cholecystitis, cystitis, colon polyps, and other diseases of the prostate (men only). One question about gastric ulcers was included to ascertain the frequency of reporting a relatively common condition that, a priori, was not believed to be related to PFOS exposure. The year of first diagnosis was asked for each condition. A brief pregnancy outcome history was asked of the women, including number of pregnancies, the month and year the pregnancy ended, the outcome of the pregnancy, and the weight of the live-born children. Several other questions were asked relating to routine screening procedures that may be related to the diagnosis of prostate disease, colon polyps, or cancer. The questionnaire also recorded tobacco use.

All questionnaires were reviewed on receipt and double entered into an electronic database. Validation of the diagnosis of the self-reported cases of prostate cancer, colon cancer, breast cancer, and melanoma was sought through medical records. Participants reporting these conditions were contacted by letter, with telephone follow-up, to request permission to contact their physician to verify the diagnosis. Signed consent and medical release forms, and the name and address of the physician or clinic of reference were obtained and sent to the physician or clinic along with a request for pathology reports, surgical notes, or any other information pertaining to the diagnosis of the reported cancer. If no response was

received from the clinic or physician, they were contacted by telephone to assure receipt of the material and encourage appropriate response.

Exposure Assessment

The exposure assessment followed the previously described method used in the mortality study.[25] This method created job-specific exposure categories based on job titles, departments, and dates of employment identified in the participant's individual work histories, and potential for PFOS exposure. The relative differences in serum PFOS concentrations by job were determined by a biological monitoring study of 186 workers in 1998, which is detailed elsewhere.[23] Because production processes have remained constant over time, a simple exposure matrix was developed based on the work history records of the study cohort. The work histories used in the exposure analysis covered the period from when the plant opened (ie, 1961) through when the work histories were collected for the original mortality study (ie, 1997).[25]

Each unique job and department combination in the work history was assigned to three major exposure categories based on the geometric mean PFOS serum concentrations of the major job categories from biological monitoring[23] and the expert judgment of plant industrial hygienists that grouped workers with similar tasks and exposures. The major exposure categories and the geometric mean serum PFOS concentrations from the biological monitoring study were as follows: 1) no direct workplace exposure to POSF-based fluorochemicals (0.11 to 0.29 ppm), 2) low-potential workplace exposure to POSF-based fluorochemicals (0.39 to 0.89 ppm), and 3) high-potential workplace exposure to POSF-based fluorochemicals (1.30 to 1.97 ppm). Hereafter, these three categories will be referred to as nonexposed, low exposure, and high exposure.

The time at each exposure level accrued from first employment until date of diagnosis of each condition, until death, or until the end of the study. This exposure metric assumes a continually increasing accumulation of PFOS exposure because the half-life for PFOS is prolonged; thus, exposures to high concentrations can result in high body burdens for a long time after exposure ceases. For this analysis, two exposure models were considered. For the primary model the workers were classified as never employed in a PFOS-exposed job, ever employed in a low-exposure job, ever employed in a high-exposure job, ever employed in a high- or low-exposure job, employed in a high- or low-exposure job for at least 1 year, and employed in a high-exposure job for at least 1 year. The second exposure model estimated cumulative exposure by assigning the no-exposure, low-exposure, and high-exposure jobs relative POSF-based job exposure weights of 1, 3, and 10, respectively. The years spent in each job were multiplied by the relative weights to develop a cumulative quantitative exposure metric. The cumulative exposures were categorized to represent the equivalent of up to 1, 1 to 5, and greater than 5 years of employment in a high-exposure job.

For each disease or condition, exposure was estimated up to the first year of diagnosis for that disease or condition. For the analysis of pregnancy outcome, exposure was estimated up to the month and year the pregnancy ended. Any health events

TABLE 1
Gender, Age, and Exposure Characteristics of Participants and Nonparticipants in the Decatur Morbidity Study

	Questionnaire Respondent						
	Yes		No		Deceased		
	N	%	*N*	%	*N*	%	Total
Gender							
Male	1137	81.2	416	84.0	177	94.1	1730
Female	263	18.8	79	16.0	11	5.9	353
Total	1400		495		188		2083
Age at end of study							
<30	5	0.4	3	0.6	8	4.3	16
30–39	65	4.6	41	8.3	21	11.2	127
40–49	294	21.0	144	29.1	40	21.3	478
50–59	604	43.1	207	41.8	55	29.3	866
60–69	352	25.1	84	17.0	43	22.9	479
70+	80	5.7	16	3.2	21	11.2	117
Years worked							
<5	437	31.2	172	34.7	52	27.7	661
5–9	148	10.6	67	13.5	33	17.6	248
10–14	111	7.9	38	7.7	26	13.8	175
15–19	120	8.6	38	7.7	18	9.6	176
20+	584	41.7	180	36.4	59	31.4	823
PFOS exposure group[a]							
Nonexposed[b]	562	40.1	179	36.2	68	36.2	809
Low							
Ever	413	29.5	121	24.4	67	35.6	601
≥1 yr	320	22.9	78	15.8	52	27.7	450
High							
Ever	624	44.6	276	55.8	82	43.6	982
≥1 yr	480	34.3	234	47.3	69	36.7	783
Low or high							
Ever	838	59.9	316	63.8	120	63.8	1274
≥1 yr	689	49.2	273	55.2	108	57.4	1070

[a]Categories are not mutually exclusive. For example, a participant could be counted as having both "ever low exposure" and "ever high exposure."

[b]Nonexposed includes workers from the film plant who never worked in the chemical plant.

diagnosed pre-employment were classified as never exposed.

Analysis

The associations between each categorical exposure level and risk of each condition are presented as odds ratios estimated with logistic regression. All models were adjusted for age and gender. The precision of the estimates for all analyses are described with 95% confidence intervals. The analyses of cancers included cases from this population identified by death certificate under the assumption that these cancers are reliably reported on the death certificates. Accordingly, the decedents as well as questionnaire respondents were included in the analyses. The analyses of cancers were conducted on all self-reported cancers, and then on the subset of cancers that were validated, including those on the death certificates. Cancer of the breast, prostate, and colon are reported with reasonable validity. Melanoma, however, is often misreported on a self-administered questionnaire and is frequently mistaken for other types of skin cancer.[27,28] The analyses for all other conditions were conducted only for questionnaire respondents as the conditions do not appear routinely on death certificates.

Pregnancy outcomes were compared across the same exposure groupings with the exposure estimate up to the time of pregnancy. For still births, only a descriptive analysis is presented because of the rarity of the event. Birth weight, reported as pounds and ounces, was converted to kilograms. Birth weight for each exposure category was compared with the no-exposure group using a Wilcoxon two-sample test. Multiple linear regression models were fit to estimate the difference in mean birth weight by exposure category. All models for birth weight included only singleton births and were adjusted for maternal age, gravidity, and smoking. All analyses were conducted with SAS 9.1 for Windows (SAS Institute Inc., Cary, NC).

TABLE 2
Frequencies of Self-Reported and Validated Cases of Cancer and Self-Reported Noncancer Health Conditions From the Survey

	Yes		No		
Condition	*N*	%	*N*	%	Total (*N*)
Self-reported cancer					
Breast	4	1.5	259	98.5	263
Colon	22	1.6	1378	98.4	1400
Liver	0	0	1400	100	1400
Melanoma	39	2.8	1361	97.3	1400
Prostate	29	2.6	1107	97.4	1137
Thyroid	0	0	1400	100	1400
Validated cancer					
Colon	12	0.9	1388	99.1	1400
Melanoma	8	0.6	1392	99.4	1400
Prostate	22	1.9	1115	98.1	1137
Noncancer conditions					
Gastric ulcer	300	21.4	1100	78.6	1400
Cystitis	269	19.2	1131	80.8	1400
Bladder calculi	23	1.6	1377	98.4	1400
Colon polyps	241	17.2	1159	82.8	1400
Cholecystitis	74	5.3	1326	94.7	1400
Cholelithiasis	119	8.5	1281	91.5	1400
Nephrolithiasis	242	17.3	1158	82.7	1400
Liver disease, including cirrhosis and hepatitis	54	3.9	1346	96.1	1400
Benign prostatic hyperplasia	211	18.6	925	81.4	1137
Prostatitis	155	13.6	981	86.4	1137

TABLE 3
Risk Estimates for Cancer Associated With PFOS Exposure for Self-Reported and Validated Cancers and Cancer Deaths

	Cumulative PFOS Exposure[a]			
	Yes (*N*)	No (*N*)	OR[b]	95% CI[c]
Colon cancer[d]				
Never	8	623	1	
Ever low or high	15	942	1.21	0.51–2.87
Low or high (≥1 yr)	14	775	1.37	0.57–3.30
High (>1 yr)	7	536	1.69	0.68–4.17
Melanoma[e]				
Never	4	627	1	
Ever low or high	7	950	1.08	0.31–3.72
Low or high (≥1 yr)	5	784	0.90	0.24–3.43
High (>1 yr)	4	544	1.01	0.25–4.11
Prostate cancer[d]				
Never	10	536	1	
Ever low or high	19	748	1.34	0.62–2.91
Low or high (≥1 yr)	16	616	1.36	0.61–3.02
High (>1 yr)	9	458	1.08	0.44–2.69

[a]Cumulative exposure estimated up to the year of diagnosis.
[b]All estimates are derived from separate models using the never exposed as the referent category and with the exception of gender-specific conditions, adjusted for age and gender.
[c]The confidence intervals presented are Wald 95% confidence limits.
[d]Self-reported cancer.
[e]Validated cancer.

Results

Of the 2083 original members of the cohort, 188 were determined to be deceased at the time the questionnaire was sent and 1400 completed and returned the questionnaire. The remaining 495 did not respond because they either declined to participate or were not reachable. Overall, 73.9% of those eligible responded. The response rates for eligible cohort members by exposure category were nonexposed, 75.8% (562 of 741); only low exposure or high exposure for less than 1 year, 81.4% (358 of 440); and high exposure for 1 year or more, 67.2% (480 of 714). The response rate for women was slightly higher than that for men and the respondents were older and less likely to have a history of working in PFOS-exposed areas of the plant (Table 1).

Melanoma ($n = 39$), prostate cancer ($n = 29$), and colon cancer ($n = 22$) were the most frequently reported malignancies on the questionnaire (Table 2). A majority of the prostate cancers ($n = 22$) and just over half of the colon cancers ($n = 12$) were confirmed with medical records, including one that was originally reported on the questionnaire as "not-sure" if it was cancer. One colon cancer was confirmed as a secondary tumor and one was clarified as not cancer by the participant on follow-up. One instance of prostate cancer was determined not to be cancer by the physician. The colon and prostate cancers not validated were either because of not obtaining a signed medical release form from the participant (colon $n = 10$, prostate $n = 6$), or because the physician of record was not able to provide the records (colon $n = 1$, prostate $n = 1$). Medical records were obtained for 22 of the reported melanomas; however, fewer than half of these were confirmed as melanoma ($n = 8$). Twelve of the reported melanomas were confirmed as nonmelanoma skin cancer (five basal cell carcinoma, six squamous cell carci-

TABLE 4
Risk Estimates for Other Health Conditions Associated With PFOS Exposure

	Cumulative PFOS Exposure[a]			
	Yes (*N*)	No (*N*)	OR[b]	95% CI[c]
Cystitis				
Never	113	468	1	
Ever low or high	156	663	0.95	0.61–1.48
Low or high (≥1 yr)	113	541	0.99	0.63–1.58
High (>1 yr)	67	399	0.91	0.55–1.51
Bladder calculi				
Never	10	553	1	
Ever low or high	13	824	0.86	0.37–1.99
Low or high (≥1 yr)	11	671	0.90	0.37–2.15
High (>1 yr)	6	473	0.66	0.23–1.84
Colon polyps				
Never	100	469	1	
Ever low or high	141	690	0.98	0.74–1.31
Low or high (≥1 yr)	114	565	0.98	0.72–1.32
High (>1 yr)	76	401	0.87	0.63–1.22
Cholelithiasis				
Never	45	521	1	
Ever low or high	74	760	1.06	0.71–1.59
Low or high (≥1 yr)	57	619	1.02	0.66–1.56
High (>1 yr)	36	439	0.91	0.57–1.46
Cholecystitis				
Never	26	538	1	
Ever low or high	48	788	1.19	0.71–1.98
Low or high (≥1 yr)	39	642	1.17	0.69–2.01
High (>1 yr)	27	452	1.15	0.65–2.06
Nephrolithiasis				
Never	110	470	1	
Ever low or high	132	688	0.97	0.69–1.37
Low or high (≥1 yr)	105	560	0.96	0.67–1.39
High (>1 yr)	79	387	0.91	0.61–1.35
Liver disease, including cirrhosis and hepatitis				
Never	28	547	1	
Ever low or high	26	799	1.08	0.54–2.17
Low or high (≥1 yr)	21	652	1.13	0.55–2.32
High (>1 yr)	17	455	1.21	0.56–2.60
Gastric ulcer				
Never	124	443	1	
Ever low or high	176	657	1.03	0.76–1.39
Low or high (≥1 yr)	143	530	1.07	0.78–1.47
High (>1 yr)	110	364	1.09	0.78–1.54
Benign prostatic hyperplasia				
Never	88	398	1	
Ever low or high	123	527	1.00	0.73–1.37
Low or high (≥1 yr)	102	425	1.06	0.76–1.47
High (>1 yr)	77	323	1.00	0.70–1.43
Prostatitis				
Never	73	415	1	
Ever low or high	82	566	0.84	0.57–1.26
Low or high (≥1 yr)	64	464	0.83	0.54–1.27
High (>1 yr)	48	352	0.80	0.50–1.27

[a]Cumulative exposure estimated up to the year of diagnosis.
[b]All estimates are derived from separate models using the never exposed as the referent category and, with the exception of gender-specific conditions, adjusted for age and gender.
[c]The confidence intervals presented are Wald 95% confidence limits.

TABLE 5
Summary of Singleton Pregnancies Reported by Women Ever Employed at Decatur for One or More Years by Exposure Classification Category

		Cumulative PFOS Exposure Till Pregnancy											
		No exposure		Ever Low		Ever High		Ever Low or High		Low or High >1 yr		High >1 yr	
	Total	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Births													
Live birth	421	312	96.9	83	95.4	38	90.5	109	93.2	99	94.3	32	91.4
Still birth	14	8	2.5	4	34.6	2	4.8	6	5.1	4	3.8	1	2.9
Missing	4	2	0.6	0		2	4.8	2	1.7	2	1.9	2	5.7
Total	439	322		87		42		117		105		35	
Birth weight (kg)[a]													
Median	3.39	3.35		3.40		3.49		3.44		3.46		3.50	
Min.	1.13	1.13		1.81		2.55		1.81		1.81		2.55	
Max.	5.44	5.44		4.31		4.39		4.39		4.39		4.39	
p value[b]		Ref		0.88		0.22		0.45		0.44		0.15	

[a]Analysis of birth weight on 439 singleton live births with a birth weight reported.
[b]*p* value from Wilcoxon two sample test comparing each exposure category to the no-exposure category.

noma, and one undetermined), and two were not cancerous lesions. The risk of colon cancer, melanoma, and prostate cancer was not associated with any of the PFOS-exposure categories for analyses that included all self-reported or only validated cancers (Table 3). The risk estimates for the four breast cancers were not computed because the numbers in the exposure strata were too small to estimate risk. One breast cancer case worked in a low-exposure job for 8 years and two other cases worked in high-exposure jobs for less than 1 year.

Cystitis, prostatic hypertrophy and prostatitis, colon polyps, cholelithiasis, and gastric ulcers were frequently reported by the respondents (Table 2). Nevertheless, there was no association between any of these conditions and having worked in a job with either low or high exposure to PFOS (Table 4).

The 263 women who completed the questionnaire reported a total of 458 pregnancies. There were 439 singleton pregnancies that resulted in either a live birth ($n = 421$) or still birth ($n = 14$), whereas four reported pregnancies had no outcome provided by the participant (Table 5). The overall median birth weight was 3.39 kg and was lowest in the never-exposed pregnancies. The frequency of still births was low, and there was no appreciable difference between exposure categories. Birth weight of the singleton births, adjusted for maternal age at birth, gravidity, and smoking status, did not vary between exposure groups (Table 6). Similar analyses were conducted, estimating exposure up to 1 year before pregnancy outcome. As with the previously reported results, there were no appreciable differences in birth weight when comparing the exposed groups to the never exposed.

TABLE 6
Regression Coefficients for Birth Weight in Kilograms of Singleton Live Births by Exposure Category Compared With Never-Exposed Pregnancies

Cumulative PFOS Exposure Group	Estimate[a]	95% CI
Ever low	−0.08	−0.25 to 0.09
Ever high	0.07	−0.14 to 0.28
High exposure for >1 yr	0.11	−0.11 to 0.33
Low or High for >1 yr	−0.03	−0.19 to 0.13
Ever low or high	−0.05	−0.20 to 0.11

[a]Estimates were adjusted for mother's age, gravidity, and smoking status (yes/no). Each coefficient was derived from a separate model.

Smoking was found to be associated with low birth weight. The effect of smoking on birth weight in these data was examined to evaluate the internal validity of the birth weight data. The reported birth weight for women who smoked during pregnancy compared with that for those who did not smoke during pregnancy, adjusting for maternal age at birth and gravidity, was significant and therefore consistent with scientific knowledge (estimate = −0.24 kg; 95% CI = −0.12 to −0.37).

Models for all conditions were reexamined using the cumulative exposure metric. No significant associations were found between the cumulative estimates of exposure to PFOS and any of the health outcomes.

Discussion

This study evaluated self-reported health outcomes in relation to occupational exposures to PFOS at a POSF-based fluorochemical manufacturing facility in Decatur, Alabama.

The study originated to investigate an excess of bladder cancer mortality in this occupational cohort, but questions pertaining to these additional outcomes were added to allow broader exploration of potential health outcomes related to working in a POSF manufacturing facility. The list of potential outcomes was based on suggestive associations seen in the mortality study and the episodes of care study,[24,25] or based on toxicological studies of this family of chemistries.[1,13,14,29,30] Ultimately, none of the conditions or birth weight of live born children were related to the mother having worked in a job in which exposure to PFOS was likely.

The participation rate of 73% in this study was in line with prevailing response rates,[31] but to the extent participation was associated with the exposures or outcomes, there is a possible bias. Systematically collected medical records for this population were not available; thus self-administered questionnaires were used to ascertain health outcomes. Given that self-administered questionnaires were used to assess medical conditions, we limited reporting to the first occurrence of the condition. It is conceivable that effects of PFOS, and other fluorochemical exposures, can manifest as recurrent problems rather than a single occurrence of relatively common events. Future studies should consider investigating this hypothesis.

Self-reporting of cancers is considered reasonably valid with a high positive predictive value in other studies.[32] The self-report of colon, breast, and prostate cancers in the Decatur cohort also appeared to be reasonably valid for those participants who agreed to allow access to their medical records.[27,28] By contrast, the reporting of melanoma was problematic, with more nonmelanoma skin cancers than actual cases of melanoma being identified through validation following a self-report of a melanoma. Nevertheless, in this study the results showed no association with occupational exposures when all reported or only validated cancers were included in the analysis. Medical validation of other self-reported conditions was not pursued; however, there did not appear to be any association between these conditions and PFOS exposure.

The potential for PFOS exposure to affect the health of developing fetuses was of particular concern given that studies of laboratory animals have demonstrated reproductive and developmental effects of PFOS. In animal studies, maternal exposure to PFOS before and during pregnancy resulted in increased fetal and perinatal mortality, lower fetal and postnatal weight gain, and some structural defects.[16,17,19,33] These effects were observed at dosage levels that also resulted in maternal weight loss during pregnancy; however, evidence suggests causation from direct toxicity to the pup, rather than maternal morbidity, as PFOS is readily transferred from the dam to the fetus in utero and to the newborn through lactation.[17,18] Exposure to human fetuses and infants could occur following occupational exposure to the mother through the same routes. The potential effects, however, would likely be subtle given the doses from occupational exposure are well below the no observable adverse effects level (NOAEL) in laboratory animals; thus, the finding of no association with birth weight is not surprising. Birth weight is considered a marker of overall fetal health and development, and maternal report of birth weight, even years after the pregnancy, is known to be quite valid.[34,35] This analysis assumed that all other determinants of birth weight, nutrition, maternal health, and maternal behavior, eg, physical activity and alcohol consumption, were constant among exposure groups. Whether these covariates differed across exposure categories is unknown; thus, it is difficult to speculate about residual confounding.

This study suggests that occupational exposure to POFS-based fluorochemicals, specifically PFOS, in adult working populations is not associated with the health endpoints examined here. These findings are encouraging in that the exposures experienced by the employees in this facility are substantially higher than exposures in the general population. Although the results in this study found no association between birth weight and PFOS exposure, it is not possible to rule out all adverse effects, including potential negative outcomes to children.

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