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**Self-Reported Medical Conditions in Perfluorooctanesulfonyl
Fluoride Manufacturing Workers**

Final Report

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Abstract

Objective: To determine whether several self-reported cancers and other health conditions in employees of a perfluorooctanesulfonyl fluoride (POSF) production facility are related to employment in a perfluorooctanesulfonate (PFOS) exposed job.

Methods: Current and former employees of the 3M facility in Decatur, Alabama who were included in a cohort mortality study were contacted and asked to complete a self-administered questionnaire as part of a health study following-up a potential excess occurrence of bladder cancer. In addition to bladder cancer, the questionnaire asked about several other cancers and health conditions that were potentially related to exposure to POSF based fluorochemicals chemicals. The female members of the cohort were also asked to complete a brief pregnancy history to determine whether these exposures prior to pregnancy were related to birth weight and still birth in their offspring. Non-respondents were contacted by telephone to ensure receipt of the study material and offered the chance to complete the questionnaire by telephone. Validation of reported melanoma and breast, prostate, and colon cancers was sought through medical records for those cases consenting to release of medical records. Death certificates were obtained for all cohort members identified as deceased and coded for underlying cause of death. A simple job exposure matrix was used to assign employment in non-exposed, low exposed and high exposed jobs. Exposure was ascertained up to the year of the diagnosis of the condition. Because PFOS is eliminated from the body slowly, all exposure prior to each reported pregnancy was included in the analysis of birth weight.

Results: The questionnaires were returned by 1,400 of the 1895 cohort members presumed alive during the study period, of which 1,137 were men and 263 were women. Melanoma (N=42), prostate cancer (N=29), and colon cancer (N=25) were the most frequently reported malignancies on the questionnaire. While prostate and colon cancer were reported with good validity, a majority of the reported melanomas for which medical records could be obtained were ultimately not melanoma (14 of 22). The overall analysis showed no association between working in a PFOS exposed job and the risk of any of the surveyed conditions (breast, colon, liver, prostate and thyroid cancer, melanoma, gastric ulcer, cystitis, urinary calculi (bladder and kidney), colon polyps, cholecystitis and cholelithiasis, liver disease, benign prostate hyperplasia

and prostatitis). Still births were too rare to evaluate. No association was observed between reported birth weight and employment in a PFOS exposed job prior to the pregnancy.

Conclusion: This study found no association between working in a PFOS exposed job and several cancers, common health conditions, and birth weight.

Background

A manufacturing facility in Decatur Alabama was one of two major 3M 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.(3M Company 2000) POSF based chemicals can degrade or be metabolized to perfluorooctanesulfonate (PFOS, $C_8F_{17}SO_3^-$), which is also used as a primary component in a limited number of specialty chemical applications.

The presence of PFOS in non-occupationally exposed populations and wildlife, particularly marine mammals and piscivorous birds, has raised concerns about the environmental and health effects of PFOS. PFOS is now recognized as a pervasive compound that persists in the environment and can accumulate in wildlife.(3M Company 2000; Giesy and Kannan 2001; Hansen et al. 2001) Moreover, PFOS has been quantified at serum concentrations of 30 to 40 parts per billion (ppb, ng/ml) in the general population.(Olsen et al. 2004; Olsen et al. 2004; Olsen et al. 2003; Olsen et al. 2005) These facts prompted the phase-out of the production of POSF-based chemicals by the major producer (3M Company).

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.(Seacat et al. 2003; Seacat et al. 2002) PFOS was not found to be a developmental toxicant in rats or rabbits.(Case et al. 2001) Higher maternal doses of PFOS increased neonatal mortality, absorptions, resorptions, and reduced weight gain in rat pups.(Lau et al. 2003; Luebker et al. 2005; Luebker et al. 2005; Thibodeaux et al. 2003) There were no effects on post-natal neurological development or on fertility and estrous cycling in offspring in multigeneration studies. Multiple genotoxicity assays indicate PFOS does not present a hazard from interaction with genetic material.(3M Company 2000) The mechanism of toxicity, though not fully understood, may be due to an effect on fatty acid transport and metabolism, membrane function, peroxisome proliferation, and/or mitochondrial bioenergetics.(Luebker et al. 2002; Starkov et al. 2001; Wallace et al. 2001)

Potential human health effects of PFOS exposure have been studied in occupationally exposed populations. PFOS has not been shown to affect clinical blood and urine chemistry analyses.(Olsen et al. 2003) A study of health insurance claims filed by workers at the Decatur site 1993-1998 evaluated the relative frequency of episodes of care for specific conditions between employees of the chemical plant (fluorochemical exposed) and the film plant (fluorochemical nonexposed).(Olsen et al. 2004) Workers employed in the PFOS production area of the plant had more frequent claims for biliary tract disorders and cystitis recurrence, which were included in the list of a priori conditions from the 424 categories of conditions identified. Claims for benign colon polyps, malignant colorectal tumors and malignant melanoma were also more frequent in the exposed population. A cohort mortality study of current and former employees of the 3M Decatur facility was conducted to evaluate the health of workers exposed to POSF based fluorochemicals.(Alexander et al. 2003) The cohort included 2083 workers who were employed for a minimum of 1 year at the Decatur facility, and the mortality experience was ascertained through December, 31, 1998. The main finding from the study was an excess of death from bladder cancer, though based only on three cases. In response to this finding a morbidity survey was conducted to ascertain incident, non-fatal bladder cancer cases. The analysis of bladder cancer occurrence based on the morbidity survey did not show evidence of a high risk of bladder cancer in relation to PFOS exposure.(Alexander 2004)

In the process of conducting the follow-up for bladder cancer, several additional health issues were addressed on the questionnaire. This study reports on these health issues in reference to occupational PFOS exposure at the 3M facility in Decatur, Alabama.

Methods

Study Population

The study site was the 3M facility in Decatur, Alabama. The plant is divided in two major sections, which are approximately 300 yards apart. The chemical plant produced specialty chemicals, including the POSF line of chemicals. The other section is the film plant, where a variety of films are produced, but little or no occupational fluorochemical exposures occur. The population of interest included all current, retired, and former Decatur employees who were eligible for the original cohort mortality study. All current employees who were not part of the original cohort, those hired after January 1, 1998, were also included in the case finding exercise, but not a primary focus of the analysis. The study required direct contact with the participants. A roster of all known addresses and telephone numbers were obtained through 3M 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 TRW/Experian, Lortan 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. Prior to recruitment a series of meetings were held with current employees and retirees to inform them of the upcoming study and allow them to ask questions about the study. Recruitment of all presumed living cohort members was initiated with a letter and brochure outlining the reasons for the study, the scope of the study, what was required of participants, and assurances of confidentiality. The study questionnaire, with cover letter and postage paid return envelope, followed the recruitment letter by approximately one week. A reminder post card was sent to all non-respondents two weeks after the questionnaire was mailed, and a second questionnaire was mailed two weeks after that. If mailings were returned with undeliverable addresses, the address information was 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 one 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 conducted in the Decatur plant workforce. The questionnaire ascertained diagnoses of cancers including melanoma, liver, prostate (men only), breast (women only), colon or rectal cancer, non-cancerous 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 or colon polyps or cancer. The questionnaire also recorded history of smoking.

All questionnaires were reviewed upon 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 were 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 if the participant agreed. Copies of the consent and medical release forms were 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.(Alexander et al. 2003) 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 comprehensive assessment, which is detailed elsewhere.(Olsen et al. 2003) In that assessment, serum PFOS concentrations were measured in 186 employees (n = 126 chemical plant; 60 = film plant) from a randomly selected sample of 232 employees. The geometric mean serum PFOS level (95% confidence interval) for chemical plant employees was 0.94 ppm (95% CI=0.79-1.13) and for film plant employees it was 0.14 ppm (95% CI=0.11-0.16). The exposure to film plant employees is thought to be influenced by environmental exposure from proximity to the chemical plant. Chemical plant jobs were classified into eight categories: cell operators, chemical operators, maintenance workers (primarily mechanics and electricians), mill operators, waste treatment plant operators, engineers/laboratory workers, supervisors/managers and administrative assistants. The highest geometric mean level of serum PFOS was observed in cell operators (2.0 ppm) followed by the waste operators (1.5), chemical operators (1.5 ppm), and maintenance workers (1.3 ppm). Supervisors/managers (0.9 ppm), mill operators (0.6 ppm), engineer/lab workers (0.4 ppm) and administrative assistants (0.4 ppm) had lower geometric mean serum PFOS levels.

Because production processes have remained relatively 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, 1961, until 1997 when the work histories were collected for the mortality study. With the knowledge of the major job-specific serum PFOS levels, a company industrial hygienist and epidemiologist assigned each unique job and department combination in the work history records to one of the following three major exposure categories:

- No direct workplace exposure to POSF-based fluorochemicals (encompasses film plant jobs).

- Low potential workplace exposure to POSF-based fluorochemicals (includes such jobs as engineers, quality control technicians, environmental, health and safety workers, administrative assistants and managers).
- High potential workplace exposure to POSF-based fluorochemicals (includes cell operators, chemical operators, maintenance workers, mill operators, waste operators and crew supervisors)

Hereafter these three categories will be referred to as the non-exposed, 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 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 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 one year
- Employed in a high exposure job for at least one year.

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 that first occurred 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 death certificate.

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 certificate. 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 being mistaken for other types of skin cancer.(Bergmann et al. 1998; Paganini-Hill and Chao 1993) 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 due to the rarity of the event. Birth weight, reported as pounds and ounces, was converted to kilograms. Birth weight for each exposure category was compared to the no exposure group using a Wilcoxon Two-Sample test. Multiple linear regression models were fit to estimate change 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 2003)

Results

Of the 2,083 original members of the cohort, 188 were determined to be deceased at the time the questionnaire was sent and 1,400 completed and returned the questionnaire. The remaining 495 did not respond either because they declined to participate or were not reachable. Overall 73.9 percent of those eligible responded. The response rates for eligible cohort members by exposure category were; non-exposed 75.8% (562 of 741), only low exposure or high exposure for less than one year 81.4% (358 of 440), and high exposure for one year or more 67.2% (480 of 714). The response rate for women was slightly higher than 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=42), prostate cancer (N=29), and colon cancer (N=25) 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 reported prostate cancer was determined not to be cancer by the physician. The remaining non-validated colon and prostate cancers were due to not obtaining a signed medical release form from the participant (colon N=10, prostate N=6) or the physician of record not being 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 non-melanoma skin cancer (5 basal cell carcinoma, 6 squamous cell carcinoma, and one undetermined), and two were not cancer. The risk of colon cancer, melanoma and prostate cancer was not associated with any of the PFOS exposure categories; this held for analysis of validated (Table 3) and all self-reported cancers including those not validated (Table 4). The odds ratio for prostate cancer was greater than one in the ever employed in a low exposure job, but the confidence intervals were very wide (OR=2.0, 95% CI=0.75-5.36). 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 one year.

Cystitis, prostatic hypertrophy and prostatitis , colon polyps, cholelithiasis, and gastric ulcers were frequently reported by the respondents (Table 5). However, there was no association between any of these conditions and having worked in a job with either low or high exposure to PFOS (Table 6).

The 263 women who completed the questionnaire reported a total of 458 pregnancies. There were 427 singleton pregnancies that resulted in either a live birth (N=409) or still birth (N=14), while 4 reported pregnancies had no outcome provided by the participant (Table 7). The overall median birth weight was 3.4 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 8).

Discussion

This study evaluated self-reported health outcomes in relation to occupational exposures to PFOS at the 3M 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 ensure full exploration of potential health outcomes related to POSF-related exposures. The list of potential outcomes was based on suggestive associations seen in the mortality study and the episodes of care study, (Alexander et al. 2003; Olsen et al. 2004) or based on toxicological studies of this family of chemistries. (3M Company 2000; Seacat and Butenhoff 2001; Seacat et al. 2002; Seacat et al. 2001; Seacat et al. 2003; Seacat et al. 2002) Ultimately, none of the conditions or birth weight of live born children were related to having worked in a job where exposure to PFOS was likely.

The logistics and cost of systematically obtaining information from medical records for a population such as this are prohibitive. The use of self-administered questionnaires to ascertain medical outcomes is feasible and can characterize the health of a population. The validity of the information collected, however, is often difficult to characterize. Self-reporting of cancers is considered reasonably valid with a high positive predictive value in other studies. (Sigurdson et al. 2003) The self-report of colon, breast, and prostate cancer in the Decatur cohort also appeared to be reasonably valid for those people who agreed to allow access to their medical records. (Bergmann et al. 1998; Paganini-Hill and Chao 1993) By contrast, the reporting of melanoma was problematic with more non-melanoma 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.

The validity of self-report of other conditions was not pursued; however there did not appear to be any association between PFOS exposure and these other conditions. A limitation of using a self-administered questionnaire for these types of conditions is the difficulty of assessing recurrent conditions. This study only ascertained the first occurrence of the condition. It is conceivable that effects of PFOS and other fluorochemical exposure can manifest as recurrent

problems, rather than a single occurrence of relatively common events. Nevertheless, the lack of any association between these conditions and the estimated PFOS exposure suggests otherwise.

The potential for PFOS exposure to affect the health of developing fetuses was evaluated by comparing birth weight of singleton births to exposure through the month and year of pregnancy. Studies of laboratory animals have demonstrated reproductive and developmental effects of PFOS. Maternal exposure to PFOS prior to and during pregnancy resulted in increased fetal and perinatal mortality, substantially lower fetal and post natal weight gain and some structural defects.(Lau et al. 2004; Lau et al. 2003; Luebker et al. 2005; Thibodeaux et al. 2003) 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/newborn in utero and through lactation.(Luebker et al. 2005; Luebker et al. 2005) 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 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.(Gayle et al. 1988; Tilley et al. 1985) This analysis assumed all other determinants of birth weight, nutrition, maternal health, and maternal behavior, e.g. physical activity and alcohol consumption, were constant between exposure groups. Whether these covariates differed across exposure categories is unknown, thus it is difficult to speculate about residual confounding.

Overall, this study offers some assurances that PFOS exposure in adult working populations is not associated with the health endpoints detailed here. While it is not possible to entirely rule out all adverse effects of PFOS exposure, the results of these analyses do not support any associations.

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Table 1. Gender, age, and exposure characteristics of participants and non-participants in the Decatur morbidity study

		Questionnaire Respondent				Deceased		Total
		Yes		No		N	%	
		N	%	N	%			
Total		1400		495		188		2083
Gender	M	1137	81.2	416	84.0	177	94.1	1730
	F	263	18.8	79	16.0	11	5.9	353
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*								
Non Exposed**		562	40.1	179	36.2	68	36.2	809
Low	Ever	413	29.5	121	24.4	67	35.6	601
	≥1 year	320	22.9	78	15.8	52	27.7	450
High	Ever	624	44.6	276	55.8	82	43.6	982
	≥1 year	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 year	689	49.2	273	55.2	108	57.4	1070

*Categories overlap

** Non exposed includes workers from the film plant who never worked in the chemical plant.

Table 2. Frequencies self-reported cancers and validated cases of cancer from the survey

	Condition	Yes		No		Total
		N	%	N	%	N
Self-Reported Cancer	Breast	4	1.5	259	98.5	263
	Colon	25	1.6	1377	98.4	1400
	Liver	0	0	1400	100	1400
	Melanoma	42	2.8	1360	97.3	1400
	Prostate	29	2.6	1107	97.4	1136
	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

Table 3. Risk estimates for cancer associated with PFOS exposure for validated cancers only (including deaths).

	Cumulative PFOS Exposure ¹	Yes N	No N	OR ²	95% CI ³
Colon Cancer	Never	5	626	1	
	Ever Low	2	472	0.50	0.10 , 2.64
	Ever High	6	698	0.95	0.29 , 3.16
	Ever Low or High	8	949	0.96	0.31 , 2.98
	Low or High (≥ 1 yr)	7	782	1.04	0.33 , 3.34
	High (> 1 yr)	6	542	1.22	0.37 , 4.05
Melanoma	Never	4	627	1	
	Ever Low	3	472	0.93	0.20 , 4.28
	Ever High	6	698	1.24	0.34 , 4.43
	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	Never	7	539	1	
	Ever Low	10	354	2.00	0.75 , 5.36
	Ever High	10	582	1.36	0.51 , 3.59
	Ever Low or High	15	752	1.50	0.61 , 3.72
	Low or High (≥ 1 yr)	13	619	1.56	0.62 , 3.96
	High (> 1 yr)	6	461	1.02	0.34 , 3.07

1. Cumulative exposure estimated up to the year of diagnosis
2. 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.
3. The confidence intervals presented are Wald 95% confidence limits.

Table 4. Risk estimates for cancer associated with PFOS exposure for all self reported cancers and cancer deaths.

	Cumulative PFOS Exposure ¹	Yes N	No N	OR ²	95% CI ³
Colon Cancer	Never	8	623	1	
	Ever Low	5	469	0.81	0.26 , 2.52
	Ever High	12	692	1.30	0.53 , 3.22
	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	Never	19	613	1	
	Ever Low	11	463	0.81	0.38 , 1.73
	Ever High	20	683	0.89	0.47 , 1.69
	Ever Low or High	23	933	0.79	0.42 , 1.46
	Low or High (≥ 1 yr)	19	770	0.78	0.41 , 1.51
	High (> 1 yr)	15	533	0.83	0.41 , 1.66
Prostate Cancer	Never	10	536	1	
	Ever Low	11	353	1.55	0.64 , 3.71
	Ever High	13	579	1.24	0.54 , 2.85
	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

1. Cumulative exposure estimated up to the year of diagnosis
2. 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.
3. The confidence intervals presented are Wald 95% confidence limits

Table 5. Frequencies of self-reported non-cancer health conditions in questionnaire respondents of the Decatur cohort.

Condition	Yes	%	No	%	Total
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	1136
Prostatitis	155	13.6	981	86.4	1136

Table 6. Risk estimates for other health conditions associated with PFOS exposure.

	Cumulative PFOS PFOS Exposure	Yes N	No N	OR ¹	95% CI ²
Cystitis	Never	113	468	1	
	Ever Low	80	317	1.14	0.67 , 1.94
	Ever High	100	514	0.53	0.53 , 1.37
	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	6	405	0.89	0.31, 2.52
	Ever High	8	615	0.68	0.27 , 1.76
	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	57	349	0.84	0.58 , 1.21
	Ever High	103	516	0.93	0.69 , 1.27
	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	34	375	1.01	0.62 , 1.66
	Ever High	52	569	0.99	0.64 , 1.53
	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	23	387	1.24	0.67 , 2.30
	Ever High	35	588	1.17	0.68 , 2.01
	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

(continued)

Table 6 (continued)

	Cumulative PFOS PFOS Exposure	Yes N	No N	OR ¹	95% CI ²
Nephrolithiasis	Never	110	470	1	
	Low	51	342	0.98	0.63 , 1.53
	Ever High	103	508	0.94	0.64 , 1.36
	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	8	393	0.90	0.35 , 2.31
	Ever High	20	594	1.06	0.51 , 2.23
	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	
	Low	76	331	1.04	0.71 , 1.51
	Ever High	138	482	1.05	0.76 , 1.45
	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	60	237	1.18	0.81 , 1.73
	Ever High	96	417	0.96	0.68 , 1.34
	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	40	259	1.05	0.64 , 1.73
	Ever High	68	445	0.87	0.57 , 1.33
	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

1. Cumulative exposure estimated up to the year of diagnosis
2. 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.
3. The confidence intervals presented are Wald 95% confidence limits.

Table 7. Summary of singleton pregnancies reported by women ever employed at Decatur for one or more years by exposure classification category.

	Total	Cumulative PFOS Exposure Till Pregnancy											
		No exposure		Ever Low		Ever High		Ever Low or High		Low or High > 1 yr		High > 1 year	
Births		N	%	N	%	N	%	N	%	N	%	N	%
Live Birth	409	301	96.5	82	96.5	38	90.5	108	93.9	98	95.2	32	91.4
Still Birth	14	9	2.9	3	3.5	2	4.8	5	4.4	3	2.9	1	2.9
Missing	4	2	0.6	0		2	4.8	2	1.7	2	1.9	2	5.7
Total	427	312		85		42		115		103		35	
Birth weight (Kg) ¹													
Median	3.40	3.35		3.42		3.48		3.46		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 ²		Ref		0.82		0.24		0.42		0.41		0.16	

1: Analysis of birth weight on 399 singleton live births with a birth weight reported.

2: p-value from Wilcoxon two sample test comparing each exposure category to the no exposure category.

Table 8. Regression coefficients for birth weight in kilograms of singleton live births by exposure category compared to never-exposed pregnancies.

Cumulative PFOS exposure group	Estimate ¹	95% CI
Ever low	-0.08	-0.23 , 0.07
Ever high	0.03	-0.16 , 0.21
High exposure for >1 yr	0.07	-0.13 , 0.27
Low or High for > 1 year	-0.03	-0.17 , 0.10
Ever Low or High	-0.05	-0.18 , 0.08

1: Estimates were adjusted for mother's age, gravidity and smoking status. Each coefficient derived from separate model.