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Birth defects associated with paternal firefighting in the National Birth Defects Prevention Study

Miriam R. Siegel DrPH[1] | Carissa M. Rocheleau PhD[1] | Brittany S. Hollerbach PhD[2] | Amel Omari PhD[1] | Sara A. Jahnke PhD[2] | Lynn M. Almli PhD[3] | Andrew F. Olshan PhD[4] | National Birth Defects Prevention Study

[1]Division of Field Studies and Engineering, National Institute for Occupational Safety and Health, Cincinnati, Ohio, USA

[2]Center for Fire, Rescue, and EMS Health Research, NDRI-USA, Inc, Leawood, Kansas, USA

[3]Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, CDC, Atlanta, Georgia, USA

[4]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Correspondence
Miriam R. Siegel, DrPH, Division of Field Studies and Engineering, National Institute for Occupational Safety and Health, 1090 Tusculum Ave, Mailstop R-15, Cincinnati, OH 45226, USA.
Email: wrm9@cdc.gov

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Abstract

Background: Few studies have evaluated birth defects among children of firefighters. We investigated associations between birth defects and paternal work as a firefighter compared to work in non-firefighting and police officer occupations.

Methods: We analyzed 1997–2011 data from the multi-site case-control National Birth Defects Prevention Study. Cases included fetuses or infants with major structural birth defects and controls included a random sample of live-born infants without major birth defects. Mothers of infants self-reported information about parents' occupations held during pregnancy. We investigated associations between paternal firefighting and birth defect groups using logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Referent groups included families reporting fathers working non-firefighting and police officer jobs.

Results: Occupational groups included 227 firefighters, 36,285 non-firefighters, and 433 police officers. Twenty-nine birth defects were analyzed. In adjusted analyses, fathers of children with total anomalous pulmonary venous return (TAPVR; OR = 3.1; 95% CI = 1.1–8.7), cleft palate (OR = 1.8; 95% CI = 1.0–3.3), cleft lip (OR = 2.2; 95% CI = 1.2–4.2), and transverse limb deficiency (OR = 2.2; 95% CI = 1.1–4.7) were more likely than fathers of controls to be firefighters, versus non-firefighters. In police-referent analyses, fathers of children with cleft palate were 2.4 times more likely to be firefighters than fathers of controls (95% CI = 1.1–5.4).

Conclusions: Paternal firefighting may be associated with an elevated risk of birth defects in offspring. Additional studies are warranted to replicate these findings. Further research may contribute to a greater understanding of the reproductive health of firefighters and their families for guiding workplace practices.

KEYWORDS

birth defects, firefighting, occupational health, paternal exposure, reproductive health

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1 | INTRODUCTION

There are over 1.1 million firefighters that protect our communities and environment in the United States today.[1] The hazardous conditions and chemicals that firefighters encounter on the job, as well as their acute and chronic safety and health effects, are well-recognized. However, studies of reproductive health in firefighters are limited, although the topic is of great concern to the fire service.[2] Research on male firefighters has supported associations with infertility,[3] reduced semen quality,[4] and reproductive cancers, including of the testes and prostate.[5–9] Some studies have focused on pregnancy and birth outcomes among female firefighters, such as miscarriage, preterm delivery, abortive outcomes, and delivery complications,[10–12] but none have evaluated birth defects—likely given the difficulties in studying a rare outcome among a small population (i.e., women comprise roughly 8% of all US firefighters[1]). Exposures among male firefighters could impact birth outcomes in children through direct (e.g., toxicity to the male reproductive system) and indirect routes (e.g., take-home exposure affecting pregnant mothers).[13,14] Nonchemical exposures among firefighters, such as heat and shiftwork, might also directly affect reproductive health.[14,15]

Only a few studies have evaluated birth defects among children of firefighters, with inconsistent findings. Most recently, an analysis of National Birth Defects Prevention Study data from 1997 to 2004 found no associations between birth defects and paternal occupation as a firefighter; however, the sample only included 81 firefighters (58 cases) for that time period.[16] A few small, older studies found positive associations between paternal firefighting and children born with birth defects, such as congenital heart defects, oral clefts, genital organ defects, urinary system defects, musculoskeletal defects, and Down syndrome, with varying magnitude of association and precision when compared to non-firefighters or police officers.[17–21] Other studies found no evidence of positive associations for birth defects among children of small numbers of firefighters.[22,23]

Recently the epidemiologic literature on the association between birth defects and maternal or paternal exposures that might be common among firefighters has grown. Relevant polycyclic aromatic hydrocarbons (PAHs), engine exhaust, organic solvents, polybrominated diphenyl ethers (PBDEs), polychlorinated organic substances, heavy metals, phthalates, and other endocrine disrupting chemicals.[24–36]

Given the age, inconsistencies, and sample size limitations of past studies, as well as a recent growth in studies that support associations between birth defects and select exposures common among firefighters, further research on birth defects among children of male firefighters is needed. Our objective was to investigate associations between birth defects and paternal work as a firefighter compared to paternal work in all other occupations and, to control for residual confounding, police officer occupations.

2 | MATERIALS AND METHODS

2.1 | Data collection

We analyzed data from the National Birth Defects Prevention Study (NBDPS), a multi-site, population-based case-control study of major structural, non-chromosomal birth defects. Previous publications have thoroughly described the NBDPS design and methods.[37,38] Briefly, families of infants and fetuses were recruited from birth defects surveillance centers in 10 states (Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah). All centers identified cases among live births, and some also included cases among stillbirths (fetal deaths at ≥20 gestational weeks) and terminations of pregnancy (any gestational age). Clinical geneticists classified all congenital heart and non-heart defect cases as isolated (i.e., no other major birth defects) or characterized by multiple major birth defects (i.e., two or more major defects occurring in different organ systems). Pediatric cardiology experts reviewed clinical records to further classify congenital heart defect cases as simple (one single heart defect or a well-defined constellation of defects recognized as one entity), associated (common, uncomplicated combinations of heart defects), or complex (three or more distinct defects). Study personnel identified control families from hospital delivery logs or vital records in the same study sites as cases and included a random sample of live births without major structural defects. All NBDPS families included deliveries on or after October 1, 1997, and with estimated dates of delivery on or before December 31, 2011. All interviewed study participants provided informed consent and institutional review board approval was obtained from each study site and the Centers for Disease Control and Prevention.

Mothers of cases and controls completed a computer-assisted telephone interview between 6 weeks and 2 years after the estimated date of delivery. The interviews, conducted in both English and Spanish, included, but were not limited to, questions about demographics, behavior, and health during pregnancy, reproductive history, and occupation.

In addition to providing information on their own jobs held during pregnancy, mothers also reported a narrative description of each job held by infants' fathers for at least 1 month in the 3 months before the estimated date of conception through the end of pregnancy. The narrative job description consisted of answers to five questions: where the father worked, what the company made or did, the father's job title, typical job duties, and any equipment or chemicals handled. The survey also collected information on estimated start/stop dates, hours worked per day, and days worked per week. Experienced coders previously assigned the 2007 North American Industry Classification System (NAICS) and 2010 Standard Occupational Classification (SOC) codes to all reported maternal and paternal jobs in NBDPS.

For the current analysis, we included all case and control families who participated in NBDPS and who reported a father working a

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specified job at some point during pregnancy. Only those paternal jobs with specified, valid SOC codes were included in firefighter-status classification and potential analysis (i.e., excluding jobs with a missing SOC code or labeled as homemaker/parent, student, various short-term jobs not otherwise specified, do not know, refused, uncodable, or blank; $n = 5519$).

2.2 | Occupation classification

We determined the firefighter status of fathers using SOC codes assigned according to job narratives reported by mothers. We classified jobs into non-mutually exclusive groups as firefighting, non-firefighting, and police-related. Firefighting-related SOC categories included 332010/332011 (Firefighters), 331020 (First-Line Supervisors of Fire Fighting and Prevention Workers), 332021 (Fire Inspectors and Investigators), and 332022 (Forest Fire Inspectors and Prevention Specialists). We reviewed job narratives for the latter three occupations to identify any jobs for which firefighting-related duties or environments could not be confirmed or determined for consideration in father-level exclusions. Jobs that had been assigned any SOC code other than those considered firefighting-related were classified as non-firefighting jobs. Jobs with listed SOC categories 331012 (First-Line Supervisors of Police and Detectives), 333050 (Police Officers), and 333051 (Police and Sheriff's Patrol Officers) were additionally considered police officer jobs.

All fathers reported to have worked at least one job within a firefighting-related SOC category during the periconceptional period of 3 months before conception through the first month of pregnancy were categorized as firefighters for the current analysis. We categorized all fathers working only non-firefighting jobs during the periconceptional period as non-firefighters. Additionally, we classified fathers as police officers if they reported at least one job within a police-related SOC during the periconceptional period.

Firefighting fathers whose only relevant job was one in which the firefighting-related duties or environments could not be confirmed or determined were excluded from all analyses ($n = 3$). We excluded firefighting fathers working as firefighters only outside of the periconceptional period ($n = 9$) and non-firefighters that held no job during the periconceptional period from analyses ($n = 1532$). Additionally, in analyses comparing firefighters to police officers (i.e., police-referent analyses), police officers that held no police-related job during the periconceptional period were excluded ($n = 19$), as were fathers that worked as both firefighter and police officer ($n < 3$). At the father level, and after exclusions, firefighter-status classifications were mutually exclusive between firefighters and non-firefighters, and firefighters and police officers.

2.3 | Outcome classification

This spectrum analysis examined all congenital heart and non-heart defects classified as isolated or multiple with sufficient sample size.[39,40] Any birth defects with less than three cases in any occupation group were not examined as individual defect groups. We grouped individual defects that did not meet the sample size criteria into larger anatomical groups where possible to include them in analyses. We additionally conducted a sensitivity analysis that restricted to isolated non-heart defect cases and isolated, simple heart defect cases (i.e., one single heart defect or a well-defined constellation of heart defects recognized as one entity). All individual defect groups included the appropriate control group in comparison to the case group (e.g., only male controls for analyzing hypospadias cases).

2.4 | Statistical analysis

We first evaluated an a priori set of family characteristics of fathers that worked as firefighters, non-firefighters, and police officers during the periconceptional period in a descriptive analysis. We calculated frequencies and percentages or means and standard deviations for study site (state) and maternal age at delivery (in years and categorical as <20, 20–34, and ≥35 years), race/ethnicity, body mass index (BMI) pre-pregnancy (underweight, <18.5 kg/m^2; normal weight, 18.5 to <24 kg/m^2; overweight, 25 to <30 kg/m^2; or obese, >30 kg/m^2), smoking during early pregnancy (i.e., 1 month before conception through the third month of pregnancy based on a period in which a fetus is most vulnerable to maternal exposure to teratogens), alcohol use during early pregnancy, and education status by paternal occupation. As done in the previous NBDPS analysis of paternal occupation, we selected maternal demographic and behavioral variables because mother-reported information on related characteristics among fathers was often missing.[16] We also assessed these covariates descriptively by paternal occupation among only control families to summarize the demographic characteristics of the base population analyzed for this study.

We calculated the number of cases for each birth defect group by paternal firefighter status. For each defect group with at least three cases in each occupation group, we investigated associations between paternal firefighting during the periconceptional period and each birth defect using logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Referent groups included (a) families reporting fathers working non-firefighting jobs during the periconceptional period, and (b) families reporting fathers working as police officers during the periconceptional period. The second comparison group reduced unmeasured confounding by paternal characteristics (e.g., age and other demographic characteristics), socioeconomic factors, work conditions, and healthy worker status that are similar between firefighters and police officers, other than some heavy chemical exposures encountered by firefighters. We included covariates in multivariable analyses where there appeared to be potentially confounding differences between firefighters and the referent group based on the distribution of frequencies and percentages in the descriptive analysis. Observations with missing covariate information were excluded from multivariable analyses

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(<1% of any exposure group for all covariates included in multivariable models). All cell sizes less than three were suppressed as a practice of confidentiality and to preserve statistical power. We repeated multivariable analyses for a sensitivity analysis restricting to isolated/simple defect cases to assess whether potential associations were driven by multiple defect cases only (i.e., a more heterogenous case population).

3 | RESULTS

A total of 44,621 paternal jobs worked at some point during pregnancy reported by mothers in NBDPS were included in firefighter-status assignment. Of these, 250 jobs were firefighting occupations and 44,371 as non-firefighting occupations based on SOC codes. Additionally, 473 paternal jobs worked at some point during pregnancy were police officer occupations based on SOC codes. Of the firefighting jobs worked at some point during pregnancy, SOC codes identified 227 (90.8%) as firefighter occupations, 15 (6.0%) as first-line supervisors of firefighting and prevention worker occupations, and 8 (3.2%) as fire inspector and investigator or forest fire inspector and prevention specialist occupations.

After father-level exclusions, including periconceptional period restrictions, 227 paternal firefighters (168 cases, 59 controls) and 36,285 non-firefighters (26,486 cases, 9,799 controls) were included in analyses. Of non-firefighters, 433 fathers were also included as police officers (318 cases, 115 controls) in police-referent analyses.

Table 1 provides a summary of NBDPS family characteristics by paternal occupation. Study site varied for NBDPS families of firefighters compared to non-firefighters. While the mean maternal age was similar across paternal occupation groups, substantially less maternal co-parents to firefighters were under the age of 20 compared to those to paternal non-firefighters (results not shown, cell size <3). Compared to maternal co-parents to non-firefighters, maternal co-parents to firefighters smoked less during early pregnancy (10% vs. 18%) and were more educated (82% had beyond a high school degree vs. 61%). More maternal co-parents to firefighters were non-Hispanic white than those to both non-firefighters and police officers (83%, 62%, and 74%, respectively). Study site, maternal age at delivery, maternal smoking during early pregnancy, and maternal education did not differ substantially between families of firefighters and police officers. Maternal BMI pre-pregnancy and alcohol use during early pregnancy did not vary by paternal occupation. The supplementary material includes a descriptive summary of covariates by paternal occupation among only control families (Supporting Information: Table S.I); note that select covariate categories were collapsed due to some non-reportable cell sizes ($n < 3$).

Table 2 provides the results of the multivariable analyses assessing associations between 29 birth defect groups and paternal firefighting in referent to non-firefighters and police officers. Non-firefighter-referent models adjusted for study site and maternal age (continuous in years), race/ethnicity (dichotomous as non-Hispanic white vs. nonwhite and Hispanic to keep consistent with police-referent models), smoking status, and education. Police-referent models adjusted for maternal race/ethnicity (dichotomous as non-Hispanic white vs. nonwhite and Hispanic to allow police-referent models to converge). Adding maternal smoking status to the adjusted police-referent models did not change results (results not shown).

Fathers of children with total anomalous pulmonary venous return (TAPVR) defect (OR = 3.1; 95% CI = 1.1–8.7), oral cleft (particularly cleft palate [OR = 1.8; 95% CI = 1.0–3.3] and cleft lip [OR = 2.2; 95% CI = 1.2–4.2]), and transverse limb deficiency (OR = 2.2; 95% CI = 1.1–4.7) were 2–3 times more likely than fathers of controls to be firefighters versus non-firefighters. The OR was also elevated for children born with an atrioventricular septal defect (AVSD) but was imprecise (OR = 2.0; 95% CI = 0.7–5.6).

In the police-referent analysis, fathers of children with a cleft palate were 2.4 times more likely to be firefighters than fathers of controls (95% CI = 1.1–5.4), which was slightly higher than found in reference to non-firefighters. Estimates for TAPVR and cleft lip in the police-referent analysis were elevated–and similar to non-firefighter-referent estimates—but were imprecise with wide CIs. For many of the remaining defects, we found no substantial evidence of elevated associations in analyses of either occupational referent group.

Results of the sensitivity analysis restricting to isolated/simple defect cases are shown in Supporting Information: Table S.II. In general, estimates were similar to those in the main analysis of isolated and multiple defect cases. The estimates for TAPVR, cleft palate, cleft lip, and transverse limb deficiency did not change directionality and were either similar, larger, or slightly attenuated. Results for six defects could not be reported due to a lack of sample size and CIs were generally very wide due to a loss in precision.

4 | DISCUSSION

The current analysis evaluated associations between paternal firefighting and individual birth defects among children in comparison to (a) paternal non-firefighters and (b) paternal police officers. The results suggested associations between paternal firefighting and several birth defects, including cleft palate, cleft lip, and TAPVR. We observed an association between firefighting and cleft palate in comparison to both non-firefighters and police officers. Effect estimates for cleft lip and TAPVR, while similarly elevated in comparison to both referent groups, were imprecise in comparison to police officers, likely due to small sample size. Transverse limb deficiency and AVSD had elevated ORs associated with paternal firefighting in comparison to non-firefighters, however, the associations were less precise in comparison to police officers.

Some previous studies of birth defects among children of male firefighters support our findings, however, many of these studies had very small numbers of exposed cases. For example, several studies found results suggestive of an association between firefighting and oral clefts.[18,19,21] A study in British Columbia was the only previous analysis to directly compare firefighters to both non-firefighters and

TABLE 1 Distribution of covariates among families of paternal firefighters, non-firefighters, and police officers, National Birth Defects Prevention Study, 1997–2011

Covariate	Firefighters[a] (n = 227)		Non-firefighters (n = 36,285)		Police[a] (n = 433)	
	n[b,c]	%[b]	n[b,c]	%[b]	n[b,c]	%[b]
Study site						
Arkansas	23	10.1	4604	12.7	51	11.8
California	26	11.5	4075	11.2	38	8.8
Georgia	10	4.4	4086	11.3	26	6.0
Iowa	25	11.0	3702	10.2	43	9.9
Massachusetts	44	19.4	4659	12.8	71	16.4
New Jersey	12	5.3	1960	5.4	36	8.3
New York	21	9.3	2630	7.3	45	10.4
North Carolina	21	9.3	2767	7.6	38	8.8
Texas	18	7.9	3842	10.6	55	12.7
Utah	27	11.9	3960	10.9	30	6.9
Maternal age at delivery						
Years (mean, SD)	29.5	4.6	28.2	6.0	29.8	4.7
Maternal race/ethnicity						
Non-Hispanic White	188	82.8	22,434	61.8	322	74.4
Non-Hispanic Black	6	2.6	3073	8.5	27	6.2
Hispanic	19	8.4	8433	23.2	70	16.2
All other non-Hispanic groups	14	6.2	2341	6.5	14	3.2
Maternal BMI pre-pregnancy						
Underweight	10	4.4	1777	5.1	11	2.6
Normal weight	123	54.4	18,169	52.2	252	58.5
Overweight	58	25.7	8068	23.2	108	25.1
Obese	35	15.5	6814	19.6	60	13.9
Maternal smoking during early pregnancy						
No	204	89.9	29,671	81.8	367	84.8
Yes	23	10.1	6592	18.2	66	15.2
Maternal alcohol use during early pregnancy						
No	131	58.0	22,552	62.4	253	59.0
Yes	95	42.0	13,603	37.6	176	41.0
Maternal education status						
No high school degree or equivalent	7	3.1	5373	14.8	10	2.3
High school degree or equivalent	34	15.0	8641	23.8	85	19.6
Some college	98	43.2	10,183	28.1	146	33.7
College degree or higher	88	38.8	12,047	33.2	192	44.3

Abbreviations: BMI, body mass index; SD, standard deviation.

[a] $n < 3$ fathers classified as firefighter and police officer were excluded from analyses with a police officer referent group.

[b] Estimates shown as n (%) except if indicated otherwise.

[c] Frequencies may not combine to sample totals where there are missing values (<5% missing for all categories).

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police officers and found that cleft lip was elevated among children of firefighters in comparison to non-firefighters (OR 4.2; 95% CI = 0.4–46.1), the estimate was diminished in comparison to police officers (OR = 1.6; 95% CI = 0.2–10.1).[18] The study was unable to analyze cleft palate due to a lack of exposed cases. A study of birth defects in Atlanta, GA also supported associations between firefighting and cleft lip in comparison to non-firefighters (OR = 13.3; 95% CI = 4.0–44.4), but did not present results for cleft palate among children of firefighters due to either an absence of sufficient cases or an absence of a strong association (i.e., OR not greater than 1.5 or less than 0.7).[19]

While no previous studies reported results for the congenital heart defects TAPVR and AVSD among children of firefighters specifically, several studies suggested associations between grouped categories of any heart defect or other heart anomalies.[19,20] The estimate for the grouped category for any heart defect was not elevated in the current analysis. Two studies suggested associations between firefighting and septal heart defects (i.e., ventricular and atrial septal defects),[18,20,21] which results in the current study did not strongly support.

Similar to our non-firefighter-referent analysis, several previous studies have suggested associations between firefighting and limb defects or other musculoskeletal anomalies in comparison to non-firefighters with varying degrees of association.[18–20] Inconsistent with our findings, the study from British Columbia found estimates for limb anomalies to increase in referent to police officers, however, only one case among police officers was included for each limb defect category.[18] On the other hand, the study from Atlanta suggested that police officer work could be associated with upper limb reduction defects.[19]

Some previous studies found results inconsistent with the current study, such as associations between paternal firefighting and defects of the digestive system (i.e., an elevated estimate for pyloric stenosis, while we found none for anorectal atresia/stenosis),[21] hypospadias/genital organs,[19,20] or no defects found at all.[16,22,23] Nonetheless, there are major differences in study design between previous studies and the current analysis, such as sample size, years of observation, geographic location, and methods of occupation or outcome ascertainment.

There are a few possible explanations for why results slightly differed between non-firefighting and police-referent analyses in the current study. It is likely that the police officer referent group helped address residual confounding because of similarities between firefighters and police officers related to demographic characteristics (e.g., age), lifestyle, physical fitness (i.e., both firefighters and police officers often must pass physical examinations for fitness-for-duty), and so forth. Also, analyses lost statistical power with diminished sample size in the police-referent group, leading to wide CIs even for defects that maintained moderately elevated estimates (i.e., cleft lip and TAPVR); or that firefighting carries some similar occupational risk factors for adverse reproductive outcomes as those in other public safety and first responder groups (e.g., shift work, diesel exhaust, and heavy metal exposure).[9,41]

The associations we identified in the current study are plausible given the many exposures firefighters face that could directly or indirectly (i.e., through maternal pathways) increase the risk of adverse birth outcomes in offspring.[14,15,24–36,42–44] For example, firefighters are heavily exposed to PAHs as combustion by-products released during fire response and training,[45–48] and their postfire urinary levels of PAH exposure are significantly higher than levels observed in office workers and the general population.[49] PAH exposure is recognized to impact reproduction and development through male and female reproductive pathways.[50] Studies have shown that maternal PAH exposure may increase the risk for several birth defects, including oral clefts.[25–27,29–31] Reports suggest that paternal exposure to PAHs and other toxic compounds can have adverse effects on future offspring through possible genetic and nongenetic (e.g., epigenetic, noncoding RNA, and microRNA) mechanisms.[51,52] Furthermore, DNA methylation, accelerated epigenetic age, changes in microRNA expression, and thyroid hormone disruption have been studied in firefighters within the context of mechanisms for carcinogenicity[53–57]; but research on the overlap between potential biomechanistic pathways for cancer and those for direct routes of developmental toxicity in firefighters is warranted.

Exposure-induced mechanistic changes that are present in the sperm could cause abnormal fetal development leading to a birth defect. Still, there is lack of research on paternally-mediated environmental exposures to children's health—despite an ever-increasing body of mechanistic data—that has been discussed in the literature.[58] A prior study showed paternal smoking (a common source of PAH exposure) appeared to induce DNA alterations in human F1 offspring that cannot be explained by maternal exposure to second-hand smoke alone[59]; this finding has also been replicated by other researchers.[60] Therefore, a mechanism for birth defects connected to paternal exposure is biologically plausible.

Indirect exposure among mothers who are co-parents to male firefighters is also possible. Contamination of firefighters' gear, clothing, skin, and workplaces is a major source of their exposure to persistent chemicals.[45,61–63] If strict decontamination procedures are not adhered to following a fire response, such as using cleansing wipes andor showering, firefighters can have chemicals that linger on their skin even after they leave the incident and fire station.[64] This contamination can lead to extended exposure for firefighters or even secondary exposure affecting pregnant mothers in the home environment. In some situations, firefighters bring contaminated gear or clothing into their personal vehicles or homes, like for cleaning or storage purposes.[65,66] Take-home exposure among firefighters is not well-measured, so little is known about the potential for secondary exposure of firefighters' families.

To our knowledge, this analysis included the largest sample of children born with birth defects among firefighters in the literature to date. This analysis nearly tripled the sample size of firefighters from a previous NBDPS analysis of paternal occupations by adding 7 years of additional, more recent, data and increased power for examining more individual defects. Furthermore, to our knowledge, this is only the second study of birth defects in children of male firefighters that

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TABLE 2 Adjusted associations between individual birth defect groups and paternal occupation as a firefighter in comparison to paternal non-firefighters and paternal police officers, National Birth Defects Prevention Study, 1997–2011

		Firefighters versus non-firefighters[a]			Firefighters versus police officers[b,c]		
Defect	**FF cases, *n*[b]**	**Non-FF cases, *n***	**OR**	**95% CI**	**Police cases, *n***	**OR**	**95% CI**
Any heart defect	61	10,162	1.01	(0.71 – 1.45)	128	0.90	(0.58– 1.39)
Conotruncal defects	19	2185	1.44	(0.85 – 2.43)	32	1.04	(0.54 – 2.03)
Tetralogy of Fallot	8	990	1.33	(0.63 – 2.80)	15	0.92	(0.35 – 2.41)
D-Transposition of the Great Arteries	7	673	1.65	(0.75 – 3.64)	11	1.14	(0.42 – 3.12)
AVSD	4	304	2.02	(0.73 – 5.63)	6	1.22	(0.33 – 4.51)
APVR	4	319	2.38	(0.85 – 6.65)	4	1.85	(0.44 – 7.70)
TAPVR	4	251	3.10	(1.11 – 8.68)	3	2.49	(0.54 – 11.55)
LVOT defects	10	1914	0.81	(0.41 – 1.60)	16	1.21	(0.51 – 2.84)
Hypoplastic left heart syndrome	3	552	0.88	(0.28 – 2.84)	7	0.85	(0.21 – 3.45)
Coarctation of the aorta	4	1015	0.61	(0.22 – 1.69)	8	0.97	(0.28 – 3.39)
RVOT defects	6	1773	0.59	(0.25 – 1.37)	23	0.50	(0.19 – 1.31)
Pulmonary valve stenosis	4	1319	0.51	(0.19 – 1.43)	18	0.43	(0.14 – 1.33)
Septal defects	20	3958	0.88	(0.53 – 1.48)	47	0.83	(0.45 – 1.53)
Perimembranous VSD	12	1401	1.52	(0.81 – 2.84)	13	1.72	(0.73 – 4.02)
Secundum ASD	6	2008	0.51	(0.22 – 1.20)	27	0.42	(0.16 – 1.08)
ASD, not otherwise specified	3	529	1.05	(0.32 – 3.46)	6	1.08	(0.26 – 4.57)
Neural tube defects	7	1806	0.65	(0.30 – 1.44)	16	0.84	(0.33 – 2.16)
Spina bifida	4	1071	0.63	(0.23 – 1.75)	11	0.69	(0.21 – 2.27)
Oral clefts	37	3963	1.67	(1.09 – 2.54)	44	1.72	(1.00 – 2.96)
Cleft palate	15	1370	1.84	(1.03 – 3.29)	13	2.40	(1.06 – 5.41)
Cleft lip with cleft palate	10	1683	1.16	(0.59 – 2.29)	20	1.04	(0.45 – 2.37)
Cleft lip without cleft palate	12	910	2.23	(1.19 – 4.20)	11	2.20	(0.91 – 5.31)
Esophageal atresia	3	628	0.77	(0.24 – 2.46)	11	0.50	(0.13 – 1.86)
Anorectal atresia/stenosis	6	873	1.21	(0.52 – 2.84)	12	0.96	(0.34 – 2.70)
Hypospadias	18	2175	1.07	(0.59 – 1.94)	30	0.88	(0.42 – 1.86)
Limb deficiency	10	1046	1.63	(0.83 – 3.20)	20	0.90	(0.39 – 2.07)
Transverse limb deficiency	8	611	2.23	(1.05 – 4.71)	12	1.26	(0.48 – 3.28)
Craniosynostosis	12	1401	1.20	(0.64 – 2.27)	20	1.17	(0.53 – 2.57)
Gastroschisis	3	1092	0.96	(0.29 – 3.15)	9	0.65	(0.17 – 2.49)

Abbreviations: AVSD, atrioventricular septal defect; CI, confidence interval; D-Transposition, Dextro-Transposition; FF, firefighter(s); L/RVOT, left/right ventricular outflow tract; OR, odds ratio; [T]APVR, [Total] anomalous pulmonary venous return; V/ASD, ventricular/atrial septal defect.

[a]Adjusting for study site and maternal age in years, race/ethnicity (dichotomous as non-Hispanic white vs. nonwhite/Hispanic to allow all models to converge), smoking status, and education.

[b]*n* < 3 fathers classified as firefighter and police officer were excluded from analyses with a police officer referent group.

[c]Adjusting for maternal race/ethnicity (as non-Hispanic white vs. nonwhite/Hispanic to allow all models to converge).

used police officers as a referent group to help control for potential residual confounding, with the first studying a non-US sample from decades earlier.[18] Still, there are limitations to the current study. Sample sizes were small for some individual defect groups, with roughly a third of defects analyzed having <5 firefighter cases, contributing to reduced statistical power and wide CIs/imprecise estimates. This limitation was greater for the police-referent analysis, for which the number of cases among children of police officers was also small for some defects.

We evaluated an a priori set of characteristics as potential confounders for which to control in the multivariable models. However, our ability to evaluate a larger number of variables as

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potential confounders was limited by our sample size. Although using a police officer referent group allowed us to control for many potential confounders that existed in the non-firefighter-referent analysis—including paternal characteristics, residual confounding could still be present in both analyses. For example, because maternal race/ethnicity was dichotomized due to small sample size, it may not have been adequately controlled for in multivariable models.

Because we examined a wide spectrum of birth defect groups, our results are subject to potential random errors introduced through multiple comparisons. Because we ran regression models for 29 birth defect groups and two referent groups, it is possible that some positive or significant estimates could have been found due to chance. Nonetheless, previous studies support our results, particularly related to oral clefts and limb defects.[18–21]

Our assessment of occupation was also subject to limitations. No specific occupational exposures were evaluated for this analysis, and exposures may have widely varied across the included sample of firefighters. Further, our analysis did not account for maternal occupation or occupational exposures. We were unable to evaluate birth defects among female firefighters, whose occupational exposures could have different or stronger reproductive effects, due to an insufficient sample size. Similar to the previous NBDPS analysis of paternal occupations, we focused on the exposure period of 3 months before conception through the first month of pregnancy as a periconceptional window during which male-mediated mechanisms of teratogenesis can occur,[16] although take-home exposure of pregnant mothers could occur through the end of the first trimester. Research delineating potential maternal and paternal routes of toxicity for firefighters and their families could be important for practice.

Because there is no clear evidence to identify whether paternally-mediated risks follow a direct biological mechanism (e.g., a direct impact on sperm or seminal fluid) or an indirect effect (e.g., take-home exposures to domestic partners), we did not exclude families in which donor sperm were used. We also did not have full data on household composition, including whether the father resided in the same household with the biological mother throughout periconception and the first trimester of pregnancy. We also did not assess non-paternity. All of these might lead to misclassification of occupation; in all these scenarios, however, the misclassification would likely lead to bias towards the null.

Lastly, the data evaluated in the current study were collected between 1997 and 2011 and may not accurately represent reproductive hazards among current firefighters. Over the past decade, research related to exposure and cancer risk for firefighters has grown rapidly.[7,8] As a result, awareness levels, control interventions, workplace practices and policies, and healthy behaviors among firefighters are also increasing.[67,68] Positively, this cultural shift, while aimed at preventing cancer, may also reduce adverse reproductive health outcomes among families of firefighters.

5 | CONCLUSIONS

The results of this study, if replicated, have implications for research and practice. National fire service organizations recognize the need for clear evidence-based guidance on how firefighting impacts reproductive health for both men and women. In early 2022, the National Fallen Firefighters Foundation released its updated Research Agenda for the Fire Service and indicated reproductive health as a critical area related to health and safety.[2] Recent research reported more than 30% of fire departments have no policy on pregnancy or reproductive health.[12] Nonetheless, fire service members, leadership, and organizations can continue to advocate for adherence to decontamination practices and control interventions aimed at reducing exposure among firefighters. While many of these interventions are aimed at reducing the risk of cancer, it is likely that many of the same practices will better protect firefighters and their families from adverse reproductive health outcomes associated with hazardous exposures. Additional research may lead to a better understanding of the reproductive health of male and female firefighters and their families and help guide policy decisions and standard operating guidelines.

AUTHOR CONTRIBUTIONS

Miriam R. Siegel led the data analysis and drafting of the manuscript. Miriam R. Siegel, Carissa M. Rocheleau, and Andrew F. Olshan contributed to conception and design of the analysis. Brittany S. Hollerbach, Sara A. Jahnke, and Lynn M. Almli contributed to drafting portions of the manuscript. Andrew F. Olshan assisted with and replicated statistical analyses. All authors provided critical review of the manuscript and approved the submission.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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John Meyer declares that he has no conflict of interest in the review and publication decision for this article.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

DATA AVAILABILITY STATEMENT

The study questionnaires and process for accessing the data used in this study are described at https://www.cdc.gov/ncbddd/birthdefects/nbdps-public-access-procedures.html. The code book and analytic code may be made available upon request.

ETHICS APPROVAL AND INFORMED CONSENT

All interviewed study participants provided informed consent. The Centers for Disease Control and Prevention Institutional Review Board (IRB), along with the IRBs for each participating site, have approved the NBDPS (CDC protocol #2087).

ORCID

Miriam R. Siegel http://orcid.org/0000-0002-0231-2564
Brittany S. Hollerbach http://orcid.org/0000-0002-6350-8210
Amel Omari http://orcid.org/0000-0002-6345-1947
Lynn M. Almli http://orcid.org/0000-0003-4399-807X

REFERENCES

1. Evarts B, Stein GP. US Fire Department Profile 2018. 2020. https://www.nfpa.org/-/media/Files/News-and-Research/Fire-statistics-and-reports/Emergency-responders/osfdprofile.pdf
2. National Fallen Firefighters Foundation. 2021 National Fire Service Research Agenda: Recommendations Report. 2022.
3. Petersen KU, Hansen J, Ebbehoej NE, Bonde JP. Infertility in a cohort of male Danish firefighters: a register-based study. *Am J Epidemiol*. 2019;188(2):339-346. doi:10.1093/aje/kwy235
4. Engelsman M, Toms LML, Wang X, Banks APW, Blake D. Effects of firefighting on semen parameters: an exploratory study. *Reprod Fertil*. 2021;2(1):L13-L15. doi:10.1530/raf-20-0070
5. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occup Environ Med*. 2014;71(6):388-397. doi:10.1136/oemed-2013-101662
6. International Agency for Research on Cancer. Painting, firefighting, and shiftwork. *IARC Monogr Eval Carcinog Risks Hum*. 2010;98:9-764.
7. Jalilian H, Ziaei M, Weiderpass E, Rueegg CS, Khosravi Y, Kjaerheim K. Cancer incidence and mortality among firefighters. *Int J Cancer*. 2019;145(10):2639-2646. doi:10.1002/ijc.32199
8. Soteriades ES, Kim J, Christophi CA, Kales SN. Cancer incidence and mortality in firefighters: a state-of-the-art review and meta-analysis. *Asian Pacific J Cancer Prev*. 2019;20(11):3221-3231. doi:10.31557/apjcp.2019.20.11.3221
9. Sritharan J, Pahwa M, Demers PA, Harris SA, Cole DC, Parent ME. Prostate cancer in firefighting and police work: a systematic review and meta-analysis of epidemiologic studies. *Environ Health*. 2017;16(1):124. doi:10.1186/s12940-017-0336-z
10. Jahnke SA, Poston WSC, Jitnarin N, Haddock CK. Maternal and child health among female firefighters in the U.S. *Matern Child Health J*. 2018;22(6):922-931. doi:10.1007/s10995-018-2468-3
11. Park J, Ahn YS, Kim MG. Pregnancy, childbirth, and puerperium outcomes in female firefighters in Korea. *Ann Occup Environ Med*. 2020;32:e8. doi:10.35371/aoem.2020.32.e8
12. Jung AM, Jahnke SA, Dennis LK, et al. Occupational factors and miscarriages in the US fire service: a cross-sectional analysis of women firefighters. *Environ Health*. 2021;20(1):116. doi:10.1186/s12940-021-00800-4
13. Burdorf A, Figa-Talamanca I, Jensen TK, Thulstrup AM. Effects of occupational exposure on the reproductive system: core evidence and practical implications. *Occup Med*. 2006;56(8):516-520. doi:10.1093/occmed/kql113
14. Jensen TK, Bonde JP, Joffe M. The influence of occupational exposure on male reproductive function. *Occup Med*. 2006;56(8):544-553. doi:10.1093/occmed/kql116
15. McDiarmid MA, Agnew J. Reproductive hazards and firefighters. *Occup Med*. 1995;10(4):829-841.
16. Desrosiers TA, Herring AH, Shapira SK, et al. Paternal occupation and birth defects: findings from the National Birth Defects Prevention Study. *Occup Environ Med*. 2012;69(8):534-542. doi:10.1136/oemed-2011-100372
17. Olshan AF, Baird PA, Teschke K. Paternal occupational exposures and the risk of Down syndrome. *Am J Hum Genet*. 1989;44(5):646-651.
18. Olshan AF, Teschke K, Baird PA. Birth defects among offspring of firemen. *Am J Epidemiol*. 1990;131(2):312-321. doi:10.1093/oxfordjournals.aje.a115500
19. Schnitzer PG, Olshan AF, Erickson JD. Paternal occupation and risk of birth defects in offspring. *Epidemiology*. 1995;6(6):577-583. doi:10.1097/00001648-199511000-00003
20. Li F. Congenital Heart Defects Among Offspring of Firemen. Dissertation. University of Calgary; 1998.
21. Olshan AF, Teschke K, Baird PA. Paternal occupation and congenital anomalies in offspring. *Am J Ind Med*. 1991;20(4):447-475. doi:10.1002/ajim.4700200403
22. Aronson KJ, Dodds LA, Marrett L, Wall C. Congenital anomalies among the offspring of fire fighters. *Am J Ind Med*. 1996;30(1):83-86. doi:10.1002/(sici)1097-0274(199607)30:1<83::Aid-ajim14>3.0.Co;2-4
23. Källén B, Pradat P. Re: "Birth defects among offspring of firemen". *Am J Epidemiol*. 1992;135(11):1318-1320. doi:10.1093/oxfordjournals.aje.a116242
24. Fazekas-Pongor V, Fekete M, Csáky-Szunyogh M, Cseh K, Pénzes M. Parental occupational exposure and congenital heart diseases in a Hungarian case-control study. *Int Arch Occup Environ Health*. 2021;94(3):515-527. doi:10.1007/s00420-020-01589-4
25. Langlois PH, Hoyt AT, Lupo PJ, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons and risk of neural tube defect-affected pregnancies. *Birth Defects Res Part A Clin Mol Teratol*. 2012;94(9):693-700. doi:10.1002/bdra.23045
26. Langlois PH, Hoyt AT, Lupo PJ, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons and risk of oral cleft-affected pregnancies. *Cleft Palate Craniofac J*. 2013;50(3):337-346. doi:10.1597/12-104
27. Lupo PJ, Langlois PH, Reefhuis J, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons: effects on gastroschisis among offspring in the National Birth Defects Prevention Study. *Environ Health Perspect*. 2012;120(6):910-915. doi:10.1289/ehp.1104305
28. Nassar N, Abeywardana P, Barker A, Bower C. Parental occupational exposure to potential endocrine disrupting chemicals and risk of hypospadias in infants. *Occup Environ Med*. 2010;67(9):585-589. doi:10.1136/oem.2009.048272

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29. O'Brien JL, Langlois PH, Lawson CC, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons and craniosynostosis among offspring in the National Birth Defects Prevention Study. *Birth Defects Res Part A Clin Mol Teratol*. 2016;106(1):55-60. doi:10.1002/bdra.23389
30. Patel J, Nembhard WN, Politis MD, et al. Maternal occupational exposure to polycyclic aromatic hydrocarbons and the risk of isolated congenital heart defects among offspring. *Environ Res*. 2020;186:109550. doi:10.1016/j.envres.2020.109550
31. Santiago-Colón A, Rocheleau CM, Chen IC, et al. Association between maternal occupational exposure to polycyclic aromatic hydrocarbons and rare birth defects of the face and central nervous system. *Birth Defects Res*. 2020;112(5):404-417. doi:10.1002/bdr2.1643
32. van Rooij IALM, Wijers CHW, Rieu PNMA, et al. Maternal and paternal risk factors for anorectal malformations: a Dutch case-control study. *Birth Defects Res Part A Clin Mol Teratol*. 2010;88(3):152-158. doi:10.1002/bdra.20649
33. Wang C, Zhan Y, Wang F, et al. Parental occupational exposures to endocrine disruptors and the risk of simple isolated congenital heart defects. *Pediatr Cardiol*. 2015;36(5):1024-1037. doi:10.1007/s00246-015-1116-6
34. Poon S, Koren G, Carnevale A, et al. Association of in utero exposure to polybrominated diphenyl ethers with the risk of hypospadias. *JAMA Pediatrics*. 2018;172(9):851-856. doi:10.1001/jamapediatrics.2018.1492
35. Chevrier C, Dananché B, Bahuau M, et al. Occupational exposure to organic solvent mixtures during pregnancy and the risk of non-syndromic oral clefts. *Occup Environ Med*. 2006;63(9):617-623. doi:10.1136/oem.2005.024067
36. Desrosiers TA, Lawson CC, Meyer RE, et al. Maternal occupational exposure to organic solvents during early pregnancy and risks of neural tube defects and orofacial clefts. *Occup Environ Med*. 2012;69(7):493-499. doi:10.1136/oemed-2011-100245
37. Reefhuis J, Gilboa SM, Anderka M, et al. The National Birth Defects Prevention Study: a review of the methods. *Birth Defects Res Part A Clin Mol Teratol*. 2015;103(8):656-669. doi:10.1002/bdra.23384
38. Yoon P, Rasmussen S, Lynberg M, et al. The National Birth Defects Prevention Study. *Public Health Rep*. 2001;116(Suppl 1):S32-S40. doi:10.1093/phr/116.S1.32
39. Botto LD, Lin AE, Riehle-Colarusso T, Malik S, Correa A. Seeking causes: classifying and evaluating congenital heart defects in etiologic studies. *Birth Defects Res Part A Clin Mol Teratol*. 2007;79(10):714-727. doi:10.1002/bdra.20403
40. Rasmussen SA, Olney RS, Holmes LB, Lin AE, Keppler-Noreuil KM, Moore CA. Guidelines for case classification for the National Birth Defects Prevention Study. *Birth Defects Res Part A Clin Mol Teratol*. 2003;67(3):193-201. doi:10.1002/bdra.10012
41. Harris MA, Kirkham TL, MacLeod JS, Tjepkema M, Peters PA, Demers PA. Surveillance of cancer risks for firefighters, police, and armed forces among men in a Canadian census cohort. *Am J Ind Med*. 2018;61(10):815-823. doi:10.1002/ajim.22891
42. Estors Sastre B, Campillo Artero C, González Ruiz Y, et al. Occupational exposure to endocrine-disrupting chemicals and other parental risk factors in hypospadias and cryptorchidism development: a case-control study. *J Pediatr Urol*. 2019;15(5):520.e1-520. doi:10.1016/j.jpurol.2019.07.001
43. Fazekas-Pongor V, Csáky-Szunyogh M, Fekete M, Mészáros Á, Cseh K, Pénzes M. Congenital heart diseases and parental occupational exposure in a Hungarian case-control study in 1997 to 2002. *Congenit Anom*. 2021;61(2):55-62. doi:10.1111/cga.12401
44. Morales-Suárez-Varela MM, Toft GV, Jensen MS, et al. Parental occupational exposure to endocrine disrupting chemicals and male genital malformations: a study in the Danish National Birth Cohort study. *Environ Health*. 2011;10(1):3. doi:10.1186/1476-069x-10-3
45. Fent KW, Eisenberg J, Snawder J, et al. Systemic exposure to PAHs and benzene in firefighters suppressing controlled structure fires. *Ann Occup Hyg*. 2014;58(7):830-845. doi:10.1093/annhyg/meu036
46. Fent KW, Toennis C, Sammons D, et al. Firefighters' and instructors' absorption of PAHs and benzene during training exercises. *Int J Hyg Environ Health*. 2019;222(7):991-1000. doi:10.1016/j.ijheh.2019.06.006
47. Fent KW, Toennis C, Sammons D, et al. Firefighters' absorption of PAHs and VOCs during controlled residential fires by job assignment and fire attack tactic. *J Exposure Sci Environ Epidemiol*. 2020;30(2):338-349. doi:10.1038/s41370-019-0145-2
48. Keir JLA, Akhtar US, Matschke DMJ, et al. Polycyclic aromatic hydrocarbon (PAH) and metal contamination of air and surfaces exposed to combustion emissions during emergency fire suppression: implications for firefighters' exposures. *Sci Total Environ*. 2020;698:134211. doi:10.1016/j.scitotenv.2019.134211
49. Keir JLA, Akhtar US, Matschke DMJ, et al. Elevated exposures to polycyclic aromatic hydrocarbons and other organic mutagens in Ottawa firefighters participating in emergency, on-shift fire suppression. *Environ Sci Technol*. 2017;51(21):12745-12755. doi:10.1021/acs.est.7b02850
50. Ramesh A, Harris KJ, Archibong AE. Reproductive toxicity of polycyclic aromatic hydrocarbons. In: Gupta RC, ed. *Reproductive and Developmental Toxicology*. 3rd ed. Academic Press; 2022:759-778.
51. Bonde JPE, Tøttenborg SS, Hougaard KS. Paternal environmental exposure and offspring health. *Curr Opin Endocr Metab Res*. 2019;7:14-20. doi:10.1016/j.coemr.2019.05.001
52. Yang J, Lu Z, Liu Z, Wang L, Qiang M. Methylation of imprinted genes in sperm DNA correlated to urinary polycyclic aromatic hydrocarbons (PAHs) exposure levels in reproductive-aged men and the birth outcomes of the offspring. *Front Genet*. 2021;11:611276. doi:10.3389/fgene.2020.611276
53. Goodrich JM, Jung AM, Furlong MA, et al. Repeat measures of DNA methylation in an inception cohort of firefighters. *Occup Environ Med*. 2022;79:656-663. doi:10.1136/oemed-2021-108153
54. Zhou J, Jenkins TG, Jung AM, et al. DNA methylation among firefighters. *PLoS One*. 2019;14(3):e0214282. doi:10.1371/journal.pone.0214282
55. Goodrich JM, Calkins MM, Caban-Martinez AJ, et al. Per- and polyfluoroalkyl substances, epigenetic age and DNA methylation: a cross-sectional study of firefighters. *Epigenomics*. 2021;13(20):1619-1636. doi:10.2217/epi-2021-0225
56. Jung AM, Zhou J, Beitel SC, et al. Longitudinal evaluation of whole blood miRNA expression in firefighters. *J Exposure Sci Environ Epidemiol*. 2021;31(5):900-912. doi:10.1038/s41370-021-00306-8
57. Trowbridge J, Gerona R, McMaster M, et al. Organophosphate and organohalogen flame-retardant exposure and thyroid hormone disruption in a cross-sectional study of female firefighters and office workers from San Francisco. *Environ Sci Technol*. 2022;56(1):440-450. doi:10.1021/acs.est.1c05140
58. Braun JM, Messerlian C, Hauser R. Fathers matter: why it's time to consider the impact of paternal environmental exposures on children's health. *Curr Epidemiol Rep*. 2017;4(1):46-55. doi:10.1007/s40471-017-0098-8
59. Laubenthal J, Zlobinskaya O, Poterlowicz K, et al. Cigarette smoke-induced transgenerational alterations in genome stability in cord blood of human F1 offspring. *FASEB J*. 2012;26(10):3946-3956. doi:10.1096/fj.11-201194
60. Linschooten JO, Verhofstad N, Gutzkow K, et al. Paternal lifestyle as a potential source of germline mutations transmitted to offspring. *FASEB J*. 2013;27(7):2873-2879. doi:10.1096/fj.13-227694

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61. Alexander BM, Baxter CS. Flame-retardant contamination of fire-fighter personal protective clothing – a potential health risk for firefighters. *J Occup Environ Hyg*. 2016;13(9):D148-D155. doi:10.1080/15459624.2016.1183016
62. Easter E, Lander D, Huston T. Risk assessment of soils identified on firefighter turnout gear. *J Occup Environ Hyg*. 2016;13(9):647-657. doi:10.1080/15459624.2016.1165823
63. Banks APW, Engelsman M, He C, Wang X, Mueller JF. The occurrence of PAHs and flame-retardants in air and dust from Australian fire stations. *J Occup Environ Hyg*. 2020;17(2-3):73-84. doi:10.1080/15459624.2019.1699246
64. Fent KW, Alexander B, Roberts J, et al. Contamination of firefighter personal protective equipment and skin and the effectiveness of decontamination procedures. *J Occup Environ Hyg*. 2017;14(10):801-814. doi:10.1080/15459624.2017.1334904
65. Macy GB, Hwang J, Taylor R, Golla V, Cann C, Gates B. Examining behaviors related to retirement, cleaning, and storage of turnout gear among rural firefighters. *Workplace Health Saf*. 2020;68(3):129-138. doi:10.1177/2165079919882951
66. Moore KJ, Koru-Sengul T, Alvarez A, et al. Safety gear decontamination practices among Florida firefighters: analysis of a text-based survey methodology. *Workplace Health Saf*. 2018;66(11):522-529. doi:10.1177/2165079918754331
67. Harrison TR, Muhamad JW, Yang F, et al. Firefighter attitudes, norms, beliefs, barriers, and behaviors toward post-fire decontamination processes in an era of increased cancer risk. *J Occup Environ Hyg*. 2018;15(4):279-284. doi:10.1080/15459624.2017.1416389
68. Louzado-Feliciano P, Griffin KA, Santiago KM, et al. Fire service organizational-level characteristics are associated with adherence to contamination control practices in Florida Fire Departments: evidence From the Firefighter Cancer Initiative. *J Occup Environm Med*. 2020;62(9):e508-e514. doi:10.1097/jom.0000000000001953

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