

## RESEARCH ARTICLE

# End-stage renal disease incidence in a cohort of US firefighters from San Francisco, Chicago, and Philadelphia

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## Abstract

**Background:** Firefighters perform strenuous work in hot environments, which may increase their risk of chronic kidney disease. The purpose of this study was to evaluate the risk of end-stage renal disease (ESRD) and types of ESRD among a cohort of US firefighters compared to the US general population, and to examine exposure–response relationships.

**Methods:** ESRD from 1977 through 2014 was identified through linkage with Medicare data. ESRD incidence in the cohort compared to the US population was evaluated using life table analyses. Associations of all ESRD, systemic ESRD, hypertensive ESRD, and diabetic ESRD with exposure surrogates (exposed days, fire runs, and fire hours) were examined in Cox proportional hazards models adjusted for attained age (the time scale), race, birth date, fire department, and employment duration.

**Results:** The incidence of all ESRD was less than expected (standardized incidence ratio (SIR) = 0.79; 95% confidence interval = 0.69–0.89, observed = 247). SIRs for ESRD types were not significantly increased. Positive associations of all ESRD, systemic ESRD, and hypertensive ESRD with exposed days were observed; however, 95% confidence intervals included one.

**Conclusions:** We found little evidence of increased risk of ESRD among this cohort of firefighters. Limitations included the inability to evaluate exposure–response relationships for some ESRD types due to small observed numbers, the limitations of the surrogates of exposure, and the lack of information on more sensitive outcome measures for potential kidney effects.

## KEYWORDS

end-stage renal disease, firefighters, longitudinal studies

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## 1 | INTRODUCTION

Firefighters may be at increased risk of developing chronic kidney disease because they perform strenuous work in hot environments. Strenuous work with heat stress and dehydration may cause renal impairment from clinical or subclinical rhabdomyolysis, hyperuricemia and urate crystalluria, and hyperosmolality-induced release of vasopressin and activation of the aldose reductase-fructokinase pathway.<sup>1-11</sup> Increased concern about these potential heat-related effects on kidney function has arisen due to an epidemic of chronic kidney disease among sugarcane workers in Central America.<sup>12</sup> Chronic kidney disease in these workers has often progressed to end-stage renal disease (ESRD).<sup>3,13</sup> Chronic kidney disease has also been observed among other heat-exposed workers and in other regions.<sup>4,12,14-17</sup> However, few data exist on the risk of kidney disease among firefighters.

Firefighters are at risk of heat stress from exposure to heat from fires, ambient heat during hot weather, and metabolic heat generated by strenuous physical work.<sup>18,19</sup> The heavy, impermeable personal protective equipment structural firefighters wear adds to their metabolic workload and impairs evaporative cooling.<sup>19</sup> Increased core body temperature and heat-related illnesses, including rhabdomyolysis and fatal heat stroke, have been documented among firefighters and trainees.<sup>20-28</sup> Firefighters are also at risk of dehydration,<sup>29</sup> which can contribute to kidney injury.<sup>30,31</sup>

We previously evaluated mortality and cancer incidence among a large National Institute for Occupational Safety and Health (NIOSH) cohort of US firefighters from the Chicago, Philadelphia, and San Francisco fire departments and found an increased risk of several cancers including kidney cancer compared to the US general population.<sup>32,33</sup> Mortality from chronic and unspecified nephritis and renal failure and other renal sclerosis, based on the underlying cause of death, was elevated among Philadelphia firefighters (standardized mortality ratio = 1.35; 95% confidence interval [CI] = 1.03-1.73) but not Chicago or San Francisco firefighters.<sup>33</sup> However, chronic kidney disease is usually not the underlying cause of death even when mentioned on the death certificate.<sup>34</sup> In this study, we evaluate ESRD incidence in the NIOSH firefighter cohort compared to the general population and relationships of ESRD with surrogates of exposure. Chicago and Philadelphia have humid continental climates, whereas San Francisco has a Mediterranean climate.<sup>35</sup> From 1981 to 2010, the average annual number of days the temperature reached 32.2°C was 17 in Chicago, 25 in Philadelphia, and 2 in San Francisco.<sup>36</sup>

## 2 | METHODS

### 2.1 | Cohort description

The previous mortality cohort included 29,992 career firefighters employed by the fire departments of Chicago (CFD), Philadelphia (PFD), and San Francisco (SFFD) for at least 1 day between the years

1950 and 2009, as described previously.<sup>32,33</sup> The current study cohort includes 26,469 members of the mortality cohort who were alive in 1977, when retrospective ascertainment of incident ESRD began, or later. Firefighters of unknown race ( $n = 727$ ) were assumed White because 81% of firefighters of known race in the current cohort were White and 70% of firefighters of unknown race were hired before 1970 when minority hiring was lower. The cohort used in the exposure-response analysis, hereafter referred to as the restricted cohort, was further limited to 18,923 male firefighters of known race hired in 1950 or later for at least 1 year.

The study received approvals from the Institutional Review Boards of NIOSH and the National Cancer Institute. Informed consent was waived for this records-based study.

### 2.2 | Exposure assessment

Exposure surrogates were calculated for the restricted cohort as described previously.<sup>37,38</sup> These surrogates were originally developed to estimate exposure to combustion byproducts of fire for a cancer study,<sup>38</sup> but are used in this study as crude surrogates of occupational heat exposure. Briefly, detailed work histories through 2009 were linked with job exposure matrices based on the job, location, and fire-fighting apparatus assignments. Data were available to calculate the number of exposed days (i.e., days worked in a job or location with potential exposure) for CFD, PFD, and SFFD firefighters; the number of fire runs for CFD and PFD firefighters; and the number of fire hours (i.e., the time spent at fires) for CFD firefighters.

### 2.3 | Ascertainment of vital status and ESRD

Vital status was ascertained through 2016 as described previously.<sup>32,33</sup> Cohort members with incident ESRD treated with dialysis or transplant from 1977 through 2014 were identified by linking the cohort with Medicare data on persons with ESRD by Social Security number (SSN), name, date of birth, and gender using the Fuzzy Lookup Transformation in Microsoft SQL Server Integration Services.<sup>39</sup> Inexact matches were manually reviewed in descending order of the overall similarity score until they were consistently judged to be false matches. All inexact matches with an exact match on the Social Security number were also manually reviewed.

Medicare data on persons with ESRD is maintained by the Centers for Medicare & Medicaid Services (CMS) and includes individuals who received Medicare-covered renal replacement therapy (dialysis or transplant) in 1977 or later. Since 1973, most persons with ESRD have been entitled to Medicare regardless of age.<sup>40</sup> Between the earliest years, when reporting was incomplete, and 1995, when reporting of all ESRD patients regardless of Medicare eligibility was mandated,<sup>41</sup> approximately 93% of ESRD patients in the United States were included in the data collected.<sup>40</sup>

**TABLE 1** Characteristics of the full and restricted cohorts

	Full cohort (N = 26,469)		Restricted cohort <sup>a</sup> (N = 18,923)	
Gender, n (%)				
Male	25,480	(96.3)	18,923	(100)
Female	989	(3.7)	–	–
Race, n (%)				
White	20,810	(78.6)	14,775	(78.1)
Other	4932	(18.6)	4148	(21.9)
Unknown	727	(2.8%)	–	–
Fire department, n (%)				
San Francisco	4679	(17.7)	3049	(16.1)
Chicago	13,559	(51.2)	10,076	(53.3)
Philadelphia	8231	(31.1)	5798	(30.6)
Vital status <sup>b</sup> , n (%)				
Alive	16,327	(61.7)	>14,118 <sup>c</sup>	(>74.6) <sup>c</sup>
Deceased	10,120	(38.2)	4794	(25.3)
Lost to follow-up	22	(0.1)	<11 <sup>c</sup>	(<0.1) <sup>c</sup>
Employment, median (IQR)				
Year hired	1973	(1955–1991)	1978	(1965–1993)
Age at hire (years)	28	(25–31)	27	(25–31)
Duration (years)	23	(11–30)	23	(12–30)

Abbreviation: IQR, interquartile range.

<sup>a</sup>Male firefighters of a known race who were hired in 1950 or later and employed for at least 1 year.

<sup>b</sup>Vital status at the end of follow-up (December 31, 2014) or the date of diagnosis, whichever was earlier.

<sup>c</sup>Cell size <11 or reporting the exact number allows a cell size <11 to be derived.

## 2.4 | Analysis

The incidence of ESRD among the overall cohort was compared to that of the US general population in R version 4.1.3<sup>42</sup> using the methods described by Calvert et al.<sup>43</sup> Since the Medicare data on ESRD are incomplete before 1977, cohort members who died before 1977 were excluded from the analyses. Person-years-at-risk (PYAR) were accumulated from the date the cohort criteria were met or January 1, 1977, whichever was later, to the first service date for ESRD, the date of death, the date last observed, or the ending date of the study (December 31, 2014), whichever was earliest. The first service date for ESRD is generally the date on which renal replacement therapy began and was used as a surrogate for the date of onset for ESRD. PYAR were stratified by gender, race (White, other), and 5-year intervals of age and calendar time and then multiplied by the appropriate US ESRD incidence rates to calculate the expected number of cases for each stratum. The US incidence rates were created from CMS Medicare data and US census data as described elsewhere.<sup>43</sup> The expected number of ESRD cases in each stratum was summed to obtain the total expected number. The standardized incidence ratio (SIR) was calculated as the ratio of the

observed to the expected number of treated ESRD cases. SIRs were also calculated for types of ESRD and for the restricted cohort. Ninety-five percent CIs were computed assuming a Poisson distribution for observed ESRD cases. Types of ESRD and the corresponding International Classification of Diseases, 9th Revision, Clinical Modification codes for the primary cause of renal failure in the CMS data are listed in Supporting Information: Table S1.

Exposure–response associations within the restricted cohort were examined with Cox proportional hazards regression using the SAS PHREG procedure.<sup>44</sup> Risk sets comprised all restricted cohort members at risk as of the attained age of the case who also matched the case on race (White, other), birth date (within 5 years), and fire department. Restricted cohort members were followed from the completion of the 1-year eligibility period or January 1, 1977, whichever was latest. The cumulative exposure metrics were lagged 10 and 20 years because chronic kidney failure generally develops over many years. In categorical models, the cut-points were selected to obtain an approximately equal number of cases in each exposure quartile. Hazard ratios (HRs) were estimated from the maximum partial likelihood ratio test and two-sided 95% CIs were based on the profile likelihood. The exposure surrogates were also analyzed as

continuous time-dependent variables in log-linear models where the HR increases exponentially with exposure or, equivalently, the log of the HR increases linearly with exposure. Because the exposure surrogates were generally right-skewed and exposure-response relationships in occupational studies are often attenuated at high exposure levels,<sup>45</sup> log-linear models were also evaluated excluding person-time in the top decile of exposure. The healthy worker survivor effect was addressed by repeating the analyses also matching on employment duration (<10, 10–<20, 20–<30, and 30+ years). Modeling analyses were restricted to analyses with 30 or more observed cases.

### 3 | RESULTS

Table 1 shows the demographic characteristics of the full and restricted cohorts. Most members of the full cohort were male (96.3%) and White (78.6%). Over three-fourths (78.1%) of the restricted cohort of male firefighters were also White. The mean employment duration for both cohorts was 21 years. At the end of the follow-up, 38.2% of the full cohort and 25.3% of the restricted cohort were deceased.

As shown in Table 2, the incidence of all ESRD was less than expected among the full (SIR = 0.79; 95% CI = 0.69–0.89; observed = 247) and restricted (SIR: 0.73; 95% CI = 0.63–0.85; observed = 177) cohorts. The median age at the time of onset was 69 years

(interquartile range = 61–77) and 67 years (interquartile range: 59–73) among the full and restricted cohorts, respectively. SIRs for ESRD due to metabolic disease (full cohort: 2.84; 95% CI = 0.76–7.26; restricted cohort: 1.92; 95% CI = 0.22–6.94) and ESRD due to collagen vascular disease (full cohort: 1.18; 95% CI = 0.32–3.01; restricted cohort: 1.17; 95% CI = 0.24–3.42) were elevated, although the CIs for these ESRD types were wide and included one. The incidence of systemic ESRD and diabetic ESRD was less than expected among the full (systemic ESRD: SIR = 0.76; 95% CI = 0.65–0.88; diabetic ESRD: SIR = 0.66; 95% CI = 0.52–0.82) and restricted (systemic ESRD: SIR = 0.71; 95% CI = 0.59–0.84; diabetic ESRD: SIR = 0.63; 95% CI = 0.49–0.81) cohorts. The incidence of ESRD caused by glomerulonephritis was also less than expected among the full cohort (SIR = 0.61; 95% CI = 0.35–0.97). The SIR for ESRD caused by glomerulonephritis among the restricted cohort was 0.66 (95% CI = 0.36–1.10).

The results of internal analyses among the restricted cohort using categorical models are shown in Table 3 (20-year lag) and Supporting Information: Table S2 (10-year lag). Results reported herein were obtained from the analyses with matching on employment duration, unless stated otherwise. HRs for all ESRD obtained from categorical models increased in the second and third quartiles of exposed days, but then decreased in the top quartile. HRs for systemic ESRD increased with each exposed-day quartile in 20- and 10-year lagged analyses. HRs for hypertensive ESRD also increased with the exposed-day quartile in 20- and 10-year lagged analyses

Type of ESRD <sup>a</sup>	Full cohort			Restricted cohort		
	Obs	SIR	95% CI	Obs	SIR	95% CI
All ESRD	247	0.79	0.69–0.89	177	0.73	0.63–0.85
Systemic ESRD	180	0.76	0.65–0.88	132	0.71	0.59–0.84
Malignancy	NR	0.83	0.27–1.94	NR	0.91	0.24–2.32
Diabetes mellitus	78	0.66	0.52–0.82	63	0.63	0.49–0.81
Metabolic disease	NR	2.84	0.76–7.26	NR	1.92	0.22–6.94
Cystic nephropathy	NR	0.69	0.22–1.60	NR	0.84	0.27–1.97
Collagen vascular disease	NR	1.18	0.32–3.01	NR	1.17	0.24–3.42
Hypertension	81	0.88	0.70–1.10	53	0.81	0.60–1.05
Obstructive nephropathy	NR	0.57	0.11–1.66	NR	0.60	0.07–2.16
Nonsystemic ESRD	22	0.67	0.42–1.02	NR	0.69	0.40–1.11
Glomerulonephritis	NR	0.61	0.35–0.97	NR	0.66	0.36–1.10
Interstitial nephritis	NR	1.05	0.34–2.45	NR	0.94	0.19–2.75
Other causes	17	1.05	0.61–1.67	NR	0.84	0.42–1.50
Unknown causes	28	1.06	0.70–1.53	17	1.00	0.58–1.61

Abbreviations: AIDS, acquired immunodeficiency syndrome; CI, confidence interval; ESRD, end-stage renal disease; NR, not reported (cell size <11 or reporting the cell size allows numbers <11 to be derived); Obs, observed; SIR, standardized incidence ratio.

<sup>a</sup>ESRD due to AIDS, sickle cell disease, and hereditary nephropathy were omitted because no cases were observed.

**TABLE 2** SIRs for ESRD among the full and restricted cohorts, 1977–2014

**TABLE 3** ESRD HRs by 20-year lagged exposure surrogates obtained from categorical models<sup>a</sup>

Type of ESRD <sup>b</sup>	Exposure surrogate (dept) Exposure category	Not adjusted for employment duration		Adjusted for employment duration	
		HR	95% CI	HR	95% CI
All ESRD	Exposed days (CFD, PFD, SFFD)				
	<2212	1.00	—	1.00	—
	2212–<4970	1.06	0.62–1.81	1.21	0.67–2.19
	4970–<6972	1.36	0.76–2.42	1.78	0.87–3.61
	6972+	0.90	0.49–1.64	1.35	0.62–2.91
	Fire runs (CFD, PFD)				
	<1577	1.00	—	1.00	—
	1577–<4491	1.11	0.63–1.97	1.16	0.63–2.15
	4491–<7614	1.18	0.64–2.18	1.20	0.60–2.41
	7614+	0.98	0.52–1.87	1.04	0.50–2.18
	Fire hours (CFD)				
	<339	1.00	—	1.00	—
	339–<986	1.34	0.60–3.01	1.47	0.62–3.50
	986–<1688	1.40	0.59–3.32	1.56	0.61–3.98
	1688+	1.04	0.42–2.60	1.14	0.41–3.11
	Systemic	Exposed days (CFD, PFD, SFFD)			
<2842		1.00	—	1.00	—
2842–<5232		1.31	0.73–2.37	1.48	0.74–2.96
5232–<7461		1.25	0.66–2.36	1.58	0.71–3.51
7461+		1.27	0.65–2.49	1.94	0.81–4.62
Fire runs (CFD, PFD)					
<2198		1.00	—	1.00	—
2198–<4670		1.37	0.74–2.55	1.45	0.74–2.86
4670–<8344		1.06	0.55–2.04	1.03	0.49–2.17
8344+		1.14	0.57–2.28	1.14	0.51–2.53
Fire hours (CFD)					
<363		1.00	—	1.00	—
363–<1071		0.90	0.38–2.15	0.99	0.39–2.50
1071–<1915		0.84	0.33–2.14	0.86	0.31–2.37
1915+		0.83	0.31–2.24	0.77	0.26–2.32
Diabetes mellitus		Exposed days (CFD, PFD, SFFD)			
	<2204	1.00	—	1.00	—
	2204–<5184	0.72	0.32–1.65	0.78	0.30–1.98
	5184–<7352	0.79	0.33–1.90	0.93	0.31–2.78
	7352+	0.56	0.23–1.40	0.87	0.27–2.82
	Fire runs (CFD, PFD)				
<1990	1.00	—	1.00	—	

(Continues)

TABLE 3 (Continued)

Type of ESRD <sup>b</sup>	Exposure surrogate (dept) Exposure category	Not adjusted for employment duration		Adjusted for employment duration	
		HR	95% CI	HR	95% CI
	1990-<5544	0.79	0.33-1.89	0.78	0.30-2.04
	5544-<8367	1.01	0.40-2.52	0.95	0.33-2.73
	8367+	0.76	0.29-1.99	0.78	0.25-2.39
	Fire hours (CFD)				
	<522	1.00	—	1.00	—
	522-<1080	1.06	0.34-3.31	0.92	0.28-3.06
	1080-<2239	0.52	0.16-1.72	0.38	0.10-1.40
	2239+	0.84	0.23-3.03	0.59	0.14-2.48
Hypertension	Exposed days (CFD, PFD, SFFD)				
	<2883	1.00	—	1.00	—
	2883-<5315	1.61	0.57-4.55	2.64	0.77-8.99
	5315-<7816	1.64	0.53-5.11	2.75	0.67-11.3
	7816+	2.32	0.70-7.67	4.51	0.97-20.9
	Fire runs (CFD, PFD)				
	<1657	1.00	—	1.00	—
	1657-<4574	1.27	0.42-3.84	1.77	0.55-5.74
	4574-<6806	1.95	0.61-6.25	2.77	0.76-10.1
	6806+	1.04	0.31-3.51	1.36	0.35-5.34
	Fire hours (CFD)				
	<345	1.00	—	1.00	—
	345-<1139	1.14	0.27-4.71	1.58	0.36-6.93
	1139-<1723	1.83	0.40-8.44	2.55	0.51-12.8
	1723+	1.27	0.25-6.30	1.59	0.28-8.96

Abbreviations: CFD, Chicago fire department; CI, confidence interval; dept, fire departments included in the analysis; ESRD, end-stage renal disease; HR, hazard ratio; PFD, Philadelphia fire department; SFFD, San Francisco fire department.

<sup>a</sup>All models were adjusted for age (time scale) and for race (White/non-White), date of birth (within 5 years), and fire department by matching. Some models were also adjusted for employment duration (<10, 10-<20, 20-<30, and 30+ years) by matching.

<sup>b</sup>All modeling analyses were conducted among the restricted cohort and included 30 or more observed ESRD cases with an approximately equal number of cases in each exposure quartile. The overall numbers of ESRD cases in the analyses of exposed days were 177 for all ESRD, 132 for systemic ESRD, 63 for diabetic ESRD, and 53 for hypertensive ESRD.

with an HR of 4.51 (95% CI = 0.97-20.9) in the top quartile in 20-year lagged analyses. HRs for diabetic ESRD increased with exposed-day quartile in 10-year lagged analyses only.

The results of internal analyses among the restricted cohort using log-linear models are shown in Table 4 (20-year lag) and Supporting Information: Table S3 (10-year lag). The HR for all ESRD was 1.11 (95% CI = 0.99-1.25) and 1.08 (95% CI = 0.98-1.18) per 1000 exposed days in 20- and 10-year lagged analyses, respectively, when person-time in the top exposure decile was excluded. In analogous linear models including person-time in the top decile of exposure, the

HR for all ESRD was 1.05 (95% CI = 0.96-1.16) and 1.07 (0.99-1.16) per 1000 exposed days in 20- and 10-year lagged analyses, respectively.

Systemic ESRD HRs per 1000 exposed days were 1.05 (95% CI = 0.95-1.18) and 1.07 (95% CI = 0.98-1.17) in 20- and 10-year lagged analyses, respectively, when person-time in the top decile of exposure was included and 1.07 (95% CI = 0.95-1.23) and 1.05 (95% CI = 0.95-1.17) in 20- and 10-year lagged analyses, respectively, when person-time in the top decile of exposure was excluded. Hypertensive ESRD HRs per 1000 exposed days were 1.09 (95%

**TABLE 4** ESRD HRs by 20-year lagged exposure surrogates obtained from log-linear models<sup>a</sup>

Type of ESRD <sup>b</sup>	Exposure surrogate <sup>c</sup>	Not adjusted for employment duration				Adjusted for employment duration			
		Including the top exposure decile		Excluding the top exposure decile		Including the top exposure decile		Excluding the top exposure decile	
		HR per 1000 <sup>d</sup>	95% CI	HR per 1000 <sup>d</sup>	95% CI	HR per 1000 <sup>d</sup>	95% CI	HR per 1000 <sup>d</sup>	95% CI
All ESRD	Exposed days	0.99	0.93–1.07	1.03	0.94–1.13	1.05	0.96–1.16	1.11	0.99–1.25
	Fire runs	0.98	0.93–1.03	1.01	0.94–1.08	0.98	0.92–1.03	1.00	0.92–1.08
	Fire hours	0.88	0.65–1.19	1.02	0.67–1.56	0.87	0.62–1.21	1.06	0.67–1.66
Systemic	Exposed days	1.00	0.93–1.09	1.03	0.94–1.15	1.05	0.95–1.18	1.07	0.95–1.23
	Fire runs	0.98	0.93–1.03	1.01	0.93–1.09	0.98	0.92–1.03	0.99	0.91–1.08
	Fire hours	0.94	0.67–1.30	1.10	0.69–1.77	0.88	0.61–1.26	1.04	0.64–1.69
Diabetes mellitus	Exposed days	0.96	0.87–1.07	0.96	0.84–1.10	1.02	0.89–1.19	1.01	0.86–1.21
	Fire runs	0.96	0.89–1.03	1.00	0.90–1.11	0.95	0.87–1.04	0.98	0.87–1.11
	Fire hours	0.79	0.50–1.25	1.10	0.60–2.07	0.69	0.40–1.14	0.94	0.48–1.83
Hypertension	Exposed days	1.04	0.91–1.19	1.10	0.93–1.32	1.09	0.93–1.29	1.13	0.93–1.40
	Fire runs	0.99	0.91–1.08	0.96	0.84–1.09	0.99	0.91–1.08	0.98	0.85–1.12
	Fire hours	1.11	0.66–1.79	1.06	0.51–2.19	1.09	0.63–1.80	0.99	0.47–2.03

Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio.

<sup>a</sup>All models were adjusted for age (time scale) and for race (White/non-White), date of birth (within 5 years), and fire department by matching. Some models were also adjusted for employment duration (<10, 10–<20, 20–<30, and 30+ years) by matching.

<sup>b</sup>All modeling analyses were conducted among the restricted cohort and included 30 or more observed ESRD cases. The overall numbers of ESRD cases in analyses of exposed days were 177 for all ESRD, 132 for systemic ESRD, 63 for diabetic ESRD, and 53 for hypertensive ESRD.

<sup>c</sup>Exposed days were available for Chicago, Philadelphia, and San Francisco firefighters; fire runs for Chicago and Philadelphia firefighters; and fire hours for Chicago firefighters.

<sup>d</sup>1000 exposed days, 1000 fire runs, or 1000 fire hours.

CI = 0.93–1.29) and 1.10 (95% CI = 0.96–1.27) in 20- and 10-year lagged analyses, respectively. When person-time in the top exposure decile was excluded, the hypertensive ESRD HRs per 1000 exposed days were 1.13 (95% CI = 0.93–1.40) and 1.09 (95% CI = 0.94–1.29) in 20- and 10-year lagged analyses, respectively. In 10-year lagged analyses, the diabetic ESRD HR per 1000 exposed days was 1.03 (95% CI = 0.92–1.17) and 1.03 (95% CI = 0.90–1.19), including and excluding person-time in the top exposure decile, respectively.

## 4 | DISCUSSION

The incidence of all ESRD, systemic ESRD, and diabetic ESRD was less than expected based on rates of ESRD in the general population, which is consistent with a healthy worker effect. Diabetes mellitus is the most common cause of ESRD in the United States with over 45% of incident ESRD attributed to diabetes in 2016.<sup>41</sup> Thus, these findings may reflect, in part, differences in the prevalence and control of diabetes mellitus among the cohort compared to the general population. This is supported by the previously reported mortality from diabetes mellitus in the mortality cohort (SMR = 0.73; 95% CI = 0.64–0.83).<sup>33</sup> A lower prevalence of hyperglycemia among male US firefighters than the general population has also been reported.<sup>46</sup>

Increasing HRs were observed for systemic and hypertensive ESRD with exposed days in 20- and 10-year lagged analyses and for diabetic ESRD with exposed days in 10-year lagged analyses using categorical models. In log-linear models, positive trends were observed for all ESRD, systemic ESRD, and hypertensive ESRD with exposed days, although the CIs included one. These associations with exposed days, but not fire runs and fire hours, may reflect the limitation of using fire runs and fire hours as surrogates for heat exposure. Firefighters are also exposed to occupational heat exposure and experience heat-related illnesses during other activities such as training.<sup>21,27</sup> For the purposes of this study, we assumed that all three exposure surrogates would estimate occupational heat exposure in addition to exposure to combustion byproducts of fire. However, the exposure surrogates are likely crude measures of exposure in this study because we were unable to include additional information in the job exposure matrices regarding risk factors for heat exposure such as environmental air temperature and humidity. Other potential reasons for observing trends with exposed days but not fire runs or fire hours include the lack of data on fire runs and fire hours for all three fire departments and the potential impact of shift work on kidney function.<sup>47,48</sup>

The positive trend in hypertensive ESRD with exposed days, although not statistically significant, raises the possibility that the

work of firefighters may exacerbate underlying hypertensive kidney disease. This trend could also potentially be due to an association between hypertension and other occupational exposures. Occupational exposures that may increase the risk of hypertension include particulate matter from fire smoke,<sup>49</sup> shift work,<sup>50</sup> work-related stress,<sup>51</sup> noise,<sup>52,53</sup> and perfluoroalkyl substances.<sup>54,55</sup> In a recent study, 69% of firefighters had hypertension and the prevalence of hypertension was higher among male firefighters than in the general population.<sup>56</sup>

In the epidemic of chronic kidney disease in Central America, kidney disease rarely co-occurred with diabetes or hypertension.<sup>57</sup> Biopsies from affected Central American workers showed interstitial nephritis.<sup>58</sup> A limitation of the current study was the inability to evaluate the association of ESRD due to interstitial nephritis with exposure surrogates due to the small number of observed cases.

The current study also does not provide information on the risk of chronic kidney disease that does not progress to ESRD. Other limitations include the lack of data on occupational heat exposure, surrogates of prolonged occupational heat exposure, and risk factors for ESRD such as hypertension,<sup>59</sup> diabetes mellitus,<sup>60</sup> and obesity.<sup>61</sup> In addition, cumulative exposure surrogates were negatively associated with leaving employment, which suggests that HRs obtained from analyses using g-estimation instead of matching on employment duration to account for the healthy worker survivor effect may be lower. The findings are also not generalizable to wildland firefighters because of differences in personal protective equipment (heavy encapsulating turnout gear with self-contained breathing apparatus vs. light, somewhat breathable fabrics and no respiratory protection), and the typical amount and duration of physical exertion (short bursts of very strenuous work for about 30 min a few times during a 24-h shift vs. relatively constant strenuous work during a 12-h shift each day during a 14-day deployment).

In summary, the firefighters in this study were not at an increased risk of ESRD compared to the general population and statistically significant associations of ESRD with exposure surrogates were not observed. Only nonstatistically significant positive associations of all ESRD, systemic ESRD, and hypertensive ESRD with exposed days were observed. Associations of ESRD due to interstitial nephritis with surrogates of exposure could not be assessed due to the small number of observed cases. Additional research using more sensitive outcome measures to evaluate potential kidney effects among firefighters is warranted.

## AUTHOR CONTRIBUTIONS

Lynne E. Pinkerton conceived the study and wrote the first draft of the manuscript. Stephen Bertke conducted the analysis. Travis L. Kubale, James H. Yiin, and Robert D. Daniels acquired the data and assembled the cohort. Matthew M. Dahm led the assessment of the exposure surrogates. All authors participated in the

interpretation and presentation of results, approved the final manuscript, and agreed to be accountable for all aspects of the work.

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## CONFLICTS OF INTEREST

Lynne E. Pinkerton currently works for Maximus, Inc., which holds contracts with CDC NIOSH for assistance, including the conduct of research studies. The remaining authors declare that there are no conflicts of interest.

## DISCLOSURE BY AJIM EDITOR OF RECORD

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

## DATA ACCESSIBILITY

The data that support the findings of this study are subjected to restrictions. Data are provided to NIOSH from third-party government agencies and are subjected to restrictions. Limited data may be available upon request to NIOSH.

## ETHICS APPROVAL AND INFORMED CONSENT

The study received approvals from the Institutional Review Boards of the National Institute for Occupational Safety and Health and the National Cancer Institute. Informed consent was waived for this records-based study.

## DISCLAIMER

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

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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