



## Original Contribution

# Infertility in a Cohort of Male Danish Firefighters: A Register-Based Study

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Our aim in this study was to examine infertility among male firefighters in Denmark. Thus, we established a cohort of 4,710 past and present male Danish firefighters through personnel and membership records obtained from employers and trade unions. Information on vital status and infertility from the Danish Civil Registration System, the In Vitro Fertilisation Register, and the National Patient Register for the period 1984–2017 was linked to cohort members using their Danish personal identification numbers. Hazard ratios and corresponding 95% confidence intervals were estimated for male-factor infertility and overall infertility through Cox regression analyses comparing the firefighters with 2 reference groups: a sample of employees and military men. Among the full-time firefighters, the risk of male-factor infertility was increased in comparison with the sample of employees (In Vitro Fertilisation Register model: hazard ratio = 1.46 (95% confidence interval: 1.10, 1.94); National Patient Register model: hazard ratio = 1.53 (95% confidence interval: 1.18, 1.98)). Results were less consistent using the military men as the reference group. Further, the increase in infertility seemed restricted to duration of time employed as a firefighter. No increase in risk of either male-factor infertility or overall infertility was seen among the part-time/volunteer firefighters. Thus, full-time firefighting was associated with a greater risk of being diagnosed with male-factor infertility in our cohort.

cohort studies; firefighters; heat; infertility; occupational exposure

Abbreviations: CI, confidence interval; CPR, Central Person Register; HR, hazard ratio; ICD-8, *International Classification of Diseases, Eighth Revision*; ICD-10, *International Classification of Diseases, Tenth Revision*; IVF, In Vitro Fertilisation; NPR, National Patient Register.

In the line of duty, firefighters face a wide range of imminent and obvious threats to both safety and health. While exposure at the scene of a fire potentially involves a multitude of different chemicals, several commonly present compounds have documented reproductive toxicity in humans (1, 2). In addition, firefighters are frequently at risk of hyperthermia—either by being directly affected by the heat from fires, during strenuous physical activity while wearing heavy turnout gear, or through subsequent use of saunas for chemical detoxification (3). Resulting genital heat stress may impair spermatogenesis and ultimately the quality of semen in males (4). Finally, emotional strain and night-shift work may also hypothetically influence fertility among firefighters (3).

Despite potential occupational exposure to reproductive hazards, no existing studies have specifically explored infertility among firefighters, to our knowledge. Only a few countries in the world have the advantage of nationwide registers with

individualized information on measures of infertility. In Denmark, all fertility treatments administered in both public and private clinics are registered through a mandatory and virtually complete reporting system (5). Fertility treatments in Denmark are generally free of charge, with a female age limit of 40 years and a restriction on use of in vitro techniques to couples without common children (5). Referral for treatment follows the internationally accepted clinical definition of infertility as failure to conceive after 1 year of trying (6). In addition, the Danish National Patient Register (NPR) contains information on sterilization procedures, conditions potentially related to infertility, and actual diagnoses of infertility from hospital contacts (7, 8).

Thus, our aim in this study was to examine infertility in relation to occupational firefighting exposure in a cohort of male Danish firefighters, through the use of data from several objective national registers.

## METHODS

### Firefighter cohort

Subjects for this study were included from a previously established cohort of 17,134 Danish firefighters (9–11). The construction of this cohort was initiated through systematic collection of personnel and membership records from fire services and firefighter unions throughout Denmark. In addition, records of persons reporting a job title in the firefighting field from the Danish Civil Registration System were added (10, 12). Apart from information on time and type of employment, a unique 10-digit personal identification number, the Central Person Register (CPR) number, was retrieved for each firefighter. Since April 2, 1968, this number has served as the key to all public administrative data, summarizing both sex and date of birth for all permanent residents in Denmark (12).

Subsequently, further information on employment history from the Danish Supplementary Pension Fund Register was linked to members of the cohort using their CPR numbers (13). Since 1964, this register has kept mandatory and permanent employment records on industry and company type by wage earners aged 16–66 years working at least 9 hours/week (13). With this additional source of information, otherwise unidentified periods of firefighting were added and previously established employment was validated (10).

### Study population

With initial evaluation of our original cohort records, inclusion of subjects for analyses on infertility was restricted to males born from January 1, 1964, to March 23, 1992, with valid CPR numbers and actual exposure to occupational firefighting, determined according to specific job titles and functions ( $n = 5,674$ ). Subsequently, firefighters employed for less than a year or only before December 31, 1992, were excluded. The remaining criteria for exclusion were emigration to Greenland or having undergone

a vasectomy or received a hospital diagnosis of a condition clearly related to infertility (see Web Table 1, available at <https://academic.oup.com/aje>) before first firefighting employment (Figure 1).

### Reference groups

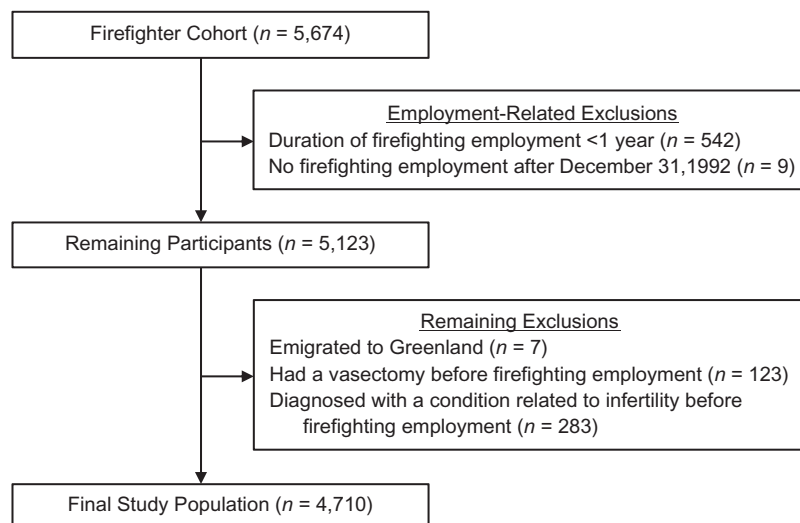
The systematic selection of healthy individuals, both upon recruitment and continuously throughout employment, may potentially bias study results when firefighters are simply compared with the general population. In order to minimize this “healthy worker effect,” we created 2 external occupational reference groups using data from the Supplementary Pension Fund Register (13).

Initially, records on male employees of all types were extracted entirely according to year of birth as a random sample reflecting the general Danish working population. Because of resemblance with firefighters regarding both baseline fitness and socioeconomic profile, all men ever employed by the Danish military were chosen as a second comparison group. With the exception of firefighting employment, these 2 reference groups were shaped according to the same criteria as the firefighter cohort, providing a comparison sample of 49,971 general Danish workers and 177,034 military men.

### Exposure

In an attempt to account for both timing of exposure and intensity of exposure, we used surrogate measures in the form of period and type of firefighting employment. For period of employment, the entire interval from the very first day of any firefighting job to the last day was considered the period in which the firefighter had been exposed.

While the larger cities in Denmark mainly employ full-time firefighters, rural areas are generally covered by either part-time or volunteer firefighters. Because the part-time and volunteer



**Figure 1.** Construction of a study population of male Danish firefighters born in 1964–1992. The cohort included men with valid Danish personal identification numbers born between January 1, 1964, and March 23, 1992, and occupationally exposed to firefighting in Denmark.

workers in this cohort had undergone essentially the same basic training and performed the same tasks, they were grouped together in analyses. Firefighters with several different types of employment were categorized as full-time workers if they had ever been such (10). According to this definition, the share of full-time workers spending at least half of their firefighting time with this employment type was 94%.

### Information on infertility

Information on diagnoses of, conditions related to, and treatments for infertility was retrieved from both the Danish In Vitro Fertilisation (IVF) Register and the Danish NPR (7, 14, 15).

Since January 1, 1994, records of all assisted reproductive technology treatments involving in vitro techniques have been gathered in the IVF Register through mandatory reporting from all public and private fertility clinics in Denmark (5). Starting in 2005, this register was expanded to include intrauterine insemination (14). Apart from the specific methods used, information on dates of treatment initiation and cause(s) of infertility was available. While the key identifier for all records is the CPR number of the woman being treated, the corresponding CPR numbers of partners involved are generally also recorded. Thus, identifying male infertility required linkage of both cohort and reference group members to women with IVF records through at least one of the following criteria: 1) registration as a partner in the actual IVF Register; 2) marriage to a woman at the time of her IVF treatment, determined by marital history from the Civil Registration System; and 3) cohabiting with a woman at the time of her IVF treatment, according to residence history from the Civil Registration System (12). Shared residence was further restricted to couples aged at least 20 years at some point during their partnership and differing by no more than 10 years in age. In addition, the address had to have been shared for at least a month with only 1 woman in the household meeting all requirements. Our infertility data from the IVF Register covered the period January 1, 1994, to March 23, 2017.

As an additional source of fertility information, the NPR contains records of all hospital admissions in Denmark since January 1, 1977. While specific diagnoses and surgeries with exact attestation of time have been documented from the introduction of this register, outpatient and treatment data were added in 1995 and 1999, respectively (8). Diagnoses were coded according to a modified Danish version of the *International Classification of Diseases, Eighth Revision* (ICD-8), and the *International Classification of Diseases, Tenth Revision* (ICD-10), with January 1, 1994, as the separating date. Similarly, classification of surgeries according to the Danish Classification of Surgical Procedures and Therapies was replaced by the Nordic Classification of Surgical Procedures in 1996 (8). Nonsurgical procedures are coded using a Danish classification for treatments, care, and prophylaxis in the Health Care Classification System (8).

Through direct linkage of CPR numbers, diagnoses of male infertility were identified for both members of the cohort and the reference groups using the ICD-8 codes 60609–60699 and the ICD-10 codes N46–N46.9 in the NPR. Information concerning conditions related to infertility (see Web Table 1 for full list) and sterility through vasectomy (procedure codes 55940–55960 and KKFD46) was added subsequently.

With the previously established linkage to women through either marriage or shared residence, female cases of infertility and connected treatments were sought out as well (associated with male factors (ICD-10 code N97.4), all causes (ICD-8 codes 62800–62899 and ICD-10 code N97), and Health Care Classification System procedures BJFL0–BJFL9). While diagnoses of male infertility were available starting from the introduction of the register in 1977, separation of female infertility according to underlying factors only emerged as an option with the implementation of the ICD-10 in 1994. Our data collection from the NPR ended on October 11, 2016.

### Statistical analysis and modeling

Because fertility is most often defined and modified through partnership, outcomes for both men and women were assessed in several models using data from either the IVF Register or the NPR (16), as follows.

1. In the male-IVF model, the definition of infertility rested on partnering with a woman at the time of her treatment for male-factor infertility according to records from the IVF Register.
2. In the all-IVF model, the definition of infertility was expanded to partnering with a woman at the time of her treatment, regardless of underlying causes, in the records from the IVF Register.
3. In the male-NPR model, the definition of infertility through NPR records included directly given diagnoses of male infertility as well as partnering with a woman at the time of her infertility diagnosis if the underlying cause was male.
4. In the all-NPR model, the definition of infertility through NPR records involved all diagnoses of infertility given either directly to the man or to a woman during the time of partnership. Fertility procedures used during the partnership were counted as well.

In the IVF models, follow-up started on the latest of either January 1, 1994, the 20th birthday, or the date of first firefighting employment for the firefighters. For the NPR models, the beginning of follow-up was the latest of either January 1, 1984, the 20th birthday, or the date of first firefighting employment. In all models, follow-up ended on the first of either the date of death, emigration, disappearance, vasectomy, diagnosis of a condition related to infertility (Web Table 1), diagnosis of infertility, or the end of the actual study period (March 23, 2017, for the IVF models and October 11, 2016, for the NPR models).

We performed Cox regression analyses to calculate hazard ratios and corresponding 95% confidence intervals. Male age (in years) was used as the time scale in all models. Calendar time was included as a time-varying covariate using 5-year intervals.

Because the indication for examining fertility typically arises from a contradiction between desire and ability to reproduce, men in relationships with female partners are intuitively at a higher risk of discovering infertility. In consequence, we restricted both cohort and reference groups to men with at least 1 female partnership during the entire follow-up period in a subanalysis. Female partnership was defined through either marriage or shared residence according to the previously applied

criteria. In addition to male age and calendar time, we also adjusted for birth year of the female partner in 5-year intervals in this analysis, acknowledging the crucial role of aging in female fertility.

Finally, we also performed an internal analysis examining potential differences in risk during exposure (employment) and after exposure ended between full-time and part-time/volunteer firefighters with at least 1 female partnership during follow-up.

Statistical analyses were conducted using Stata, version 14.2 (StataCorp LLC, College Station, Texas).

## RESULTS

Among the male Danish firefighters who were eligible for infertility analyses, 1,253 were full-time employees and the remaining 3,457 worked only part-time or volunteered. The firefighters were generally slightly older than both reference groups at the beginning of follow-up, because their time at risk

started at first employment. However, the most evident difference between the groups related to the number of female partners during follow-up. While more than 85% of the firefighters had a female partner as defined through either marriage or shared residence during follow-up, the corresponding numbers for the military personnel and the sample of employees were 66.8% and 73.1%, respectively. Selected characteristics of both cohort and reference groups are listed in Table 1.

For the full-time firefighters, the number of infertility cases observed ranged from 49 in the most restrictive model (male IVF) to 99 in the broadest model (all NPR) (Table 2). While the periods of follow-up differed significantly between the IVF and NPR models, the infertility data retrieved from the separate registers overlapped somewhat in the shared interval. In all models, hazard ratios were increased for the full-time firefighters as compared with both of the 2 reference populations. In addition, the models strictly assessing male-factor infertility yielded the highest hazard ratios among the full-time firefighters (hazard ratio (HR) = 1.46 (95% confidence interval (CI): 1.10,

**Table 1.** Characteristics of the Male Firefighter Cohort and Reference Groups, Danish Firefighter Study, 1984–2017

Characteristic	Firefighter Cohort						Reference Group					
	Full-Time Firefighters			Part-Time/Volunteer Firefighters			Military Employees			Sample of Danish Employees		
	No. of Persons	%	Mean (SD)	No. of Persons	%	Mean (SD)	No. of Persons	%	Mean (SD)	No. of Persons	%	Mean (SD)
Male subjects												
No. eligible for analysis	1,253			3,457			177,034			49,971		
Mean birth year	1973			1975			1973			1977		
Age at entry in the male IVF model <sup>a</sup>	27.0 (4.9)			28.1 (6.1)			22.8 (3.3)			21.9 (3.0)		
Age at entry in the male NPR model <sup>b</sup>	26.0 (5.2)			27.8 (6.2)			20.0 (0)			20.0 (0)		
Children <sup>c</sup>												
Mean no. of children	1.4 (1.0)			1.4 (1.1)			1.6 (1.2)			1.2 (1.2)		
Total no. of children												
0	272	21.7		861	24.9		42,143	23.8		19,025	38.1	
1	450	35.9		1,012	29.3		34,337	19.4		12,169	24.4	
2	383	30.6		1,076	31.1		66,719	37.7		12,620	25.3	
≥3	148	11.8		508	14.7		33,835	19.1		6,157	12.3	
Female partners and relationships												
No. of female partners during follow-up <sup>d</sup>												
0	109	8.7		485	14.0		58,845	33.2		13,432	26.9	
≥1	1,144	91.3		2,972	86.0		118,189	66.8		36,539	73.1	
Mean birth year	1973			1975			1974			1977		

Abbreviations: IVF, In Vitro Fertilisation; NPR, National Patient Register; SD, standard deviation.

<sup>a</sup> In the male IVF model, infertility was defined as partnering with a woman being treated for male-factor infertility according to records from the IVF Register.

<sup>b</sup> In the male NPR model, infertility was defined as a diagnosis of male infertility given directly to the male, as well as partnering with a woman at the time of her infertility diagnosis if the underlying cause was male, according to records from the NPR.

<sup>c</sup> At the end of follow-up on March 23, 2017.

<sup>d</sup> Partnership was defined through either marriage or shared residence.

1.94) in the male IVF model and HR = 1.53 (95% CI: 1.18, 1.98) in the male NPR model, with the sample of employees used as the reference group) after adjustment for male age and calendar time (Table 2).

In the subanalyses restricting the data to males with a minimum of 1 female partner during follow-up, as defined through either marriage or shared residence, and adjusting for birth year of the female partner (in 5-year intervals), male age, and calendar time, results were essentially unchanged using the sample of employees as the reference group, with similar hazard ratios for the full-time firefighters, especially in the male models (HR = 1.30 (95% CI: 0.96, 1.74) in the male IVF model and HR = 1.31 (95% CI: 1.00, 1.73) in the male NPR model) (Table 2). Comparing the full-time firefighters with the military men, the increases in hazard ratios observed in the main analyses were generally reduced in the subanalyses. For the part-time/volunteer firefighters,

hazard ratios were generally not increased in comparison with either reference group (Table 2).

Finally, the internal analysis of firefighters with at least 1 female partner during follow-up showed marked increases in hazard ratios for the full-time firefighters in both of the male models during exposed time at risk and no increase after employment ended (for exposed time, HR = 2.15 (95% CI: 1.34, 3.45); for unexposed time, HR = 1.00 (95% CI: 0.45, 2.21) in the male IVF model with the part-time/volunteer firefighters used as the reference group) (Table 3).

**DISCUSSION**

With this study on infertility among male firefighters, we assessed several nationwide register-based models. We found a clear indication of increased risk of male-factor infertility in the

**Table 2.** Relationship Between Type of Firefighting and Infertility Among 4,710 Male Danish Firefighters, Determined Using a Sample of Danish Employees and Military Men as Reference Groups, Danish Firefighter Study, 1984–2017

Infertility Model and Type of Analysis	Firefighter Cohort and Reference Group										
	No. of Cases	Full-Time Firefighters (n = 1,253)				Part-Time/Volunteer Firefighters (n = 3,457)					
		Sample of Danish Employees		Military Men		No. of Cases	Sample of Danish Employees		Military Men		
	HR	95% CI	HR	95% CI	HR		95% CI	HR	95% CI	HR	95% CI
Male IVF model <sup>a</sup>											
Crude <sup>b</sup>	49	1.40	1.05, 1.86	1.42	1.07, 1.89	66	0.88	0.69, 1.13	0.90	0.71, 1.15	
Adjusted <sup>c</sup>	49	1.46	1.10, 1.94	1.40	1.06, 1.86	66	0.86	0.67, 1.11	0.83	0.65, 1.06	
Subanalysis <sup>d</sup>	46	1.30	0.96, 1.74	1.18	0.88, 1.57	63	0.80	0.62, 1.03	0.72	0.56, 0.92	
All-IVF model <sup>e</sup>											
Crude	88	1.15	0.93, 1.41	1.10	0.89, 1.35	173	1.09	0.93, 1.26	1.04	0.90, 1.21	
Adjusted	88	1.21	0.98, 1.49	1.09	0.88, 1.33	173	1.06	0.91, 1.24	0.95	0.82, 1.11	
Subanalysis	83	1.04	0.84, 1.30	0.88	0.71, 1.10	170	0.97	0.83, 1.13	0.81	0.70, 0.94	
Male NPR model <sup>f</sup>											
Crude	59	1.49	1.15, 1.94	1.37	1.06, 1.77	98	1.21	0.98, 1.48	1.10	0.91, 1.35	
Adjusted	59	1.53	1.18, 1.98	1.36	1.05, 1.75	98	1.19	0.97, 1.46	1.00	0.82, 1.22	
Subanalysis	54	1.31	1.00, 1.73	1.10	0.84, 1.44	92	1.08	0.87, 1.33	0.84	0.68, 1.03	
All-NPR model <sup>g</sup>											
Crude	99	1.40	1.14, 1.71	1.41	1.16, 1.72	167	1.15	0.99, 1.35	1.16	1.00, 1.36	
Adjusted	99	1.40	1.14, 1.71	1.41	1.16, 1.72	167	1.14	0.98, 1.34	1.12	0.96, 1.30	
Subanalysis	95	1.22	0.99, 1.50	1.11	0.91, 1.36	161	1.03	0.88, 1.21	0.89	0.76, 1.04	

Abbreviations: CI, confidence interval; HR, hazard ratio; IVF, In Vitro Fertilisation; NPR, National Patient Register.

<sup>a</sup> In the male IVF model, infertility was defined as partnering with a woman being treated for male-factor infertility according to records from the IVF Register.

<sup>b</sup> HRs were adjusted for male age (in years) as the time scale.

<sup>c</sup> HRs were adjusted for male age (in years) as the time scale and calendar time in 5-year intervals (time-dependent).

<sup>d</sup> Subanalysis including only men with a minimum of 1 female partner, as defined through either marriage or shared residence, during the entire period of follow-up. HRs were adjusted for male age (in years) as the time scale, calendar time in 5-year intervals (time-dependent), and birth year of the female partner (in 5-year intervals).

<sup>e</sup> In the all-IVF model, infertility was defined as partnering with a woman being treated for infertility, regardless of underlying causes, according to the IVF Register.

<sup>f</sup> In the male NPR model, infertility was defined as being directly given a hospital diagnosis of male infertility, as well as partnering with a woman at the time of her infertility diagnosis if the underlying cause was male, according to records from the NPR.

<sup>g</sup> The all-NPR model included all diagnoses of infertility given either directly to the man or to a woman during the time of partnership, according to records from the NPR. Fertility procedures used during the partnership that were listed in this register were counted as well.



**Table 3.** Relationship Between Employment Status and Infertility Among 4,116 Male Danish Firefighters With a Minimum of 1 Female Partner During the Entire Follow-up Period, Danish Firefighter Study, 1984–2017

Infertility Model <sup>a</sup> and Type of Firefighting	Employment Period							
	During Employment				After Employment			
	No. of Person-Years	No. of Cases	HR	95% CI	No. of Person-Years	No. of Cases	HR	95% CI
Male IVF model <sup>b</sup>								
Full-time workers	14,064	38	2.15	1.34, 3.45	3,599	8	1.00	0.45, 2.21
Part-time workers/volunteers	24,260	34	1.00	Referent	12,901	29	1.00	Referent
Male NPR model <sup>c</sup>								
Full-time workers	15,261	43	1.70	1.12, 2.59	3,153	11	1.05	0.54, 2.06
Part-time workers/volunteers	25,217	50	1.00	Referent	11,671	42	1.00	Referent

Abbreviations: CI, confidence interval; HR, hazard ratio; IVF, In Vitro Fertilisation; NPR, National Patient Register.

<sup>a</sup> HRs were adjusted for male age (in years) as the time scale, calendar time in 5-year intervals (time-dependent), and birth year of the female partner (in 5-year intervals).

<sup>b</sup> In the male IVF model, infertility was defined as partnering with a woman being treated for male-factor infertility according to records from the IVF Register.

<sup>c</sup> In the male NPR model, infertility was defined as being directly given a hospital diagnosis of male infertility, as well as partnering with a woman at the time of her infertility diagnosis if the underlying cause was male, according to records from the NPR.

Danish full-time firefighters as compared with a sample of male employees. When comparing the full-time firefighters with military employees, results were more ambiguous. In an internal subanalysis using part-time/volunteer firefighters as the reference group, the increase in risk among the full-time firefighters seemed to be confined to their employed time at risk. The part-time/volunteer workers, who were presumably less firefighting-exposed, had no significant increase in risk of either male-factor infertility or overall infertility.

Because maturing cells in the testicles may be affected by potential occupational or environmental exposures, the approximately 74 days required for spermatogenesis constitutes a window of male reproductive susceptibility (17). Once damage has been induced, sperm cells have a limited capacity for repairs, and resulting changes can often be detected in the volume, concentration, motility, and morphology of sperm in semen (6, 16).

In the case of firefighters, a range of potential occupational hazards may mediate impairment of male fertility. At present, the most plausible mechanism behind disturbances in the reproductive ability of firefighters involves genital heat stress incurred through frequent hyperthermia experienced either at the fire scene or subsequently with systematic chemical detoxing regimens using saunas (3, 4, 18). Aside from the extrinsic heat radiating directly from a fire, firefighters may also be affected by intrinsic hyperthermia generated through severe physical activity while wearing heavy and insulating turnout gear (3). Even slight, transient increases in scrotal temperatures may modify the quality of maturing semen negatively (4).

As a second potential source of adverse fertility outcomes in firefighters, several chemicals commonly present during firefighting operations have shown reproductive toxicity in males, mediated through either endocrine disruption or direct cytotoxicity (1, 19). Among the exposures primarily relevant to firefighters, polychlorinated and polybrominated biphenyls, polycyclic

aromatic hydrocarbons, benzene, trichloroethylene, vinyl chloride, perfluoroalkyl substances, cadmium, and lead are either known for or suspected of impairing male fertility (1, 19, 20). While several of these chemicals may appear at the scene of a fire in relation to combustion, others are released through extinguishing agents or structural components as ceilings and walls are pulled apart (21). In addition, emotional trauma or stress added through unpredictable rescue assignments may reduce male testosterone levels, weaken the libido, or ultimately cause impotence (3). Finally, exposure to noise, physical exertion, and night work have also been suggested as contributing factors (3).

In our study, infertility was measured either through partnering with a woman enlisted for infertility treatment (IVF models) or receiving a hospital-based diagnosis of actual infertility (NPR models). Clinical infertility differs from most epidemiologic outcomes, as the capacity to reproduce is typically only assessed during actual attempts at pregnancy, and both the inability to conceive within a given time frame and the resulting behavior in seeking medical help to do so are affected by several somewhat unpredictable factors, both male and female (6, 22). Interpretation of results should, therefore, aim to reflect these limitations.

In our choice of reference groups, we attempted to account for both male general health status and socioeconomic profile. Despite these expected similarities between firefighters and the reference groups, especially the military employees, we found notable differences in the percentage with at least 1 female partner as defined through either marriage or shared residence during follow-up (Table 1). In industrialized countries, most pregnancies are planned, and being in an established partnership may indicate a desire to have a family and ultimately facilitate visits to a fertility clinic (6). In our subanalyses, the observed increase in male-factor infertility remained

after restriction of follow-up to males with a minimum of 1 established female partner, using the sample of employees as the reference group. With the military men as the reference group, the observed increase in male-factor infertility was notably reduced in these analyses. The similarities in risk between the full-time firefighters and the military men may originate in similar types of lifestyle confounding. However, military men may also be exposed to various occupational hazards, potentially affecting their reproductive capacity.

Considering the notable differences in both age at entry and percentage with partnerships between the respective reference groups and the firefighters, we also performed an internal analysis differentiating risk according to employment status. Compared with the part-time/volunteer workers, the hazard ratios for male infertility were only elevated among the full-time firefighters during active employment, which is suggestive of an occupational dose-dependent association (Table 3). Confounding factors potentially related to either male or female infertility would also most likely remain stable across these changes in occupational status (23). In this scenario, reproductive damage was temporary, with no long-term deficits. On the limiting side, the distribution of years at risk was notably skewed in this analysis among both types of firefighters with the greatest amount of follow-up time contributed in the exposed category. With a marked imbalance in risk time, the possibility for bias in these estimates cannot be completely rejected.

An important further limitation in our study was the relatively low number of full-time firefighters in the cohort. While occupational information on our cohort is collected and confirmed through multiple sources, type and time of employment are only surrogate measures for actual toxic exposure. However, several previous studies have documented far greater fire attendance among full-time firefighters in comparison with both part-time and volunteer workers, justifying the perception of this group as more exposed (24–26).

In Denmark, less than half of the adult population is married. Sharing a residence with a person of the opposite sex may not necessarily equal partnership as assumed in our analyses. In order to limit errors from this type of misclassification, we applied restrictions on age and other potential partners at the same address. Finally, we had no information on potentially important lifestyle factors, such as smoking, alcohol consumption, physical activity, and diet.

On the positive side, our study had a very long follow-up period (more than 32 years in the most comprehensive model) and high-quality infertility data from several nationwide health registries. Few countries in the world have the advantage of individualized register data on fertility and assisted reproductive technology treatments collected through mandatory reporting from both the public and private health-care sectors in a system with free medical access (5). This approach allows for accurate identification of both male-factor infertility and overall couple infertility, as well as exclusion or censoring of subjects choosing permanent contraception (vasectomy procedures) or suffering from conditions potentially related to infertility.

In our study of a Danish cohort, male full-time firefighters had an increased risk of being diagnosed with male-factor infertility in comparison with a random sample of employees. Results were less consistent when comparing the firefighters with a military reference group. The increase in risk seemed confined

to actual firefighting employment time, potentially indicating an occupational association. Because the inability to conceive within a given time frame and the resulting measures taken to alleviate reproductive problems are influenced by several somewhat unpredictable factors, both male and female, further studies assessing (especially) the biological consequences of firefighting on male fertility are needed. In the meantime, awareness of potentially preventable or reducible aspects of occupational exposure to heat and toxic chemicals should be emphasized among firefighters.

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