Nested Case-Control Study of Selected Systemic Autoimmune Diseases in World Trade Center Rescue/Recovery Workers

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an ‘Accepted Article’, doi: 10.1002/art.39059
© 2015 American College of Rheumatology
Received: Jul 24, 2014; Revised: Dec 23, 2014; Accepted: Jan 29, 2015
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Running title: Autoimmune Diseases and World Trade Center Work

Acknowledgements: This publication was made possible by NIOSH cooperative agreement #1U01OH010513-01. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NIOSH.

Competing financial interests: The authors declare no competing interests.
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Abstract

Objective: To test the *a priori* hypothesis that acute (arrival time at the World Trade Center site) and chronic (months of World Trade Center-related work) exposures were associated with risk of new onset systemic autoimmune diseases.

Methods: We performed a nested case-control study by individually matching each rheumatologist-confirmed case diagnosed between 9/12/2001 and 9/11/2013 (n=59) to 4 randomly selected controls (n=236) that were matched for year of hire (±1 year), gender, race and work assignment (firefighter or Emergency Medical Service). Rheumatologists were blinded to exposure status. Conditional odds ratios (COR) and 95% confidence intervals (95% CI) were derived from exact conditional logistic models.

Results: Rheumatoid arthritis (37%) was the most common autoimmune diagnosis, followed by spondyloarthritis (22%), inflammatory myositis (14%), systemic lupus erythematosus (12%), systemic sclerosis (5%), Sjögren’s syndrome (5%), antiphospholipid syndrome (3%) and granulomatosis with polyangiitis (Wegener’s) (2%). The COR of autoimmune disease increased by 13% for each additional month worked at the site (95% CI 1.02-1.26) and was independent of the association between high acute exposure (working during the morning of 9/11/2001) and disease outcome, which was elevated, but not statistically significant (COR 1.85 95% CI 0.86-3.89).

Conclusion: Prolonged work at the WTC site, independent of acute exposure, was an important predictor of post-9/11 systemic autoimmune diseases. The World Trade Center Health Program
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should expand surveillance efforts for those with extended exposures as early detection can facilitate early treatment, which has been shown to minimize organ damage and improve quality of life.

244 words
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Genetic factors are known to influence the development of autoimmune diseases, although heritability studies using identical twins suggest only low to moderate concordance rates (1), depending on the disease, implying that environmental, occupational, or other factors also play an important role in disease development. Compared with the growing body of genetic research, fewer resources have been allocated to studying environmental/occupational exposures. One well-studied environmental exposure is silica, a basic component of soil, sand, granite, and many other minerals, which has been associated with rheumatoid arthritis (2), systemic sclerosis (3, 4), systemic lupus erythematosus (5), dermatomyositis (1), Sjögren’s syndrome (6) and risk of ANCA-associated vasculitis (7). Autoimmune diseases have also been associated with environmental exposures to metals, ozone, hydrocarbons, organic solvents, pesticides, particulates, and, in the case of cigarette smoking, has been shown to increase the formation of autoantibodies (8-11). In general, these autoimmune conditions were associated with chronic environmental exposures acquired over years or even decades, presumably in individuals with genetic predispositions.

The terrorist attacks on the World Trade Center (WTC) buildings and the subsequent building collapses and fires exposed rescue/recovery workers and residents to aerosolized WTC Dust – an amalgam of pulverized cement, glass fibers, silica, asbestos, lead, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and polychlorinated furans and dioxins (12). While it is widely known that most of the Fire Department of the City of New York (FDNY) workforce of firefighters and Emergency Medical Service (EMS) workers arrived at the disaster site within days or even hours of 9/11/2001, it may be less well known that many continued to work at the site for up to 10 months, potentially experiencing chronic exposures to re-suspended particulate...
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matter. Evidence of the effects of this intense WTC-exposure, both acute and chronic, is abundant, as more than 70% of FDNY workers reported one or more respiratory and aerodigestive symptoms in the first post-9/11/2001 year, which, over time, led to physician-diagnosed chronic conditions including asthma, chronic bronchitis, rhinosinusitis, gastroesophageal reflux disease and cancer (13, 14). We have also documented dramatic post-9/11/2001 declines in lung function consistent with the increased incidence of these respiratory conditions (15, 16).

The full spectrum of health consequences of WTC-exposure remains unknown. The FDNY-WTC Health Program (FDNY-WTCHP) follows a cohort of nearly 16,000 firefighters and EMS workers who worked at the WTC site. Clinical observations of rare systemic autoimmune diseases (SAID) in these mostly male workers triggered a preliminary medical-record review. The current nested case-control study was designed to assess whether acute or chronic 9/11/2001-related work exposures were associated with incident SAID including: systemic lupus erythematosus, antiphospholipid syndrome, systemic sclerosis, inflammatory myositis, Sjögren’s syndrome, rheumatoid arthritis (RA), spondyloarthritis, granulomatosis with polyangiitis (Wegener’s), and eosinophilic granulomatosis with polyangiitis (Churg-Strauss).
METHODS

Data sources

We obtained information from FDNY employee databases (race, gender, FDNY hire date); from self-administered health questionnaires (smoking status, symptoms of post-traumatic stress disorder (PTSD), and acute and chronic WTC-related exposures); and from rheumatologist-confirmed case records.

Health Questionnaires

Cigarette smoking was characterized as “ever/never” by combining current and former smokers into a single “ever” category. Smoking status was taken from participants’ most recent questionnaires. The earliest questionnaire date was 2008, the most recent was 2014, and the median was 2013. Symptoms of PTSD were assessed from the PCL-17 checklist (17), which, since 2005, is routinely administered as part of the mental health questionnaire. We considered symptoms of PTSD as present if the participant attained a total score of ≥44 and scored into each of the three domains (re-experiencing, avoidance, and hyper-arousal) (18). PTSD status was taken from participants’ first mental health questionnaire. The earliest questionnaire date was 2006, the most recent was 2014, and the median was 2007.

Exposure Ascertainment

Measures of WTC-exposure were defined as acute or chronic. Acute exposure was based on earliest time of arrival at the WTC site, and was taken from the first post-9/11/2001 health questionnaire, which was administered starting October 2001. We categorized arrival time into
two groups: arriving on the morning of 9/11/2001 versus arriving any time thereafter until 7/25/2002 (19), when the site was closed to FDNY workers. Questions about chronic exposure, or duration of work, were added to the monitoring questionnaires in 2002. Members were asked to indicate the months in which they worked at least 1 day at the WTC site. Duration was measured by summation of the number of months a member worked between 9/11/2001 and 7/25/2002 (20). Since all study participants reported work at the WTC site, the minimum exposure duration was 1 month.

Study population

The FDNY-WTCHP schedules monitoring evaluations of the active and retired WTC-exposed workforce every 12 to 18 months. The monitoring visit includes a physical exam and completion of self-administered physical and mental health questionnaires. In 2005 we amended the physical health questionnaire to include a question about doctor-diagnosed autoimmune disease and, in 2009, created an autoimmune registry to capture potential cases in two ways. Most commonly, potential cases were reported in the physical health questionnaires. Specifically the question asks: “Since your last FDNY WTC annual medical, has a doctor or health professional told you that you have arthritis or any autoimmune disease listed below?” Answer choices include “rheumatoid arthritis,” “lupus,” “polymyositis/dermatomyositis,” and “other, for example, psoriatic arthritis or scleroderma.” Individuals are not limited to one response. Additionally, the registry is populated by potential cases that were reported by a patient to an FDNY physician either during a medical monitoring exam or during a treatment visit. This information is recorded as part of the patient medical history.
The registry clinician (NJ) calls every potential case in the autoimmune registry. During the study period there were 738 potential cases of self-reported SAID. After a brief phone call, 522 (71%) were determined to be “reporting errors,” mostly people who had osteoarthritis and not rheumatoid arthritis. Of the 216 possible cases (i.e., not reporting errors), we were unable to contact 59, either by phone or mail; 72 were contacted and determined to be “possible cases,” but they failed to submit adequate documentation by the study close. The final population consisted of 59 medically confirmed cases, 51 cases originating from the annual monitoring questionnaires and 8 additional cases originating from FDNY physician notes.

Medically confirmed cases required diagnostic documentation from their treating physician/rheumatologist. Documentation from the treating rheumatologist must include the specific SAID diagnosis and approximate diagnosis date (month and year). If there was any supporting lab work, imaging, pathology, or relevant treatment notes, we asked that it also be sent to the registry clinician for review. Before final confirmation, all cases were re-reviewed by our SAID case consultation group which included two rheumatologists (JB and QB) blinded to WTC-exposure history. Unanimous agreement was required for confirmation. Only confirmed cases were used for analyses.

The population at-risk consisted of 15,484 WTC-exposed firefighters and EMS workers. Inclusion criteria required: having completed a monitoring questionnaire during or after 2005, thereby having had the potential to self-report; not having a pre-9/11/2001 SAID diagnosis; not having an unconfirmed SAID diagnosis in the autoimmune registry; having known exposure to the WTC site (known time and date of first arrival and number of months worked at the WTC...
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site); having a working telephone number; and having provided written consent for research.

After these exclusions, the study population totaled 13,617 (87.9%).

For the current analysis, post-9/11/2001 diagnoses of interest included rheumatologist-confirmed diagnoses of any of the following: systemic lupus erythematosus, antiphospholipid syndrome, systemic sclerosis (both diffuse and limited), inflammatory myositis (dermatomyositis, polymyositis, or inclusion-body myositis), Sjögren’s syndrome, rheumatoid arthritis (RA), spondyloarthritis (i.e., psoriatic arthritis and ankylosing spondylitis), granulomatosis with polyangiitis (Wegener’s) and eosinophilic granulomatosis with polyangiitis (Churg-Strauss). All diagnoses met American College of Rheumatology criteria (21-27). The primary analyses combined all SAID as the outcome of interest; additional analyses were performed for the SAID outcome with the greatest incidence – RA.

We accrued cases of SAID diagnosed between 9/12/2001 and 9/11/2013. After accrual was closed, we randomly selected 4 matched controls per case using incidence density sampling based on the following criteria: year of FDNY hire (within 1 year), gender, race and work assignment (firefighter or EMS). We did not match on age, as in this cohort, age and year of hire are highly correlated (r=0.91). Potential controls were called by the registry clinician to verify their non-case status as of two years prior to the diagnosis date of their matched case (28).

Consistent with incidence density sampling, controls were eligible to become a case at a later date and could also serve as a control for more than one case.
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This study has been approved by the institutional review board at Montefiore Medical Center, Bronx, New York and is in compliance with the Helsinki Declaration.

Statistical Analysis

Preliminary analyses included examination of demographic and other characteristics, including acute and chronic exposure, by case or control status. Acute exposure (arrival time) was categorized as arriving on the morning of 9/11 versus arriving after. Chronic exposure (duration) was treated as a continuous variable (per month) and was also grouped into high versus low using a median split. For univariable and multivariable analyses we constructed exact conditional logistic regression models for the odds of being a SAID case and separately, for the odds of being a case of RA, the most common individual diagnosis. The exact method was appropriate given our small sample size (29). The primary predictors of interest were acute and chronic exposure, but based on factors suggested in the literature, we also examined the possible effects of smoking history (8) and PTSD symptoms (30) (present/absent) on the SAID outcome, and separately, on the RA outcome. Conditional odds ratios (COR) and 95% confidence intervals (95% CI) were derived from these conditional models.

To adjust for possible disease latency, we performed a sensitivity analysis where we constructed an exact conditional logistic model after removing 5 case strata in which the cases were diagnosed within 2 years of 9/11/2001. Similarly, we carried out a sensitivity analysis for the model predicting RA, removing the 3 strata with cases diagnosed within 2 years of 9/11/2001.

All analyses were performed using the statistical software SAS (version 9.4; SAS Institute Inc.,
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Cary, N.C., USA) using α=0.05 to indicate statistical significance.

RESULTS

Overall, we confirmed 59 cases of SAID; the most common individual diagnosis was RA (22 cases or 37.3%). The number of diagnoses increased after 2004, peaking between 2005 – 2010 (Table 1). Most cases (n=56; 94.9%) occurred in men. Characteristics of cases and controls are displayed in Table 2. Ascertainment of exposure, both acute and chronic, usually occurred well before diagnosis. The median time between ascertainment of arrival time to the WTC site from the monitoring questionnaire and diagnosis of SAID was 5 years; the median time between ascertainment of duration of exposure from the monitoring questionnaire and diagnosis of SAID was 3 years because duration questions were a later addition to our monitoring program. In all final models (Table 3), cases were significantly more likely to have reported prolonged work exposure to the WTC site. Using duration of exposure as a continuous variable, the COR of SAID was 1.13 (95% CI 1.02-1.26) or 13% increase for each month worked at the WTC site. As a dichotomous variable (median split at 2 month), the COR for duration of exposure was 2.40 (95% CI 1.16-5.23). Results were similar in models where we removed all EMS cases (n=5) and their matched controls (n=20) (data not shown).

In the sensitivity analysis to adjust for potential disease latency, we removed 5 case strata diagnosed within 2 years of 9/11/2001. The effect of duration as a continuous variable increased to 17% per month (COR, 1.17 [95% CI, 1.05-1.31]) and similarly increased when we used a median split for duration of work at the site (COR 3.11 [95% CI 1.40-7.51]).
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We also examined acute WTC-exposure and found that cases were somewhat more likely to have arrived at the WTC site during the morning of 9/11/2001, although the effect of early arrival was not statistically significant in either univariable (COR 1.85 [95% CI 0.86-3.89]) or multivariable models. In a model with a term controlling for duration, the effect of arriving at the WTC site during the morning was similar (COR 1.80 [95% CI 0.84-3.80]). The COR for duration (continuous) with arrival time in the model was 1.13 (95% CI 1.02-1.26) per month. There was no interaction between acute exposure and duration of exposure. Neither of the other potential correlates ("ever/never" smoking or PTSD symptoms) was associated with SAID in this cohort. Models using an outcome of RA found similar CORs for acute and chronic exposures, smoking and PTSD symptoms as the model combining all SAID outcomes, although no factors attained statistical significance at the 0.05 level (not shown), perhaps due to low power.
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Discussion

This first study of post-9/11/2001 SAID in WTC rescue/recovery workers finds a strong independent effect of prolonged work at the WTC disaster site. The effect of chronic exposure increased by about 13% for each month worked at the WTC site. Based on this model, for those who worked the full 10 months compared with those who worked for 1 month, we estimate the COR for SAID incidence as 3.09 (95% CI 1.21-7.94). When we modeled duration of exposure using a median split, those who worked 2 or more months at the site incurred a risk more than double that of workers who worked less. These results are consistent with non-WTC-related studies of chronic occupational exposures and disease outcomes. For example, silicosis usually takes at least 10 years after exposure to develop, but may develop sooner after a large exposure (31). To the best of our knowledge, acute and chronic WTC-exposures have been associated with respiratory conditions like asthma (20, 32, 33) and PTSD (34-36) previously, but not with the new onset of systemic autoimmune diseases other than sarcoidosis (37-39).

The cause or causes of SAID are unknown and likely multi-factorial. One common hypothesis postulates a series of events that result in initiation of an autoimmune reaction. Genetic susceptibility may be the crucial first factor; next, an antigenic event like an infection or environmental exposure occurs; and then, through various immunologic-inflammatory-oxidative pathways, an autoimmune response occurs ultimately resulting in clinical symptoms and disease. Just as genetic susceptibility may involve multiple genetic-risk factors, the triggering event may also involve multiple environmental factors or multiple factors at different periods or in a specific time sequence (8).
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The SAID included in this study have diverse immuno-genetic-inflammatory mechanisms, but they all can lead to uncontrolled inflammation, pain, disability, and often, tissue destruction (40, 41). Many components of adaptive and innate immunity come into play in each of these diseases and any attempt to group them by pathophysiology seems problematic. More work is needed to correctly define the dominant pathways for each disease. We excluded sarcoidosis as we previously reported that incident sarcoidosis, primarily involving intrathoracic disease, increased after WTC-exposure in FDNY firefighters and EMS workers (38). A high point-prevalence was similarly reported in two other WTC-exposed cohorts (37, 42), and two case series described workers with sarcoid arthropathies (43, 44). We included diagnoses of granulomatosis with polyangiitis (Wegener’s) and eosinophilic granulomatosis with polyangiitis (Churg-Strauss) in our analyses, but found no cases of the latter. In the future, as we begin to understand more about the different parts of the immune system that contribute to these various diseases, further sub-groupings may be possible. Until then, however, attempts to force categorization may not just be premature, but may be misleading because they will fail to capture the complexity of the underlying disease mechanisms.

We are confident in the results of the current study for several reasons. First, our cohort existed prior to 9/11/2001, eliminating recruitment bias. Second, although self-reported physician diagnoses usually started the documentation process, all persons in the cohort had the opportunity to report diagnoses on their monitoring questionnaires, which were then confirmed by our rheumatology case consultative review panel. Third, it is unlikely that members of our cohort had unrecognized pre-9/11/2001 SAID because the physical demands of firefighting and EMS work would have made concealment difficult. Fourth, we examined possible lack of bio-plausibility by carrying out sensitivity analyses, removing those diagnosed within 2 years of
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9/11/2001 and found similar results, despite lower statistical power. Fifth, we believe that our control subjects were truly non-diseased, as they were selected based on an absence of self-report and physician diagnoses of SAID in our electronic medical record database. Each control was then called to confirm non-disease status as of two years prior to the case diagnosis date, arguing against misclassification of disease outcomes in the control population. Finally, information about WTC-exposures was collected from questionnaires completed by all cohort members regardless of symptoms and, in most cases, was obtained years prior to the date of diagnosis, arguing against recall bias, or differential recall of WTC-exposure among affected individuals.

Our findings have important clinical implications for the estimated 409,000 WTC-exposed workers and residents (45), of whom ~120,000 have already enrolled in WTC Health Programs at FDNY, the WTC Responder Health Consortium or the WTC Health Registry at the New York City Department of Health. Autoimmune diseases in North American and European populations have been thought to predominantly affect women (>75% of cases). Since men predominate in the FDNY (96%) and the other WTC worker populations (78% at WTC Health Registry (46) and 87% at WTC Health Program Consortium (47)), our findings are unexpected and highlight the need for increased clinician awareness of the possibility of these and perhaps other autoimmune disorders in their WTC-exposed male patients. Our findings also reveal the lack of comparison rates of autoimmune disorders in various non-WTC-exposed populations, specifically in men. Population-based prevalence studies have been inconsistent in their methodology and have reported varying results. For example, two meta-analyses indirectly estimated population rates by comprehensively reviewing the published literature and applying rates in samples to the US population (48, 49), although neither included estimates by sex. In 1996, Jacobson reported the total population prevalence of 19 autoimmune diseases in the US as
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1 in 31 or 3.2% (49). In 2009, Cooper estimated the total population prevalence of 29 autoimmune diseases, which differed from the diseases included in Jacobson’s study, as 7.6%-9.4% (50). Both Jacobson and Cooper estimated the incidence of autoimmune diseases as less than 0.5% per year (48, 49). Incidence rates as estimated from other populations, both in the US and abroad, however, may not be applicable to specific populations like our cohort, which is comprised mostly of healthy white men. Our nested case-control study takes on added significance for this very reason.

A limitation of our study is that it involves a relatively small sample size with a largely white, male population. But, since we matched on these characteristics, this limitation should not have affected our primary goal of estimating the association between WTC-exposure (whether acute or chronic) and SAID. Each case was randomly matched to 4 controls based on gender, race, work assignment and hire year, so that cases and controls had similar levels of training, access to personal protective equipment, and work exposures throughout their careers. We did not match on age, as in previous studies we found that matching on year of hire was sufficient to control for age, a decision supported by the median ages of cases and controls at the conclusion of the study (57.2 versus 56.4 years). Thus, we are confident that our findings are not the result of confounding by smoking status, PTSD, or other known factors, but rather describe the effects of acute and chronic work exposure to the WTC site. We cannot, however, rule out the possibility that confounding by unknown and unmeasured factors could have influenced our study results. For example, our duration variable does not differentiate between those with one day vs. many days of exposure in a given month. In the mid-portion of this study period, the number of cases diagnosed increased. We cannot determine whether this was a biologic effect or increased awareness. Regardless, these factors should have had a similar impact on our controls.
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In addition, case ascertainment may have been incomplete after 2010, as there was a time lag of about 2 years between obtaining a SAID diagnosis and having the opportunity to self-report the diagnosis on the medical monitoring questionnaire. Final study limitations include the lack of information about family history of SAID and about non-WTC-related exposures, both work-related and recreational.

Conclusions

SAID are relatively rare, but their effects on disability and activity limitation are great. This is the first study of WTC-related SAID. We found a strong association between prolonged work at the WTC disaster site such that the odds of SAID increased by about 13% for each month at the site, or more than 3-fold for those who worked at the site for the full 10 months duration.

Accordingly, we suggest enhanced surveillance for WTC-exposed worker and resident cohorts to assess our findings and to provide early access to care. The stakes are high because enhanced surveillance can lead to early SAID detection and treatment, which has been shown to improve quality of life and reduce or delay organ damage including erosive joint destruction, kidney failure, pulmonary fibrosis, and hypertension. (40, 41).
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Table 1. Distribution of Systemic Autoimmune Diseases (SAIDs) in the FDNY Cohort

<table>
<thead>
<tr>
<th>Type of SAID</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>59</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>22 (37.3)</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>13 (22.0)</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>11 (18.6)</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Spondyloarthritis (axial &amp; peripheral, without ankylosis)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Inflammatory Myositis</td>
<td>8 (13.6)</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>6 (10.2)</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>7 (11.9)</td>
</tr>
<tr>
<td>Systemic Sclerosis (Scleroderma)</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>Sjogren's Syndrome</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>Antiphospholipid Syndrome</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis (Wegener’s)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Year of Diagnosis**

<table>
<thead>
<tr>
<th>Year of Diagnosis</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>2002-2004</td>
<td>10 (16.9)</td>
</tr>
<tr>
<td>2005-2007</td>
<td>19 (32.2)</td>
</tr>
<tr>
<td>2008-2010</td>
<td>17 (28.8)</td>
</tr>
<tr>
<td>2011-2013</td>
<td>13 (22.0)</td>
</tr>
</tbody>
</table>

Abbreviations: SAIDs = Systemic Autoimmune Diseases; FDNY = Fire Department of New York.

*a* Due to rounding percentages do not add to 100%

*b* Case ascertainment may be incomplete for this time period
Table 2. Characteristics of Systemic Autoimmune Diseases (SAIDs) Cases and Controls

<table>
<thead>
<tr>
<th></th>
<th>Case n (%)</th>
<th>Control n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>59 (94.9)</td>
<td>236 (94.9)</td>
<td>295</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>56 (94.9)</td>
<td>224 (94.9)</td>
<td>280</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (5.1)</td>
<td>12 (5.1)</td>
<td>15</td>
</tr>
<tr>
<td>African American</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>56 (94.9)</td>
<td>224 (94.9)</td>
<td>280</td>
</tr>
<tr>
<td>Female</td>
<td>3 (5.1)</td>
<td>12 (5.1)</td>
<td>15</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fire</td>
<td>54 (91.5)</td>
<td>216 (91.5)</td>
<td>270</td>
</tr>
<tr>
<td>EMS</td>
<td>5 (8.5)</td>
<td>20 (8.5)</td>
<td>25</td>
</tr>
<tr>
<td><strong>Age at hire (median, range)</strong></td>
<td>26.9 (21-36.1)</td>
<td>26.5 (19-36.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at diagnosis (median, range)</strong></td>
<td>50.4 (28.4-69.4)</td>
<td>50.2 (26.8-71.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Age on 9/10/13 (median, range)</strong></td>
<td>57.2 (36.7-75.9)</td>
<td>56.4 (34.3-78.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic Exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High (2 or more months on Site)</td>
<td>43 (72.9)</td>
<td>132 (55.9)</td>
<td>175</td>
</tr>
<tr>
<td>Low (1 Month on Site)</td>
<td>16 (27.1)</td>
<td>104 (44.1)</td>
<td>120</td>
</tr>
<tr>
<td><strong>Acute Exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/11/01 AM Arrival</td>
<td>16 (27.1)</td>
<td>41 (17.4)</td>
<td>57</td>
</tr>
<tr>
<td>Later Arrival</td>
<td>43 (72.9)</td>
<td>195 (82.6)</td>
<td>238</td>
</tr>
</tbody>
</table>

Abbreviations: SAIDs = Systemic Autoimmune Diseases
Table 3. Final Conditional Logistic Models for Duration of WTC-Exposure and Risk of any SAID

<table>
<thead>
<tr>
<th>Model</th>
<th>Odds of SAID</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duration as Continuous Duration with Median Split</td>
</tr>
<tr>
<td></td>
<td>Exact Odds Ratio (95% CI)</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td></td>
</tr>
<tr>
<td>Months of WTC work (duration)</td>
<td>1.13 (1.02, 1.26)</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
</tr>
<tr>
<td>Tobacco History</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>1.14 (1.02, 1.27)</td>
</tr>
<tr>
<td>History</td>
<td>1.16 (0.62, 2.20)</td>
</tr>
<tr>
<td>PTSD</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>1.13 (1.02, 1.25)</td>
</tr>
<tr>
<td>PTSD</td>
<td>1.40 (0.58, 3.14)</td>
</tr>
<tr>
<td><strong>Sensitivity Analysis</strong></td>
<td></td>
</tr>
<tr>
<td>Remove strata with case diagnosed</td>
<td></td>
</tr>
<tr>
<td>within 2 years of 9/11/2001</td>
<td>1.17 (1.05, 1.31)</td>
</tr>
</tbody>
</table>

Abbreviations: WTC = World Trade Center; SAID = Systemic Autoimmune Disease; PTSD = Post-Traumatic Stress Disorder.

*a*5 strata with a case diagnosed between 9/12/2001 and 9/11/2003 were removed. A total of 54 case strata remained in the model.