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Occupational and Hobby Exposures Associated with Myositis Phenotypes in a National Myositis Patient Registry

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Abstract

Objective: To investigate occupational and hobby exposures to silica, solvents, and heavy metals and odds of idiopathic inflammatory myositis (IIM) phenotypes, dermatomyositis (DM) and polymyositis (PM) versus inclusion body myositis (IBM), lung disease plus fever or arthritis (LD+), and systemic autoimmune rheumatic disease-overlap myositis (OM).

Methods: The sample included 1390 patients (598 DM, 409 PM, and 383 IBM) ages ≥18 years from a national registry. Of these, 218 (16%) were identified with LD+, i.e., self-reported lung disease with fever and/or arthritis, and 166 (12%) with OM. Questionnaire data on jobs, hobbies, and exposures before diagnosis were evaluated using a rules-based protocol and expert assessment of silica dust, solvents, and heavy metals exposure. We calculated adjusted odds ratios (OR) and 95% confidence intervals (CI) and explored joint effects with smoking.

Results: High silica exposure was associated with an increased odds of having DM (OR=2.02; 95%CI 1.18–3.46, compared to no exposure; p-trend=0.004), LD+ (1.75; 1.10–2.78; p-trend=0.005, versus no LD), and OM (2.07; 1.19–3.61; p-trend=0.020). Moderate to high heavy metals exposure was associated with greater odds of having LD+ (1.49; 1.00–2.14; p-trend=0.026) and OM (1.59; 0.99–2.55, p-trend=0.051). Greater odds of LD+ were seen among smokers with moderate to high silica exposure versus non-smokers with low or no exposure (high-certainty assessment, 2.53; 1.31–4.90; p-interaction=0.061).

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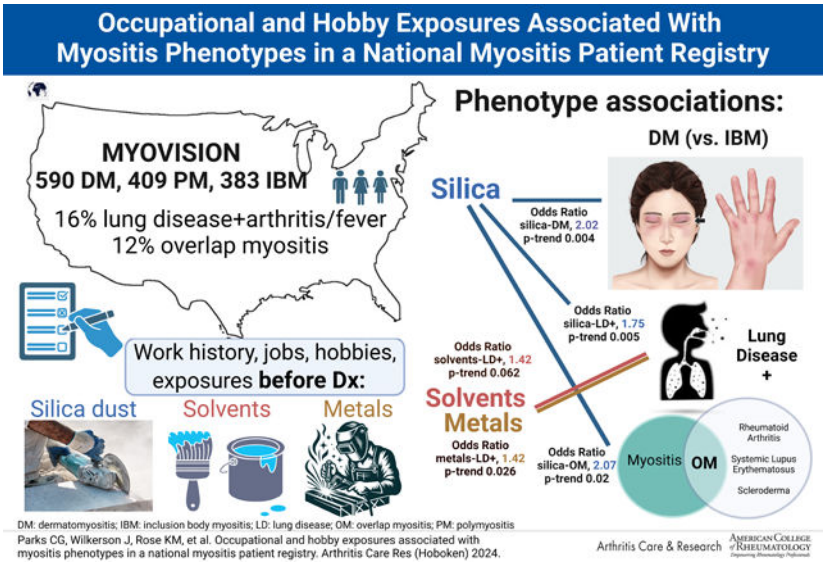
Conclusion: These findings, based on a systematic exposure assessment, suggest that occupational and hobby exposures to silica and heavy metals contribute to adult IIM phenotypes, including DM, OM, and LD+, a possible marker for anti-synthetase or other autoantibody-associated lung disease.

Graphical abstract



Keywords

occupation exposures; environment; myositis; lung disease; silica; heavy metals; solvents; dermatomyositis; polymyositis; anti-synthetase syndrome; overlap myositis

Introduction

The idiopathic inflammatory myopathies (IIM), including three classical phenotypes dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM), are rare systemic rheumatic autoimmune diseases (SARDs) characterized by muscle weakness, distinctive autoantibodies and clinical features (1–3). Interstitial lung disease (ILD), accompanied by arthritis and fever, is a defining feature of the anti-synthetase syndrome (ASynS), a severe phenotype seen in up to 25% of adult patients (4–6). Overlap myositis (OM), occurring with other SARDs, is another recognized phenotype associated with ILD, Raynaud's, arthritis, and dysphagia, with implications for therapies and relapse (7–9).

Genetic risk factors have been identified for IIM, ASynS, and OM (10–12), but little is known about environmental risk factors for IIM and IIM phenotypes (13–15). Studies have shown risk of SARDs associated with occupational exposures. Respirable silica dust, from rock, sand, and derivative products, is one of the best-known occupational risk factors for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and scleroderma/systemic sclerosis (SSc) (16–20). Solvents and metals have also been associated with SARDs (16, 17, 21, 22). Limited data suggests a role for respirable occupational exposures in IIM, especially among patients with ASynS (7, 18, 3). In a large trans-national European myositis registry,

patients with the IBM and ILD phenotypes were more likely than other IIM patients to have prior exposure to environmental toxins, including asbestos, silica, fiberglass, solvents, or coal dust (7). Most studies of environmental risk factors for IIM and ASynS, have been relatively small, lacked details on exposure assessment, and did not consider gender or hobby exposures, limiting their interpretation.

To address these research gaps, we evaluated occupational and hobby exposures to silica, solvents, and heavy metals using a systematic expert review and rules-based exposure-assessment in 1390 adults from MYOVISION, a national myositis patient registry in the United States (U.S.) (24–26). We investigated associations of these exposures with phenotypic differences among IIM patients, including the classical IIM subgroups (DM and PM versus IBM), and IIM-associated symptoms of lung disease plus fever or arthritis (LD+), as a proxy for ASynS or other myositis autoantibody-associated lung disease, and OM phenotypes. Given prior evidence of stronger associations of silica with SARDs and ILD among smokers and interactions of smoking with other inhaled exposures (16, 27, 28), we also evaluated effect modification by smoking.

Methods

Population and Sample

The design and sample for MYOVISION, a U.S. national myositis patient registry, have been described previously (26). Participants were recruited through The Myositis Association, and specialty physicians and clinics. The study was approved by institutional review boards at Cincinnati Children's Medical Center and the National Institutes of Health. Written informed consent was obtained from all participants. Most data were collected by mailed questionnaires, except for 18% who enrolled online; 85% of participants completed telephone interviews to clarify or fill-in missing data. Questions included disease-related information, demographics, and occupational and hobby exposures prior to IIM diagnosis (26).

Of 1956 individuals who returned questionnaires, 1806 met probable or definite Bohan and Peter criteria for DM or PM, or Griggs' criteria for possible IBM (29, 30); Diagnoses were confirmed for 105 (87%) of 121 who were patients at the NIH (26). The current study sample was limited to 1390 patients diagnosed at ages ≥18 years, who reported ≥1 full- or part-time paid or unpaid job for ≥1 year and ≥10 hours per week *before* their IIM diagnosis. This included 598 DM, 409 PM, 383 IBM patients; 218 were identified with LD+, and 166 met criteria for OM.

Data collection

Questions used to define disease phenotype are presented in the Appendix. In addition to defining questions on the classical IIM phenotypes, patients were asked about the main problems experienced with their myositis, including joint swelling, fever, and lung disease (LD) causing chronic cough or shortness of breath. We defined symptoms of LD+ as a phenotype including LD plus joint swelling (hereafter called "arthritis") and/or fever. Patients were also asked if they had been diagnosed with one or more of 4 SARDs, i.e.,

RA or juvenile idiopathic arthritis (JIA), SLE, and SSc, used to define OM. Covariate data included diagnosis age, gender, race/ethnicity, and smoking history.

Occupational and hobby-related questions are listed in the Appendix. These included paid or unpaid, for ≥1 year and ≥10 hours per week, (prior to diagnosis with myositis) for 12 types of jobs and factory work, with 7 specific factory types, write-in option for “other” factory jobs, and whether work was in production or an office. Patients were asked about any other job they wished to report, which was updated to include longest-held job in telephone interviews completed by 85% of participants. Questions on hobbies included gardening, painting, outdoor sports/activities, and a write-in option for “other hobbies”. Other questions asked about exposures from jobs or hobbies, including silica dust (i.e., from rock, sand, clay, tile, or brick), solvents (e.g., gasoline, lubricating oils, or other petroleum products; benzene, toluene,, dyes/inks, paint thinners, stains/ varnishes, glues/adhesives), metals (e.g., mercury, cadmium), and hours per week, months per year, and years started and stopped.

Exposure assessment

Methods followed a gold standard approach in occupational epidemiology, using a systematic rules-based protocol (25). Blinded to demographic and clinical phenotypes, expert reviews of self-reported occupation and hobby questionnaire data were performed by 2 occupational epidemiologists (CP and CR), and an MPH student (AF), rating potential exposure to crystalline silica, metals, and solvents. Exposures and write-in data on factory work, longest held job (or, other job, for 15% who did not complete telephone interviews), and other hobbies, were evaluated using custom job/hobby-exposure matrices, supported by industrial hygiene literature and using reported hours per week to rank potential exposure intensity (i.e., high, moderate, low, or no exposure) and certainty of assessment (i.e., high or low certainty based on all available evidence; see Appendix). Differences among reviewers were resolved by consensus, supported by additional industrial hygiene reviews to achieve final agreement. A ranking was assigned based on the highest intensity exposures prior to diagnosis. Patients with different data sources from non-overlapping periods were assigned the highest intensity ratings.

Analysis

We examined frequencies and associations across classical disease subgroups, and LD+ and OM phenotypes, overall and stratified by gender. Multinomial logistic regression models with a generalized logit link function were used to calculate the odds of exposure associated with the disease subgroups (DM or PM) to the referent subgroup (IBM). Binary logistic regression models calculated the odds of exposure associated with the phenotypes LD+ and OM. All models were adjusted for age and gender and were run on the overall sample and limited to those with high certainty ratings. Some exposure levels were combined to achieve sufficient cell sizes (e.g., moderate/high heavy metals exposure) or groupings of high/moderate versus low/no for the joint effects of smoking and silica (differences by smoking were also explored for solvents and metals). Effect modification was evaluated, including a product term in a model that included smoking and the exposure (results shown for high certainty ratings).

We explored additional gender-stratified analyses, and considered an additive score of high certainty silica, metals, and solvent exposure, in two sets of models (1) *adjusting* for smoking and previously identified occupation or hobby-associated ultraviolet radiation (UV) exposure (25), and (2) *adding* smoking and the UV variables to the other exposures. Analyses were performed using SAS (version 9.4, Cary, NC, U.S.A.).

Results

Sample characteristics and self-reported exposures.

Patient ages ranged from a median of 47 years for DM and PM, to 62 years for IBM (Table 1). DM and PM patients were predominantly female (83% and 74%, respectively), while 60% of IBM patients were male, and most reported non-Hispanic white race/ethnicity. Symptoms of LD+ were reported by 22% of DM, 18% PM, and 4% IBM patients, while OM was seen in 14% of DM, 15% PM, and 5% of IBM patients. Most DM and PM patients (65%) were never smokers, versus 51% of IBM. Self-reported job or hobby exposure to silica was similar across subtypes (8–10%). Solvent-related exposures were commonly reported (11–19%), while heavy metal exposures were less common (6–9%).

The median age of patients with LD+ and OM was 47 years; 80–85% were female (Table 2). Patients with LD+ included 12% with RA/JIA (97% with onset>16 years of age), 7% SLE, and 6% SSc, while 28% of OM patients had LD+. Most LD+ and OM patients were non-smokers (59–61%). Self-reported silica and heavy metals exposures were highest (12%) in LD+, while OM patients reported greater use of paints or paint thinners (22%).

Associations of exposures with myositis phenotypes

Based on expert assessment, silica exposure was strongly associated with having DM versus IBM (OR=2.02: 95%CI 1.18–3.46 for high intensity versus no exposure; p-trend=0.004), overall, and for the high certainty exposure assessment (2.44:1.26–4.74; p-trend=0.011; Table 3). An elevated odds of PM versus IBM was associated with high intensity silica exposure (1.58:0.92–2.70; p-trend=0.077). DM patients were less likely than IBM patients to have solvent exposure (e.g., low-level exposure 0.58:0.34–1.00). Low exposure to heavy metals was associated with DM versus IBM, but only for high certainty ratings (3.10:1.15–8.38), and no association was seen for moderate or higher exposures. Similar, attenuated associations were seen for PM with solvents and metals exposure.

The odds of having LD+ versus no LD were greater among those with high intensity silica exposure (overall, OR=1.75: 95%CI 1.10–2.78, p-trend=0.005; high certainty, 2.03:1.15–3.60, p-trend=0.037; Table 4). When limited to DM and PM, results were slightly attenuated (high exposure, 1.53:0.94–2.50p-trend=0.029). High intensity solvent exposure was associated with LD+ among DM or PM patients (overall, 1.61:1.01–2.57, p-trend=0.054; high certainty, 1.61:0.96, 2.70; p-trend 0.072). Moderate to high metals exposure was also associated with LD+ (overall, 1.49;1.00–2.24, p-trend=0.026; high certainty, 2.63; 1.46–4.73, p-trend=0.003). Limiting to DM and PM patients, findings were similar (overall, 1.43;0.93–2.18; p-trend=0.44; high certainty, 2.46; 1.33–4.53, p-trend=0.010.)

The odds of OM were greater for those with high intensity silica exposure (overall, 2.07:1.19–3.61, p-trend=0.020; high certainty 2.75:1.37–5.50; p-trend=0.008; Table 5). Odds of OM were not associated with solvent exposure but were elevated for moderate to high metals exposure (1.59; 0.99–2.55, p-trend=0.051), although this was attenuated when limited to high certainty exposure ratings (1.16:0.56–2.40, p-trend=0.536).

Joint associations of exposures and smoking

Compared to non-smokers with low or no silica exposure, the odds of DM or PM (versus IBM) were greater among smokers with high or moderate silica exposure (OR=2.79:95%CI 1.31–5.94 for DM; and 2.07:0.96–4.47 for PM), but interactions were not significant (interaction p=0.347 and 0.175; Figure 1). The odds of LD+ were greater for smokers with high/moderate silica exposure, versus non-smokers with low/no exposure (OR=2.53:95%CI 1.31–4.90) but were not higher among silica-exposed non-smokers (1.13:0.64–1.98; interaction p=0.061). The joint effects of high/moderate silica exposure and smoking on OM were less apparent (1.74:0.78–3.90) versus non-smokers with low/no silica exposure (interaction-p=0.560).

We saw no interactions of smoking with solvents (Supplemental Figure 1) or heavy metals exposures on myositis phenotypes (Supplemental Figure 2). Patients with high/moderate solvent exposure and smoking had greater odds of having LD+ (1.96; 1.17–3.28) compared with non-smokers with low/no solvent exposure, while the odds of LD+ were higher among those with heavy metals exposure regardless of smoking (moderate/high versus low/no: smokers, 3.65:1.70–7.88; non-smokers, 2.33:1.11–4.89).

Gender-stratified analyses

Distributions of age and race/ethnicity of myositis subgroups, and LD+ or OM were similar to overall frequencies by gender (Supplemental Table 1). Smoking (current or past) ranged from 29% among female PM patients to 57% among males with LD+. Occupational or hobby-related silica exposures were reported by 6–11% of female patients and 12–16% of males. Solvent-related exposures ranged from 7–13% of female patients to 27–40% of males, while heavy metals-related exposures were reported by 4–11% of females and 9–24% of males. The top jobs among male patients were in construction/roadbuilding (28% of DM and 27% LD+), while housekeeping/janitorial work was most frequently reported among females (13% of DM and 14% LD+; Supplemental Table 2).

More than a third of males had high intensity silica exposure (32% of IBM to 44% of PM; Supplemental Tables 3.1 and 3.2). Males showed no associations of high silica exposure with DM (versus IBM) (Supplemental Table 3.1); however, ORs increased after adjustment for solvent exposure (high silica, OR 2.41:95%CI 0.90–6.42). In male LD+ patients, 48% had high silica exposure, and 70% had moderate/high metals exposure; however, ORs were not calculated due to a lack of unexposed patients. Similarly in OM, all male patients had exposure to silica and solvents, and none were unexposed. Thus, we conducted a secondary analysis combining low and no-exposure categories for all exposures in males and females (Supplemental Table 3.2). In males, high silica exposure was associated with increased odds of LD+ (2.09: 0.98–4.48, compared with low/no exposure), as was high/moderate heavy

metals exposure (2.03: 1.01–4.07). No significant ORs were seen for OM. In females, high silica exposure was more frequent in DM (14%) versus IBM (7%) patients (2.90:1.22–6.89, versus no exposure), and high silica exposure was associated with OM (18% exposed; 2.03:1.11–3.71; Supplemental Table 3.1), while high solvent exposure was associated with LD+ (22% exposed; 1.67: 1.03–2.71). Most associations were similar in females when low exposure was included in the referent group (Supplemental Table 3.2). However, a stronger association was seen for high/moderate heavy metals exposure and LD+ (2.03: 1.01–4.07).

Multiple exposures

Cumulative exposures to silica, solvents, and heavy metals (dichotomous variables for high/moderate versus low /no exposure) are listed in Supplemental Table 4. Adjusting for smoking and occupational and/or hobby UV-exposure (previously associated with DM in this sample) (25), we saw no increased odds of DM or PM (versus IBM), or of OM, among those with 2–3 high/moderate exposures versus none. Greater odds of LD+ were associated with having 2–3 elevated exposures (overall, OR=2.14; 95%CI 1.35–3.41), both in males (2.95: 1.18–7.39) and females (1.84: 1.03–3.31). Next, considering the sum of these 5 exposures (i.e., silica, solvents, metals, plus smoking and UV exposure), having more exposures (3–5) was not associated with greater odds of DM or PM, nor OM. But the odds of LD+ associated with 3–5 exposures was elevated overall (2.80: 1.64–4.77) and in females (2.31: 1.12–4.77).

Discussion

In this large nationwide U.S. registry study, we provide novel evidence of IIM phenotypes associated with silica, solvents, and heavy metals exposure from jobs and hobbies using a systematic exposure assessment protocol combining rules-based approach and expert review to assign levels of exposure intensity and certainty of assessment. Our results showed that high intensity silica exposure increases the odds of having DM (vs. IBM), and the LD+ and OM phenotypes, and suggest that exposures to metals and solvents may also contribute to symptoms of LD+, a potential indicator of ASynS and other myositis autoantibody-associated LD, severe IIM phenotype (4,5). These differences among IIM phenotypes are notable, given prior evidence of silica and other respiratory occupational exposures associated with SARDs and idiopathic ILD (15–18, 20, 21, 31), supporting the need for future research comparing different IIM phenotype to population controls.

Within the classical IIM phenotypes, robust results were seen for silica associated with DM (vs. IBM), with a significant trend for more intense exposures. Silica exposure has been considered as a potential risk factor for DM (15), and in a study of construction workers (a traditional “dusty trade” industry, silica dust exposure was associated with hospitalization with DM, SLE or SSc (32). In the current study, silica exposure was associated with DM among female patients, who infrequently worked in dusty trades like roadbuilding or construction. We highlight potential silica exposures in other occupations, for example in dental laboratories in the Appendix. Females also showed greater odds of DM associated with high/moderate metals exposure (vs. IBM). An association was also seen for silica and PM (vs. IBM), though confidence intervals included the null. We saw no increased ORs

for DM or PM, and some were inversely associated with greater solvent exposure versus IBM, which could have contributed to a lack of apparent exposure response when multiple exposures were considered. Another reason for the lack of stepwise increases for DM could be confounding or conflicting effects of jobs with multiple co-exposures.

Interstitial Lung Disease, such as in ASynS, represents one of the more severe IIM phenotypes (33). While we lacked data on clinically diagnosed ASynS and other ILD, our findings showed that most silica-associated symptoms of LD reported by patients in relation to their myositis diagnosis occurred among smokers. Heavy metals were associated with LD+ regardless of smoking. A role of metals in ILD has been described (34, 35). Metal fumes often include both heavy metals, as well as hard metals, so further investigation is warranted to determine potential causal agents. In gender-stratified analyses, most males with LD+ had at least one of the exposures examined (silica, solvents, or metals), and we saw greater odds of LD+ associated with having more than one of these exposures, adjusting for smoking and UV exposure. In females, the odds of LD+ were increased when multiple exposures also included smoking and occupational or hobby UV-exposure. These findings support the need to consider diverse occupational risk factors for ILD phenotype in all patients, regardless of gender.

Within this cohort of IIM patients, we saw associations of silica exposures with the OM phenotype, which is notable given prior literature on silica and other SARDs (16–20). OM was also reported by 1 in 5 patients with LD+; ILD has been seen in other SARDs (36),and in OM with SSc has been associated with severe outcomes (37). These overlap phenotypes may represent heterogenous conditions and warrant specific autoantibody and clinical characterizations in future studies.

Mechanisms by which silica could impact DM, ASynS and OM phenotypes, may follow a shared initial pathway. Intense respirable exposures (i.e., very small particles inhaled into the deep alveolar spaces of the lung) may lead to accumulation in the lung parenchyma and associated lymph nodes. Some individuals may develop a fibrotic response in the lung, while silica accumulation may also lead to increased apoptosis of immune cells attempting to remove the foreign body, leading to release of self-antigens in an inflammatory milieu, triggering and promoting the development of autoantibodies (38, 39). Silica is not destroyed, thus perpetuating a cycle of immune activation and local inflammation. The rare intersection of silicosis and IIM provides a classic example of this process (40). Our findings for LD+ also support the idea that smoking interacts with silica exposure to contribute to the ASynS phenotype. Potential synergistic effects of smoking and silica on the risk of ILD are supported by experimental studies showing enhanced toxicity of silica in the context of smoking (41, 42). Other silicates may contribute to IIM phenotype. For example, individuals exposed to Libby asbestiform amphiboles, an amorphous fibrous silicate, had more myositis-related autoantibodies (anti-Jo1, -PM100, -NXP2, and -Mi2a autoantibodies) than individuals exposed to chrysotile asbestos (43). Mechanisms by which respiratory metals impact ASynS may share some features as silica exposure, as well as unique effects of specific metals (34, 35). Growing experimental evidence shows that stimulation of type I interferon (IFN-1) genes may play a key role in silica-induced pulmonary inflammation (44). A single acute dose of silica was associated with upregulated IFN-1 signaling genes in

a lupus model (45), providing a potential pathway by which silica exposure may play a role in DM pathogenesis relative to IBM, where IFN-1is not prominent (46).

Our findings are strengthened by the large national sample and inclusion of patients with diverse histories of paid and unpaid work, the detailed occupational and hobby exposure data, and systematic exposure assessment protocol, blinded to clinical and demographic data, which increased both sensitivity and specificity by integrating multiple types of data on jobs, hobbies, tasks, and exposures (47). Our protocol combined a “gold standard” expert assessment of write-in data on other factories, jobs, and hobbies and a rules-based approach to evaluate exposure intensity (48), assigning certainty ratings to further increase specificity. We focused on maximal or peak potential exposure intensity, hypothesizing that intense exposures were more likely to trigger disease. Cumulative exposures and latency were not examined due to the complexity of summarizing exposures across multiple jobs with varying exposure and certainty levels. A study of RA and multiple inhaled occupational exposures, including silica, found that duration was less clearly associated with disease risk than having multiple exposures (16). Our findings for additive scores across the three exposure types and an interaction of smoking with silica are consistent with this idea. Like another study showing IBM patients had greater exposure to asbestos, silica, fiberglass, solvents, or coal dust compared with other IIM patients (7), we saw somewhat greater reporting of specific exposures and high intensity exposures ratings among IBM patients. However, after *adjusting models for age and gender* we found greater odds of DM associated with silica exposure compared with IBM. Gender is an important determinant of IIM phenotype, job history, and exposures at work, so we also conducted stratified analyses to consider gender-patterned exposure frequencies and sources, which warrants greater attention in future studies, given female predominance in many SARD, including DM and PM.

This study has some limitations. Our sample included patients who were healthy enough to participate and may not be generalizable to clinic populations or patients with difficult management and poorer outcomes, such as SSc-overlap, which comprised a larger proportion of OM in the European registry (7). Genetic and environmental factors may contribute to diverse causal pathways; thus, more detailed clinical and myositis autoantibody characterization and genotyping may help identify unique or specific risk factors for different IIM phenotypes, as recently described for RA (13, 49). Conversely, evaluating risk factors across phenotypes may suggest common pathways, as the silica association with DM, LD+, and OM. While the IIM phenotypes in our study were based on self-report, their frequencies, relative distributions, and associated demographics are reassuringly like other studies, including a trans-European clinical registry (7, 8). The exposure associations with LD+ need to be confirmed in a clinical cohort with evaluation of ILD and testing for anti-synthetase autoantibodies, as well as other subgroups, including anti-MDA5 and myositis-associated autoantibodies (4).

Throughout their lifetime, individuals may be exposed to many different types of occupational exposures, including complex mixtures. We did not assess a broader range of inhaled exposures (e.g., wood dust or fumes), focusing instead on deep information for three specific exposures, while exploring interactions with smoking and simple additive models to consider multiple exposures, which also included occupational/hobby UV-exposure and

smoking. Our assessment protocol was limited by self-reported data, subject to recall error and misclassification; participants enrolled on average 9 years after diagnosis, though this did not vary by disease type – minimizing the influence of differential recall (26). Our assessment integrated multiple types of data evaluated by established population-based job exposure matrices, additional questionnaire data, and industrial hygiene literature reviews. However, future studies using prospective data may benefit from combining traditional epidemiologic exposure data with exposure biomarkers to better characterize a patient's "exposome" (50). Occupational exposures may be related to socioeconomic factors, and this study lacked individual data on socioeconomic status, e.g., education or income; but residual confounding would impact results only if these factors were strongly related to disease phenotype.

Due to a lack of population controls, our study could not directly evaluate the association of exposures with IIM risk. These findings do not imply causal associations with onset of any specific phenotype – rather the development of one phenotype versus another. Although the frequencies of occupations (e.g., construction/roadbuilding) followed expected differences by gender, comparisons in this volunteer registry to population data were limited by inherent differences in the registry compared to other types of surveys. Differences in questionnaire data and coding precluded comparisons with the National Health and Nutrition Examination Survey, for example, which has standardized occupational coding data on longest held job, and a specific question including broader range of mineral dusts (e.g., also including concrete, asbestos, coal, and soil) than queried in our survey (51). Population-based or occupational cohort studies of IIM are needed to replicate the findings for silica and other SARD, such as RA and SLE. Results for PM should be cautiously interpreted, as the classical clinical diagnosis of PM is being questioned based on new autoantibody and muscle pathology data, suggesting a lower prevalence and misclassification of historically diagnosed cases (52). Alternative diagnoses may include OM, immune-mediated necrotizing myopathy, and the ASynS phenotypes based on new classification criteria (1, 2).

Our analyses of major IIM phenotypes comparing DM and PM with IBM, assume underlying etiologic differences. As the most common myopathy in patients over age 45 to 50 years, IBM manifests distinct clinical and pathologic features (53, 54). Genetic differences and autoantibodies may help to distinguish IBM from DM/PM, e.g., in the HLA-region and other genes (4, 10, 54). We did not find prior studies of occupational risk factors for IBM. he inverse associations of solvents with DM could reflect a positive association of solvents with IBM (versus DM), and warrants further consideration, given the high prevalence of solvent exposure reported by IBM patients.

In conclusion, using detailed data collection and a systematic exposure assessment in a large national myositis registry, our results indicated robust associations of silica with DM and OM phenotypes and multiple exposures associated with LD+. Prospective studies are needed in large well-defined clinical populations, including a healthy control group from the general population, to evaluate the impact of past and ongoing occupational exposures on disease and phenotype risks and outcomes. These findings support taking a comprehensive occupational history among patients to determine potential risks and opportunities for mitigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Lundberg IE, Fujimoto M, Vencovsky J, Aggarwal R, Holmqvist M, Christopher-Stine L, et al. Idiopathic inflammatory myopathies. Nat Rev Dis Primers. 2021;7(1):86. [PubMed: 34857798]
2. Selva-O'Callaghan A, Pinal-Fernandez I, Trallero-Araguás E, Milisenda JC, Grau-Junyent JM, Mammen AL. Classification and management of adult inflammatory myopathies. Lancet Neurol. 2018;17(9):816–28. [PubMed: 30129477]
3. Ashton C, Paramalingam S, Stevenson B, Brusch A, Needham M. Idiopathic inflammatory myopathies: A review. Intern Med J. 2021;51(6):845–52. [PubMed: 34155760]
4. McHugh NJ, Tansley SL. Autoantibodies in myositis. Nature Reviews Rheumatology. 2018;14(5):290–302. [PubMed: 29674612]
5. Hallowell RW, Paik JJ. Myositis-associated interstitial lung disease: A comprehensive approach to diagnosis and management. Clin Exp Rheumatol. 2022;40(2):373–83. [PubMed: 33769263]
6. Connors GR, Christopher-Stine L, Oddis CV, Danoff SK. Interstitial lung disease associated with the idiopathic inflammatory myopathies: What progress has been made in the past 35 years? Chest. 2010;138(6):1464–74. [PubMed: 21138882]
7. Lilleker JB, Vencovsky J, Wang G, Wedderburn LR, Diederichsen LP, Schmidt J, et al. The Euromyositis registry: An international collaborative tool to facilitate myositis research. Annals Rheumatic Diseases. 2018;77(1):30–9.
8. Maundrell A, Proudman S, Limaye V. Prevalence of other connective tissue diseases in idiopathic inflammatory myopathies. Rheumatol Int. 2019;39(10):1777–81. [PubMed: 31385080]
9. Nuño-Nuño L, Joven BE, Carreira PE, Maldonado-Romero V, Larena-Grijalba C, Llorente Cubas I, et al. Overlap myositis, a distinct entity beyond primary inflammatory myositis: A retrospective analysis of a large cohort from the Remicam registry. Int J Rheum Dis. 2019;22(8):1393–401. [PubMed: 30968571]
10. Lamb JA. The genetics of autoimmune myositis. Front Immunol. 2022;13:886290.
11. Rothwell S, Chinoy H, Lamb JA, Miller FW, Rider LG, Wedderburn LR, et al. Focused HLA analysis in Caucasians with myositis identifies significant associations with autoantibody subgroups. Annals Rheumatic Diseases. 2019;78(7):996–1002.
12. Acosta-Herrera M, Kerick M, González-Serna D, Wijmenga C, Franke A, Gregersen PK, et al. Genome-wide meta-analysis reveals shared new loci in systemic seropositive rheumatic diseases. Annals Rheumatic Diseases. 2019;78(3):311–9.
13. Miller FW, Lamb JA, Schmidt J, Nagaraju K. Risk factors and disease mechanisms in myositis. Nature Reviews Rheumatology. 2018;14(5):255–68. [PubMed: 29674613]
14. Che WI, Lundberg IE, Holmqvist M. Environmental risks for inflammatory myopathies. Rheum Dis Clin North Am. 2022;48(4):861–74. [PubMed: 36333000]
15. Bax CE, Maddukuri S, Ravishankar A, Pappas-Taffer L, Werth VP. Environmental triggers of dermatomyositis: A narrative review. Ann Transl Med. 2021;9(5):434. [PubMed: 33842655]

16. Tang B, Liu Q, Ilar A, Wiebert P, Hägg S, Padyukov L, et al. Occupational inhalable agents constitute major risk factors for rheumatoid arthritis, particularly in the context of genetic predisposition and smoking. Annals Rheumatic Diseases. 2023;82(3):316–23.
17. Woo JMP, Parks CG, Jacobsen S, Costenbader KH, Bernatsky S. The role of environmental exposures and gene-environment interactions in the etiology of systemic lupus erythematous. J Intern Med. 2022;291(6):755–78. [PubMed: 35143075]
18. Prisco LC, Martin LW, Sparks JA. Inhalants other than personal cigarette smoking and risk for developing rheumatoid arthritis. Curr Opin Rheumatol. 2020;32(3):279–88. [PubMed: 32141952]
19. Blanc PD, Trupin L, Yelin EH, Schmajuk G. Assessment of risk of rheumatoid arthritis among underground hard rock and other mining industry workers in Colorado, New Mexico, and Utah. JAMA Netw Open. 2022;5(10):e2236738.
20. Ingegnoli F, Ughi N, Mihai C. Update on the epidemiology, risk factors, and disease outcomes of systemic sclerosis. Best Pract Res Clin Rheumatol. 2018;32(2):223–40. [PubMed: 30527428]
21. Rubio-Rivas M, Moreno R, Corbella X. Occupational and environmental scleroderma. Systematic review and meta-analysis. Clin Rheumatol. 2017;36(3):569–82. [PubMed: 28091808]
22. Parks CG, Meyer A, Beane Freeman LE, Hofmann JN, Sandler DP. Farming tasks and the development of rheumatoid arthritis in the agricultural health study. Occup Environ Med. 2019;76(4):243–9. [PubMed: 30760605]
23. Labirua-Iturburu A, Selva-O'Callaghan A, Zock J-P, Orriols R, Martínez-Gómez X, Vilardell-Tarrés M. Occupational exposure in patients with the antisynthetase syndrome. Clinical Rheumatology. 2014;33(2):221–5. [PubMed: 24384826]
24. Hossain MM, Wilkerson J, McGrath JA, Farhadi PN, Brokamp C, Khan MTF, et al. The geospatial distribution of myositis and its phenotypes in the United States and associations with roadways: Findings from a national myositis patient registry. Front Med (Lausanne). 2022;9:842586.
25. Parks CG, Wilkerson J, Rose KM, Faiq A, Noroozi Farhadi P, Long CS, et al. Association of ultraviolet radiation exposure with dermatomyositis in a national myositis patient registry. Arthritis Care & Research. 2020;72(11):1636–44. [PubMed: 31478597]
26. Feldon M, Farhadi PN, Brunner HI, Itert L, Goldberg B, Faiq A, et al. Predictors of reduced health-related quality of life in adult patients with idiopathic inflammatory myopathies. Arthritis Care & Research. 2017.
27. Zeng P, Chen Z, Klareskog L, Alfredsson L, Bengtsson C, Jiang X. Amount of smoking, duration of smoking cessation and their interaction with silica exposure in the risk of rheumatoid arthritis among males: Results from the Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA) study. Annals Rheumatic Diseases. 2018;77(8):1238–41.
28. Wheeler AM, Baker JF, Poole JA, Ascherman DP, Yang Y, Kerr GS, et al. Genetic, social, and environmental risk factors in rheumatoid arthritis-associated interstitial lung disease. Semin Arthritis Rheum. 2022;57:152098.
29. Griggs RC, Askanas V, DiMauro S, Engel A, Karpati G, Mendell JR, et al. Inclusion body myositis and myopathies. Ann Neurol. 1995;38(5):705–13. [PubMed: 7486861]
30. Bohan A, Peter JB. Polymyositis and dermatomyositis (parts 1 and 2). N Engl J Med. 1975;292:344–7,−403–7.
31. Huntley CC, Patel K, Mughal AZ, Coelho S, Burge PS, Turner AM, et al. Airborne occupational exposures associated with pulmonary sarcoidosis: A systematic review and meta-analysis. Occup Environ Med. 2023;80(10):580–9. [PubMed: 37640537]
32. Blanc PD, Järvholm B, Torén K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. Am J Med. 2015;128(10):1094–101. [PubMed: 26007670]
33. Long K, Danoff SK. Interstitial lung disease in polymyositis and dermatomyositis. Clin Chest Med. 2019;40(3):561–72. [PubMed: 31376891]
34. Kelleher P, Pacheco K, Newman LS. Inorganic dust pneumonias: The metal-related parenchymal disorders. Environ Health Perspect. 2000;108 Suppl 4(Suppl 4):685–96.
35. Assad N, Sood A, Campen MJ, Zychowski KE. Metal-induced pulmonary fibrosis. Curr Environ Health Rep. 2018;5(4):486–98. [PubMed: 30298344]

36. Joy GM, Arbiv OA, Wong CK, Lok SD, Adderley NA, Dobosz KM, et al. Prevalence, imaging patterns and risk factors of interstitial lung disease in connective tissue disease: A systematic review and meta-analysis. Eur Respir Rev. 2023;32(167):220210.
37. Paik JJ. Myopathy in scleroderma and in other connective tissue diseases. Curr Opin Rheumatol. 2016;28(6):631–5. [PubMed: 27548651]
38. Eleftheriadis T, Pissas G, Zarogiannis S, Liakopoulos V, Stefanidis I. Crystalline silica activates the T-cell and the B-cell antigen receptor complexes and induces T-cell and B-cell proliferation. Autoimmunity. 2019;52(3):136–43. [PubMed: 31119949]
39. Langley RJ, Kalra R, Mishra NC, Hahn FF, Razani-Boroujerdi S, Singh SP, et al. A biphasic response to silica: I. Immunostimulation is restricted to the early stage of silicosis in lewis rats. Am J Respir Cell Mol Biol. 2004;30(6):823–9. [PubMed: 14742293]
40. Yang Y, Fujita J, Tokuda M, Bandoh S, Dobashi H, Okada T, et al. Clinical features of polymyositis/dermatomyositis associated with silicosis and a review of the literature. Rheumatol Int. 2001;20(6):235–8. [PubMed: 11563582]
41. Sager TM, Umbright CM, Mustafa GM, Yanamala N, Leonard HD, McKinney WG, et al. Tobacco smoke exposure exacerbated crystalline silica-induced lung toxicity in rats. Toxicol Sci. 2020;178(2):375–90. [PubMed: 32976597]
42. Hanson KM, Hernady EB, Reed CK, Johnston CJ, Groves AM, Finkelstein JN. Apoptosis resistance in fibroblasts precedes progressive scarring in pulmonary fibrosis and is partially mediated by toll-like receptor 4 activation. Toxicol Sci. 2019;170(2):489–98. [PubMed: 31020321]
43. Pfau JC, McLaurin B, Buck BJ, Miller FWJ. Amphibole asbestos as an environmental trigger for systemic autoimmune diseases. Autoimmun Rev. 2024;Aug 20. Online ahead of print.
44. Benmerzoug S, Rose S, Bounab B, Gosset D, Duneau L, Chenuet P, et al. STING-dependent sensing of self-DNA drives silica-induced lung inflammation. Nat Commun. 2018;9(1):5226. [PubMed: 30523277]
45. Chauhan PS, Wagner JG, Benninghoff AD, Lewandowski RP, Favor OK, Wierenga KA, et al. Rapid Induction of Pulmonary Inflammation, Autoimmune Gene Expression, and Ectopic Lymphoid Neogenesis Following Acute Silica Exposure in Lupus-Prone Mice. Front Immunol. 2021;12:635138.
46. Pinal-Fernandez I, Casal-Dominguez M, Derfoul A, Pak K, Plotz P, Miller FW, Milisenda JC, et al. Identification of Distinctive Interferon Gene Signatures in Different Types of Myositis. Neurology. 2019;93e1193–31204.
47. Ge CB, Friesen MC, Kromhout H, Peters S, Rothman N, Lan Q, et al. Use and reliability of exposure assessment methods in occupational case-control studies in the general population: Past, present, and future. Ann Work Expo Health. 2018;62(9):1047–63. [PubMed: 30239580]
48. Sauvé JF, Friesen MC. Using decision rules to assess occupational exposure in population-based studies. Curr Environ Health Rep. 2019;6(3):148–59. [PubMed: 31297745]
49. Klareskog L, Rönnelid J, Saevarsdottir S, Padyukov L, Alfredsson L. The importance of differences; on environment and its interactions with genes and immunity in the causation of rheumatoid arthritis. J Intern Med. 2020;287(5):514–33. [PubMed: 32176395]
50. Parks CG, Costenbader KH. The exposome: what it is, really, and does it help to understand environmental influences on human health and rheumatic disease? Arthritis Rheumatol. 2024; Jan 29. Doi: 10.1002/art.42816. Online ahead of print.
51. Doney B, Kurth L, Syamlal G. Chronic bronchitis and emphysema among workers exposed to dust, vapors, or fumes by industry and occupation. Arch Environ Occup Health. 2022;77(7):525–9. [PubMed: 34309492]
52. Leclair V, Notarnicola A, Vencovsky J, Lundberg IE. Polymyositis: Does it really exist as a distinct clinical subset? Curr Opin Rheumatol. 2021;33(6):537–43. [PubMed: 34494607]
53. Chinoy H, Lilleker JB. Pitfalls in the diagnosis of myositis. Best Pract Res Clin Rheumatol. 2020;34(1):101486.
54. McLeish E, Slater N, Sooda A, Wilson A, Coudert JD, Lloyd TE, et al. Inclusion body myositis: The interplay between ageing, muscle degeneration and autoimmunity. Best Pract Res Clin Rheumatol. 2022;36(2):101761.

55. Rothwell S, Cooper RG, Lundberg IE, Gregersen PK, Hanna MG, Machado PM, et al. Immune-array analysis in sporadic inclusion body myositis reveals HLA-DRB1 amino acid heterogeneity across the myositis spectrum. Arthritis Rheumatol. 2017;69(5):1090–9. [PubMed: 28086002]

Significance and Innovations

- In a large myositis patient registry, using a systematic expert exposure assessment, we examined associations of phenotype (subgroup, lung disease, and overlap myositis) with occupational and hobby exposures to silica, solvents, and metals.
- Occupational silica exposure was associated with dermatomyositis, overlap myositis, and having symptoms of lung disease plus fever or arthritis, a potential marker of anti-synthetase syndrome and other myositis autoantibody-related interstitial lung disease.
- Lung disease plus fever or arthritis was more strongly associated with silica dust among smokers and was also associated with heavy metals and solvent exposures.
- These findings may assist clinicians in identifying at-risk patients for early preventive or mitigation therapies.

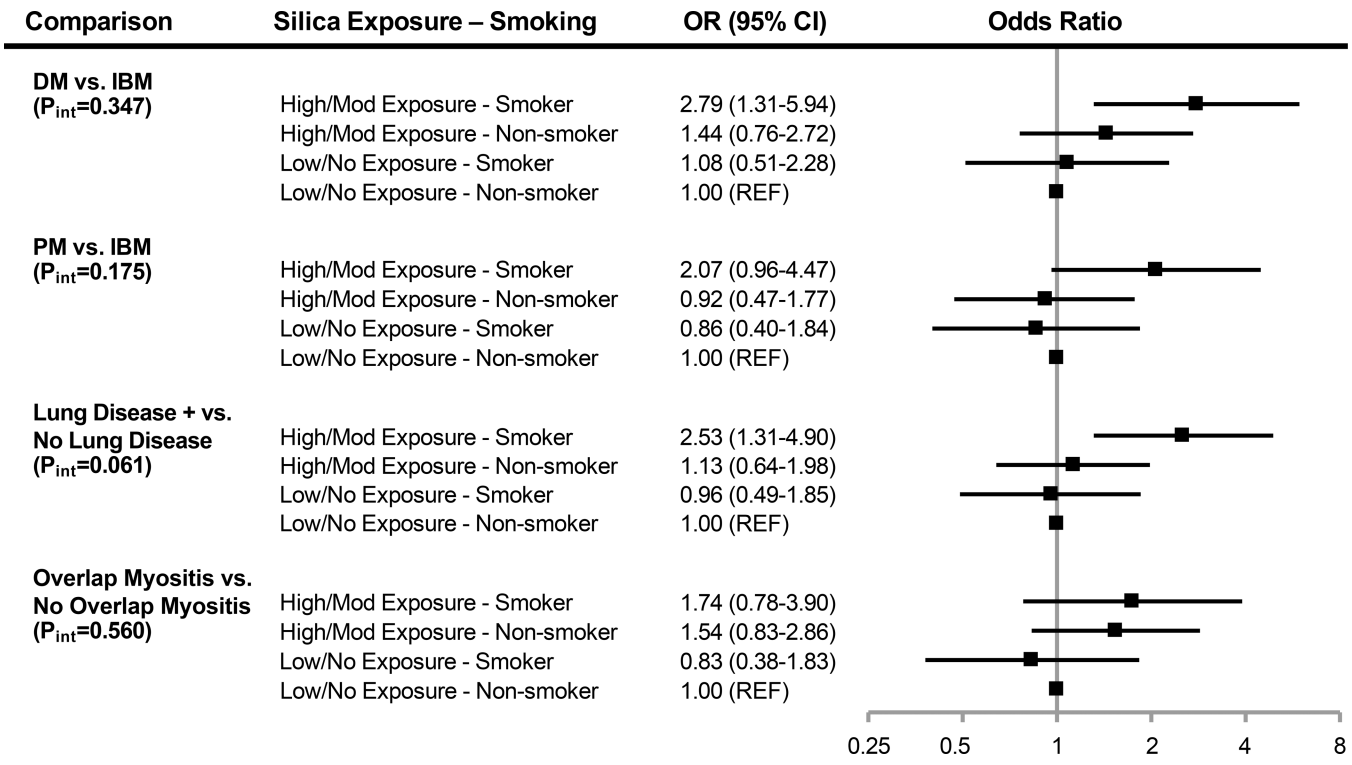

Figure 1.

Associations of myositis phenotypes with silica: joint effects of high certainty occupational exposures with smoking

Odds Ratios (OR) and 95% Confidence Interval (CI) are calculated by logistic regression, adjusted for age and gender. Models testing interaction also included a variable for smoking, the main exposure (silica), and a product term for smoking X exposure. Interaction P-value (P_{int})=0.061 for LD+ is considered statistically significant. All other interaction p-values were considered non-statistically significant, with P_{int}>0.10.

Abbreviations: OR, Odds Ratio; 95% CI, Confidence Interval; DM, Dermatomyositis; PM, Polymyositis; IBM, Inclusion Body Myositis; LD+, LD+, lung disease symptoms related to myositis diagnosis plus fever and/or arthritis; No LD, no lung disease symptoms, also without fever or arthritis; OM, Overlap Myositis.

Table 1.

Characteristics and self-reported exposures of 1390 adult-onset myositis patients in the MYOVISION registry by clinical subgroup.

Characteristic	IBM N=383 N (%)	DM N=598 N (%)	PM N=409 N (%)
Diagnosis age, years – Median [IQR]	62 [55, 68]	47 [38, 54]	47 [38, 56]
Gender			
Female	152 (40)	497 (83)	303 (74)
Male	231 (60)	101 (17)	106 (26)
Race/Ethnicity			
Non-Hispanic White	362 (95)	518 (87)	335 (83)
Non-Hispanic African	10 (3)	27 (5)	42 (10
American	7 (2)	20 (3)	8 (2)
Hispanic American	4 (1)	33 (6)	24 (6)
Other/multiple			
Lung Disease + (LD+)*			
Yes	15 (4)	129 (22)	74 (18)
LD Only	44 (11)	51 (9)	49 (12)
No LD	324 (85)	418 (70)	286 (70)
Overlap Myositis (OM)†			
RA/JIA	14 (4)	44 (7)	34 (8)
SLE	4 (1)	39 (7)	17 (4)
SSc	0 (0)	20 (3)	15 (4)
Smoking Status			
Current	20 (5)	49 (8)	30 (7)
Former	167 (44)	159 (27)	111 (27)
Never	195 (51)	386 (65)	264 (65)
Missing	1	4	4
Job/Hobby Exposures‡			
Silica dust (sand or rock)	37 (10)	46 (8)	33 (8)
Solvents	73 (19)	67 (11)	65 (16)
Gasoline/petroleum	96 (25)	81 (14)	72 (18)
Paints, paint thinners	73 (19)	108 (18)	67 (16)
Stains, varnishes	57 (15)	64 (11)	36 (9)
Dyes or inks	26 (7)	45 (8)	37 (9)
Heavy metals	36 (9)	40 (7)	23 (6)

Abbreviations: IBM, Inclusion Body Myositis; DM, Dermatomyositis; PM, Polymyositis; IQR, interquartile range; LD, Lung Disease; LD+, symptoms of lung disease plus arthritis and/or fever; RA, rheumatoid arthritis; JIA, juvenile idiopathic arthritis; SLE, systemic lupus erythematosus; SSc, scleroderma/systemic sclerosis.

* LD+ defined as self-reported symptoms of lung disease *plus* fever and/or arthritis. LD-only are 144 patients reporting symptoms of lung disease *without* fever or arthritis. LD-only are 144 patients reporting symptoms of lung disease *without* fever or arthritis.

[†]Overlap Myositis (12% of total cases) with a diagnosis of IIM and one or more of these four systemic autoimmune rheumatic diseases: RA or JIA, SLE, and SSc.

[‡]Self-reported exposures at jobs or hobbies before myositis diagnosis. Silica dust specified as dust from sand, rock, clay, tile, or brick. Solvents specified included benzene, toluene, xylene, naphthalene, trichloroethylene (TCE), tetrachloroethylene (PERC), and Solvene; Heavy metals specified were mercury and cadmium.

Table 2.

Characteristics and self-reported exposures of 1390 adult-onset patients in the MYOVISION registry, by lung disease plus arthritis and/or fever, and overlap myositis phenotypes.

	LD+*		Overlap Myositis†	
	No LD N=1,028	Yes N=218	No N=1224	Yes N=166
Characteristic	N (%)	N (%)	N (%)	N (%)
Age, years - Median [IQR]	52 [41, 61]	47 [38, 56]	52 [42, 61]	47 [39, 54]
Gender				
Female	689 (67)	174 (80)	811 (66)	141 (85)
Male	339 (33)	44 (20)	413 (34)	25 (15)
Race/Ethnicity				
Non-Hispanic White	918 (89)	176 (81)	1,073 (88)	142 (85)
Non-Hispanic Black	42 (4)	25 (11)	64 (5)	15 (9)
Hispanic	27 (3)	4 (2)	32 (3)	3 (2)
Other/multiple	41 (3)	13 (6)	55 (4)	6 (4)
LD+*				
Yes	0 (0)	218 (100)	172 (14)	46 (28)
No LD	1,028 (100)	0 (0)	922 (75)	106 (64)
Overlap myositis†				
RA/JIA	58 (6)	26 (12)	0 (0)	92 (55)
SLE	40 (4)	15 (7)	0 (0)	60 (36)
SSc	20 (2)	12 (6)	0 (0)	35 (21)
Smoking status				
Current	65 (6)	21 (10)	82 (7)	17 (10)
Former	321 (32)	69 (32)	389 (32)	48 (29)
Never	633 (62)	128 (59)	744 (61)	101 (61)
Missing	9	0	9	0
Self-reported exposures‡				
Silica dust	81 (8)	26 (12)	101 (8)	15 (9)
Solvents	144 (14)	40 (18)	185 (15)	20 (12)
Gasoline/petroleum	176 (17)	38 (17)	225 (18)	24 (15)
Paints, paint thinners	177 (17)	43 (20)	211 (17)	37 (22)
Stains, varnishes	108 (11)	27 (12)	134 (11)	23 (14)
Dyes or inks	71 (7)	26 (12)	93 (8)	15 (9)
Heavy metals	66 (6)	25 (12)	82 (7)	17 (10)

Abbreviations: LD, lung disease; LD+, lung disease plus arthritis and/or fever; IQR, interquartile range; RA, rheumatoid arthritis; JIA, juvenile idiopathic arthritis.

*LD+ defined as self-reported symptoms of lung disease *plus* fever and/or arthritis. LD-only are 144 patients reporting symptoms of lung disease *without* fever or arthritis. Table excludes 144 patients who reported isolated lung disease without reported fever or arthritis (shown in Table 1).

†Overlap Myositis (12% of total cases) with a diagnosis of IIM and one or more of these four systemic autoimmune rheumatic diseases: RA, JIA, SLE, and SSc.

[‡]Self-reported exposures at jobs or hobbies before myositis diagnosis. Silica dust specified as dust from sand, rock, clay, tile, or brick. Solvents specified were benzene, toluene, xylene, naphthalene, trichloroethylene (TCE), tetrachloroethylene (PERC), and Solvene; Heavy metals specified included mercury and cadmium.

Table 3.

Occupational/hobby exposures and odds of dermatomyositis or polymyositis versus inclusion body myositis

Exposure certainty/ intensity levels*		IBM N (%)	DM N (%)	Odds Ratio† (95% CI)	PM N (%)	Odds Ratio† (95% CI)
Silica						
Any certainty						
	High	86 (22)	107 (18)	2.02 (1.18–3.46)	82 (20)	1.58 (0.92–2.70)
	Moderate	93 (24)	140 (23)	1.50 (0.90–2.50)	83 (20)	1.04 (0.62–1.75)
	Low	138 (36)	227 (38)	1.15 (0.72–1.82)	147 (36)	0.92 (0.57–1.47)
	No	66 (17)	124 (21)	1.00 (REF)	97 (24)	1.00 (REF)
	Total N	383	598		409	
	p-trend			*0.004*		*0.077*
High certainty						
	High	49 (28)	63 (23)	2.44 (1.26–4.74)	40 (22)	1.68 (0.85–3.30)
	Moderate	53 (30)	68 (25)	1.39 (0.77–2.53)	39 (21)	0.97 (0.52–1.81)
	Low	11 (6)	21 (8)	1.08 (0.36–3.21)	13 (7)	0.90 (0.29–2.75)
	No	61 (35)	120 (44)	1.00 (REF)	90 (49)	1.00 (REF)
	Total N	174	272		182	
	p-trend			*0.011*		*0.237*
Solvents						
Any certainty						
	High	86 (22)	97 (16)	0.90 (0.55–1.48)	90 (22)	1.10 (0.67–1.80)
	Moderate	167 (44)	262 (44)	1.17 (0.76–1.79)	145 (35)	0.86 (0.55–1.34)
	Low	58 (15)	70 (12)	0.58 (0.34–1.00)	59 (14)	0.68 (0.39–1.18)
	No	72 (19)	169 (28)	1.00 (REF)	115 (28)	1.00 (REF)
	Total N	383	598		409	
	p-trend			*0.577*		*0.685*
High certainty						
	High	69 (26)	66 (17)	0.74 (0.43–1.27)	71 (25)	1.04 (0.61–1.78)
	Moderate	94 (35)	110 (29)	0.91 (0.56–1.50)	66 (23)	0.73 (0.43–1.21)
	Low	36 (13)	45 (12)	0.49 (0.26–0.92)	40 (14)	0.65 (0.35–1.23)
	No	70 (26)	163 (42)	1.00 (REF)	108 (38)	1.00 (REF)
	Total N	269	384		285	
	p-trend			*0.521*		*0.970*
Heavy Metals						
Any certainty						
	High/Moderate	174 (45)	190 (32)	1.31 (0.82–2.09)	135 (33)	1.09 (0.68–1.76)
	Low	147 (38)	269 (45)	1.13 (0.72–1.79)	176 (43)	1.01 (0.64–1.62)
	No	62 (16)	139 (23)	1.00 (REF)	98 (24)	1.00 (REF)
	Total N	383	598		409	
	p-trend			*0.248*		*0.695*
High certainty						
	High/Moderate	60 (49)	47 (23)	1.16 (0.57–2.34)	41 (29)	1.18 (0.58–2.37)

Exposure certainty/ intensity levels*	IBM N (%)	DM N (%)	Odds Ratio† (95% CI)	PM N (%)	Odds Ratio† (95% CI)
Low	13 (11)	33 (16)	3.10 (1.15–8.38)	13 (9)	1.56 (0.55–4.46)
No	49 (40)	126 (61)	1.00 (REF)	86 (61)	1.00 (REF)
Total N	122	206		140	
p-trend			*0.579*		*0.710*

Abbreviations: 95% CI, Confidence Interval; REF, referent; IBM, Inclusion Body Myositis; DM, Dermatomyositis; PM, Polymyositis.

*Any certainty includes all assessments, regardless of high or low certainty of assessment, High certainty includes only high certainty assessments. Exposure assessment intensity was rated as high, moderate, low or no.

†Logistic regression, odds of DM or PM versus IBM, adjusted for age and gender.

Table 4.

Occupational/hobby exposures and odds of anti-synthetase syndrome.

	All Myositis			DM/PM only		
Exposure certainty/ intensity levels*	**No LD N (%)**	**LD+† N (%)**	**Odds Ratio‡ (95% CI)**	**No LD N (%)**	**LD+† N (%)**	**Odds Ratio‡ (95% CI)**
Silica						
Any Certainty						
High	197 (19)	53 (24)	1.75 (1.10–2.78)	124 (18)	50 (25)	1.53 (0.94–2.50)
Moderate	224 (22)	50 (23)	1.21 (0.77–1.90)	148 (21)	46 (23)	1.10 (0.68–1.76)
Low	394 (38)	68 (31)	0.86 (0.56–1.30)	276 (39)	62 (31)	0.78 (0.50–1.21)
No	213 (21)	47 (22)	1.00 (REF)	156 (22)	45 (22)	1.00 (REF)
Total N	1,028	218		704	203	
p-trend			*0.005*			*0.029*
High certainty						
High	107 (23)	31 (29)	2.03 (1.15–3.60)	66 (21)	28 (28)	1.71 (0.93–3.15)
Moderate	119 (26)	24 (22)	1.10 (0.63–1.94)	73 (23)	21 (21)	0.94 (0.51–1.73)
Low	34 (7)	7 (7)	0.95 (0.39–2.29)	24 (8)	7 (7)	1.01 (0.40–2.50)
No	202 (44)	45 (42)	1.00 (REF)	149 (48)	43 (43)	1.00 (REF)
Total N	462	107		312	99	
p-trend			*0.037*			*0.181*
Solvents						
Any certainty						
High	192 (19)	47 (22)	1.49 (0.96–2.32)	121 (17)	46 (23)	1.61 (1.01–2.56)
Moderate	421 (41)	90 (41)	1.24 (0.85–1.81)	283 (40)	82 (40)	1.22 (0.82–1.81)
Low	142 (14)	26 (12)	1.02 (0.61–1.70)	92 (13)	24 (12)	1.09 (0.63–1.88)
No	273 (27)	55 (25)	1.00 (REF)	208 (30)	51 (25)	1.00 (REF)
Total N	1,028	218		704	203	
p-trend			*0.062*			*0.054*
High certainty						
High	149 (21)	34 (23)	1.42 (0.87–2.33)	89 (19)	34 (24)	1.61 (0.96–2.70)
Moderate	200 (29)	42 (28)	1.28 (0.81–2.03)	122 (26)	38 (27)	1.31 (0.80–2.13)
Low	89 (13)	20 (13)	1.18 (0.66–2.10)	59 (13)	19 (14)	1.32 (0.72–2.42)
No	262 (37)	53 (36)	1.00 (REF)	199 (42)	49 (35)	1.00 (REF)
Total N	700	149		469	140	
p-trend			*0.142*			*0.072*
Heavy Metals						
Any certainty						
High/Moderate	353 (34)	88 (40)	1.49 (1.00–2.24)	208 (30)	83 (41)	1.43 (0.93–2.18)
Low	454 (44)	78 (36)	0.81 (0.55–1.21)	329 (47)	70 (34)	0.71 (0.47–1.08)
No	221 (21)	52 (24)	1.00 (REF)	167 (24)	50 (25)	1.00 (REF)
Total N	1,028	218		704	203	
p-trend			*0.026*			*0.044*

	All Myositis			DM/PM only		
Exposure certainty/ intensity levels*	**No LD N (%)**	**LD+† N (%)**	**Odds Ratio‡ (95% CI)**	**No LD N (%)**	**LD+† N (%)**	**Odds Ratio‡ (95% CI)**
High certainty						
High/Moderate	96 (28)	33 (39)	2.63 (1.46–4.73)	50 (21)	30 (38)	2.46 (1.33–4.53)
Low	48 (14)	5 (6)	NC	36 (15)	5 (6)	NC
No	194 (57)	46 (55)	1.00 (REF)	150 (64)	44 (56)	1.00 (REF)
Total N	338	84		236	79	
p-trend			*0.003*			*0.010*

Abbreviations: 95% CI, Confidence Interval; REF, referent; LD, lung disease without fever or arthritis; LD+, lung disease plus arthritis and/or fever; NC, Not Credible due to cell count of 5 or less

*Any certainty includes all assessments, regardless of high or low certainty of assessment, High certainty includes only high certainty assessments. Exposure assessment intensity was rated as high, moderate, low or no.

†LD+ defined as self-reported lung disease symptoms related to myositis diagnosis plus fever and/or arthritis. “DM/PM only” excludes IBM patients (15 LD+ cases and 324 with no LD).

‡Logistic regression models, odds of LD+ versus no LD, adjusted for age and gender

Table 5.

Occupational/hobby exposures and odds of overlap myositis.

Exposure Certainty and Intensity Levels*		Overlap Myositis† No N (%)	Overlap Myositis† Yes N (%)	Odds Ratio‡ (95% Confidence Interval)
Silica				
Any certainty				
	High	241 (20)	34 (20)	2.07 (1.19–3.61)
	Moderate	279 (23)	37 (22)	1.51 (0.89–2.57)
	Low	445 (36)	67 (40)	1.55 (0.96–2.51)
	No	259 (21)	28 (17)	1.00 (REF)
	Total	1,224	166	
	p-trend			*0.020*
High Certainty				
	High	133 (24)	19 (26)	2.75 (1.37–5.50)
	Moderate	142 (26)	18 (25)	1.51 (0.78–2.92)
	Low	36 (6)	9 (12)	2.37 (1.01–5.55)
	No	244 (44)	27 (37)	1.00 (REF)
	Total	555	73	
	p-trend			*0.008*
Solvents				
Any certainty				
	High	250 (20)	23 (14)	0.81 (0.47–1.39)
	Moderate	501 (41)	73 (44)	1.25 (0.83–1.87)
	Low	162 (13)	25 (15)	1.23 (0.72–2.09)
	No	311 (25)	45 (27)	1.00 (REF)
	Total	1,224	166	
	p-trend			*0.844*
High Certainty				
	High	193 (23)	13 (12)	0.60 (0.31–1.15)
	Moderate	241 (29)	29 (27)	1.06 (0.64–1.78)
	Low	102 (12)	25 (15)	1.33 (0.74–2.41)
	No	296 (36)	45 (27)	1.00 (REF)
	Total	832	106	
	p-trend			*0.244*
Heavy Metals				
Any certainty				
	High/Moderate	440 (36)	59 (36)	1.59 (0.99–2.55)
	Low	519 (42)	73 (44)	1.23 (0.79–1.92)
	No	265 (22)	34 (20)	1.00 (REF)
	Total	1,224	166	
	p-trend			*0.051*

Exposure Certainty and Intensity Levels*	Overlap Myositis†		
	No	Yes	Odds Ratio‡
	N (%)	N (%)	(95% Confidence Interval)
High/Moderate	135 (33)	13 (23)	1.16 (0.56–2.40)
Low	49 (12)	10 (18)	1.85 (0.83–4.12)
No	228 (55)	33 (59)	1.00 (REF)
Total	412	56	
p-trend			*0.536*

Abbreviations: REF, Referent

*Any certainty includes all assessments, regardless of high or low certainty of assessment, High certainty includes only high certainty assessments. Exposure assessment intensity was rated as high, moderate, low or no.

†Overlap Myositis (12% of total cases) with a diagnosis of idiopathic inflammatory myopathy and one of four systemic autoimmune rheumatic diseases: rheumatoid arthritis or juvenile idiopathic arthritis, systemic lupus erythematosus, and systemic sclerosis.

‡Logistic regression models, odds of Overlap Myositis versus not, adjusted for age and gender