REVIEW

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Environmental and occupational contributors to autoimmune, inflammatory, and musculoskeletal rheumatic disease: a review of emerging evidence and clinical implications

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Purpose of review
Autoimmune and inflammatory rheumatic diseases as well as certain musculoskeletal diseases treated by rheumatologists result from a complex interplay between genetic predisposition and environmental factors.

Recent findings
Accumulating research has examined the possible roles of physical trauma, psychological stress, pollutants, and occupational exposures as triggers or influencers of disease. We review and summarize existing evidence for these contributors for conditions including rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, spondyloarthritis, systemic sclerosis, Sjogren's syndrome, vasculitis, myositis and fibromyalgia. We highlight findings from case–control, cohort, and twin studies that associate trauma, chronic stress and environmental exposure with immune dysregulation and increased disease risk. We apply the GRADE framework to assess the strength of evidence and identify key research gaps. Summary tables are included to guide clinical assessment which could also support interdisciplinary communication in medico-legal contexts.

Summary
These data have implications for disease etiopathogenesis; management; historical appreciation; public health, policy and safety; and legal considerations.

Keywords
autoimmune disease, environment exposures, occupational risk, rheumatology, trauma

INTRODUCTION

Autoimmune and inflammatory rheumatic diseases (AIRDs) such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), spondyloarthritis (SpA), systemic sclerosis (SSc), Sjogren's syndrome, myositis, and vasculitis are complex disorders that are influenced by an interplay between genetic and environmental influences [1–11]. While genetic predisposition is fundamental to disease vulnerability, increasing observations explore the role of environmental and psychosocial exposures as significant contributors to disease onset, progression, or expression. Separately, fibromyalgia syndrome (FMS), while not generally considered autoimmune, shares many clinical overlapping clinical features with AIRDs and has also been linked to environmental factors [12–14]. These exposures include inhaled agents (e.g. silica, solvents, cigarette smoke, air pollution, and industrial gases); metals, solvents and industrial coatings such as lacquers; physical trauma (defined here as significant tissue injury, repetitive biomechanical strain, or musculoskeletal insult), and psychological trauma (e.g. posttraumatic and chronic stress) [4,15▪,16–19].

Environmental factors such as proximity to traffic and industrial zones may also impact exposure to

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Curr Opin Rheumatol 2025, 37:000–000

DOI:10.1097/BOR.0000000000001130

KEY POINTS

- This review provides a framework for clinicians to assess environmental and occupational exposures related to the onset, expression, and progression of autoimmune and inflammatory rheumatic conditions.
- It highlights the importance of considering factors such as trauma, stress, silica, solvents, and mechanical factors in the pathogenesis of these diseases.
- The article offers valuable guidance for counseling patients regarding disability, workplace accommodations, and injury-related claims stemming from environmental and occupational exposures.

air quality, stress, and socioeconomic influences. Although causal relationships are difficult to establish, emerging data suggest these exposures may perturb host immune and neuroendocrine pathways and affect disease in susceptible individuals. Observational research includes epidemiologic reports, cohort studies, and case–control analyses [6,20–24].

Although causality is difficult to establish, claims of association arise frequently in disability evaluations, workers' compensation, and tort litigation. Literature relating to occupational medicine also summarizes those recognized and suspected environmental risk factors for autoimmune and other rheumatic diseases [25] including some that are relevant to medicolegal contexts [26].

We therefore reviewed and summarized the pertinent available literature regarding possible relationships of environmental, occupational, physical, and psycho-social contributions to rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, spondyloarthritis, systemic sclerosis, Sjogren's syndrome, vasculitis, myositis, and fibromyalgia. We highlighted findings from case–control, cohort, and twin studies that associate trauma, chronic stress and environmental exposure with immune dysregulation and increased disease risk. We applied the American College of Rheumatology GRADE framework to assess the strength of evidence and identify key research gaps. We discuss the implications of these observations for disease etiopathogenesis; management; historical appreciation; public health, policy and safety; and legal considerations.

ENVIRONMENTAL EXPOSURE AND AUTOIMMUNE AND INFLAMMATORY RHEUMATIC DISEASES

We performed a literature review using PubMed, focusing on human studies published in English between January 1990 and May 2025. Observational and interventional studies were screened at the title-and-abstract stage. Additional references were identified from article bibliographies and relevant reviews. Eligible studies included exploration of an association between at least one environmental or psychosocial exposure and the incidence or clinical course of one of the diseases of interest.

Studies were grouped into five exposure categories: physical trauma or biomechanical stress; psychological stress or trauma; inhaled pollutants and particulates (e.g. silica, air pollution, cigarette smoke); metals, solvents, and industrial chemicals; and animal and domestic exposures.

For each study, data were extracted including design, population characteristics, comparator definition, follow-up duration, primary outcome, and reported effect estimates. Key data extracted included study design, population, comparator groups, duration, primary outcome, and strength of association. When available, findings were integrated into summary evidence tables.

Exposures related to diet, allergens, and drug-induced autoimmune syndromes were excluded and considered beyond the scope of this review. Pet ownership or animal contact were also excluded unless they were explicitly assessed in human epidemiologic studies. Non-English studies were excluded unless full-text translation was available.

For each observational study we applied the American College of Rheumatology adaptation of the GRADE framework and rated the certainty of each exposure–disease association as high, moderate, low, or very low considering study design, risk of bias, result consistency, evidence of a dose–response gradient, and biological plausibility (see Table 1). Findings were summarized by exposure category (see Tables 2–4). Tables 2–4 present detailed data from primary studies reporting associations between specific exposures and rheumatic diseases. For each entry, we summarized study design, participant numbers, duration, comparator groups, and primary outcomes to provide a structured and comparative overview of the literature.

Physical trauma and biomechanical stress (see Tables 1–4 for additional details and GRADEs)

In RA, observational and case-based data suggest a possible link between injury and disease onset although the data were limited. Early case series and historical reports, including a three-patient series of RA or PsA-like disease following finger joint trauma, a case of seronegative monoarticular arthritis of the elbow after a radial head fracture with persistent synovitis for over seven years, and a 2024 case of

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Table 1. Observational evidence outlining occupational risks and rheumatic disease

Disease	Occupation or risk factor	Increased risk?	Grade level of evidence*	Comments
RA (Wallace) [112]	Emotional or physical trauma	Possibly (aggravation more than causation)	Low	Several studies suggest stress and trauma can exacerbate existing disease Weak support for initiating disease
RA (Karlson *et al.*) [6]	Smoking Silica	Yes	Low	Smoking: Most consistently demonstrated environmental risk factor stronger association in ACPA+ RA; dose–response relationship present Silica: Multiple cohort and case–control studies show consistent dose–response relationship
RA (Anaya *et al.*) [4]	Smoking, silica, mineral oil	Yes	Low	Smoking interacts with HLA-DRB1 shared epitope Silica linked to Caplan's syndrome
RA (Di Giuseppe *et al.*) [67]	Smoking	Yes	Moderate	Meta-analysis (10 studies) found dose–response relationship, with risk plateauing beyond 20 pack-years Stronger for RF-positive RA (RR 2.47)
RA (Tobon *et al.*) [19]	Smoking	Yes	Moderate	Strong, consistent evidence from cohort and case–control studies
RA (Sigaux *et al.*) [113]	Silica	Yes	Moderate	Dust Exposure Life-Course Questionnaire used
RA (Ajeganova *et al.*) [15▪]	Fine particulate matter PM2.5, coarse particles (PM_{10}), other gases including sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen oxides (NOx)	Yes	Moderate	Fire smoke–related PM2.5 exposure is associated with increased risk of incident RA Exposure to fossil fuel–related NOx was most strongly associated with RA overall and with seronegative RA Associations persisted even among never-smokers
RA, SLE (Barragan-Martinez *et al.*) [5]	Smoking, Silica, solvents	Yes	Low	Meta-analysis with subgroup analysis showed consistent association Supported by additional case–control studies; heterogeneity noted
SLE (Edwards *et al.*) [114]	Silica, silicone, aromatic amines, hydrazines, vinyl chloride, solvents, metals, smoking, infections	Yes	Low	Theoretical mechanisms outlined
SLE (Goldshen *et al.*) [54▪▪]	PTSD	Yes	Moderate	Prospective cohort studies and large epidemiologic database Behavioral factors including smoking may be related
SLE (Parks *et al.*) [22]	Silica	Likely	Moderate	Association noted but smaller and less consistent than for SSc
SLE (Barbhaiya *et al.*) [16]	Smoking, silica	Yes	Moderate	Smoking remains a key modifiable risk factor in SLE
SLE (Parperis *et al.*) [115▪▪]	PTSD (including from combat, 9/11 exposure, childhood trauma, military service)	Yes	Moderate	All included studies reported positive association
SLE (Gardner *et al.*) [91]	Mercury exposure in gold mining	Yes	Low	Mercury-exposed Brazilian gold miners had higher ANA, and pro-inflammatory cytokines vs. nonexposed miners Cross-sectional field study
PsA (Stober *et al.*) [116]	Trauma, biomechanical stress, obesity	Yes	Low	Promotes biomechanical stress at entheses Increasing risk of transition from Psoriasis to PsA; dose-dependent risk

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Table 1 (*Continued*)

Disease	Occupation or risk factor	Increased risk?	Grade level of evidence*	Comments
PsA (Hseih *et al.*) [36]	Physical trauma	Possible	Moderate	~9% PsA patients report trauma prior to onset vs. 1–2% in RA/SpA Supported by retrospective case series and case–control studies
SSc (Kettanah *et al.*) [76]	Organic solvents	Yes	Moderate	Meta-analysis of 11 studies (n = 1291 SSc, 3,435 controls) found OR 2.4 (95% CI 1.7–3.4), higher risk in men (OR 3.0) than women (OR 1.8) Heterogeneity and publication bias noted
SSc (Aryal *et al.*) [93]	Organic solvents	Yes	Moderate	Meta-analysis of eight studies (7 case–control, 1 cohort) identified increased relative risk with solvents and disease (RR = 2.9, 95% CI 1.6–5.3) Limitations included heterogeneity
SSc (Mora *et al.*) [77]	Silica, aromatic hydrocarbons	Possible	Low	Occupational silica exposure a known risk; solvent evidence growing
SSc (Garabrant *et al.*) [104]	Organic solvents Paint thinners and removers	Possibly (weak association)	Low	Some studies show increased risk, mostly in men Associations inconsistent
SSc (Rubio *et al.*) [81]	Silica	Yes	Moderate	13 case–control studies with data from 2,107 patients
Myositis (Costa) [1]	Environmental exposures (e.g., birds, mold, feather pillows)	Yes	Low	Retrospective observational study; 59% of patients reported exposures, 74% among those with pulmonary onset Suggests link between environmental antigens and disease phenotype
FMS (Wolfe *at al.*) [117]	Physical trauma: motor vehicle accidents, surgery, work injury, whiplash	Not clear	Low	Most of the supporting studies are low-quality, with selection, recall, or measurement bias
FMS (White *et al.*) [118]	Physical trauma	Possibly	Low	More high quality research needed including prospective design, psychological profile, long term follow up and litigation must be addressed

* Evidence grading: the quality of evidence for each exposure–disease relationship was assessed using the GRADE framework. Studies were classified as high, moderate, low, or very low quality based on judgement about study design, consistency of findings, presence of dose–response, risk of bias, and biological plausibility. Prospective cohort studies with consistent findings and mechanistic support were graded higher than single case–control or retrospective studies.

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Table 2. Summary of trials surrounding rheumatologic disease and environmental exposure (trauma)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Trauma: RA					
A case–control study examining the role of physical trauma and the onset of rheumatoid arthritis [29]	Multicenter retrospective case–control	262 RA	N/A	262 controls	55/262 (21%) RA patients reported physical trauma within six months prior to onset
Trauma: PsA					
Interplay between environmental factors, articular involvement, and HLA-b27 in patients with psoriatic arthritis [35]	Retrospective case–control	138 PsA	N/A	138 RA	12/138 (9%) PsA reported preceding acute medical disorder <10 days prior vs. 2/138 RA
Clinical, laboratory and immunogenetic aspects of post-traumatic psoriatic arthritis: a study of 25 patients [33]	Case series with a comparison cohort	300 PsA	1–7 years	300 RA 100 SpA	25/300 PsA with preceding trauma <3 months prior to disease onset
Association between environmental factors and onset of psoriatic arthritis in patients with psoriasis [37]	Case–control	159 PsA	N/A	159 Psoriasis	PsA associated with heavy lifting (OR ~2.9) and infections requiring antibiotics (OR ~1.7) Injuries showed a borderline association, smoking was protective (OR ~0.5)
Physical trauma recorded in primary care is associated with the onset of psoriatic arthritis among patients with psoriasis [34]	Matched cohort	15,416 PsA with trauma	N/A	55,230 controls without trauma	Multivariate HR 1.32 (95% CI 1.13–1.54); joint trauma HR 1.50 (1.19–1.90); bone trauma HR 1.46 (1.04–2.04)
Trauma: SpA					
Seronegative spondyloarthropathy initiated by physical trauma [40]	Cross-sectional	288 SpA	N/A	N/A	12 patients identified with physical trauma 1 month prior to SpA
Trauma: SSc					
Scleroderma and occupational exposure to hand-transmitted vibration [43]	Case–control	76 Ssc	>6 months of job exposure	213 controls	Ssc men more likely than controls to have had exposure to hand-transmitted vibration (OR ~1.5) or silica (OR ~5.2) but the association was not statistically significant
Trauma: FMS					
Role of road traffic accidents and other traumatic events in the onset of chronic widespread pain: results from a population based prospective study [48]	Case–control	241 with chronic widespread pain	4 years	N/A	Road traffic accidents associated with higher risk of chronic widespread pain (OR 1.84), but association lost significance after adjusting for psychological and sleep factors (OR 1.50)

Table 2 (*Continued*)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Mechanical injury and psychosocial factors in the workplace predict the onset of widespread body pain: a 2 year prospective study among cohorts of newly employed workers [49]	Prospective cohort	1,081 respondents	2 years	896 free of pain	New widespread pain associated with: lifting >15 pounds 1 hand, >24 pounds 2 hands, pulling >56 pounds, squatting and prolonged work with hands Psychosocial factors include job satisfaction
A case–control study examining the role of physical trauma and the onset of fibromyalgia syndrome [12]	Retrospective case–control	136 FMS	N/A	152 controls	53/136 (39%) FMS patients reported trauma 6 months prior to onset 22/102 adults with neck injury developed FMS 1 year after injury compared to 1/59 adults with lower extremity fractures
Increased rates of fibromyalgia following cervical spine injury. A controlled study of 161 cases of traumatic injury [45]	Cohort	102 adults neck injuries	Mean 3.2 months post injury	59 lower extremity fractures	FMS diagnosed in 21.6% of neck injury patients vs. 1.7% of controls ($P = 0.001$), FMS 13 × more frequent after neck injury
Does physical trauma lead to an increase in the risk of new onset widespread pain? [47]	Prospective cohort	376 crash-exposed	6 months	114 non-crash controls	New onset widespread pain at 6 months: 8% in crash group vs 4% in non-crash Association not statistically significant after adjustment for psychological factors
The role of workplace low-level mechanical trauma, posture and environment in the onset of chronic widespread pain [14]	Prospective cohort	1,658 adults	Baseline, 12 month, and 36 month follow-up	Exposed vs unexposed to workplace mechanical, postural, and psychosocial risk factors	Mechanical risk factors: Pushing/pulling heavy weights (RR 1.5) Repetitive wrist movements (RR 1.8) Kneeling (RR 1.7)

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Table 3. Summary of trials surrounding rheumatologic disease and environmental exposure (stress)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Environment: stress RA					
A twin study of the association between PTSD symptoms and rheumatoid arthritis [53]	Prospective observational	3,143 twin pairs	4 years	PTSD symptom quartiles; within-pair twin analyses controlling for familial/ genetic factors	Highest PTSD symptom quartile had 3.8× higher odds of RA (95% CI 2.1–6.1) vs. lowest quartile Association persisted within twin pairs
Elevated risk for autoimmune disorders in Iraq and Afghanistan veterans with posttraumatic stress disorder [52]	Cohort	666,269 Veterans	Median follow up 4.1 years	Veterans with no psychiatric disorders	PTSD doubled risk of autoimmune disorders overall (ARR 2.0 vs. no psychiatric diagnoses), with elevated risk for RA and SLE
Post-traumatic stress disorder and risk for incident rheumatoid arthritis [51]	Prospective cohort	54,224 female nurses	22 years	N/A	Higher PTSD symptoms associated with increased RA risk (HR 1.76, 95% CI 1.16–2.67) Risk rose with number of PTSD symptoms ($P = 0.01$)
Role of stress in the development of rheumatoid arthritis: a case-control study [50]	Case–control	76 RA	N/A	76 controls	RA patients had higher stress scores (167 vs 83, $p < 0.001$) RA patients reported more stressful life events (5.4 vs 2.7, $p < 0.001$)
Environment: Stress SLE					
Elevated risk for autoimmune disorders in Iraq and Afghanistan veterans with posttraumatic stress disorder [52]	Retrospective cohort	666,269 Veterans	Median follow-up: 4.9 years	PTSD vs. No psychiatric diagnosis	Veterans with PTSD had a 58% increased risk of developing AIRDs (adjusted HR 1.58; 95% CI 1.47–1.69)
Association of trauma and posttraumatic stress disorder with incident systemic lupus erythematosus (SLE) in a longitudinal cohort of women [32]	Longitudinal	54,763 female nurses	24 years	N/A	73 women developed SLE Probable PTSD (4–7 symptoms) was significantly associated with an almost three-fold increased risk of SLE (HR 2.94, 95% CI: 1.19–7.26, $p<0.05$)
The association of trauma with self-reported flares and disease activity in systemic lupus erythematosus (SLE) [31]	Cross-sectional	252 SLE	N/A	N/A	Any traumatic event (excluding illness) was associated with more than double the odds of a self-reported flare in SLE (OR 2.27, 95% CI 1.24–4.17)

Table 3 (*Continued*)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Association of stress-related disorders with subsequent autoimmune disease [55]	Cohort	1,064,640 patients with stress related disorders	10 years	Matched 1,064,640 unexposed persons 126,652 full siblings	Patients with stress-related disorders had an increased risk of autoimmune disease (HR = 1.36) PTSD: autoimmune disease was higher (HR = 1.46) This risk more pronounced for multiple (≥ 3) AIRDs (HR = 2.29)
Perceived stress independently predicts worse disease activity and symptoms in a multi-racial/ethnic systemic lupus cohort [56▪▪]	Prospective longitudinal cohort	260 SLE	3 years	N/A	Perceived stress independently associated with greater physician-assessed disease activity ($p = 0.015$), greater self-reported disease activity ($p < 0.001$), more pain ($p = 0.019$), and more fatigue ($p < 0.001$)
Environment: Stress SpA					
Influence of environmental factors on disease activity in spondyloarthritis: a prospective cohort study [58]	Prospective cohort	272 SpA	3 years	N/A	Significant temporal relationship between stressful life events and increased SpA disease activity (95% CI 0.4–0.7)
Infection and work stress are potential triggers of ankylosing spondylitis [8]	Retrospective population survey	1,080 SpA	N/A	102 patients with chronic back pain	SpA patients were more likely to report workplace stress in the 12 months before symptom onset compared to the prior year (OR 1.51, 95% CI 1.07–2.14)
Post-traumatic stress disorder prior to diagnosis is as rare in spondyloarthritis as in non-inflammatory rheumatic conditions and rheumatoid arthritis [7]	Observational cohort	510 SpA (167 ankylosing spondylitis, 140 PsA, 130 non–radiographic axSpA, and 51 peripheral SpA)	N/A	365 patients with non–inflammatory rheumatic control diagnoses 514 RA	PTSD prevalence prior to diagnosis: SpA: 4.9% RA: 6.6% Non-inflammatory controls: 6.0% Differences not statistically significant
Environment: Stress Sjogren's Syndrome					
Stress, coping strategies and social support in patients with primary Sjogren's syndrome prior to disease onset: a retrospective case–control study [60]	Case–control	47 Sjogren's	N/A	35 patients with lymphoma 120 healthy controls	Experiencing more than one negative stressful life event increased the risk of disease onset fourfold when compared to healthy controls (OR = 4.25, 95% CI: 1.57 to 11.49)

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Study	Design	Participants	Duration	Comparator groups	Primary outcome
Association between stressful life events and female primary Sjogren's syndrome and thie role in disease activity [59]	Case–control	67 Sjogren's	N/A	67 controls	Negative-event score associated with increased risk (OR 1.31, 95% CI 1.19–1.43); negative events correlated with disease activity ($p < 0.05$)
Environment: Stress FMS					
Traumatic experiences, major life stressors, and self-reporting a physician-given fibromyalgia diagnosis [63]	Cross-sectional	10,424 adults	N/A	Trauma-exposed vs non-trauma-exposed	FMS significantly associated with lifetime physical (OR 1.38) and sexual abuse (OR 1.41), even after adjustment for age, sex, race, and education.
Vulnerability to traumatic stress in fibromyalgia patients: 19 month follow-up after the great East Japan disaster [46]	Prospective observational	60 FMS	19 months	23 RA 26 healthy controls	FMS patients had significantly higher trauma scores than RA or controls with more depression symptoms
Posttraumatic stress disorder, tenderness, and fibromyalgia syndrome: are they different entities? [64]	Cross-sectional	124 men (55 PTSD, 20 depression, 49 healthy controls)	N/A	49 healthy controls	49% of PTSD patients met ACR criteria for FMS vs. 5% with depression and 0% controls Strong correlation between PTSD severity and tender point burden

Table 4. Summary of trials surrounding rheumatologic disease and environmental exposure (pollution, solvents, and pets)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Environment: RA					
Occupational exposure to respirable silica and risk of autoimmune rheumatic disease: a nationwide cohort study [68]	Cohort	1,541,505 men and 1,470,769 women (12,268 RA)	1979–2015	Non-exposed workers	Men exposed to high levels of respirable crystalline silica had an increased incidence rate ratio (IRR) for RA of 1.57 (95% CI 1.41–1.75)
Rheumatoid arthritis among women in the agricultural health study: risk associated with farming activities and exposures [87]	Case–control	135 RA	10 years	675 controls	Pesticides: no strong associations Any welding activity, whether on or off the farm, was associated with a 2.1-fold increased risk of RA (OR = 2.1, 95% CI: 0.8–5.4)
Exposure to traffic pollution and increased risk of rheumatoid arthritis [23]	Cohort	90,297 female nurses	28 years	Exposure to high vs. low long-term $PM_{2.5}$ levels (air pollution)	Women living <50 meters of major road had a 31% higher risk of RA compared to controls (HR 1.31, 95% CI: 0.98–1.74) Particularly pronounced among nonsmokers, 62% increased risk of RA (HR 1.62, 95% CI: 1.04–2.52)
Silica exposure among male current smokers is associated with a high risk of developing ACPA positive rheumatoid arthritis [21]	Case–control	1,419 RA	10 years	1,674 controls	Increased risk of developing RA (HR 1.31) associated with traffic-related air pollution
Association between occupational exposure to mineral oil and rheumatoid arthritis: results from the Swedish EIRA case-control study [10,119]	Case–control	1,598 RA	N/A	2,514 controls	Association of silica exposure with RA risk, especially in ACPA-positive men Mineral oil exposure associated with increased risk of RF+ RA in men (OR up to 2.1); no association in women
Insecticide use and risk of rheumatoid arthritis and systemic lupus erythematosus in the women's health initiative observational study [89]	Cohort	76,861 postmenopausal women	Mean follow up 7.6 years	Never vs. personal insecticide use; frequent vs. infrequent exposure, with/without farm history	Personal and residential insecticide use associated with increased RA/SLE risk; strongest effect with frequent use (HR 2.04) and among farm-exposed women (HR 2.73)
Genetic susceptibility and the link between cat exposure and rheumatoid arthritis [98]	Case–control	98 RA	N/A	77 controls	Increased RA risk in those with DRB1 0401, *0404, or *1501 and intimate cat exposure (OR up to 8.4)
Rheumatoid arthritis: are pets implicated in its etiology? [97]	Case–control	132 RA	N/A	Cat ownership vs. none 132 matched controls	Non-significant trend toward increased RA risk with cat exposure; supports hypothesis of microbial antigen role but not conclusive
Occupation, occupational exposure to chemicals and rheumatological disease: a register based cohort study [86]	Cohort	515,174 Swedish workers (375,035 men, 140,139 women), aged 35–74 in 1980, with ≥10 years in same occupation	1981-1983	Occupational exposures based on a job-exposure matrix (e.g. organic solvents, mineral oils) vs. unexposed	Exposure to organic solvents was associated with an odds ratio (OR) of 2.3 for developing RA

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Table 4 (*Continued*)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Occupations and exposures in the work environment as determinants for rheumatoid arthritis [30]	Case–control	293 RA	20 year latency	Population control	OR for RA by exposure: Male conductors OR 17.8 (95% CI 1.5–207.8) Farmers OR 2.4 (1.1–5.2) Asbestos exposure OR 2.5 (1.0–6.8) Vibrations OR 2.0 (0.9–4.4)
Silica dust exposure increases risk for rheumatoid arthritis [120]	Case–control	141 RA	2007–2016 (after 2-year washout)	549 controls	Among men with high cumulative exposure to solvents, OR for ACPA-positive RA was 1.54 (95% CI 1.10 to 2.16).
Are cleaning activities a source of exposure to crystalline silica in women with rheumatoid arthritis? A case-control study [120]	Case–control	31,139 RA	N/A	Matched controls smoking, age, sex	RA had significantly higher occupational exposure scores for cleaning activities (p=0.02) and dusty work clothes (p=0.01) High exposure to silica exposure associated with ILD (OR 6.5, 95% CI 1.3–32.6)
Air pollution exposure increases the risk of rheumatoid arthritis: a longitudinal and nationwide study [121]	Cohort	97 RA	10 years	Quartiles of yearly averages	Increased risk of RA in participants exposed to nitrogen dioxide (NO2) (HR 1.07, 1.63, 1.49)
Air pollution as a potential determinant of rheumatoid arthritis: a population based cohort study in Taiwan [71]	Cohort	3,895 RA	10 years	Compared with entire cohort 322,301	Long-term $PM_{2.5}$ exposure showed no clear increase in RA Individuals in the highest NO_2 quartiles had ≈50% higher adjusted risk of developing RA.
Occupational exposure to respirable silica and risk of autoimmune rheumatic disease: a nationwide cohort study [68]	Cohort	1,541,505 men (3,490 RA) 1,470 769 women (9,190 RA)	1979-2015	No exposure	Incidence rate RA: Men: RR 1.57 (95% CI 1.41–1.75) Women: RR 1.42 (95% CI 1.29–1.56)
Associations of fire smoke and other pollutants with incident rheumatoid arthritis and rheumatoid arthritis–associated interstitial lung disease [70■■]	Case–control	9,701 RA (531 with RA-ILD)	5–9 years of exposure data	68,851 controls	Fire smoke–related PM2.5 associated with increased risk of RA-ILD (OR = 1.98) NO associated with increased risk of RA overall
Occupational exposure to organic dusts and risk of developing rheumatoid arthritis: findings from a Swedish population-based case–control study [69]	Case–control	12,582 RA	Exposure estimates by job history	129,335 controls	Seropositive RA: OR 1.2 (95% CI: 1.1–1.4) Seronegative RA: OR 1.3 (95% CI: 1.1–1.5) Dose-response relationship animal dust OR 1.4 (95% CI: 1.1–1.8)
Systemic autoimmune disease mortality and occupational exposures [85]	Mortality-based case-control	36,178 RA 7,241 SLE 5,642 SSc 4,270 other	N/A Death certificate data	Occupational groups (e.g., farming, animal contact, industrial work) vs. general population	Farming: increased risk death AIRDs (OR 1.3, 95% CI 1.2–1.4) Mining machine operators: increased risk of death AIRDs (OR 1.3, 95% CI 1.1–1.5) Hand painting, hand coating and hand decorating: increased risk of death AIRDs (OR 1.8, 95% CI 1.0–2.9)

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Table 4 (*Continued*)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Predicting the impact of air quality index on rheumatoid arthritis disease activity [72■]	Retrospective observational study	1,185 female 341 male	Variable	N/A	NO: significantly linked with DAS28 (Disease Activity Score assessing 28 joints) (P = 0.0024) PM_{10}: negative coefficient and was significantly linked with DAS28 (P=0.0098) O_3: significantly linked with DAS28 (P = 0.0057)
Environment: SLE					
Occupational and environmental exposures and risk of systemic lupus erythematosus: silica, sunlight, solvents [20]	Case-control	258 SLE	N/A	263 controls	Silica and SLE: OR 2.1 (95% CI 1.1–4.0)
Associations between ambient fine particulate levels and disease activity in patients with systemic lupus erythematosus (SLE) [73]	Cohort	237 SLE	7 years	N/A	No significant association between $PM_{2.5}$ exposure and overall disease activity (SLEDAI-2K) Short-term increases in $PM_{2.5}$ were significantly associated with presence of anti-dsDNA antibodies (OR 1.34, 95% CI 1.02–1.77)
Acute effects of air pollution on lupus nephritis in patients with systemic lupus erythematosus: a multicenter panel study in China [74]	Cohort	8,552 SLE	4 years	N/A	$PM_{2.5}$: OR 1.16 (95% CI 1.08–1.19) NO_2: OR 1.19 (95% CI 1.12–1.26) SO_2: OR < 1 (protective) CO, O_3: no significant association
Cluster of systemic lupus erythematosus (SLE) associated with an oil field waste site: a cross sectional study [90]	Cross-sectional	Residents of a subdivision exposed to petroleum products and mercury	N/A	Community comparison	Increased prevalence of SLE and other rheumatic diseases in the exposed community (OR 19.33, 95% CI 1.96–190.72 for SLE and OR 10.78, 95% CI 4.14–28.12 for rheumatic diseases)
Association of systemic lupus erythematosus with uranium exposure in a community living near a uranium-processing plant [88]	Case–control	25 SLE	18 years	99 controls 150 RA	High uranium exposure including occupational linked to nearly a fourfold increased risk of SLE (OR 3.92) Not found in RA
Association of perfluoroalkyl and polyfluoroalkyl substances (PFASs) exposures and the risk of systemic lupus erythematosus: a case–control study in China [75]	Case–control	100 SLE	N/A	100 controls	PFASs are risk factors for SLE and PFASs exposures are associated with SLE risk in a dose–response manner Lifetime exposure assessed
Occupational exposure to crystalline silica and risk of systemic lupus erythematosus [92]	Case–control	265 SLE	N/A	355 controls	Silica: increased risk medium exposure (OR 2.1, 95% CI 1.1–4.0), high exposure (OR 4.6, 95% CI 1.4–15.4)
Fine particulate air pollution and systemic autoimmune rheumatic disease in two Canadian provinces [65]	Population based	Approximate total population of around 7,977,960 residents	Alberta (1993-2007) Quebec (1996-2011)	Within group comparison	Positive relationship between PM2.5 exposure and AIRDs including SLE
Environment: SSc					
Systemic sclerosis and occupational risk factors: role of solvents and cleaning products [44]	Case- control	93 SSc	N/A	206 controls	Higher $PM_{2.5}$ levels associated with increased risk
Prospective study to evaluate the association between systemic sclerosis and occupational exposure and review of the literature [18]	Case–control	100 SSc	N/A	300 controls	Organic solvents associated with increased risk of SSc (OR ~2.0)

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Table 4 (*Continued*)

Study	Design	Participants	Duration	Comparator groups	Primary outcome
Occupational silica exposure in an Australian systemic sclerosis cohort [78]	Prospective cohort	1,640 SSc (126 reported silica exposure)	12 years	Ssc without exposure	Silica exposure associated with increased odds of SSc (adjusted OR = 1.65; 95% CI: 1.17–2.32); association stronger in men (OR = 2.61)
Occupational quantitative exposure to crystalline silica, solvents and pesticides and risk of clinical forms of systemic sclerosis [79]	Cross-sectional	228 SSc	N/A	N/A	Silica and pesticide exposures underestimated; job-exposure matrices revealed higher prevalence. Non-significant trends toward increased risk in pulmonary fibrotic phenotype (OR 3.12) and vascular phenotype (OR 2.89)
What is the contribution of occupational environmental factors to the occurrence of scleroderma in men? [122]	Case–control	56 SSc	N/A	41 controls	No significant association between SSc and occupational exposure to silica, solvents, or epoxy resins
Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers [83]	Prospective cohort	240,983 male construction workers	13 years	Unexposed workers	In combined group (SSc, SLE, RA, dermatomyositis): Silica exposure: RR 1.39 (95% CI 1.17–1.64)· Other inorganic dusts: RR 1.31 (95% CI 1.11–1.53)
Environment: Sjogrens Syndrome					
Primary Sjogren's syndrome and occupational risk factors: a case–control study [17]	Case–control	175 Sjogren's	4 years	350 matched controls	Exposure to any type of solvent was associated with increased risk (OR 2.76, 95% CI 1.70–4.47)
Systemic autoimmune rheumatic disease risk is associated with long-term exposure to fine particulate matter [66▪▪]	Population-based cohort	7,482,397 adults	19 years	N/A	O verall: $PM_{2.5}$ linked to increased incidence (HR 1.036, 95% CI 1.002–1.070, per IQR; HR 1.012, 95% CI 1.002–1.021, per decile increase in mixture) Sjogren's syndrome: Stronger effect (HR 1.41, 95% CI 1.00–1.99, per IQR)
Environment: Myositis					
Occupational exposure in patients with the antisynthetase syndrome [11]	Case–control	32 patients with antisynthetase syndrome	N/A	32 patients with myositis without antisynthetase antibodies	High exposure to dusts, gases, or fumes: 16/32 (50%) antisynthetase syndrome vs 7/32 (22%) myositis controls ($p < 0.05$)
Environment: Vasculitis					
Impact of exposure to environmental particulate matter on the onset of giant cell arteritis [96▪]	Case-crossover study	232 GCA	Mean follow-up 38 months	Each patient served as own control	PM_{10} exposure: Odds of GCA increased by 27.1% (95% CI 5.8–52.6) per 10-μg/m^3 rise within 60 days; in patients ≥70 years, risk increased by 38.8% at a 60-day lag

monoarticular RA in the knee following injury, offered anecdotal support [9,27,28]. A multicenter case–control study reported that recent musculoskeletal trauma was more common in RA patients than controls [29]. Another case–control study found that long term exposure to vibration was associated with increased risk of RA [odds ratio (OR) 2.2, 95% confidence interval (CI): 1.3–3.8] with the highest risks observed in farming, freight/transport, and printmaking [30]. While not an acute traumatic event, vibration may result in repetitive mechanical strain and micro-injury, supporting its inclusion in the trauma category.

The role of physical trauma in SLE is not well defined. Some studies assessing trauma exposures in SLE included both physical and psychological domains, complicating categorization. In cross sectional cohort data, higher lifetime exposures including serious accidents, physical assaults, and early life adversity was associated with significantly increased disease flares (OR 2.27, 95% CI 1.24–4.17) and disease activity [31]. Longitudinal cohort data that included both physical and psychological events (e.g., car accidents, assaults, natural disasters), found that exposure was associated with a significantly increased risk of developing SLE [hazard ratio (HR) =2.87; 95% CI: 1.31–6.28] [32]. However, because these studies did not isolate physical trauma as an independent exposure – and the observed associations likely reflected psychological stress mechanisms – they were not included in the physical trauma exposure summary tables.

In PsA, case series suggested that a higher proportion of patients had a history of trauma preceding symptom onset when compared with RA or SpA populations [33–36]. In one series, 25 of 300 PsA patients reported preonset trauma compared to RA or SpA controls [33] while another found only three of 138 PsA patients with prior articular trauma [35]. More robust evidence from a large population-based cohort study found that psoriasis patients who experienced physical trauma had an increased risk of developing PsA, particularly after joint trauma and bone trauma [34]. A case–control study of psoriasis patients, PsA was independently associated with lifting heavy loads (OR 2.8) and physical injuries (OR 2.1) [37].

In SpA, small studies and case series reported preceding physical trauma [38–42] with new-onset seronegative spondyloarthropathy, Reiter's syndrome (the now-discarded term found in the older literature), or peripheral arthritis development within weeks of injuries such as falls, car crashes or joint trauma. Inflammatory symptoms often localized to the site of injury, suggesting a potential role for biomechanical triggers in disease expression [39,40,42]. Although patient numbers were small, findings were consistent across SpA subtypes. A separate case series described trauma-related complications in ankylosing spondylitis but did not establish trauma as an initiating factor and was therefore excluded from the summary table [41].

SSc data was sparse. In a case–control study of male construction workers, hand–arm vibration from power tools was linked to a higher risk of Raynaud's phenomenon, but not SSc and was difficult to separate from concurrent silica exposure [43]. Another case–control study reported an OR of 3.9 (0.8–19) for vibration and SSC, which was nonsignificant due to the limited number of cases [44].

We were not aware of eligible studies linking physical trauma to the onset of Sjogren's syndrome, myositis, or vasculitis.

In FMS, case–control and prospective studies have found increased risk of chronic widespread pain following motor vehicle accidents and other physical injuries, particularly when accompanied by psychological distress [12,13,45–49]. A case–control study found increased number of FMS patients reported significant physical trauma in the 6 months prior to disease onset, compared to controls [12]. This provided low to moderate-quality evidence, limited by retrospective self-report and modest sample size. A cross-sectional study found FMS in 21.6% of 102 patients with cervical spine injury vs. 1.7% of and 59 leg fracture controls. This provided moderate-quality evidence for a trauma-associated FMS subset [13]. In contrast, another study found low incidence of chronic widespread pain following motor vehicle accidents (MVA) attributing modest associations to psychological distress [47].

Psychological trauma and stress

Psychological trauma, including posttraumatic stress disorder (PTSD), early life adversity, and chronic emotional stress, has been investigated as a potential contributor to autoimmune disease onset, flare activity and symptom severity [50].

In RA, several large epidemiologic studies have reported an increased risk associated with PTSD and early life adversity. Women with PTSD had a significantly higher risk of developing RA over a 24-year follow-up period after adjusting for smoking and other confounders [51]. This relationship has been confirmed in cohort data when compared to veterans with no psychiatric history [52]. A retrospective twin-control study found a dose-dependent relationship between PTSD symptom burden and adult-onset RA [53]. This represented moderate quality evidence due to large sample sizes and prospective design.

Multiple prospective and cohort studies have demonstrated trauma exposure to SLE risk [32,54▪▪,55,56▪▪]. One study found a three-fold increased risk of subsequent incident SLE compared with women without trauma exposure when controlling for confounders [32]. Another study of 666 000 post9/11 veterans linked PTSD to SLE [risk ratio (RR) = 1.65; 95% CI: 1.14–2.40; $P = 0.008$] [52]. In the California Lupus Epidemiology Study (CLUES) cohort a rise in perceived stress over three years correlated with higher disease activity, pain, and fatigue [56▪▪]. This was moderate quality evidence although reliance on self-reported stress was a limitation.

In a case–control study initially discussed in the physical trauma section linking mechanical exposures and PsA onset, emotional stressors such as bereavement, divorce, job changes, unemployment, and treatment for depression or anxiety were assessed but none were significantly associated suggesting discrete life events may not independently trigger PsA onset [37].

A large nationwide cohort study of over 3.7 million individuals found that stress was associated with AIRDs including psoriasis (HR 1.42, 95% CI: 1.37–1.47) [7]. A separate cross-sectional report found psoriasis patients were more likely than dermatology controls to report emotional abuse, substance exposure, and traumatic experiences across lifespan, although PsA was not assessed [57].

In SpA, a prospective cohort of 272 patients found that stressful life events were associated with disease activity ($P < 0.005$) [58]. A population survey of 1080 patients reported more physical stress, work problems, and infections in the year prior to symptom onset [8]. In contrast, a cohort study comparing 510 SpA patients with 514 RA and 365 non-inflammatory controls found no significant differences in PTSD provenance prior to diagnosis [7].

We were not aware of evidence linking stress to SSc.

For Sjogren's syndrome, limited but consistent evidence suggested higher frequency of stress prior to disease onset compared to controls. Case–control studies reported more negative stressful life events in the year preceding disease onset among Chinese women with primary Sjo?gren's syndrome compared to controls (OR = 2.59; 95% CI: 1.87–3.58) [59] and more major negative life events compared with healthy and lymphoma controls [60]. This provided low quality due to recall bias and absence of large sample size.

Limited evidence suggested an association between emotional stress and increased risk for AIRDs, with some datasets potentially including vasculitis among the outcomes, although it was not reported as a distinct category. However, for myositis, we did not identify direct data linking emotional trauma or stress to disease onset or activity.

Multiple studies indicated a significant association between FMS and psychological stress, emotional trauma, and PTSD [61,62]. A large population-based sample found that individuals with a history of physical or sexual abuse had significantly higher odds of reporting a fibromyalgia diagnosis [63]. Following a national disaster, acute stress was associated with disease onset [46] and in a male veteran cohort, nearly half of those with PTSD met fibromyalgia criteria [64]. A 2018 systematic review of 31 studies reported consistent associations between FMS and early-life trauma, particularly sexual and physical abuse. Because it did not examine occupational exposures, it was excluded from Table 1, which is restricted to observational and pooled analyses of occupational risk factors [61]. This represented low quality evidence as these cases are observational in nature.

Environmental and chemical exposures (see Tables 1–4 for additional details and GRADEs)

To clarify the diverse environmental factors implicated in AIRDs, we classified them into three categories: inhaled pollutants and particulates, including both ambient air pollution (e.g., $PM_{2.5}$, NO_2, and wildfire smoke), occupational dusts (e.g., silica, asbestos, and textile fibers), and indoor air contaminants (e.g., mold and secondhand smoke); metals, solvents, pesticides and industrial chemicals, capturing systemic toxins such as organic solvents, metals, pesticides, and epoxy resins that may be absorbed through inhalation, skin contact, or ingestion; and animal and domestic exposures, including pet ownership, farm animal contact, and household or hobby-related exposures which may influence immune dysregulation and disease onset. We excluded behavioral exposures (e.g., alcohol use), drug-induced syndromes (e.g., hydralazine, procainamide, and penicillamine), and dietary triggers (e.g., allergens and specific food antigens).

Inhaled pollutants and particulates (see Tables 1–4 for additional details and GRADEs)

Emerging evidence suggested that ambient air pollution may contribute to the development of AIRDs [65,66▪▪]. In a population-based cohort of over 7.4 million adults, long-term exposure to fine particulate matter ($PM_{2.5}$) was associated with a small but significant increased risk of AIRDs including SLE, Sjogren's, and SSc (HR 95% CI: 1.00–1.02) [66▪▪]. This represented high-quality evidence due to the

large cohort, robust exposure modeling, and outcome validation.

In RA, a meta-analysis of ten studies (seven case–control and three cohorts) identified a dose–response relationship to smoking [67]. A nationwide cohort of over 3 million workers found an association between high cumulative silica exposure with increased risk [68] linked silica to ACPA-positive disease (OR 1.67; 95% CI: 1.13–2.48) [21]. In >12 000 RA cases and 129 000 controls, animal and textile dust exposure increased risk for RA (OR 1.6) [69]. Mineral dust (OR 2.5) and asbestos exposure (OR 1.6) were also associated to RA as well as vibration exposure (see trauma section) [30].

Air pollution studies showed consistent associations: a U.S. veteran case–control study [9701 RA, 531 RA interstitial lung disease (ILD)] found NO_x, ozone, and PM_{10} was associated with higher risk, while fire smoke-related $PM_{2.5}$ increased RA-ILD risk (OR 1.98) [70▪▪]. In a Nurses' Health Study (>90 000) traffic related air pollution increased risk of developing RA (HR 1.31), particularly among nonsmokers (HR 1.62) [23]. A Taiwanese cohort study (>322 000) linked CO (HR 1.17), NO_2 (HR 1.54), and O_3 (HR 1.37) to new RA with no significant PM_{10}, and modest SO_2 association (HR 1.02) [71]. Recently, a retrospective observational study in Kuwait found NO_2 and O_3 exposure to be linked to disease activity [72▪]. These findings represented moderate quality evidence supported by large sample sizes, prospective design, and consistency across cohorts.

In SLE, a multicenter case–control study (258 cases) found that outdoor work, silica exposure, and use of art-related chemicals were associated with increased risk [20]. From the same Canadian cohort, one study found no link between short-term $PM_{2.5}$ exposure and total SLEDAI-2K scores [16] while another reported increased antidsDNA positivity and renal casts following higher $PM_{2.5}$ levels, suggesting subclinical immune activation [73]. A multicenter longitudinal (>8500) found short-term increases in $PM_{2.5}$ and NO_2 associated with increased lupus nephritis risk [74]. A separate case–control study linked five PFASs compounds to SLE with a dose–response relationship [75]. These findings represented moderate-quality evidence supported by large sample size, although limitations included potential regional confounding and reliance on ambient exposure estimates [74].

We were not aware of studies linking inhaled pollutants to SpA or PsA.

For SSc, silica was a well established environmental risk factor [44,76–79]. A meta-analysis of >20 studies found strong associations (ORs 2–37) as well as with solvents (OR ~2) [80]. Another pooled data analysis of 15 case–control studies (OR 2.81, 95% CI: 1.86–4.23) and 4 cohort studies (RR 17.52, 95% CI: 5.98–51.37) confirmed this relationship [81,82]. A case–control study (80 cases, 160 controls) found that silica occupational exposure significantly increased disease risk (OR 4.0, 95% CI: 1.6–9.9) [18]. In the Australian Scleroderma Cohort Study (n= 1670) silica exposure was linked to earlier disease onset, more joint contractures (OR 1.8), anti-Scl-70 positivity, and worse disability (OR 1.4) [78]. One UK case–control study did not find associations with silica, solvents, or epoxy resins [83].

For Sjogren's syndrome, a cohort in Quebec assessed the impact of $PM_{2.5}$ and AIRD's and found 3268 incident cases as well as increased risk (HR 1.41, 95% CI: 1.00–1.99) [66▪▪]. Another study (175 cases, 350 controls) found associations between dichloromethane (OR 9.28), toluene (OR 4.18), white spirit (OR 3.60), and chlorinated solvents (OR 2.95) [17].

For myositis, a case–control study of 32 patients with antisynthetase syndrome (ASS) and 32 myositis controls without antisynthetase antibodies found high exposure to dust, gases, or fumes in 50% of ASS patients vs. 22% of controls ($P < 0.05$). This provided low quality evidence, limited by small sample size but supported by antibody-defined subtyping [11]. Isolated case series also suggested links between silica and solvent exposure to myositis, although these were limited by small sample size [84].

In vasculitis, a meta-analysis (33 studies) found a significant association between solvent exposure and AIRDs, including primary systemic vasculitis (OR 1.54; 95% CI: 1.25–1.92) [5]

We were not aware of direct or specific evidence linking pollution to FMS.

Metals, solvents, and industrial chemicals (see Tables 1–4 for additional details and GRADEs)

Industrial occupations surrounding solvent, metal and machinery exposure have been associated with increased risk of systemic autoimmune diseases. A national mortality study identified elevated risk of death from RA, SLE, and SSc among workers in occupations such as machine operation (RA OR 1.5), textile processing, and hand painting or coating (SSc OR 4.4) [85].

For RA, a case–control study (715 cases, >2200 controls) linked farming, freight/transport work, and printmaking with increased risk [30]. In a Swedish cohort (>500 000 workers) organic solvents exposures were associated with increased RA risk (RR= 1.2). particularly among spray-painters, lacquer workers, and machinery repairmen [86]. In 76 000 postmenopausal women, self-reported insecticide use was associated with increased risk of RA and

SLE (HR 2.04 for frequency, HR 1.97 duration ≥20 years) [22]. The Agricultural Health Study found no overall pesticide association but elevated risk for lindane and welding [87]. Others found no relationship between RA and uranium exposure [88]. A large case–control study (12 582 RA cases, 129 335 controls) found associations with animal dust (OR 1.2–1.3) and textile dust ($P=0.014$) [69]. This represented moderate grade evidence due to large sample size, multiple high-quality cohorts, and dose–response evidence despite some exposure classification limitations.

Insecticide use has been linked to increased risk of SLE [22,89]. A case–control study of 258 patients with SLE and 263 controls found occupational exposures including outdoor work, use of paints or dyes, nail polish application, metals and pottery was associated with increased risk [20]. A prospective study of nurses found dose-dependent increase in SLE risk with occupational solvent exposure (HR 1.59, 95% CI 1.05–2.42) [16]. A community comparison study found increased SLE prevalence in the petroleum and mercury-exposed community compared to controls [90]. In Brazilian miners, mercury exposure in gold mining was associated with increased ANA titers and pro-inflammatory cytokines [interleukin (IL)-1β, tumor necrosis factor alpha (TNF-α), interferon gamma (IFN-γ)] compared to diamond and emerald miners [91]. SLE development was found to be almost four-fold higher in uranium exposures [88]. Higher SLE prevalence has also been reported in silica-exposed occupations, including uranium miners, scouring powder factory workers, and silicosis patients, with one Swedish registry study noting a more than 20-fold increased hospitalization risk in those with silicosis [92]. However, other studies have found no association between SLE and pesticides [85].

For PsA and SpA current evidence did not establish a consistent or causal association with specific environmental or occupational exposures.

In SSc, a 2001 meta-analysis of 8 studies found increased risk of solvent exposure and disease (RR 2.9) [93]. A 2008 meta-analysis of 11 studies confirmed this relationship in an occupational setting [76]. A larger systematic review and meta-analysis of 33 studies reported that exposure to organic solvents was significantly associated with increased AIRDs (OR 1.54; 95% CI: 1.25–1.92), including SSc and vasculitis [5]. A case–control study of 93 patients with SSc and 206 controls found occupational exposure to solvents was significantly associated with increased risk (OR = 3.23; 95% CI: 1.58–6.63) [44]. Additional case–control and observational studies have identified similar associations for epoxy resins, pesticides, and welding fumes [81,85]. Overall this represented moderate to high-quality evidence, supported by pooled estimates, sensitivity analyses, and minimal publication bias, although heterogeneity in exposure assessment remained a limitation.

A case–control study investigated the association between Sjogren's syndrome and solvent exposure and demonstrated significantly elevated odds ratios for multiple solvents, including dichloromethane (OR 9.28), perchloroethylene (OR 2.64), benzene (OR 3.30), and toluene (OR 4.18). Overall exposure to any solvent (OR 2.76) and to chlorinated or aromatic solvents was associated with higher risk [17]. There was no significant association with pesticide exposure.

A case of polymyositis with antihistidyl-t-RNA synthetase (Jo-1) antibody syndrome was reported following extensive vinyl chloride exposure [94].

Two case reports described systemic vasculitis following prolonged exposure to organic solvents in male workers (electrician and painter), suggesting a possible temporal association [95]. A questionnaire-based study comparing 53 patients with granulomatosis with polyangiitis (GPA) to controls reported possible links between mercury and lead exposure, as well as allergy history, although findings were limited by small sample size [2]. A case cross-over study of 232 patients with giant cell arteritis (GCA) revealed increased odds of disease onset with PM10 particulate exposure, and this effect was stronger in individuals aged ≥70 years and in chronically exposed individuals [96▪].

For FMS the overall body of research was limited, inconsistent, or inconclusive for these factors.

Animal and domestic exposures (see Tables 1–4 for additional details and GRADEs)

Animal and domestic exposures have been proposed as potential triggers for systemic autoimmune diseases. A national mortality study found that occupational animal exposure was associated with increased risk of death from all AIRDs, with the most consistent association with RA [85]. In a case–control study of 122 RA patients, prepubertal exposure to cats was significantly associated with increased risk (OR 4.9; 95% CI: 2.7–9.0), with a reported dose–response effect [97]. A follow-up genetic analysis found that exposure was strongly associated with RA risk (OR 4.2; 95% CI: 2.1–8.5) [98].

We were not aware of data regarding epidemiological data on human exposure to animals and the development of PsA, SpA, SSc, vasculitis, or FMS.

One hundred eighteen patients with polymyositis, dermatomyositis, or ASS, were studied with exposure to household exposures to mold, birds, and feather pillows using questionnaires. However,

specific results regarding animal-related exposures were not reported, and therefore no conclusions can be drawn from this study regarding animal exposure and myositis risk [11].

DISCUSSION

This review summarized the environmental and occupational exposures to autoimmune, inflammatory and musculoskeletal disease. It covered a broad scope of exposures, including physical trauma, psychological stress, and various chemical agents like silica and solvents. We applied the GRADE framework (Table 1) to evaluate the strength of the evidence and address the clinical and legal implications of these findings, providing a comprehensive review for clinicians to consider when assessing exposure history and injury related claims. The review intentionally excluded several areas of study to maintain focus. We did not cover the potential roles of diet, nutrition, or complementary and alternative medicine, nor historical perspectives of environmental or occupation exposures. For more information on these topics, please see the provided references [25,99–101].

Our review found several key patterns relating environmental exposures to rheumatic disease (Tables 2–4). Certain exposures, such as physical stress, psychological stress, silica, solvents and airborne pollutants had consistent associations with disease onset or exacerbation, although the strength of evidence varied. The evidence for physical trauma and psychological stress was mixed and often depended on the specific disease and context [4,54▪▪,102]. Psychological stress has been identified in large populations as associated with SLE and other autoimmune diseases, with moderate-level evidence from prospective cohorts and epidemiologic databases [32,54▪▪,56▪▪]. The link between silica exposure and diseases including RA [4,15▪,16] and SSc [4–6,18,21,76,77,81,82,103,104] was particularly strong and well documented. Overall, the findings suggested a nuanced relationship where environmental factors can act as triggers in presumably genetically susceptible individuals.

These observations highlight how rheumatic disease may develop in predisposed individuals. For example, the increased prevalence of RA after the industrial revolution, associated with increased availability of sugar, perhaps associated with periodontal disease and a trigger like *Porphyromonas gingivalis* perhaps leading to disease, supports the concept that new environmental exposures may contribute importantly to disease [105]. This underscores the importance of gene-environment interactions and the historical search for infectious or environmental triggers. The concept of "therapeutic windows" in preclinical disease is also relevant, suggesting that understanding these triggers may allow for earlier intervention [106]. Further insight could help guide intervention strategies, including workplace modifications and providing preventive counseling for patients in high-risk occupations. This knowledge also supports targeted screening in exposed populations, potentially leading to earlier diagnosis and treatment.

This review also contributes to the historical understanding of rheumatic diseases, which have long been understood as complex and multifactorial. Certain diseases have not been thought to have been recognized in antiquity, supporting the notion that recent and environmental factors may contribute to their etiology. Nor do we really know what causes (most) rheumatic diseases. We have seen thoughts over the years about humors, infections, food and diets, viruses, amoebae, mycoplasma, other microbes, immune dysregulation, the microbiome, even space aliens!, and now the environment [99,105,107]. This perspective is particularly relevant today as our understanding of complex environmental contributions to disease pathogenesis continues to evolve.

The implications from these findings extend to public health and policy. There is a clear need for stricter occupational safety standards and environmental regulations to protect workers and the general population. Recognizing links between exposure and disease can support a more equitable approach to compensation systems for those affected.

LEGAL IMPLICATIONS

Question of relationships of environmental factors, occupation, trauma, and physical and psycho-social stress frequently arise in disability and legal contexts. While scientific evidence is evolving, legal standards require substantiated proof as well as preponderance of medical evidence when addressing issues of causation and aggravation.

From a medicolegal standpoint, physicians must navigate standards of causation and apportionment. Courts have emphasized that apportionment requires medical evidence and explanation (e.g. Escobedo [108], Gonzales [109]), that aggravation of preexisting conditions may be compensable (Sweat [109]), and that misapplication of psychiatric vs. physical injury standards can undermine physician opinions (Villa [110]). Selected illustrative cases are summarized in Table 5.

CONCLUSION

Environmental exposures are important, although variably supported, contributors to AIRDs and rheumatic disease. Understanding these exposures

Table 5. Legal implications

Legal/jurisdiction principle	Illustrative cases	Outcome and specific rationale	Medical evidence used
Aggravation of preexisting conditions	*Sweat v. Superior Industries, Inc.* [109]	The Tennessee Supreme Court found a preexisting, asymptomatic disease compensable when employment activities caused an "actual progression" of the disease. The court placed the burden of proving the nonindustrial portion of the progression on the employer, noting the "inability to precisely quantify" the allocation.	Physician testified that in PsA repetitive, strenuous, weight-bearing activities resulted in permanent joint injury.
Apportionment to causation	*Gonzales v. Team Infinity, Inc* [108]	The court confirmed that apportionment must be based on a physician's analysis of causation. "Vocational apportionment" by nonphysicians cannot negate a valid medical opinion.	Medical experts provided opinions that a preexisting arthritic condition was a contributing cause of disability.
Causation standard for stress related vs. physical injury	*Villa v. Calavo Growers, Inc.* [110]	The court determined the physician incorrectly applied the stricter psychiatric injury standard to a physical injury (FMS) caused by stress.	The case involved a rheumatologist's opinion that the employee's symptoms were best explained by a preexisting psychiatric condition and did not sufficiently explain the causation related to the physical injury.
Burden of proof and substantial medical evidence	*Brophy v. WCAB* [123]	The court emphasized that the defendant has the burden of proving a valid basis for apportionment. A physician must adequately explain "how and why" a nonindustrial factor caused a portion of the disability.	Physician determined that heavy smoking and obesity caused 80% of a pulmonary condition. The report was found to be inadequate when the physician could not explain the apportionment between two injuries beyond stating they were close in time.
Medical treatment vs. causation	*County of Santa Clara v. WCAB* [124]	The court clarified that the employer is not responsible for disability without apportionment if medical treatment is not the sole cause of permanent disability. Apportionment is required if other factors, like a preexisting condition, contribute to the disability.	Diagnostic studies showing preexisting severe osteoarthritis, which led to the need for surgery, served as the basis for a 50% nonindustrial apportionment.
Requirement for substantive apportionment analysis	*Linda Becerra v. Conifer Health Solution* [125]	The court ruled that the doctor's apportionment analyses did not meet standard for substantial evidence because they failed to provide a detailed explanation of "how and why" the disability was causally related to specific nonindustrial factors or prior injuries.	In the apportionment analysis, the physician noted contribution including multiple factors, such as work stresses and orthopedic injuries, without a specific and individualized assessment of how and why each factor is at present contributing.

provides a critical framework in the evolving understanding of disease pathogenesis and has implications for management, public health and safety, historical perspectives about our diseases, and too considerations in our legal system. Despite growing interest, key gaps remain. Future research should prioritize objective and detailed exposure assessment and outline clear temporal relationships to disease onset [111▪]. This may inform public health policy, refine workplace protections, and support intervention in high-risk individuals. In the meantime, clinicians should maintain vigilance for environmental and psychosocial contributors as part of comprehensive rheumatologic care [126▪,127▪▪,128▪,129▪▪].

Acknowledgements

The authors thank Attorneys Kenneth Kingston and Randy Pollack for their advice and helpful discussions.

Financial support and sponsorship

None.

Conflicts of interest

The authors do not have financial interests that are directly or indirectly related to the work submitted for publication.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Costa AN, Kawano-Dourado L, Shinjo SK, *et al.* Environmental exposure in inflammatory myositis. Clin Rheumatol 2014; 33:1689–1690.
2. Albert D, Clarkin C, Komoroski J, *et al.* Wegener's granulomatosis: possible role of environmental agents in its pathogenesis. Arthritis Care Res 2004; 51: 656–664.
3. Stojanovich L, Marisavljevich D. Stress as a trigger of autoimmune disease. Autoimmun Rev 2008; 7:209–213.
4. Anaya JM, Ramirez-Santana C, Alzate MA, *et al.* The autoimmune ecology. Front Immunol 2016; 7:139.
5. Barragán-Martínez C, Speck-Hernández CA, Montoya-Ortiz G, *et al.* Organic solvents as risk factor for autoimmune diseases: a systematic review and meta-analysis. Chaturvedi S, ed. PLoS ONE 2012; 7:e51506.
6. Karlson EW, Deane K. Environmental and gene-environment interactions and risk of rheumatoid arthritis. Rheum Dis Clin N Am 2012; 38:405–426.
7. Fan A, Glace B, Pereira B, *et al.* Posttraumatic stress disorder prior to diagnosis is as rare in spondyloarthritis as in non-inflammatory rheumatic conditions and rheumatoid arthritis. Joint Bone Spine 2023; 90:105500.
8. Zochling J, Bohl-Bühler MHJ, Baraliakos X, *et al.* Infection and work stress are potential triggers of ankylosing spondylitis. Clin Rheumatol 2006; 25: 660–666.
9. Williams KA, Scott JT. Influence of trauma on the development of chronic inflammatory polyarthritis. Ann Rheum Dis 1967; 26:532–537.
10. Miller FW. Is occupational exposure to mineral oil a risk factor for rheumatoid arthritis? Nat Clin Pract Rheumatol 2006; 2:130–131.
11. Labirua-Iturburu A, Selva-O'Callaghan A, Zock JP, *et al.* Occupational exposure in patients with the antisynthetase syndrome. Clin Rheumatol 2014; 33:221–225.
12. Al-Allaf AW. A case–control study examining the role of physical trauma in the onset of fibromyalgia syndrome. Rheumatology 2002; 41:450–453.
13. Buskila D, Mader R. Trauma and work-related pain syndromes: risk factors, clinical picture, insurance and law interventions. Best Pract Res Clin Rheumatol 2011; 25:199–207.
14. McBeth J. The role of workplace low-level mechanical trauma, posture and environment in the onset of chronic widespread pain. Rheumatology 2003; 42:1486–1494.
15. ■ Ajeganova S, Sokolove J. Air pollution's hidden toll: risks for rheumatoid arthritis and rheumatoid arthritis–associated lung disease. Arthritis Rheumatol 2025; 77:789–791.

This editorial highlights a higher risk of RA associated interstitial lung disease (ILD) related to fine particulate matter (PM2.5) exposure and underscores the broader public health risks posed by air pollutants for both RA and RA-ILD.

16. Barbhaiya M, Costenbader KH. Environmental exposures and the development of systemic lupus erythematosus. Curr Opin Rheumatol 2016; 28: 497–505.
17. Chaigne B, Lasfargues G, Marie I, *et al.* Primary Sjögren's syndrome and occupational risk factors: a case–control study. J Autoimmun 2015; 60: 80–85.
18. Marie I, Gehanno JF, Bubenheim M, *et al.* Prospective study to evaluate the association between systemic sclerosis and occupational exposure and review of the literature. Autoimmun Rev 2014; 13:151–156.
19. Tobón GJ, Youinou P, Saraux A. The environment, geo-epidemiology, and autoimmune disease: rheumatoid arthritis. Autoimmun Rev 2010; 9: A288–A292.
20. Cooper GS, Wither J, Bernatsky S, *et al.* Occupational and environmental exposures and risk of systemic lupus erythematosus: silica, sunlight, solvents. Rheumatology 2010; 49:2172–2180.
21. Stolt P, Yahya A, Bengtsson C, *et al.* Silica exposure among male current smokers is associated with a high risk of developing ACPA-positive rheumatoid arthritis. Ann Rheum Dis 2010; 69:1072–1076.
22. Parks C, De Roos A. Pesticides, chemical and industrial exposures in relation to systemic lupus erythematosus. Lupus 2014; 23:527–536.
23. Hart JE, Laden F, Puett RC, *et al.* Exposure to traffic pollution and increased risk of rheumatoid arthritis. Environ Health Perspect 2009; 117:1065–1069.
24. Wu Q, Xu Z, Dan YL, *et al.* Association between traffic-related air pollution and hospital readmissions for rheumatoid arthritis in Hefei, China: a time-series study. Environ Pollut 2021; 268 (Pt A):115628.
25. DeQuattro K, Panush R. Occupational, environmental, and recreational musculoskeletal disorders. In: *Kelley and Firestein's Textbook of Rheumatology*. 11th ed. Elsevier; 2025:chapter 35.
26. Archer C, Gordon DA. Silica and progressive systemic sclerosis (scleroderma): evidence for workers' compensation policy. Am J Ind Med 1996; 29:533–538.
27. Currey J, Therkildsen LHK, Bywaters EGL. Monarticular rheumatoid-like arthritis of seven years' duration following fracture of the radial head. Ann Rheum Dis 1986; 45:783–785.
28. Kembhavi R, Bagewadi RM, *et al.* Incidental arthroscopic finding of rheumatoid arthritis in a posttraumatic ligamentous injury to knee joint. *J Orthop Case Rep.* 2024;14:88–93.
29. Al-Allaf AW. A case–control study examining the role of physical trauma in the onset of rheumatoid arthritis. Rheumatology 2001; 40:262–266.
30. Olsson ÅR, Skogh T, Axelson O, Wingren G. Occupations and exposures in the work environment as determinants for rheumatoid arthritis. Occup Environ Med 2004; 61:233–238.
31. Katz P, Patterson SL, DeQuattro K, *et al.* The association of trauma with self-reported flares and disease activity in systemic lupus erythematosus (SLE). Rheumatology 2023; 62:2780–2788.
32. Roberts AL, Malspeis S, Kubzansky LD, *et al.* Association of trauma and posttraumatic stress disorder with incident systemic lupus erythematosus in a longitudinal cohort of women. Arthritis Rheumatol 2017; 69:2162–2169.
33. Punzi L, Pianon M, Bertazzolo N, *et al.* Clinical, laboratory and immunogenetic aspects of posttraumatic psoriatic arthritis: a study of 25 patients. Clin Exp Rheumatol 1998; 16:277–281.
34. Thorarensen SM, Lu N, Ogdie A, *et al.* Physical trauma recorded in primary care is associated with the onset of psoriatic arthritis among patients with psoriasis. Ann Rheum Dis 2017; 76:521–525.
35. Scarpa R, Del Puente A, Di Girolamo C, *et al.* Interplay between environmental factors, articular involvement, and HLA-B27 in patients with psoriatic arthritis. Ann Rheum Dis 1992; 51:78–79.
36. Hsieh J, Kadavath S, Efthimiou P. Can traumatic injury trigger psoriatic arthritis? A review of the literature. Clin Rheumatol 2014; 33:601–608.
37. Eder L, Law T, Chandran V, *et al.* Association between environmental factors and onset of psoriatic arthritis in patients with psoriasis. Arthritis Care Res 2011; 63:1091–1097.
38. Olivieri I, Gemignani G, Christou C, *et al.* The triggering role of physical injury in the onset of peripheral arthritis in seronegative spondyloarthropathy. Rheumatol Int 1991; 10:251–253.
39. Masson G, Thomas P, Bontoux D, Alcalay M. Influence of trauma on initiation of reiter's syndrome and ankylosing spondylitis. Ann Rheum Dis 1985; 44: 860–861.
40. Jun JB, Kim TH, Jung SS, *et al.* Seronegative spondyloarthropathy initiated by physical trauma. Clin Rheumatol 2000; 19:348–351.
41. Goldberg Andrew L, Keaton Nancy L, Rothfus William E, Daffner Richard H. Ankylosing spondylitis complicated by trauma: MR findings correlated with plain radiographs and CT. Skeletal Radiol 1993; 22:233.
42. Olivieri I, Gherardi S, Bini C, *et al.* Trauma and seronegative spondyloarthropathy: rapid joint destruction in peripheral arthritis triggered by physical injury. Ann Rheum Dis 1988; 47:73–76.
43. Bovenzi M, Barbone F, Pisa FE, *et al.* Scleroderma and occupational exposure to hand-transmitted vibration. Int Arch Occup Environ Health 2001; 74: 579–582.
44. Maître A, Hours M, Bonneterre V, *et al.* Systemic sclerosis and occupational risk factors: role of solvents and cleaning products. J Rheumatol 2004; 31:2395–2401.
45. Buskila D, Neumann L, Vaisberg G, *et al.* Increased rates of fibromyalgia following cervical spine injury. A controlled study of 161 cases of traumatic injury. Arthritis Rheum 1997; 40:446–452.
46. Usui C, Hatta K, Aratani S, *et al.* Vulnerability to traumatic stress in fibromyalgia patients: 19 month follow-up after the great east japan disaster. Arthritis Res Ther 2013; 15:R130.
47. Wynne-Jones G, Macfarlane GJ, Silman AJ, Jones GT. Does physical trauma lead to an increase in the risk of new onset widespread pain? Ann Rheum Dis 2006; 65:391–393.
48. Jones GT, Nicholl BI, McBeth J, *et al.* Role of road traffic accidents and other traumatic events in the onset of chronic widespread pain: Results from a population-based prospective study. Arthritis Care Res 2011; 63:696–701.
49. Harkness EF, Macfarlane GJ, Nahit E, *et al.* Mechanical injury and psychosocial factors in the work place predict the onset of widespread body pain: a two-year prospective study among cohorts of newly employed workers. Arthritis Rheum 2004; 50:1655–1664.
50. Germain V, Scherlinger M, Barnetche T, *et al.* Role of stress in the development of rheumatoid arthritis: a case–control study. Rheumatology 2021; 60: 629–637.
51. Lee YC, Agnew-Blais J, Malspeis S, *et al.* Posttraumatic stress disorder and risk for incident rheumatoid arthritis. Arthritis Care Res 2016; 68:292–298.
52. O'Donovan A, Cohen BE, Seal KH, *et al.* Elevated risk for autoimmune disorders in Iraq and Afghanistan veterans with posttraumatic stress disorder. Biol Psychiatry 2015; 77:365–374.
53. Boscarino JA, Forsberg CW, Goldberg J. A twin study of the association between PTSD symptoms and rheumatoid arthritis. Psychosom Med 2010; 72:481–486.

54. Goldschen L, Ellrodt J, Amonoo HL, *et al.* The link between posttraumatic ■■ stress disorder and systemic lupus erythematosus. Brain Behav Immun 2023; 108:292–301.

This study explored the relationship between PTSD and SLE, contributing to the understanding of how psychological factors may influence the onset and progression of autoimmune diseases.

55. Song H, Fang F, Tomasson G, *et al.* Association of stress-related disorders with subsequent autoimmune disease. JAMA 2018; 319:2388.

56. Patterson S, Trupin L, Hartogensis W, *et al.* Perceived stress and prediction of ■■ worse disease activity and symptoms in a multiracial, multiethnic systemic lupus erythematosus cohort. Arthritis Care Res 2023; 75:1681–1689.

Large longitudinal study which examined the association between psychological stress and disease outcomes in systemic lupus erythematosus (SLE).

57. Simonić E, Kaštelan M, Peternel S, *et al.* Childhood and adulthood traumatic experiences in patients with psoriasis. J Dermatol 2010; 37:793–800.

58. Zeboulon-Ktorza N, Boelle PY, Nahal RS, *et al.* Influence of environmental factors on disease activity in spondyloarthritis: a prospective cohort study. J Rheumatol 2013; 40:469–475.

59. Meng F, Ren S, Meng Y, *et al.* Association between stressful life events and female primary Sjogren's syndrome and their role in disease activity: a retrospective case–control study in china. Neuropsychiatr Dis Treat 2021; 17:213–220.

60. Karaiskos D, Mavragani CP, Makaroni S, *et al.* Stress, coping strategies and social support in patients with primary Sjögren's syndrome prior to disease onset: a retrospective case–control study. Ann Rheum Dis 2009; 68:40–46.

61. Yavne Y, Amital D, Watad A, *et al.* A systematic review of precipitating physical and psychological traumatic events in the development of fibromyalgia. Semin Arthritis Rheum 2018; 48:121–133.

62. Edwards RR, Bingham CO, Bathon J, Haythornthwaite JA. Catastrophizing and pain in arthritis, fibromyalgia, and other rheumatic diseases. Arthritis Care Res 2006; 55:325–332.

63. Haviland MG, Morton KR, Oda K, Fraser GE. Traumatic experiences, major life stressors, and self-reporting a physician-given fibromyalgia diagnosis. Psychiatry Res 2010; 177:335–341.

64. Amital D, Fostick L, Polliack ML, *et al.* Posttraumatic stress disorder, tenderness, and fibromyalgia syndrome: are they different entities? J Psychosom Res 2006; 61:663–669.

65. Bernatsky S, Smargiassi A, Barnabe C, *et al.* Fine particulate air pollution and systemic autoimmune rheumatic disease in two Canadian provinces. Environ Res 2016; 146:85–91.

66. Geslin M, Vachon J, Zhao N, *et al.* Systemic autoimmune rheumatic disease ■■ risk is associated with long-term exposure to fine particulate matter. Arthritis Rheumatol 2025; doi: 10.1002/art.43276. [Epub ahead of print].

This large-scale, population-based cohort study found a positive association between long-term exposure to fine particulate matter (PM2.5) and its various chemical components (including ammonium, mineral dust, nitrate, sulfate, and organic matter) and the risk of developing AIRDs.

67. Di Giuseppe D, Discacciati A, Orsini N, Wolk A. Cigarette smoking and risk of rheumatoid arthritis: a dose–response meta-analysis. Arthritis Res Ther 2014; 16:R61.

68. Boudigaard SH, Schlünssen V, Vestergaard JM, *et al.* Occupational exposure to respirable crystalline silica and risk of autoimmune rheumatic diseases: a nationwide cohort study. Int J Epidemiol 2021; 50:1213–1226.

69. Ilar A, Gustavsson P, Wiebert P, Alfredsson L. Occupational exposure to organic dusts and risk of developing rheumatoid arthritis: findings from a Swedish population-based case–control study. RMD Open 2019; 5:e001049.

70. Kronzer VL, Yang Y, Roul P, *et al.* Associations of fire smoke and other ■■ pollutants with incident rheumatoid arthritis and rheumatoid arthritis-associated interstitial lung disease. Arthritis Rheumatol 2025; 77:808–816.

This study reported s approximately two-fold higher risk of RA-ILD related to exposure to fire smoke $PM_{2.5}$.

71. Jung CR, Hsieh HY, Hwang BF. Air pollution as a potential determinant of rheumatoid arthritis: a population-based cohort study in Taiwan. Epidemiol Camb Mass 2017; 28 (Suppl 1):S54–S59.

72. Alsaber A, Al-Herz A, Al-Mazedi M, *et al.* Predicting the impact of air quality ■ index on rheumatoid arthritis disease activity. Arthritis Care Res 2025; 0:1–10.

This study explored the relationship between air quality and RA disease activity in Kuwait, providing insights into how specific air pollutants, such as nitrogen dioxide and ozone, influence the Disease Activity Score in RA patients.

73. Bernatsky S, Fournier M, Pineau CA, *et al.* Associations between ambient fine particulate levels and disease activity in patients with systemic lupus erythematosus (SLE). Environ Health Perspect 2011; 119:45–49.

74. Bai H, Jiang L, Li T, *et al.* Acute effects of air pollution on lupus nephritis in patients with systemic lupus erythematosus: a multicenter panel study in China. Environ Res 2021; 195:110875.

75. He Y, Qu C, Tian J, *et al.* Association of perfluoroalkyl and polyfluoroalkyl substances (PFASs) exposures and the risk of systemic lupus erythematosus: a case–control study in china. Environ Health 2023; 22:78.

76. Kettaneh A, Al Moufti O, Tiev KP, *et al.* Occupational exposure to solvents and gender-related risk of systemic sclerosis: a metaanalysis of case-control studies. J Rheumatol 2007; 34:97–103.

77. Mora GF. Systemic sclerosis: environmental factors. J Rheumatol 2009; 36: 2383–2396.

78. Patel S, Morrisroe K, Proudman S, *et al.* Occupational silica exposure in an Australian systemic sclerosis cohort. Rheumatology 2020; 59: 3900–3905.

79. Galli G, De Pous-Gerardin C, Hanguehard R, *et al.* Occupational quantitative exposure to crystalline silica, solvents and pesticides and risk of clinical forms of systemic sclerosis. Rheumatology 2024; 63:3397–3406.

80. Dospinescu P, Jones GT, Basu N. Environmental risk factors in systemic sclerosis. Curr Opin Rheumatol 2013; 25:179–183.

81. Rubio-Rivas M, Moreno R, Corbella X. Occupational and environmental scleroderma. Systematic review and meta-analysis. Clin Rheumatol 2017; 36:569–582.

82. McCormic ZD, Khuder SS, Aryal BK, *et al.* Occupational silica exposure as a risk factor for scleroderma: a meta-analysis. Int Arch Occup Environ Health 2010; 83:763–769.

83. 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; 128:1094–1101.

84. Yang Y, Fujita J, Tokuda M, *et al.* Clinical features of polymyositis/dermatomyositis associated with silicosis and a review of the literature. Rheumatol Int 2001; 20:235–238.

85. Gold LS, Ward MH, Dosemeci M, Roos AJD. Systemic autoimmune disease mortality and occupational exposures. Arthritis Rheum 2007; 56:3189–3201.

86. Lundberg I, Alfredsson L, Plato N, *et al.* Occupation, occupational exposure to chemicals and rheumatological disease: a register based cohort study. Scand J Rheumatol 1994; 23:305–310.

87. De Roos AJ, Cooper GS, Alavanja MC, Sandler DP. Rheumatoid arthritis among women in the agricultural health study: risk associated with farming activities and exposures. Ann Epidemiol 2005; 15:762–770.

88. Lu-Fritts P, Kottyan LC, James JA, *et al.* Association of systemic lupus erythematosus with uranium exposure in a community living near a uranium-processing plant: a nested case–control study. Arthritis Rheumatol 2014; 66:3105–3112.

89. Parks CG, Walitt BT, Pettinger M, *et al.* Insecticide use and risk of rheumatoid arthritis and systemic lupus erythematosus in the women's health initiative observational study. Arthritis Care Res 2011; 63:184–194.

90. Dahlgren J, Takhar H, Anderson-Mahoney P, *et al.* Cluster of systemic lupus erythematosus (SLE) associated with an oil field waste site: a cross sectional study. Environ Health 2007; 6:8.

91. Gardner RM, Nyland JF, Silva IA, *et al.* Mercury exposure, serum antinuclear/antinucleolar antibodies, and serum cytokine levels in mining populations in Amazonian Brazil: a cross-sectional study. Environ Res 2010; 110:345–354.

92. Parks CG, Cooper GS, Nylander-French LA, *et al.* Occupational exposure to crystalline silica and risk of systemic lupus erythematosus: a population-based, case–control study in the Southeastern United States. Arthritis Rheum 2002; 46:1840–1850.

93. Aryal BK, Khuder SA, Schaub EA. Meta-analysis of systemic sclerosis and exposure to solvents. Am J Ind Med 2001; 40:271–274.

94. Serratrice J, Granel B, Pache X, *et al.* A case of polymyositis with antihistidyl-t-RNA synthetase (jo-1) antibody syndrome following extensive vinyl chloride exposure. Clin Rheumatol 2001; 20:379–382.

95. Brautbar N, Richter ED, Nesher G. Systemic vasculitis and prior recent exposure to organic solvents: report of two cases. Arch Environ Health Int J 2004; 59:515–517.

96. Bond M, Tomelleri A, Reatini MA, *et al.* Impact of exposure to environmental ■ particulate matter on the onset of giant cell arteritis. Arthritis Care Res 2025; 77:30–37.

97. Bond C, Cleland L. Rheumatoid arthritis: are pets implicated in its etiology? Semin Arthritis Rheum 1996; 25:308–317.

98. Penglis PS, Bond C, Humphreys I, *et al.* Genetic susceptibility and the link between cat exposure and rheumatoid arthritis. Semin Arthritis Rheum 2000; 30:111–120.

99. Cerk B, Panush RS. Food, diet, nutrition & rheumatic diseases. Rheumatol 2021; 15:37–39.

100. Panush RS, Wise LM. Complementary and alternative remedies in rheumatic disorders. UpToDate (an educational program on CD-ROM). SM Helfgott, Section Editor for Rheumatology, SM Case, Deputy Editor for Rheumatology, JR O'Dell and DS Pisetsky, Editors for Rheumatology, T Post, Editor-in-Chief, Waltham, MA. Wolters Kluwer Health, 1997.

101. Stoyler L, Matteson EL, Panush RS. The antiquity of rheumatic diseases as in Giovanni Morgagni's 1761 "de sedibus et causis morborum per anatomen indagatis (the seats and causes of diseases as investigated by anatomy)". *Pharos* 2021; 84:28–36.

102. Evers AWM, Zautra A, Thieme K. Stress and resilience in rheumatic diseases: a review and glimpse into the future. Nat Rev Rheumatol 2011; 7:409–415.

103. Lescoat A, Cavalin C, Macchi O, *et al.* Silica-associated systemic sclerosis in 2017: 60 years after Erasmus, where do we stand? Clin Rheumatol 2017; 36: 1209–1210.

104. Garabrant DH, Dumas C. Epidemiology of organic solvents and connective tissue disease. Arthritis Res 2000; 2:5–15.

105. Panush RS. Rheum with a view. Clinical and immunopathologenetical significance of antibodies to cyclic citrullinated proteints. or, why did RA begin in 1800? Rheumatologist 2012; 40–41.

106. Deane KD, El-Gabalawy H. Pathogenesis and prevention of rheumatic disease: focus on preclinical RA and SLE. Nat Rev Rheumatol 2014; 10: 212–228.
107. DeQuattro K, Trupin L, Patterson S, *et al.* Positive psychosocial factors may protect against perceived stress in people with systemic lupus erythematosus with and without trauma history. Lupus Sci Med 2024; 11:e001060.
108. *Gonzalez v. Team Infinity et al.* Raymond F. Correio (Workers' Compensation Appeals Board (WCAB) of the State of California, 2023).
109. *Joey Sweat v. Superior Industries, Inc.* (Supreme Court of Tennessee Workers' Compensation Appeals Panel 1998).
110. *Bibiana Bravo Villa v. Calavo Growers, Inc.; Travelers Property Casualty Company of America* (Workers' Compensation Appeals Board.(WCAB) of the State of California 2024).
111. ▪ Hart JE, Costenbader KH. Environment and systemic autoimmune rheumatic diseases: what do we know after more than 15 years of research? Arthritis Rheumatol 2025; 0:1–2.
This editorial highlighted the strengths of utilizing large, population-based samples and assessing individual PM2.5 components to gain more insight into the sources of air pollution that may contribute to AIRDs.
112. Wallace DJ. The role of stress and trauma in rheumatoid arthritis and systemic lupus erythematosus. Semin Arthritis Rheum 1987; 16:153–157.
113. Sigaux J, Biton J, André E, *et al.* Air pollution as a determinant of rheumatoid arthritis. Joint Bone Spine 2019; 86:37–42.
114. Edwards CJ, Cooper C. Early environmental exposure and the development of lupus. Lupus 2006; 15:814–819.
115. ▪▪ Parperis K, Papachristodoulou M, Derk C, *et al.* Posttraumatic stress disorder and systemic lupus erythematosus: insights from a systematic review. Rheumatology 2025; 00:1–8.
This systematic review assessed the current medical literature on the impact of PTSD on the development of SLE and affirms the high prevalence and its significant effect on patient-reported outcomes.
116. Stober C. Pathogenesis of psoriatic arthritis. Best Pract Res Clin Rheumatol 2021; 35:101694.
117. Wolfe F, Häuser W, Walitt BT, *et al.* Fibromyalgia and physical trauma: the concepts we invent. J Rheumatol 2014; 41:1737–1745.
118. White KP, Carette S, Harth M, Teasell RW. Trauma and fibromyalgia: Is there an association and what does it mean? Semin Arthritis Rheum 2000; 29: 200–216.
119. Sverdrup B, Källberg H, Bengtsson C, *et al.* Association between occupational exposure to mineral oil and rheumatoid arthritis: results from the swedish EIRA case–control study. Arthritis Res Ther 2005; 7:R1296.
120. Sigaux J, Cavalin C, Lescoat A, *et al.* Are cleaning activities a source of exposure to crystalline silica in women with rheumatoid arthritis? A case–control study. RMD Open 2023; 9:e003205.
121. Chang KH, Hsu CC, Muo CH, *et al.* Air pollution exposure increases the risk of rheumatoid arthritis: a longitudinal and nationwide study. Environ Int 2016; 94:495–499.
122. Silman AJ, Jones S. What is the contribution of occupational environmental factors to the occurrence of scleroderma in men? Ann Rheum Dis 1992; 51: 1322–1324.
123. *Brophy v. Workers' Compensation Appeals Board.* (Court of Appeal. Workers' Compensation Appeals Board.(WCAB) of the State of California 2021).
124. *County of Santa Clara v. Workers' Compensation Appeals Board.*(Court of Appeal. Workers' Compensation Appeals Board.(WCAB) of the State of California 2020).
125. Linda Becerra v. Conifer Health Solution, Permissibly Self-Insured, Administered by Sedgwick Claims Management Services.(Workers' Compensation Appeals Board.(WCAB) of the State of California 2023).
126. ▪ Tian D, Li P, Chen L, *et al.* Soft water exposure increases the effect of genetic susceptibility on the risk of rheumatoid arthritis. Seminars in Arthritis and Rheumatism 2025; 74:152788.
This observational study reported that exposure to soft water was associated with an increased risk of RA.
127. ▪▪ Nielsen HB, Sejbaek CS, Dreyer LW, *et al.* Occupational history of psychosocial work environment exposures and risk of autoimmune rheumatic diseases–a Danish register-based cohort study. Scand J Work Environ Health 2025; 51:226–236.
This study of a cohort of over 2.3 million Danish workers suggested that certain occupational stress and recent adverse psychosocial and physical violence contributed to rheumatic disease incidence.
128. ▪ Wang Y, Liu J, Zhu Z, *et al.* The association between exposure to brominated flame retardants and arthritis, osteoarthritis, and rheumatoid arthritis: a cross-sectional study. BMC Public Health 2025; 25:2272.
An analysis of U.S. National health data identified associations between flame retardants and the prevalence of RA.
129. ▪▪ Feng BB, Zhang YX, Dai XY, *et al.* Association of ambient air pollution with incident rheumatoid arthritis, subsequent respiratory diseases, and death: a multi-state analysis of a prospective cohort. Ecotoxicol Environ Saf 2025; 302:118557.
This prospective study associated higher exposure to air pollution, including $PM_{2.5}$, PM_{10}, NO_2, and NO with increased risk of RA, respiratory disease, and mortality.