RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Are cleaning activities a source of exposure to crystalline silica in women with rheumatoid arthritis? A case–control study

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To cite: 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. doi:10.1136/rmdopen-2023-003205

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2023-003205).

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Received 3 April 2023
Accepted 30 June 2023

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ABSTRACT

Introduction Inhalation of crystalline silica (silicon dioxide, SiO_2) is associated with a wide range of acute and chronic diseases, including rheumatoid arthritis (RA). The objectives of this work were to identify the main sources of exposure to SiO_2 in a series of patients with RA not selected on the basis of their professional activity, compared with a representative sample of the French general population, and to assess the association between silica exposure and disease features.

Methods The Dust Exposure Life-Course Questionnaire (DELCQ) is a tool that enables retrospective quantification of both occupational and non-occupational lifetime exposure to SiO_2. DELCQ—previously validated in a large representative sample of the French general population—was administered to 97 consecutive RA patients, and exposure scores were compared between cases and age, gender and smoking status-matched controls (1:4). The main sources of SiO_2 exposure were identified in cases and controls, and source-specific exposure levels were compared. The association between DELCQ scores and disease variables in cases was tested via univariable and multivariable analyses.

Results In women with RA, the main sources of SiO_2 exposure were cleaning activities and dusty clothes laundry, with higher exposure levels from these sources versus the general population ($p<0.005$). Across the whole series of RA patients, high SiO_2 exposure was independently associated with mediastinal lymphadenopathy (OR 6.3, 95% CI 1.4 to 27.7).

Conclusion Cleaning activities and dusty clothes laundry may be underestimated sources of SiO_2 exposure in women with RA.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Inhalation of crystalline silica (silicon dioxide, SiO_2) is associated with rheumatoid arthritis (RA).
⇒ Research on the role of SiO_2 in human disease has been traditionally focused on occupational exposures, with male workers as the main target population.
⇒ Substantial exposure from both occupational and non-occupational sources may occur in both men and women over the life course.

WHAT THIS STUDY ADDS

⇒ The Dust Exposure Life-Course Questionnaire (DELCQ), is a novel tool that allows to quantify retrospectively both occupational and non-occupational lifetime exposure to SiO_2.
⇒ Women with RA have high lifetime exposure to SiO_2 from sources that are currently neglected in research: cleaning activities and dusty clothes laundry.
⇒ High occupational DELCQ scores were associated with mediastinal lymphadenopathy, a proxy of crystalline silica exposure.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the importance of daily-life sources of exposure to crystalline silica, particularly in household products, and their association with RA in women.

INTRODUCTION

Inhalation of crystalline silica (silicon dioxide, SiO_2) is associated with a wide range of acute and chronic diseases,[1] including rheumatoid arthritis (RA).[2] In a recent meta-analysis of epidemiological studies, occupational exposure to SiO_2 was associated with a 2.59-fold higher odds of RA.[3] Exposure to SiO_2 has been identified as a risk factor for incident RA in the Swedish population,[4] showing a closer association with seropositive RA[5 6] and positive interaction with smoking.

SiO_2 is present in diverse polymorphs like quartz, cristobalite and tridymite; quartz is the most common form found in nature, and the main component of the crystalline silica dust that may be emitted in manufacturing processes.[5] SiO_2 is used in a wide range of

industrial activities. High exposure to crystalline silica dust may occur in blast furnace, electronics glass, cement and ceramic manufacturing. It may also occur in other sectors such as mining (historically the main sector of exposure to SiO_2 and subsequent silicosis), farming and construction.[7]

Since these activities may involve intense exposure for workers, research on SiO_2 in human diseases has historically focused on occupational exposure and on male workers as the main target population.[8] However, SiO_2 is ubiquitous in the environment. Over a lifetime, both men and women may experience substantial exposure across many professional activities and even beyond occupational contexts.

SiO_2 is present in a wide range of products (scouring powders, cat litter, rubber tires, etc) that may emit airborne particles. Thus, an accurate measure of actual lifetime exposure to crystalline silica remains a challenging task.[9]

The Dust Exposure Life-Course Questionnaire (DELCQ) is a novel tool that enables retrospective quantification of both occupational and non-occupational lifetime exposure to SiO_2.[10]

A multidisciplinary team of epidemiologists, social scientists, occupational health and medicine collaborators developed the questionnaire to identify situations likely to expose people to SiO_2. The exposures were based on an extensive list of products and activities summarised by the International Agency for Research on Cancer[11] and complemented by medical and statistical surveys of the general population[12–14] as well as data from the literature about exposure to SiO_2 and inorganic particles in occupational or environmental settings.[9 15]

DELCQ was administered in 2016 to a representative sample of the French general population (ELIPSS cohort, ELIPSSilice2 survey) selected from the French national rolling census by the French National Institute of Statistics and Economic Studies (INSEE). This population serves as a control for case–control studies of lifetime exposure to SiO_2 in patients with specific diseases such as RA and systemic sclerosis.[10] Using DELCQ, we recently found that both male and female RA patients had higher occupational exposure to SiO_2 than their respective controls, and that women with RA also had higher non-occupational exposure than controls.[10]

In this case–control study, we sought to identify the actual sources of SiO_2 exposure in patients with RA, and to explore the association between the level of SiO_2 exposure and major disease features and outcomes.

PATIENTS AND METHODS

Patients

The case and control populations and SiO_2 exposure assessment are detailed elsewhere.[10] In short, 97 patients who were diagnosed with RA according to 2010 ACR/EULAR classification criteria and followed by the Department of Rheumatology of Avicenne Teaching Hospital (GHUPSSD, APHP, Bobigny, France) were consecutively recruited in a retrospective observational study between June and December 2016.

A specially trained interviewer administered DELCQ to all patients. The interviews typically lasted 45–60 min and were conducted in person for 56 patients and by phone for 41.

Clinical, laboratory and radiological data were retrieved from patient files.

For a subgroup of patients, high-resolution CT (HRCT) images of the chest were available. HRCT was not performed on purpose for this study, and had been carried out in the setting of patient usual care or prior initiating a targeted treatment. Two investigators evaluated HRCT images of the chest while blinded to the results of the SiO_2 exposure evaluations (LSesé, P-YB). The investigators determined the presence and extent of interstitial lung disease (ILD), and the presence of emphysema, mediastinal lymphadenopathy (LA), nodules and micronodules (number and shape). They assessed the presence and extent of ILD according to the Fleischner Society criteria.[16] The most relevant CT signs of ILD are reticular patterns, traction bronchiectasis, ground-glass opacity and honeycombing. We also included ILAs (interstitial lung abnormalities) in our definition of ILD. ILAs are described as non-dependent abnormalities affecting more than 5% of any lung zone.[17] Mediastinal LAs were measured along their short axis and considered significant if >10 mm.

Controls

For each patient, up to four gender, age and smoking-status matched controls were randomly sampled from the ELIPSSilice2 cohort (online supplemental figure 1). Briefly, ELIPSSilice2 is composed of subjects sampled by INSEE, based on national rolling census data and representative of the French general population (aged 18–76 at the time of the census), that is, independent of any health considerations. Subjects (n=2 739) completed the DELCQ questionnaire in 2016. The questionnaire was self-administered on tablets.

Patient and public involvement

Patients and the public were neither involved in the design and conduct of the study, nor the choice of outcome measures, nor the recruitment.

Assessment of silica exposure

The design and the content of DELCQ are thoroughly described elsewhere.[10]

Briefly, DELCQ addresses both occupational and non-occupational exposure over a lifetime through more than 130 questions (online supplemental data 1 and 2).

The questionnaire was conducted by phone or in-person interview by a trained interviewer (OM or SER) who was unaware of the results of clinical, immunological and pulmonary assessments. A score from 0 to 5 (based on the cumulative exposure duration and level

of protection) was given for each specific exposure. Both the occupational (OES) and non-occupational exposure scores (NOES) were calculated by adding up the scores for each specific exposure. The two scores were analysed separately.

Statistical analysis

The occupational and non-occupational DELCQ scores related to each single source of exposure were compared between women with RA and controls using the Wilcoxon test. The Bonferroni correction was applied to avoid alpha-risk inflation due to multiple comparisons. The associations between DELCQ score quartiles and patient variables (for both male and female patients) were analysed with the Chi-square test or Fisher's exact test and expressed with OR and 95% CIs. A logistic regression model including age, gender, disease duration, anticitrullinated protein antibody (ACPA)/rheumatoid factor (RF) positivity and smoking status (defined as never, current or former smoker) was used to assess the association between SiO_2 exposure and HRCT abnormalities at multivariable analysis. Patients with an exposure score in the fourth quartile were considered to be highly exposed, and were compared with patients in the first to third quartiles. For all tests, the significance level was set at $p<0.05$. All statistical analyses were performed with R and RStudio V.2022.07.0 software.

Role of the funding source

The SILICOSIS project was funded with an Advanced Grant from the European Research Council. As such, its principal investigator Paul-André Rosental of the Centre for European Studies and Comparative Politics (Sciences Po, Paris) and his team are solely responsible for the design of the study; the data collection, analysis and interpretation; the writing of publications; and decisions to submit written outputs for publication in journals or books.

RESULTS

A total of 97 patients with RA (mean age: 59.4±13.2 years; 76 women and 21 men) completed the DELCQ questionnaire (table 1).

Mean RA duration was 13.1±11 years, most patients were RF and/or ACPA positive, and 61.9% were never smokers (19% of male vs 73% of female patients, $p<0.05$). At least one HRCT scan of the chest was available for 63.9% of patients.

As previously reported,[10] RA patients had significantly higher OES than their matched controls, whereas no difference appeared for non-occupational exposures. However, women with RA had both higher occupational and non-occupational exposures to SiO_2 than their female matched controls. We therefore sought to uncover the most relevant sources of SiO_2 exposure in female patients by studying and comparing the distribution of occupational and non-occupational sources of SiO_2 exposure in women with RA and their controls.

Sources and levels of occupational and non-occupational silica exposure in women with RA and controls

Cleaning activities are the most important source of occupational exposure, accounting for 31% of women's total occupational exposure (15.7% from 'proper' cleaning activities+15.3% from laundry for dusty work clothes). Then came farming (9.1%), steel welding (4.2%) and construction (3.0%) activities (data not shown). The sources of occupational SiO_2 exposures in controls were also primarily cleaning activities (15.2% from 'proper' cleaning activities+6.2% from laundry for dusty work clothes=21.4%) and farming activities (19.6%) (data not shown).

We then compared the mean score allocated to each main occupational and non-occupational source for women with RA versus controls (table 2).

Within occupational activities, women with RA had higher exposure scores for cleaning activities (1.03±1.71 vs 0.46±1.32, $p=0.02$) and laundry for dusty work clothes (1.00±1.86 vs 0.19±0.86, $p=0.01$).

Among non-occupational SiO_2 exposure sources, women with RA had higher scores than controls for cleaning activities (8.03±4.29 vs 3.92±4.48, $p<0.0001$).

Association between silica exposure and patient variables

Ever-smoker RA patients (active or former) were more likely to be in the highest quartile of SiO_2 OES than never-smoker patients ($p=0.002$), but no difference was observed for NOES ($p=0.18$) (table 3).

Being in the highest quartile of SiO_2 exposure (occupational or non-occupational) showed no association with ACPA or RF status, radiographic erosion, or the need for biologic disease-modifying antirheumatic drugs (DMARDs). Conversely, high occupational exposure to SiO_2 was associated with ILD, emphysema and mediastinal LA (all $p<0.05$, table 3).

The association between high occupational SiO_2 exposure, ILD and mediastinal LA at HRCT persisted after adjustment for smoking status (ie, ever-smoker or never-smoker), with a sixfold increased risk for patients in the highest OES quartile (table 4). Further adjusting for ACPA and/or RF status, gender and disease duration had no bearing on the associations.

DISCUSSION

This study shows that women with RA, not selected on the basis of their professional activity, have high lifetime exposure to SiO_2 from sources that are currently neglected in research: cleaning activities and dusty clothes laundry. The use of an accurate questionnaire derived from social sciences enabled identification of these unconventional sources of SiO_2 exposure.

Cleaning activities in particular were a relevant source of exposure to SiO_2 in both occupational and non-occupational contexts. Given that around 60% of the women in the series were retired or officially unemployed, our study's retrospectivity allowed us to identify

Table 1 RA patient characteristics

General characteristics	Overall RA population (n=97)	Female RA (n=76)	Male RA (n=21)	P value
Age (years)	59.4±13.2	57.4±13.0	66.4±12.2	<0.01
RA duration (years)	13.1±11.0	13.4±10.9	12.1±11.6	NS
ACPA positive	78 (83.0)	57 (75.0)	21 (100)	<0.05
RF positive	76 (84.4)	58 (76.3)	18 (85.7)	NS
Erosive RA	80 (84.2)	61 (80.3)	19 (90.5)	NS
Tobacco users				
Never a smoker	60 (61.9)	56 (73.7)	4 (19.0)	<0.0001
Current smoker	14 (14.4)	9 (11.8)	5 (23.8)	NS
Former smoker	23 (23.7)	11 (14.5)	12 (57.1)	<0.001
Occupation				
Never worked or student	6 (6.4)	6 (7.9)	0 (0)	NS
Active worker	29 (30.8)	23 (30.3)	6 (28.6)	NS
Non-active worker (retired or unemployed)	59 (62.8)	48 (63.2)	11 (52.4)	NS
RA treatments				
MTX	53 (54.6)	42 (55.3)	11 (52.5)	NS
bDMARDs	54 (55.7)	44 (57.9)	10 (47.6)	NS
Never bDMARDs user	30 (30.9)	23 (30.3)	7 (33.3)	NS
bDMARD 1st line	37 (38.1)	31 (40.8)	6 (28.6)	NS
bDMARD 2nd line	18 (18.6)	13 (17.1)	5 (23.8)	NS
bDMARD 3rd line	6 (6.2)	5 (6.6)	1 (4.8)	NS
bDMARD >3rd line	6 (6.2)	4 (5.3)	2 (9.5)	NS
Chest HRCT scan	62 (63.9)	50 (65.8)	12 (57.1)	NS
Normal HRCT chest scan	12 (19.3)	12 (24.5)	0 (0)	NS
ILD	11 (18.0)	7 (14.3)	4 (16.7)	NS
Emphysema	12 (19.7)	5 (10.2)	7 (58.3)	<0.001
Mediastinal lymph nodes	17 (27.4)	12 (24.5)	5 (41.7)	NS
Pulmonary nodules*	18 (29.0)	13 (26.5)	5 (41.7)	NS

Data are expressed as absolute number and percentage (%) or mean (SD).
*Nodules or micronodules.
ACPA, anticitrullinated protein antibody; bDMARD, biologic disease-modifying antirheumatic drug; HRCT, high-resolution CT; ILD, interstitial lung disease; MTX, methotrexate; NS, not significant; RA, rheumatoid arthritis; RF, rheumatoid factor.

substantial exposure to SiO_2 in a population that would not usually be considered at risk.

Like cigarette smoke, SiO_2 is an airborne agent that may initiate an inflammatory response in lung tissue. In predisposed individuals, local inflammation is conducive to the activation of adaptive immunity, production of autoantibodies and progression towards systemic disease.[5 6]

The association between high occupational exposure to SiO_2 and incident RA is supported by several observational studies.[3 18] A Swedish nationwide study also found an association between the risk of incident RA and a job-matrix score based on occupations with established high exposure to SiO_2.[8] However, all these studies focused on specific jobs known to expose workers to high levels of SiO_2.

Conversely, the novelty of this study was the assessment and quantification of SiO_2 exposure in an unselected sample of consulting RA patients. In a previous study, we showed that patients (men and women with RA) primarily differ from their (respective) matched controls on the level of lifetime occupational exposure.[10] Consistent with the literature, men and women with RA had higher occupational exposure to SiO_2 than both (respective) gender-matched controls. Occupational exposure was mainly attributable to male-dominated activities such as construction, glass, mining, agriculture, ceramics and electronics.[7]

The novelty of this work lies in its measurement of non-occupational exposure, and of occupational exposure from occupational activities that are not necessarily identified as at-risk. In the case of women, we had

Table 2 Main sources of occupational and non-occupational silica exposure in women with RA versus controls (expressed as the mean and SD of exposure score)

	RA women n=76		Control women n=308			
Activities	**Mean**	**SD**	**Mean**	**SD**	**P value***	**Bonferroni correction†**
Main occupational activities (OES)						
Construction	0.19	1.71	0.12	1.22	0.99	NS
Farming	0.60	2.64	0.60	2.52	0.72	NS
Stone	0.09	0.57	0.03	0.32	0.13	NS
Wood	0.00	0.00	0.10	1.05	0.39	NS
Cleaning	1.03	1.71	0.46	1.32	<0.001	†
Metallurgy	0.05	0.46	0.03	0.51	0.29	NS
Painting	0.06	0.41	0.06	0.40	0.99	NS
Plumbing	0.00	0.00	0.00	0.00	–	NS
Steel welding	0.27	1.48	0.03	0.33	0.02	NS
Dusty work clothes laundry	1.00	1.86	0.19	0.86	<0.001	†
Main non-occupational activities (NOES)						
Farming	2.30	4.07	1.06	1.88	0.13	NS
DIY	1.05	1.61	0.80	1.40	0.19	NS
Wood	0.32	0.97	0.29	0.96	0.73	NS
Cleaning	8.03	4.29	3.92	4.48	<0.001	†
Dusty work clothes laundry	2.55	3.71	1.76	3.30	0.064	NS
Cat litter	0.47	0.79	0.82	0.95	0.003	†
Mud bath	0.49	0.64	0.81	0.94	0.03	NS

*Wilcoxon test, level of significance p<0.05.
†Bonferroni correction, level of significance p<0.004 for occupational activities, p<0.006 for non-occupational activities.
NOES, non-occupational exposure score; OES, occupational exposure score; RA, rheumatoid arthritis.

previously shown that our sample of female RA patients were more exposed to SiO_2 from both occupational and non-occupational than their matched controls randomly sampled from the general population.[10] Moreover, while tobacco plays a role in the pathogenesis of RA, since the vast majority of these female patients were non-smokers,

Table 3 Association between SiO_2 exposure (occupational and non-occupational, by quartile) and patient characteristics

	Occupational exposure score			Non-occupational exposure score		
RA patient variable	**Q1–Q3**	**Q4**	**P value***	**Q1–Q3**	**Q4**	**P value***
Ever-smoking, n (%)	21 (28.8)	16 (66.7)	0.002	25 (33.8)	12 (55.2)	0.18
ACPA-positivity, n (%)	56 (78.9)	22 (95.6)	0.16	61 (85.9)	17 (73.9)	0.31
Erosive RA patients, n (%)	61 (84.7)	19 (82.6)	0.93	62 (84.9)	18 (81.8)	0.98
bDMARD treatment n (%)	44 (60.3)	10 (41.7)	0.17	38 (51.3)	16 (69.6)	0.19
ILD, n (%)	5 (10.9)	6 (37.5)	0.04*	9 (19.1)	2 (13.3)	0.9
Emphysema, n (%)	5 (10.9)	7 (43.7)	0.004*	8 (17.4)	4 (25.0)	0.51
Mediastinal LA, n (%)	9 (19.6)	8 (50.0)	0.04*	14 (28.0)	3 (25.0)	0.88
Lung micronodules, n (%)	4 (8.7)	3 (18.7)	0.27	5 (10.6)	2 (13.3)	0.77

*χ^2 test, level of significance p<0.05.
ACPA, anticitrullinated protein antibody; bDMARD, biologic disease-modifying antirheumatic drug; ILD, interstitial lung disease; LA, lymphadenopathy; RA, rheumatoid arthritis.

Table 4 Association between occupational silica exposure (by quartile) and HRCT lung abnormalities

HRCT abnormality	OES (quartiles)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Mediastinal lymphadenopathy	Q1–Q3	(ref)	(ref)
	Q4	4.1 (1.2 to 13.9)	6.3 (1.4 to 27.7)
Interstitial lung disease	Q1–Q3	(ref)	(ref)
	Q4	6.3 (1.5 to 26.6)	6.5 (1.3 to 32.6)
Emphysema	Q1–Q3	(ref)	(ref)
	Q4	6.4 (1.6 to 24.7)	2.9 (0.6 to 13.7)

ORs adjusted for smoking status, gender, disease duration, anticitrullinated protein antibody and rheumatoid factor status.
HRCT, high-resolution CT; OES, occupational exposure score.

SiO_2 may be a major contributor to the pathogenesis of the disease in this subgroup.

The thoroughness of DELCQ enables the identification of specific sources of SiO_2 exposure in women with RA. The main sources are related to cleaning activities. Contact with SiO_2 comes from household cleaning products[19] and from the manipulation of clothes belonging to workers directly exposed to high levels of SiO_2 (dusty work clothes laundry). As those activities (mainly performed by women) are not considered to be associated with SiO_2 hazards, specific protections are rarely (if ever) implemented. Even fewer protections are considered when these activities are practiced at home. Hence, the absence of protection during house chores impacted the DELCQ score and led us to identify hitherto unrecognised sources of non-occupational exposure to SiO_2.

According to DELCQ, people who perform housekeeping activities are exposed to SiO_2, which many detergents contain. However, the use of cleansing agents has not been demonstrated to result in substantial SiO_2 exposure, and the association with RA may be due to other compounds contained in the detergents. In the Swedish Epidemiological Investigation of Rheumatoid Arthritis cohort, a strong association between occupational exposure to detergents and the risk of both ACPA-positive and ACPA-negative RA was found. Detergents were the most prevalent occupational inhalant for men (percentage exposed: 31%) and women (51%) with RA.[20]

In a Swedish cross-sectional study of 40 000 workers, the prevalence of RA was higher in women working as cleaners; doctors and nurses; nurse assistants; textile workers; shop assistants; bank, postal and telegraph personnel; and housewives.[21] The study hypothesised the action of an environmental factor, but SiO_2 was not mentioned as a possible one. Another epidemiological study found a looser association with RA in women working as hairdressers or beauticians, especially those exposed to hair products. No information was provided about the composition of the products, including any possible SiO_2 content.[20]

Interestingly, Colinet's patients (whose description was used for the Caplan-Colinet syndrome[22]) were employees of a soap factory, involved in silica-scouring powder packing.[23]

Our female patient sample includes a vast majority of housewives from low-income households, partially reflecting Avicenne hospital's location in a poor urban area. Their cumulative exposure may be compared with an occupational one, even though housecleaning products may differ from those used in occupational contexts. A documented association between low socioeconomic status and RA exists,[24 25] but no study has ever considered the potential role of SiO_2 exposure in this association.

The association of high occupational DELCQ scores with HRCT abnormalities, notably mediastinal LA, provides external validity to the questionnaire. Since mediastinal LA is a common characteristic of silicosis, it can be considered a proxy for high SiO_2 exposure.[26 27] A similar association with high occupational DELCQ scores was demonstrated in a series of scleroderma patients.[28]

High occupational SiO_2 exposure was also independently associated with ILD after adjusting for potential confounders. This association is intriguing as it links SiO_2 exposure with a type of rheumatoid lung involvement. However, this association may only be due to chance and needs to be confirmed in larger series. In addition, we may have overestimated the proportion of ILD and the strength of the association. As chest HRCT had been performed only for some patients in the setting of their usual care or prior initiating a targeted treatment, a selection bias based on the presence of pulmonary involvement or on the severity of RA is likely present.

No association was found between the DELCQ and other markers of disease severity like radiographic erosion, ACPA/RF positivity and level, or the need for biologic DMARDs therapy.

The main limitation of the study is the limited sample size and the recruitment of patients from a single centre located in a poor urban area, which may result in under or overestimating relevant sources of exposure among RA patients. This may reduce the generalisability of the results and larger studies in more heterogeneous populations are needed to confirm this finding. However, the patients were recruited from a 2 million inhabitants

territory that stretches over two different administrative areas, one of which displays a sociodemographic profile corresponding to that of the French society. In fact, the main sources of exposure that we have identified did not greatly differ from those of controls extracted from a representative sample of the French general population. Another limitation is that the questionnaire administration method differed between the controls (self-administered questionnaire on digital tablets) and the cases (administered by a trained interviewer by phone or in person), potentially introducing an evaluation bias. We estimated and discussed the impact of that potential bias elsewhere,[10 29] as we compared the DELCQ scores of our hospital cohort of patients with RA to those of self-reported RA patients inside the general population panel from which the healthy controls were selected (ELLIPSILICE 1 and 2). Although occupational (but not non-occupational) scores were lower in self-declared patients, the difference was not major and may be partly explained by higher diagnostic accuracy in a hospital setting. More importantly, inside the general population sample, the DELCQ score was able to discriminate between healthy subjects and self-reported patients both on occupational and non-occupational scores. Thus, although the different mode of administration might have led to overestimate the size of the difference, this is unlikely to affect the validity of the analysis.

The study's main strength lies in the tool we used to assess SiO_2 exposure. DELCQ is a detailed questionnaire that is not excessively time-consuming but enables quantification of lifetime SiO_2 exposure, accounting for the source of SiO_2, context of exposure (occupational vs non-occupational), cumulative duration of exposure and use of protection.

In conclusion, this study identifies underestimated sources of potential SiO_2 exposure in women with RA. Both mechanistic and larger epidemiological studies are warranted to explore the relevance of SiO_2 exposure from those sources and the possible need for preventive strategies.

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Funding SILICOSIS Project, led by Paul-André Rosental, Centre for European Studies and Comparative Politics, Sciences Po (Paris, France), sponsored by the European Research Council (ERC); (grant number ERC-2011-ADG_20110406, project ID 295817).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by CLEA (Comité local éthique Avicenne), N° 2016-256. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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