


Joint surgery rates in lupus: a long-term cohort study

Johannes Nossent ^{1,2}, Helen Isobel Keen,^{1,3} David Brian Preen,⁴ Charles A Inderjeeth^{1,5}

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¹Medical School, The University of Western Australia, Perth, Western Australia, Australia

²Department of Rheumatology, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia

³Rheumatology, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

⁴School of Population & Global Health, The University of Western Australia Faculty of Medicine, Dentistry and Health Sciences, Perth, Western Australia, Australia

⁵Department of Rheumatology and Aged Care, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia

Correspondence to

Dr Johannes Nossent; johannes.nossent@uwa.edu.au

ABSTRACT

Aim With scarce data on the need and type of joint surgery in SLE, we investigated the long-term rates and underlying causes for arthroplasty, arthrodesis and synovectomy in patients with SLE.

Methods Procedure dates for arthroplasty, arthrodesis or synovectomy were retrieved from the state-wide Hospital Morbidity Data Collection between 1985 and 2015 for patients with SLE (n=1855) and propensity-matched controls (n=12 840). Patients with SLE with ≥two additional diagnostic codes for rheumatoid arthritis were classified as rhupus. ORs and incidence rates (IRs) per 100 person-years for joint procedures (JPs) were compared among patients with rhupus, patients with other SLE and controls across three study decades by regression analysis.

Results More patients with SLE than controls underwent a JP (11.6% vs 1.3%; OR 10.8, CI 8.86 to 13.24) with a higher IR for JP in patients with SLE (1.9 vs 0.1, rate ratio 19.9, CI 16.83 to 23.55). Among patients with SLE, patients with rhupus (n=120, 60.5%) had the highest odds of arthroplasty (OR 4.49, CI 2.87 to 6.92), arthrodesis (OR 6.64, CI 3.28 to 12.97) and synovectomy (OR 9.02, CI 4.32 to 18.23). Over time, the IR for overall JP in patients with rhupus was unchanged (8.7 to 8.6, R²=0.004, p=0.98), although the IR for avascular necrosis underlying arthroplasty decreased for all patients with SLE (0.52 to 0.10, p=0.02). Patients with other SLE also had significantly higher OR and IR for all three JPs than controls with insignificant decreases in synovectomy and increases in arthroplasty over time in this group.

Conclusions The overall burden of joint surgery in SLE is high and despite a reduction in avascular necrosis, arthroplasty and arthrodesis rates have not decreased over time. These data indicate a need for increased efforts to prevent joint damage in patients with lupus.

INTRODUCTION

Arthritis and arthralgias are among the most prominent symptoms in SLE.^{1,2} Clinically manifest arthritis is included across classification schemes and disease activity scores for SLE, but imaging by ultrasound or MRI has demonstrated a significant burden of subclinical articular inflammation.^{2,3} Generally, arthritis in SLE is considered to be mild and non-erosive despite a subset of patients developing joint abnormalities compatible with rheumatoid arthritis (RA)

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Higher rates of hip arthroplasty in patients with SLE have been reported in two observational studies; no data are available on other types of joint surgery.

WHAT THIS STUDY ADDS

- ⇒ The first studies to detail and compare the odds and incidence rate over three decades for arthroplasty, arthrodesis and synovectomy in a large SLE cohort.
- ⇒ Among 1855 patients with SLE, 11.6% required joint surgery, more frequently in the subgroup of patients with rhupus (35%) than those with other SLE (10.2%).
- ⇒ Arthroplasty, arthrodesis and synovectomy rates were all significantly higher in patients with SLE than age and sex-matched controls.
- ⇒ Patients with rhupus had higher rates of arthroplasty and arthrodesis than patients with other SLE, who in turn had higher rates than controls.
- ⇒ Overall arthroplasty and arthrodesis rates in patients with SLE did not change significantly over three decades.
- ⇒ The incidence of osteonecrosis decreased in all patients with SLE, while the incidence of osteoarthritis increased.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The results support a more aggressive approach towards arthritis management in SLE, such as now commonplace in rheumatoid arthritis. This could help reduce joint damage and surgery in patients with lupus.

which is regularly described as ‘rhupus’.⁴ Musculoskeletal damage is one of the most prominent features in studies on organ damage accrual in SLE^{1,5,6} and joint damage contributes up to 4 points (10%) in the prognostically important SLE Damage Index regarding erosive or deforming arthritis, tendon rupture and avascular necrosis (AVN), while muscle atrophy or weakness associated with osteoarthritis (OA) and fractures can contribute another 2 points.⁷ Despite the frequency and potential impact of arthritis on SLE and in contrast to RA, there are no specific data or guidelines for arthritis management in SLE, which is typically treated

with non-steroidal or antimalarial drugs and/or steroid injections.^{8,9} Joint surgery is reserved for progressive, deforming or persistent joint disease, but there is scarce information on the need and type of surgical joint interventions in SLE other than arthroplasty. The risk of hip and knee arthroplasty has been increasing in patients with SLE in the USA with a notable increase in OA as the underlying complication,^{10,11} while in Taiwan, hip but not knee replacement surgery was more frequent in patients with SLE than in controls.¹² The total number of hip and knee arthroplasties in Western Australia (WA) has steadily been rising over the last decades to 500 per 100,000 in 2021 (see <https://aoanjrr.sahmri.com/annual-reports-2022/supplementary>), but SLE-specific data are not available. We investigated the rates of overall and site-specific arthroplasty, arthrodesis or synovectomy among patients with SLE subclassified as rhupus or other SLE and a matched control group in WA over a 30-year period.

PATIENTS AND METHODS

This was a population-based retrospective observational study using prospectively collected, state-wide longitudinal health data for patients with lupus as recorded in the Western Australian Rheumatic Disease Epidemiological Registry (WARDER), as described earlier.¹³ WARDER data were extracted and linked through the Western Australian Data Linkage System that covers all public and private hospitals in WA (population 2.5 million) and applied probabilistic matching to link all compulsory registered health contacts over time for participants with inflammatory rheumatic diseases in the Hospital Morbidity Data Collection (HMDC), Mortality Registry or Emergency Department Data Collection (EDDC). This

results in a longitudinal health record for each participant containing sociodemographic data, length and type of any admission (eg, intensive care), all principal and secondary diagnoses (up to 20) and procedure codes (up to 10) for each hospital contact as well as details from death notices for each participant.

For this study, we included patients with SLE aged 15–75 years with prevalent lupus defined as having at least one International Classification of Diseases (ICD-9-CM or ICD-10-AM) code for lupus (online supplemental table 1) in the HMDC and EDDC between 1 January 1985 and 31 December 2014. This algorithm for identifying patients has been demonstrated to have high specificity for systemic rheumatic diseases.^{13–15} As there is no uniform definition on hand, we defined patients with rhupus as patients with SLE with at least two additional diagnostic discharge codes more than 30 days apart for RA as done in an earlier study.⁴ We also added linked health data from a control group (n=12840) of individuals without inflammatory rheumatic disease, propensity matched by sex, age and index year (ie, year of first SLE admission). Arthroplasty, arthrodesis and synovectomy were defined as a registered joint procedure (JP) by ICD-9-CM (up to 1999) and the Australian Classification of Health Interventions procedural codes (since 1999) upon hospital discharge (see online supplemental table 1 for all conditions and procedure definitions).

Primary outcomes were ORs, incidence rates (IRs) per 100 person-years and incidence rate ratio (IRR) as well as trends over 10-year periods for overall and specific JP. Secondary outcomes were cause-specific JP rates due to AVN, OA and fractures (hip and vertebral) as recorded in the HMDC (see online supplemental table 1 for relevant ICD codes).

Table 1 Overall comparison of descriptors and joint procedure rates and types between patients with rhupus, patients with other SLE and controls

	Rhupus (n=120)	Other SLE (n=1735)	OR/IRR Rhupus/other SLE	Controls (n=12840)	OR/IRR Other SLE/ controls
Entry age	49.5 (42–62.5)	39 (29–54)	–	40 (22–75)	–
Females	103 (85.8)	1492 (85.9)		11 462 (88.9)	–
Indigenous Australian	9 (7.5%)	145 (8.4%)	0.9 (0.41 to 1.7)	37 (0.3)	31.5 (22.1 to 45.9)
Lupus nephritis	34 (18.9)	328 (28.3)	0.61 (0.42 to 0.90)	–	–
Additional CTD diagnosis	33 (27.5)	177 (10.2)	3.71 (2.40 to 5.68)	–	–
Nr undergoing joint surgery	42 (35)	174 (10.2)	4.82 (3.19 to 7.23)	171 (1.3)	8.26 (6.64 to 10.27)
Total person-years	1510	21 983	–	202 249	–
Nr undergoing arthroplasty	33 (27.5)	135 (7.8)	4.5 (2.9 to 6.9)	79 (0.6)	13.6 (10.8 to 18.1)
Arthroplasty incidence rate	4.8 (3.8–6.1)	1.2 (1.03–1.32)	3.6 (2.4 to 5.2)	0.04 (0.03–0.05)	14.1 (10.8 to 18.5)
Nr undergoing arthrodesis	13 (10.8)	31 (1.8)	6.7 (3.3 to 12.9)	51 (0.4)	4.5 (2.9 to 7.1)
Arthrodesis incidence rate	1.6 (1.07–2.4)	0.18 (0.12–0.24)	4.1 (3.2 to 5.4)	0.03 (0.02–0.04)	5.6 (3.6 to 8.7)
Nr undergoing synovectomy	13 (10.8)	23 (1.3)	9.0 (4.3 to 18.2)	47 (0.4)	3.7 (2.2 to 5.9)
Synovectomy incidence rate	1.45 (0.91–2.2)	0.16 (0.12–0.23)	8.9 (5.2 to 15.1)	0.02 (0.01–0.03)	7.0 (4.6 to 10.9)

Figures indicate median with IQR, number (percentage), OR, incidence rate/100 person-years and IRR with 95% CIs. CTD, connective tissue disease; IRR, incidence rate ratio.

Statistical analyses

Descriptive statistics include median and IQR for continuous variables compared by non-parametric methods (Kruskal-Wallis), and categorical data described with a frequency and proportion and group comparisons tested with ORs and Fisher's exact test. JP IRs were calculated per 100 person-years with 95% CI derived from Poisson distribution and compared using IRRs. Changes in IR over time were assessed by linear least squares regression analysis using the coefficient of determination (R^2) as the goodness-of-fit measure where higher coefficients (range 0–1) indicated a better fit for increasing or decreasing IRs over time with p values derived from analysis of variance. Given the discrepancy between requiring one SLE diagnostic code and two RA diagnoses, we also performed a sensitivity analysis in patients with SLE with at least two diagnostic codes >30 days apart. All statistical analyses were performed using SPSS software V.28.0 (IBM) and OpenEpi software with two-sided $p < 0.05$ considered to be statistically significant.

RESULTS

Patients with SLE ($n=216$) underwent a JP more often than controls ($n=171$) (11.6% vs 1.3%; OR 10.8, CI 8.86 to 13.24), and the IR for any JP was higher in patients with SLE (1.92, CI 1.74–2.11 vs 0.1, CI 0.08 to 0.12) for a rate ratio of 19.9 (CI 16.83 to 23.55). More patients with SLE underwent more than one JP (12.9% vs 3.5%, $p < 0.01$), while median age at arthroplasty (61 years) was similar

in both groups. Among patients with SLE, 120 (6.5%) fulfilled rhupus criteria with a mean time between SLE and a first recorded RA diagnosis of 2.7 years (CI 1.7 to 3.6) (table 1). While the proportion of female and Indigenous patients was similar, patients with rhupus were significantly older at index admission than patients with other SLE (49.5 vs 39 years, $p < 0.01$) with a lower rate of renal involvement (18.7% vs 28.3%, $p = 0.012$). During a comparable follow-up period of 12 years, the proportions and time-adjusted IRs for all individual JPs were significantly higher in the rhupus than other SLE groups (table 1). However, patients with other SLE also had significantly higher proportions and IRs for all JPs than controls, especially for arthroplasty (OR 13.6, CI 10.8 to 18.11) (table 1). The sensitivity analysis including only patients with SLE with at least two diagnostic codes >30 days ($n=1408$; 76% of full cohort) demonstrated (online supplemental table 2) that despite the change in absolute numbers, both the descriptors and overall odds and IRRs for all three joint surgery types only slightly differed from the figures for the full cohort.

While the overall IR for any JP changed little over time in patients with rhupus (figure 1), it increased slightly in patients with SLE (from 1.59 (CI 1.07 to 2.27) to 2.68 (2.40 to 2.98), $p = 0.12$) in parallel with findings in controls (online supplemental table 3 for details). Regarding specific procedures, the IR for arthroplasty (figure 2A) was stable in patients with rhupus, while it increased

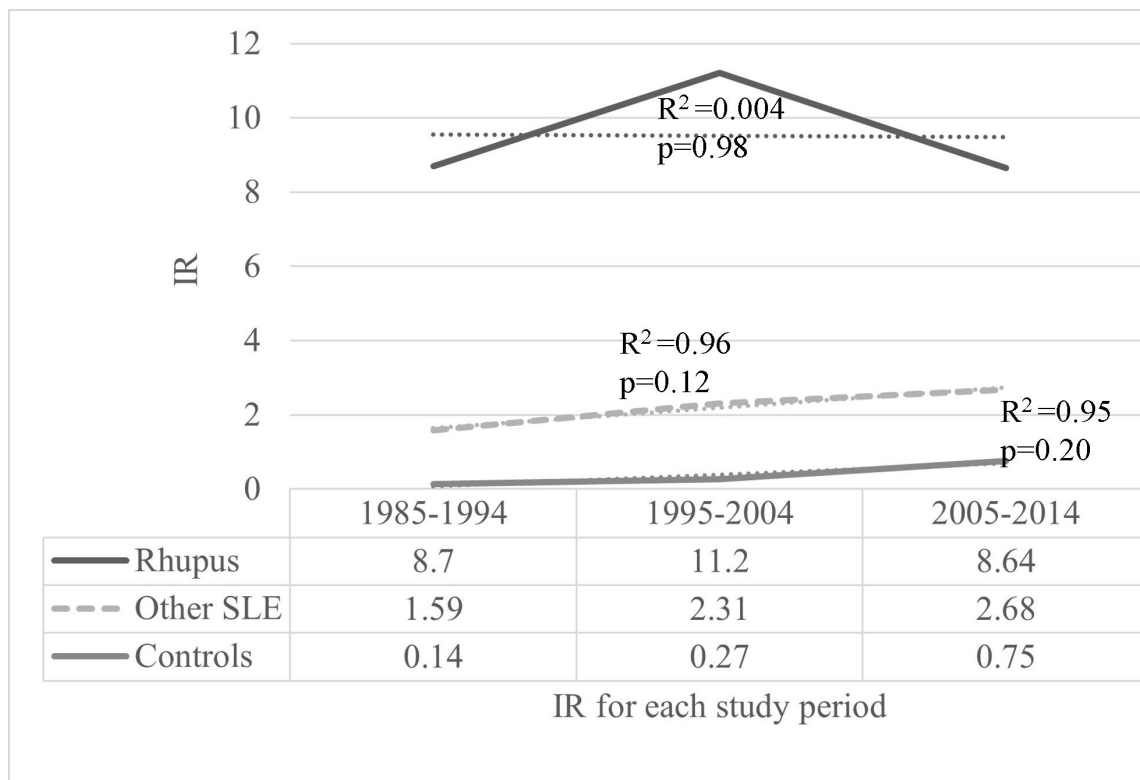


Figure 1 Temporal development of incidence rate (IR) per 100 patient-years for any joint procedure over three study decades in patients with rhupus, patients with other SLE and controls. Data table shows IR per decade for each subgroup and dotted line represents line of best fit with associated R^2 coefficient and p value.

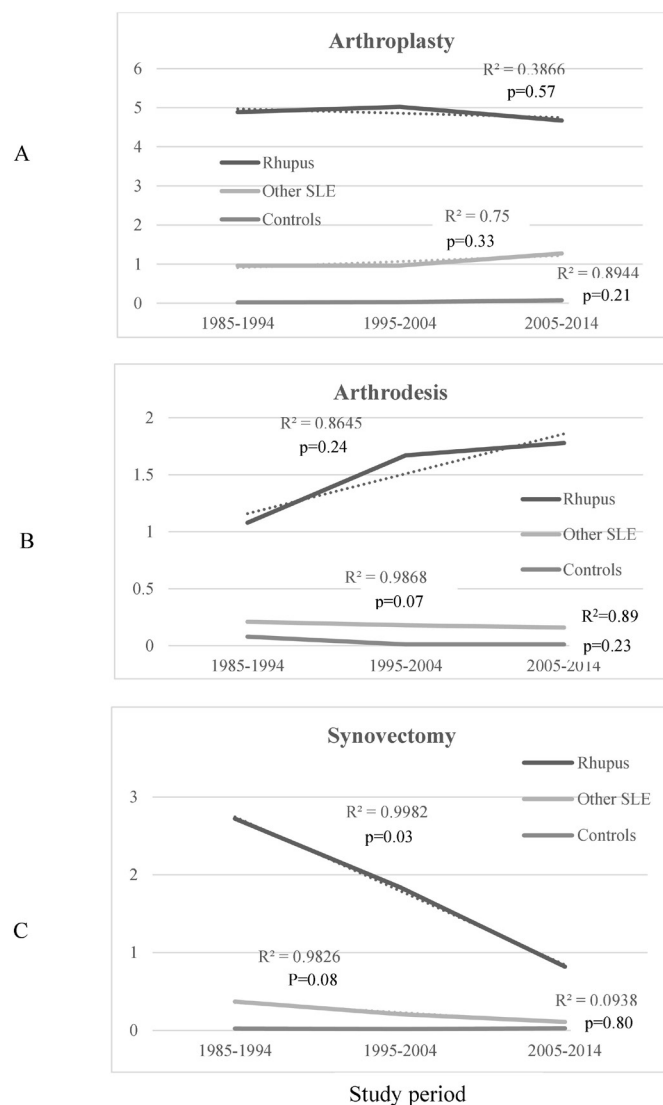


Figure 2 Incident rates per 100 patient-years over three study decades for arthroplasty (A), arthrodesis (B) and synovectomy (C) in patients with rhupus, patients with other SLE and controls. Dotted line represents line of best fit with associated R^2 coefficient and p value.

slightly for other SLE and controls. The IR for arthrodesis (figure 2B) increased somewhat in only patients with rhupus, while the IR for synovectomy decreased in both lupus groups (figure 2C).

Analysis of the surgical site for JP in patients with SLE (figure 3) demonstrated that the proportion of hip arthroplasties was higher in patients with other SLE than patients with rhupus (49.8% vs 28.3%, $p=0.02$), who had a higher proportion of wrist (16.2% vs 4.3%) and shoulder (9.6% vs 3.8%) arthroplasties. The proportion of wrist arthrodesis (40% vs 32%, $p=0.25$) was similar, but ankle arthrodesis was more frequent in patients with rhupus (48% vs 39.5%, $p=0.05$) and vertebral fusion more frequent in patients with other SLE (8% vs 34%, $p=0.04$). Knee synovectomies were more frequent in patients with rhupus (48.2% vs 33.3%, $p=0.03$).

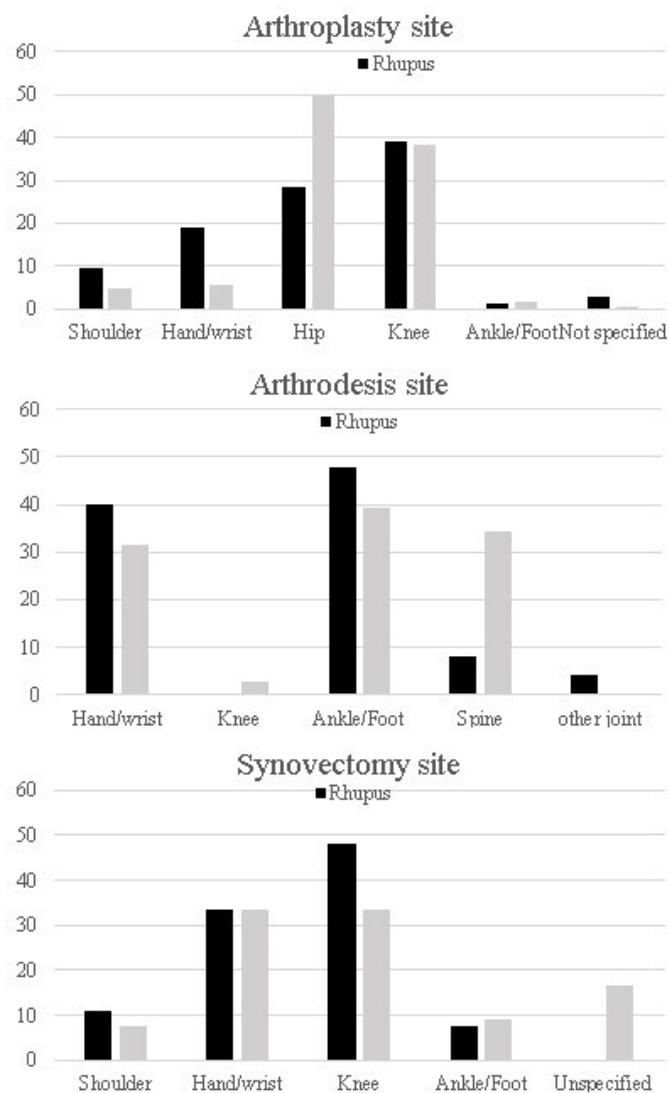


Figure 3 Site-specific frequencies (%) of orthopaedic procedures in patients with rhupus and patients with other SLE.

AVN was diagnosed in 4 patients with rhupus (3.3%) and 28 patients with other SLE (1.6%) (OR 2.1, CI 0.62 to 5.67), and the proportion of male patients was 25% in both AVN groups. The median age at first AVN episode was 36 years (IQR 24–45) after disease duration of 34 months (IQR 22–84), and AVN resulted in a total of 80 separate admissions. The overall IR for AVN hospitalisation decreased from 0.52 to 0.19 per 100 patient-years over time with a steeper decline observed in patients with rhupus (figure 4). A total of 23 patients with AVN (72%) progressed to arthroplasty with similar proportions in patients with rhupus and patients with other SLE (75% vs 71.4%, $p>0.6$).

Osteoarthritis was diagnosed in 190 patients overall (10.2%) with a higher proportion in patients with rhupus than patients with other SLE (OR 2.96, CI 1.86 to 4.62). Osteoarthritis was the main indication (64.2%) for all patients with SLE undergoing arthroplasty ($n=168$) with the lowest IR of new-onset osteoarthritis in patients with

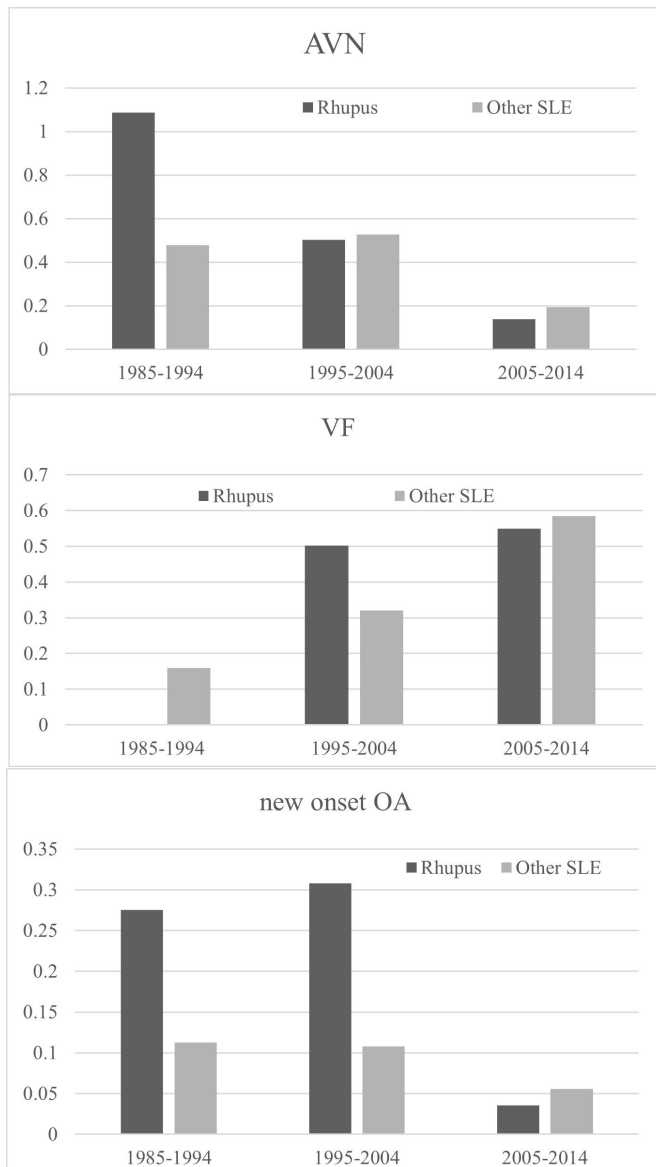


Figure 4 Incidence rates per 100 patient-years for avascular necrosis (AVN), vertebral fracture (VF) and osteoarthritis (OA) for patients with rhupus and patients with other SLE per study decade.

SLE diagnosed in the last study decade. Arthroplasty due to hip fracture ($n < 5$, 0.05%) was infrequent, while spinal arthrodesis was also uncommon ($n = 15$, 0.8%) despite an increase in IR for spinal fractures over time (figure 4).

DISCUSSION

In this longitudinal study of a sizeable and population-wide SLE cohort, the IRs for arthroplasty, arthrodesis and synovectomy were significantly higher than in a matched control group. Within the SLE group, 6.5% classified as having rhupus had joint surgery rates four times higher than for patients with other SLE and for whom arthroplasty and arthrodesis rates did not decline over time. Importantly, for patients with other SLE, joint surgery rates were also very much higher than in matched

controls. Fortunately, the incidence of AVN in patients with SLE decreased significantly over time, while arthroplasty rates increased in line with new-onset OA.

Arthroplasty was performed in 9.1% of all patients with SLE with the incidence per 100 person-years in patients with rhupus (4.8) higher than in patients with other SLE (1.2). In a recent Taiwanese study in patients with SLE newly diagnosed since 2002, arthroplasty of the hip or knee was performed in 3.2% over a 10-year period, while similar to our data, arthroplasty IRs were two to eight times higher than in a control cohort.¹² A US-based study using administrative health data found a significant increase in rates of arthroplasties from 0.17 to 0.38 per 100.000 population for patients with SLE between 1991 and 2005, which followed the increase in joint replacement rates for non-inflammatory conditions.¹⁰ These results fit with the increase in arthroplasty IR (0.9–1.3 per 100 person-years) seen in patients with other SLE in this study. AVN is one of the feared complications in SLE that may necessitate arthroplasty. A recent paper from the Hopkins Lupus cohort reported an AVN incidence of 0.65 per 100 person-years over the approximate same study period with a 50% drop over the last 20 years,¹⁶ while in this study, IR for AVN was 0.53 per 100 person-years initially and dropped to 0.19 per 100 person-years since 2005 with rate drops observed in both patients with rhupus and patients with other SLE. The increased focus on minimising corticosteroid usage in patients with SLE is likely a contributing factor to this improvement.

Arthrodesis is an irreversible but effective procedure to reduce symptoms from end-stage joint disease. Aside from case reports or mixed case series, we were unable to find any literature data on this definitive procedure in patients with SLE. Arthrodesis rates increased over time in patients with rhupus, while the rate remained stable in patients with other SLE, although at a higher rate than in controls. This could suggest that subclinical inflammation may have contributed to erosive disease in patients with rhupus especially, and this supports the need for more advanced imaging and/or medical therapy of subclinical disease.³

Synovectomy is an intermediate surgical procedure for treatment-resistant arthritis and aims to provide temporary rather than definite local disease control where the need for synovectomy indicates that a joint is at risk of damage development and further surgery. Unfortunately, we were unable to find comparable literature data for synovectomy in patients with SLE, but the decrease in synovectomy rates observed in both SLE groups most likely results from improved medical disease control in line with a similar decline observed in patients with RA over the same time period.^{17 18}

Rhupus is an incompletely understood condition for which there are no validated diagnostic or classification criteria or treatment strategies, and as a result, the real burden of rhupus remains unknown. A recent systematic review reported the prevalence of rhupus among patients with SLE to be between 0.1% when using late RA

complications such as radiographic erosions or rheumatoid nodules in the definition and 9.7% when systematically applying MRI to delineate rhupus in cross-sectional studies.⁴ In our longitudinal study, rhupus was defined as having at least two physician-based diagnoses of RA separated in time and the 6.5% prevalence falls well within the reported range.²⁹ Also, with no sex difference, higher age and less renal involvement, the characteristics of our patients with rhupus were in line with other studies.^{19–21} The lower rate of renal involvement remains unexplained but has been attributed to a different serological profile in patients with rhupus with a lower risk of nephritogenic autoantibody formation, which is, to some extent, supported by the higher rate of overlap syndromes observed in patients with rhupus.² In contrast, the joint disease in patients with rhupus was clearly more aggressive than in patients with other SLE given the significantly higher and unchanged rates of arthroplasty and arthrodesis. The stable rate of these hard outcomes suggests that joint damage in patients with rhupus has remained a significant problem during a time when effective biologicals for immune arthritis such as tumour necrosis factor or Janus kinase inhibitors have contributed to reduced joint damage in patients with RA.^{22,23} These drugs are not readily available through Medicare support for Australian patients with SLE, although the present and other data indicate that rhupus arthropathy management should follow recommendations for RA.²⁴

Our data clearly indicate that joint damage requiring surgical intervention is not restricted to patients with rhupus with joint surgery performed in 10% of other patients with SLE with the odds of arthroplasty, synovectomy and arthrodesis significantly higher than controls. This highlights the potential for non-RA-like arthritis in SLE to damage joints, likely due to persistent subclinical joint involvement, with newer imaging modalities showing erosive damage in up to 40% of patients.³ Combined with the rhupus findings, this strongly supports a need to re-evaluate the investigation and management of all SLE-related arthritis in clinical practice.⁹

Limitations for this study include the possibility that we have excluded especially younger patients with SLE with less severe disease, patients who have never been admitted to hospital, although data show that this concerns only a small number of patients with SLE over an 11-year period.²⁵ Our definition of rhupus was based on a clinical diagnosis made by the consulting physicians (mainly rheumatologists and immunologists), which is not the same as fulfilment of RA classification criteria. While the use of administrative health data allows study of hard outcomes such as hospital-based JPs, more detailed clinical data such as inflammatory markers, autoantibody profiles and antirheumatic drug treatment were not available in our deidentified dataset. We were therefore unable to evaluate these factors as potential contributors to rhupus and the risk of needing joint surgery. Also, our study observation time ended in 2015 and more recent data may show different outcomes. The strengths of this study lie

in the large number and population-wide representation of patients with SLE, a median follow-up of more than 10 years, a 30-year study period to allow trend analysis of validated outcomes over time and the inclusion of three separate JPs.

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Contributors All authors are members of the steering committee that procured the WARDER dataset. JN designed the current study and was responsible for extraction and analysis of the data. All authors contributed to interpretation of the data and were involved in drafting the manuscript and revising the final manuscript critically. JN as guarantor accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was performed in accordance with the Helsinki Declaration of 1964 and its later amendment. Approval for use of de-identified data was obtained from the Human Research Ethics Committee at the WA Department of Health (WADOH HREC# 2016.24). As this study was considered low risk by the WA Health HREC and due to the de-identified nature of the linked health dataset, the requirement for patient consent was waived. WA Health is proprietor of this administrative health dataset.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study were used under licence from WA Health Data Linkage Branch. Restrictions apply to the availability of these data, but upon reasonable request and following permission of WA Health and WA Data Linkage Branch, data are available from the authors.

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ORCID iD

Johannes Nossent <http://orcid.org/0000-0002-2833-7997>

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