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Comparative Fracture Risks among US Medicaid Enrollees with and without Systemic Lupus Erythematosus

Sara K. Tedeschi, MD, MPH[1], **DR. Seoyoung C. Kim, MD, ScD**[1,2], **Hongshu Guan, PhD**[1], **Jennifer M. Grossman, MD**[3], and **Karen H. Costenbader, MD, MPH**[1]

[1]Division of Rheumatology, Immunology and Allergy, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

[2]Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

[3]Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA

Abstract

Objective: Poor bone health is common in SLE patients. We evaluated fracture risks among low-income SLE and lupus nephritis patients compared to those without SLE.

Methods: We performed a cohort study within Medicaid 2007–2010, among SLE patients and age- and sex-matched non-SLE comparators. SLE was defined by ≥3 ICD-9 codes for SLE; lupus nephritis patients additionally had ≥2 codes for renal disease. The primary outcome was fracture of the pelvis, wrist, hip, or humerus. Demographics, prescriptions, and comorbidities were assessed during the 180-day baseline period. We calculated fracture incidence rates (IR) and 95% confidence intervals (CI) in SLE, lupus nephritis, and non-SLE comparator cohorts, and estimated adjusted hazard ratios (HR) for fractures. Sensitivity analyses evaluated the impact of glucocorticoids and comorbidities. We compared subsets of SLE patients with and without lupus nephritis.

Results: Among 47,709 SLE patients (19.8% with lupus nephritis) matched to 190,836 non-SLE comparators, mean age was 41.4 years and 92.6% were female. Fracture IR was highest among SLE patients with nephritis (4.60/1,000 person-years). SLE patients had two-fold higher fracture risk than matched comparators (HR 2.09 [95% CI 1.85, 2.37]). Lupus nephritis patients had the greatest fracture risks versus matched comparators (HR 3.06 [2.24, 4.17]), and 1.6 times higher risk than SLE patients without nephritis (HR 1.58 [1.20, 2.07]). Adjustment for glucocorticoid use and comorbidities slightly attenuated risks.

Conclusion: Fracture risks were elevated in SLE patients, particularly those with lupus nephritis, compared to matched non-SLE Medicaid patients. Elevated risks persisted after adjustment for baseline glucocorticoids and comorbidities.

Correspondence/Reprint Requests: Sara K. Tedeschi, MD, MPH, Brigham and Women's Hospital, Division of Rheumatology, Immunology and Allergy, 60 Fenwood Road, Suite 6016, Boston, MA 02115 USA, stedeschi1@bwh.harvard.edu, Phone: 617-732-5325 | Fax: 617-732-5766.

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Keywords

SLE; fracture; lupus nephritis

INTRODUCTION

Poor bone health may occur in systemic lupus erythematosus (SLE) patients for several reasons. High circulating levels of inflammatory cytokines stimulate bone resorption and greater SLE activity has been associated with low bone mineral density.[1] The adverse effects of glucocorticoids on bone health are widely recognized.[2–5] Both the cumulative dose and daily dose of glucocorticoids have been associated with low bone mineral density. Patients with lupus nephritis may be at particularly high risk for fracture due to secondary or tertiary hyperparathyroidism and vitamin D deficiency. SLE typically affects pre-menopausal women who may be at disproportionately high risk for fracture due to these factors.[6]

Few large cohort studies have compared fracture risks among SLE patients to age- and sex-matched individuals.[4,7] Fracture risks among racially and ethnically diverse, low-income SLE patients—who are at particularly high risk for SLE complications—have not been investigated. Lupus nephritis patients are likely at increased fracture risk, but have not been well studied.[8] We determined fracture incidence rates within a large cohort of low-income SLE and lupus nephritis patients, compared relative risks for fracture vs. matched comparators, and evaluated subgroups of SLE patients with lupus nephritis and by age.

METHODS

Data source and study design

We performed a cohort study to evaluate fracture incidence rates and relative risks using claims data for adults aged 18–65 years old enrolled in Medicaid. Medicaid is the US public health insurance program that covers >70 million low-income, racially and ethnically diverse individuals. Claims data were obtained from the Medicaid Analytic eXtract (MAX) for 2007–2010, provided as billing claims from the 29 most populated states. Data were obtained through a data use agreement with the Center for Medicaid and Medicare Studies providing access to claims data from 2007–2010; results are presented according to Federal data reporting standards (cell sizes <11 are suppressed).

SLE cohort

We identified a prevalent SLE cohort defined by ≥3 ICD-9 codes for SLE (710.0) ≥30 days apart as in prior work.[9–12] Among SLE patients, lupus nephritis was defined by ≥2 ICD-9 codes for nephritis, proteinuria, and/or renal failure ≥30 days apart on or after the SLE definition.[11–13] The index date was the date fulfilling SLE or lupus nephritis definition. In the event that all required codes occurred within <180 days, the next SLE or nephritis code occurring after 180 days defined the index date.

Non-SLE comparator cohort

The comparator cohort included Medicaid patients with no ICD-9 codes for SLE during the baseline period, matched 4:1 to SLE patients on index date, age (±1 year), and sex. The index date for non-SLE comparators was the date of a claim ±30 days of the index date for matched SLE patients.

Baseline and follow-up periods

We required a baseline period 180 days prior to and including the index date for all subjects. Follow-up started the day after index date and ended with the first fracture event, Medicaid disenrollment, death, or study period end (12/31/2010). We excluded any patient with fracture during baseline.

Assessment of fracture events

Pelvis, wrist, hip, and humeral fractures were defined by a claims-based algorithm using diagnosis and procedure codes (positive predictive value [PPV] >90% for each fracture site).[14] We did not include vertebral fractures due to the poor performance of a claims-based algorithm for vertebral fractures (PPV <50%).[15] The primary outcome was the first occurrence of fracture at any of these sites (“any fracture”). The first fracture at each site was a secondary outcome.

Covariates

Demographics, medications, and comorbidities were assessed during the 180-day baseline period; age was assessed at index date. US Census median household income by zip code was assessed as a marker of socioeconomic status. Race/ethnicity was categorized as White, African-American, Hispanic, or Other (Asian, Native American, or Other). Prescription claims for hydroxychloroquine, azathioprine, mycophenolate mofetil, cyclophosphamide, cyclosporine, tacrolimus, leflunomide, methotrexate or rituximab were treated as binary (ever vs. never during baseline). Mean oral and intravenous glucocorticoid use during baseline were calculated in prednisone equivalents using filled prescription claims, categorized as none (0 mg/day), low-dose (mean prednisone equivalent >0 to <7.5 mg/day), or high-dose (mean prednisone equivalent ≥7.5 mg/day).[16] The Charlson-Deyo Comorbidity Index indicated the presence/absence of claims for 17 conditions including rheumatic illness, renal disease, and malignancy. We defined end-stage renal disease as ≥1 ICD-9 code 585.6 during baseline.

Statistical analyses

We calculated crude fracture incidence rates (IR) and 95% confidence intervals (CI) in the SLE, lupus nephritis, and non-SLE comparator cohorts using Poisson models. The proportional hazards assumption was testing using Schoenfeld residuals. Multivariable Cox regression models estimated hazard ratios (HR) and 95% CI for any fracture and for fractures at each anatomic site, adjusting for age, sex, and race/ethnicity. Sensitivity analyses evaluated the impact of baseline glucocorticoid use on relative fracture risks and adjusted for the Charlson-Deyo Comorbidity Index.

In secondary analyses, we evaluated fracture risks among patients with and without lupus nephritis. We compared fracture risks in lupus nephritis patients versus matched non-SLE comparators, and then compared SLE patients with and without lupus nephritis. We compared fracture risks in SLE patients without nephritis to matched non-SLE comparators. We also stratified the SLE and non-SLE cohorts at <50 vs. ≥50 years old to compare fracture risks in younger vs. older patients.[7]

Analyses were performed using SAS v9.4 (SAS Institute, Cary, N.C). A two-sided $p < 0.05$ was considered significant. The Partners HealthCare Institutional Review Board approved all aspects of the study; formal consent was not required.

RESULTS

We identified 47,709 SLE patients matched to 190,836 non-SLE comparator patients. Lupus nephritis was present in 9,449 (19.8%) patients in the SLE cohort. Baseline characteristics are summarized in Table 1. Mean age in both cohorts was 41.4 years; 92.6% were female. The proportion of African-American patients was higher in the SLE cohort. Glucocorticoid use was uncommon among non-SLE comparators (5.7%), while 41.2% of SLE patients were prescribed glucocorticoids. Less than half of the SLE cohort was prescribed hydroxychloroquine. Bisphosphonate prescriptions were very rare and were more frequent in SLE (5.8%) than age- and sex-matched non-SLE comparators (0.7%).

Fracture incidence rates

Among SLE patients, the IR for any fracture was 4.32/1,000 person-years (Table 2). The IR was slightly higher among the subset of SLE patients with lupus nephritis: 4.60/1,000 person-years. Non-SLE patients had a lower IR for any fracture: 2.40/1,000 person-years. Pelvic fractures were the most frequent fracture type in SLE, with an IR 1.72/1,000 person-years and were more frequent in the subset with lupus nephritis (IR 2.23/1,000 person-years). Wrist fractures were the most common fracture type in non-SLE comparator patients (IR 1.04/100,000 person-years).

Comparative fracture risks

SLE patients had a two-fold higher fracture risk compared to age- and sex-matched non-SLE comparators (adjusted HR 2.09 [95% CI 1.85, 2.37]) (Table 3). Fracture risk was slightly attenuated after additionally adjusting for baseline glucocorticoid use (HR 1.78 [1.55, 2.05]) and comorbidities (HR 1.74 [1.53, 1.99]). SLE patients were at particularly high risk for hip fracture (HR 3.22 [2.33, 4.46]) and pelvic fracture (HR 2.63 [2.13,3.24]) compared to non-SLE patients. Risks for humerus fracture (HR 1.82 [1.34, 2.47]) and wrist fracture (HR 1.57 [1.27, 1.94]) were also elevated in SLE patients vs. non-SLE comparators. SLE patients without nephritis had 1.9 times greater risk than their matched comparators.

Fracture risks were greatest in the subset of SLE patients with lupus nephritis. Lupus nephritis patients had a three-fold elevated fracture risk compared to matched non-SLE patients (HR 3.06 [2.24, 4.17]) (Table 3). SLE patients with nephritis patients had 1.6 times greater fracture risk (HR 1.58 [1.20, 2.07]) than SLE patients without nephritis. Adjusting for baseline glucocorticoid use and comorbidities mildly attenuated this risk.

Younger SLE patients had 2.3 times higher fracture risks compared to younger non-SLE patients (HR 2.28 [1.90, 2.74]) (Table 3). Comparative fracture risk in SLE patients was attenuated but remained two-fold elevated after adjusting for baseline glucocorticoids and comorbidities. Among patients aged ≥50 years, SLE was also associated with a two-fold fracture risk (HR 1.92 [1.61, 2.28]); this risk was mildly attenuated after adjusting for baseline glucocorticoids and comorbidities.

DISCUSSION

Among >47,000 racially/ethnically diverse SLE patients compared to age- and sex-matched non-SLE patients enrolled in Medicaid, we identified a two-fold higher adjusted fracture risk. Fracture risks were particularly elevated among patients with lupus nephritis, with three-fold risk compared to matched non-SLE patients and 1.6-fold risk compared to SLE patients without nephritis. Adjustment for glucocorticoid use slightly attenuated fracture risks among SLE patients, consistent with prior literature on the detrimental effects of glucocorticoids on bone health. SLE was associated with a 2.3-fold fracture risk among younger patients, and a 1.9-fold risk among older patients.

We identified lupus nephritis patients as a particularly at-risk group for fracture, especially pelvic fracture. Even after adjusting for glucocorticoids and comorbidities (including renal disease), lupus nephritis patients had approximately 2.5-fold elevated fracture risk compared to non-SLE patients. Lupus nephritis patients had 1.6 times higher fracture risks compared to SLE patients without nephritis; the risk was essentially unchanged after adjusting for baseline glucocorticoid use. Adjustment for the Charlson-Deyo Comorbidity Index, which includes renal disease, attenuated fracture risks in lupus nephritis reflecting the role that renal disease plays in fracture risk.

Medicaid SLE patients had a higher relative risk of incident fracture compared to previous large studies. Wang et al. studied incident hip fractures among ~14,500 Taiwanese SLE patients and ~14,500 non-SLE patients, mean age 38.[7] Hip fracture incidence rate was 0.86/1,000 person-years, similar to our estimate of 0.76/1,000 person-years. SLE patients had twice the risk of hip fracture compared to non-SLE patients (incidence rate ratio [IRR] 2.23) in that study, whereas we detected a three-fold greater risk for hip fracture. Wang et al. identified a six-fold higher risk of hip fracture in SLE patients age <50 compared to age-matched comparators, with a wide confidence interval (IRR 6.29 [2.36–21.03]). SLE patients age <50 in our study had 2.3 times the risk of age-matched comparators, higher than the 1.9-fold relative risk among older SLE patients. Bultink et al. studied incident fractures in ~4,000 SLE patients and ~21,000 matched comparators, mean age 46, seen in general practice clinics in the UK.[4] The incidence rate for fracture of the spine, hip, forearm or humerus was 15.5/1,000 person-years, higher than our observed incidence rate (4.32/1,000 person-years), but our composite outcome did not include spine fractures and did include pelvic fractures. UK SLE patients had 58% higher risk for fracture than comparators (age- and sex- adjusted relative risk [RR] 1.58 [1.41–1.76]). Adjustment for past fracture and use of glucocorticoids, hydroxychloroquine, calcium/vitamin D supplements, benzodiazepines and proton pump inhibitors attenuated the RR to 1.22 [1.05–1.42].

Differences in study populations and methodology may explain the slightly higher fracture risks that we observed compared to prior studies. Suboptimal SLE treatment among Medicaid enrollees and poor outcomes in this population, as has been shown in prior work, may have contributed to elevated fracture risks.[11,12] More than 40% of SLE patients in our study used glucocorticoids during the baseline period, and hydroxychloroquine—a mainstay of SLE treatment—was used by less than half. Based on these practice patterns, it is possible that SLE patients in our cohort had worse bone health due to SLE itself or as a consequence of glucocorticoid use. African-American race was more frequent in the SLE cohort than the non-SLE cohort, and was associated with lower fracture risk in multivariable models (data not shown). We chose to include race in our final models because was an important confounder of fracture risk. In contrast to the Bultink et al. study, we did not include spinal (i.e. vertebral) fractures as these are frequently asymptomatic and difficult to detect accurately using claims data.[15] Also in contrast, we elected not to include SLE medications in our primary multivariable model. Glucocorticoids and hydroxychloroquine were very infrequently used in non-SLE patients, and we considered them indicators of SLE as well as potential mediators of fracture risk. Adjustment for medications that were more frequently used in SLE patients than non-SLE patients likely attenuated fracture risk estimates among SLE patients in the UK.

The American College of Rheumatology has published glucocorticoid-induced osteoporosis prevention guidelines, recommending bisphosphonates for patients with long-term glucocorticoid use and moderate or high fracture risks.[16,17] However, renal disease often contraindicates preventive treatment with bisphosphonates. In our study population, bisphosphonate use was infrequent among SLE and non-SLE patients and it was unclear if bisphosphonate use would be associated with lower fracture risk due to its biological effect, or higher fracture risk due to confounding by indication (e.g. preferential prescribing to patients perceived to be at highest fracture risk). Therefore we did not include bisphosphonates in our models.

We performed this analysis using Medicaid billing data, which have limitations. We were not able to assess history of fracture or covariates prior to the 180-day baseline period. We were also not able to adjust for lifetime exposure to glucocorticoids prior to index date, potentially leading to underestimation of relative risks. Additionally, medication claims data may not reflect the medications or doses patients actually take. For example, patients may have been taking glucocorticoids differently than prescribed at baseline. The fracture algorithm required only one code for pelvic fracture, which may have overestimated pelvic fracture rates in both SLE and non-SLE cohorts.[14] We were unable to adjust for calcium and vitamin D due to concern for poor ascertainment, as these are often purchased over-the-counter, nor for frailty, physical activity, and body mass index. We did not have access to bone density measurements so could not determine if these were osteoporotic fractures, but we included anatomic sites that are typical for low-trauma fractures. Our SLE and lupus nephritis cohorts included patients with prevalent disease and we were unable to determine disease duration. We could not assess SLE disease activity. Our SLE cohort had a lower proportion of lupus nephritis cases than other population-based cohorts, likely due to our stringent algorithm requiring at least five ICD-9 codes separate in time, limited duration of follow-up available, and because end-stage renal disease patients in the US often receive

insurance through Medicare (not Medicaid). Because we conducted this analysis among Medicaid enrollees, our results may not generalize to other SLE patients with higher socioeconomic status.

Our work had several key strengths, including a large sample of >47,000 racially/ethnically diverse SLE patients and age- and sex-matched comparators. We applied established algorithms to identify SLE, lupus nephritis, and fractures at four anatomic sites using billing claims data. While the relative risk for fracture was two- to three-fold elevated in SLE and lupus nephritis patients, absolute fracture rates were moderate. Fracture IRs were of a similar magnitude as in other SLE cohorts, suggesting that claims data are reliable for identifying fragility fractures. We omitted patients with a prior history of fracture, leading to conservative estimates of relative fracture risks. We were able to adjust for both oral and intravenous glucocorticoid use based on filled prescriptions, and other potential confounders.

Within a racially and ethnically diverse, low-income Medicaid population, SLE patients had two-fold greater risk for fractures compared to non-SLE patients. Greater risk (HR 3.06) was present in the subset of lupus nephritis patients. Glucocorticoid use during the baseline accounted for some, but not all, of increased risk. This work underscores the importance of identifying high-risk SLE and lupus nephritis patients for fracture prevention.

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REFERENCES

1. Lee C, Almagor O, Dunlop DD, Manzi S, Spies S, Chadha AB, et al. Disease damage and low bone mineral density: An analysis of women with systemic lupus erythematosus ever and never receiving corticosteroids. Rheumatology (Oxford) 2006;45:53–60. [PubMed: 16278288]
2. Ramsey-Goldman R, Dunn JE, Huang CF, Dunlop D, Rairie JE, Fitzgerald S, et al. Frequency of fractures in women with systemic lupus erythematosus: Comparison with united states population data. Arthritis Rheum 1999;42:882–90. [PubMed: 10323443]
3. Zonana-Nacach A, Barr SG, Magder LS, Petri M. Damage in systemic lupus erythematosus and its association with corticosteroids. Arthritis Rheum 2000;43:1801–8. [PubMed: 10943870]
4. Bultink IE, Harvey NC, Lalmohamed A, Cooper C, Lems WF, van Staa TP, et al. Elevated risk of clinical fractures and associated risk factors in patients with systemic lupus erythematosus versus matched controls: A population-based study in the united kingdom. Osteoporos Int 2014;25:1275–83. [PubMed: 24297094]
5. Cramarossa G, Urowitz MB, Su J, Gladman D, Touma Z. Prevalence and associated factors of low bone mass in adults with systemic lupus erythematosus. Lupus 2017;26:365–72. [PubMed: 27522094]
6. Carli L, Tani C, Spera V, Vagelli R, Vagnani S, Mazzantini M, et al. Risk factors for osteoporosis and fragility fractures in patients with systemic lupus erythematosus. Lupus Sci Med 2016;3:e000098. [PubMed: 26848397]
7. Wang SH, Chang YS, Liu CJ, Lai CC, Chen WS, Chen TJ, et al. Association of systemic lupus erythematosus with a higher risk of cervical but not trochanteric hip fracture: A nationwide population-based study. Arthritis Care Res (Hoboken) 2013;65:1674–81. [PubMed: 23592551]

8. Le B, Waller JL, Radhakrishnan R, Oh SJ, Kheda MF, Nahman NS Jr., et al. Osteoporotic fractures in patients with systemic lupus erythematosus and end stage renal disease. Lupus 2018;27:17–24. [PubMed: 28530467]

9. Barbhaiya M, Feldman CH, Guan H, Gomez-Puerta JA, Fischer MA, Solomon DH, et al. Race/ethnicity and cardiovascular events among patients with systemic lupus erythematosus. Arthritis Rheumatol 2017;69:1823–31. [PubMed: 28598016]

10. Feldman CH, Marty FM, Winkelmayer WC, Guan H, Franklin JM, Solomon DH, et al. Comparative rates of serious infections among patients with systemic lupus erythematosus receiving immunosuppressive medications. Arthritis Rheumatol 2017;69:387–97. [PubMed: 27589220]

11. Feldman CH, Hiraki LT, Winkelmayer WC, Marty FM, Franklin JM, Kim SC, et al. Serious infections among adult medicaid beneficiaries with systemic lupus erythematosus and lupus nephritis. Arthritis Rheumatol 2015;67:1577–85. [PubMed: 25772621]

12. Chen SK, Barbhaiya M, Fischer MA, Guan H, Lin TC, Feldman CH, et al. Lipid testing and statin prescription among medicaid recipients with systemic lupus erythematosus, diabetes mellitus and the general medicaid population. Arthritis Care Res (Hoboken) 2018 4 12 **doi:** 10.1002/acr.23574 **[Epub ahead of print]doi:[Epub ahead of print]**

13. Chibnik LB, Massarotti EM, Costenbader KH. Identification and validation of lupus nephritis cases using administrative data. Lupus 2010;19:741–3. [PubMed: 20179167]

14. Ray WA, Griffin MR, Fought RL, Adams ML. Identification of fractures from computerized medicare files. J Clin Epidemiol 1992;45:703–14. [PubMed: 1619449]

15. Curtis JR, Mudano AS, Solomon DH, Xi J, Melton ME, Saag KG. Identification and validation of vertebral compression fractures using administrative claims data. Med Care 2009;47:69–72. [PubMed: 19106733]

16. Grossman JM, Gordon R, Ranganath VK, Deal C, Caplan L, Chen W, et al. American college of rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010;62:1515–26. [PubMed: 20662044]

17. Buckley L, Guyatt G, Fink HA, Cannon M, Grossman J, Hansen KE, et al. 2017 american college of rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Rheumatol 2017;69:1521–37. [PubMed: 28585373]

Table 1.

Baseline Traits of SLE and Non-SLE Cohorts, 2007-2010

	SLE cohort n=47,709	Non-SLE comparator cohort n=190,836
Age at index date, years [+]	41.4 (12.3)	41.4 (12.3)
Female [+]	92.6	92.6
Median household income by zip code, US dollars	45,322 (16,931)	47,581 (17,278)
Race/ethnicity		
White	34.7	46.4
African-American	42.5	22.1
Hispanic	16.1	24.4
Other [*]	6.8	7.2
Mean prednisone equivalent/day, mg		
0	58.8	94.3
>0 to <7.5	28.6	5.3
≥7.5	12.6	0.4
Hydroxychloroquine use	35.7	0.2
Immunosuppressant use [**]	19.6	0.5
Bisphosphonate use	5.8	0.7
Charlson-Deyo Comorbidity Index	2.0 (1.5)	0.5 (1.3)
End-stage renal disease	5.4	0.6

Values presented as mean (SD) or %

[+] Cohorts were matched on age and sex

[*] Asian, Native American, or Other

[**] Azathioprine, mycophenolate, cyclophosphamide, cyclosporine, tacrolimus, leflunomide, methotrexate, or rituximab

Table 2.

Fracture Events and Incidence Rates among Adult Medicaid Enrollees

	SLE cohort (n=47,709)			Lupus nephritis cohort (n=9,449)			Non-SLE comparator cohort (n=190,836)		
	Fractures	**Person-years**	**IR/1,000 p-y (95% CI)**	**Fractures**	**Person-years**	**IR/1,000 p-y (95% CI)**	**Fractures**	**Person-years**	**IR/1,000 p-y (95% CI)**
Any fracture *	381	88,295	4.32 (3.91, 4.78)	68	14,773	4.60 (3.63, 5.83)	734	305,316	2.40 (2.23, 2.58)
Pelvis	152	88,576	1.72 (1.47, 2.02)	33	14,814	2.23 (1.59, 3.14)	220	305,949	0.72 (0.63, 0.82)
Wrist	122	88,630	1.38 (1.16, 1.65)	17	14,833	1.15 (0.71, 1.85)	317	305,787	1.04 (0.93, 1.16)
Hip	67	88,693	0.76 (0.60, 0.97)	12	14,838	0.81 (0.46, 1.43)	85	306,106	0.28 (0.23, 0.35)
Humerus	59	88,709	0.67 (0.52, 0.86)	NR	NR	NR	138	306,045	0.45 (0.38, 0.53)

p-y: person-years NR: not reportable per Centers for Medicare and Medicaid requirements due to <11 humerus fractures

* Any fracture includes fracture of the pelvis, wrist, hip, or humerus

Table 3.

Multivariable Hazard Ratios (95% CI) for Any Fracture among Adult Medicaid Enrollees with SLE and Lupus Nephritis

	Model 1 (age, sex, race/ethnicity)	Model 2 (glucocorticoids)*	Model 3 (comorbidities)**
SLE			
SLE cohort (n=47,709)	2.09 (1.85, 2.37)	1.78 (1.55, 2.05)	1.74 (1.53, 1.99)
Non-SLE comparator cohort (n=190,836)	1.00 (ref)	1.00 (ref)	1.00 (ref)
SLE without nephritis (n=38,260)	1.88 (1.63, 2.17)	1.63 (1.39, 1.91)	1.60 (1.38, 1.86)
Matched non-SLE comparators (n=153,040)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Lupus nephritis			
Lupus nephritis cohort (n=9,449)	3.06 (2.24, 4.17)	2.61 (1.83, 3.74)	2.33 (1.59, 3.40)
Matched non-SLE comparators (n=37,796)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Lupus nephritis cohort (n=9,449)	1.58 (1.20, 2.07)	1.50 (1.14, 1.97)	1.30 (0.97, 1.74)
SLE without nephritis (n=38,260)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age <50			
SLE cohort (n=34,274)	2.28 (1.90, 2.74)	1.74 (1.40, 2.15)	1.97 (1.61, 2.41)
Non-SLE comparator cohort (n=137,083)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Age ≥50			
SLE cohort (n=13,435)	1.92 (1.61, 2.28)	1.78 (1.48, 2.15)	1.60 (1.34, 1.92)
Non-SLE comparator cohort (n=53,753)	1.00 (ref)	1.00 (ref)	1.00 (ref)

*Model 2: Model 1 additionally adjusted for baseline prednisone equivalent dose (none, >0 to <7.5 mg/day, ≥7.5 mg/day)

**Model 3: Model 1 additionally adjusted for Charlson-Deyo Comorbidity index