World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

HOW MUCH GLUCOCORTICOID IS RISKY FOR BONE IN SYSTEMIC LUPUS ERYTHEMATOSUS? A REVIEW OF DOSE AND FRACTURE RISK IN SLE

Mumtahina Alam [1], Awalia, Sp PD-KR FINASIM [2,*] and Sri Purwaningsih, M. Kes [3]

[1] International Undergraduate Programme, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2] Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[3] Department of Anatomy, Histology and Pharmacology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
* Corresponding Author

World Journal of Advanced Research and Reviews, 2026, 32(02), 1431–1439

Publication history: Received on 09 October 2026; revised on 17 November 2026; accepted on 19 November 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.32.2.2949

Copyright © 2026 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution License 4.0

ABSTRACT

Glucocorticoids (GCs) are crucial in the treatment of systemic lupus erythematosus (SLE), however they play a major role in damaging bone integrity. This narrative review summarises current guideline targets and the main studies relating GC dose to bone density and pathological fractures in SLE. The 2023 EULAR recommendations lowered the acceptable maintenance dose from 7.5 to 5 mg/day prednisone equivalent, and the 2022 ACR guideline advises fracture-risk assessment for adults taking 2.5 mg/day or more for over three months. There is mixed evidence on the association between dose and bone loss. The Hopkins Lupus Cohort found that a mean prednisone dose of 7.5 mg/day or more roughly doubled the hazard of osteoporotic fracture, and a 2026 analysis from the same group found that a mean prednisone dose above 5 mg/day independently predicted osteoporosis. In contrast, a 28-year London cohort found no significant association between dose and fragility fractures. Meta-analyses show lower bone density in SLE than in controls but no clear effect of GC use on density. Differences in how dose is measured, confounding by disease activity, outcome definitions and cohort selection probably explain much of the disagreement. GC dose has been shown to be unsafe for bone in lupus in doses above 2,5 mg/day. In clinical practice, fracture risk should be assessed when GC therapy starts, the lowest effective dose should be used with steroid-sparing therapy, and calcium, vitamin D and antiresorptive treatment should follow risk category.

Keywords: Systemic Lupus Erythematosus; Glucocorticoids; Osteoporosis; Fracture Risk; Dose-Response

1 INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that produces widespread inflammation and can cause lasting tissue damage in multiple organs, including the skin, joints, kidneys, heart, lungs, blood and nervous system [1,2]. It has an estimated global incidence of about 5 per 100,000 person-years and a prevalence of 44 per 100,000 [3]. Women make up the majority of patients, and those aged 15 to 44 years are affected about thirteen times as often as men in that age range [1]. The disease follows a pattern of flares and remissions that affects both short- and long-term outcomes. SLE has a complex, multifactorial etiology involving genetic, hormonal, environmental and

immunological factors [2]. Consequently, its manifestations are highly variable and require comprehensive clinical and laboratory examination to meet the American College of Rheumatology (ACR) or European Alliance of Associations for Rheumatology (EULAR) criteria. Disease activity is measured using the SLE Disease Activity Index (SLEDAI), where scores of 1 to 5 indicate mild, 6 to 10 moderate and 11 or more high activity [4,5]. Classification relies on the 1997 ACR criteria [6] or the 2019 EULAR/ACR criteria [7]. These scores matter because they determine the treatment and its dosage.

Glucocorticoids (GCs) are vital in treating lupus and are one of the most effective first-line treatments for SLE [8,9]. As potent anti-inflammatory and immunosuppressant agents, GCs help reduce the severity of flares through high intravenous or oral doses that bring disease activity down to a milder level. However, they are also associated with various adverse effects, such as osteoporosis, cataract, myopathy and other conditions [10,11]. This narrative review mainly targets osteoporosis and whether GC dose level affects bone outcomes in patients with SLE. It summarises guideline targets, then examines studies of GC dose and bone outcomes in SLE, explains why their results differ, and draws out implications for practice. It is not a systematic review, and it focuses on the key SLE-specific studies and the guidelines that frame them.

2 GLUCOCORTICOID-INDUCED OSTEOPOROSIS

2.1 Epidemiology

GCs are widely prescribed to manage a broad spectrum of diseases, including inflammatory arthritis, connective tissue disease, lung disease and other chronic indications. Their use is prevalent worldwide: at any time, 1.0% to 4.6% of UK and US adults are taking oral GCs, and 27% to 65% of these patients will receive long-term (≥3 months) GC treatment [12]. The prevalence of osteoporosis in SLE is 10% to 20%, with up to 20% of patients experiencing vertebral fractures. Osteoporosis has been associated with higher cumulative doses and prolonged administration of GCs [8].

Premenopausal women may be at increased risk of vertebral fractures (VF), up to 29%, owing to high doses of GCs, with similar figures in young adult males. Younger subjects most often receive less preventive care for osteoporosis, as they are usually not the main population at risk [13].

Patients with SLE are mostly young women, so premature ovarian insufficiency and pregnancy planning are relevant to bone and to drug choice [14]. Systemic inflammation itself contributes to bone loss: a higher flare rate has been linked to greater bone mineral density (BMD) loss, and GCs may have a dual role by damaging bone directly while reducing inflammation-driven loss [14]. Lupus nephritis develops in up to 60% of patients at some point and can bring renal bone disease [14]. Morphometric vertebral fractures are common, found in 13.7% to 50% of patients in cross-sectional and cohort studies, and about one in three patients with such fractures has normal BMD, so densitometry alone misses much of the risk [14,15].

2.2 Pathophysiology

GC use has been linked to glucocorticoid-induced osteoporosis (GIOP) during long-term use and is one of the most common secondary causes of osteoporosis, especially in young adults [13]. GCs damage bone by causing an imbalance between bone resorption and bone formation: they promote osteoclastogenesis while keeping osteoprotegerin production low [16]. This causes rapid bone loss during the first 3 to 6 months of treatment [17]. Continued GC exposure reduces osteoblast proliferation and differentiation while increasing their apoptosis, which suppresses bone formation [18]. In short, an early burst of osteoclast activation is followed by reduced osteoblast proliferation and increased apoptosis of osteoblasts and osteocytes [17].

2.3 GC dose

GC doses are grouped into several categories (low, medium, high, very high and pulse) and are prescribed according to SLE disease activity and the severity of manifestations (Table 1) [19,20].

Guidelines such as those of the ACR and EULAR recommend acceptable long-term doses for patients, the most common being a maintenance dose of 7.5 mg/day or less (EULAR 2019), lowered to 5 mg/day or less in the 2023 update[9,19]; however, osteoporosis, fracture, cataract and ischaemic heart disease have still been reported at these levels (Table 2) [21]. Even doses above 2.5 mg/day have been associated with osteoporosis, fracture and infection in lupus [8,22,23]. However, these thresholds do not mainly concern osteoporosis but indicate organ damage, and they do not set a true threshold for a safe long-term dose.

Table 1: Glucocorticoid dose categories (prednisone equivalent)

Dose category	Daily dose
Low	7.5 mg/day or less
Medium	>7.5 to 30 mg/day
High	>30 to 100 mg/day
Very high	Over 100 mg/day
Pulse	>250 mg for a few days

Sources: [19,20].

The ACR 2022 guideline strongly recommends assessing fracture risk as soon as possible after GC initiation, within 6 months, using clinical risk factors, dual-energy X-ray absorptiometry (DXA) with vertebral fracture assessment or spine radiography, and the Fracture Risk Assessment Tool (FRAX) in adults aged 40 years or older [17]. It recommends osteoporosis therapy for adults at moderate, high or very high fracture risk [17].

Table 2: Glucocorticoid dose thresholds in guidelines

Source	Threshold	What it triggers
EULAR 2019	7.5 mg/day or less	Acceptable maintenance dose [19]
EULAR 2023	5 mg/day or less, withdraw when possible	Acceptable maintenance dose [9]
ACR 2022 GIOP	2.5 mg/day or more for over 3 months	Fracture-risk assessment and prevention [17]
ACR 2022 GIOP	Over 7.5 mg/day	FRAX correction: major osteoporotic fracture risk ×1.15, hip ×1.2 [17]
ACR 2022 GIOP	30 mg/day or more for over 30 days, or 5 g or more cumulative in a year	Very high fracture-risk category [17]

2.4 GIOP diagnosis

Diagnostic examination uses DXA and quantitative computed tomography to detect early BMD changes, and plain radiographs reveal vertebral compression fractures or hip fractures [17]. DXA is a non-invasive imaging method used to assess the quantity of bone mineral content per unit cross-sectional area (g/cm^2) [24]. Two X-ray beams with different energy levels are directed at a specific area of the patient's body, and a representative image of bone density is produced by removing the soft tissue. The reductions in low- and high-energy photon emissions are measured and merged to generate a planar image that evaluates bone mass per unit area (g/cm^2). The parts of the body examined are the lumbar spine, hip, forearm and whole body [24].

DXA results are expressed in standard deviations from the reference value, as a T-score or a Z-score (Table 3). The T-score, set by the World Health Organization (WHO), is applicable to postmenopausal women and men aged 50 years and older, as it indicates how many standard deviations the patient's BMD is from the mean of a young healthy adult reference population matched for sex and race [25,26]. The Z-score, established by the International Society for Clinical Densitometry (ISCD), is used in premenopausal women and men younger than 50 years, as it reflects how many standard deviations the patient's score is above or below the average of individuals of the same age [26].

Beyond the evaluation of osteoporosis, BMD results can be used to assess fracture risk. FRAX incorporates clinical risk factors, with or without BMD measurements, to pinpoint individuals at risk of osteoporosis or fractures [27]. Established by the WHO in 2008, FRAX is used to estimate the likelihood of a fracture occurring within a decade [27]. The clinical risk factors included in FRAX are age, sex, ethnicity, height, weight, body mass index (BMI), a history of fractures, parental history of hip fracture, use of oral glucocorticoids, rheumatoid arthritis, other secondary causes of osteoporosis, smoking and alcohol consumption of three or more drinks per day. The country where a patient resides is also taken into account in the assessment [27].

Table 3: Interpretation of DXA T-scores and Z-scores

Category	Score	Interpretation
T-score (World Health Organization)	−1.0 or above	Normal bone density for postmenopausal women and men aged 50 and older
	Between −1.0 and −2.5	Low bone mass, commonly called osteopenia, for postmenopausal women and men aged 50 and older
	−2.5 or below	Osteoporosis by the applicable densitometric classification for postmenopausal women and men aged 50 and older
Z-score (International Society for Clinical Densitometry)	−2.0 or lower	Below the expected range for age
	Above −2.0	Within the expected range for age

Sources: [25,26].

Guidelines generally recommend assessing fracture risk for individuals who are beginning or continuing GC therapy for more than three months [22]. Some guidelines depend solely on BMD, while newer approaches use country-specific FRAX estimates to determine the 10-year risk of hip and major osteoporotic fractures, with or without BMD [22]. Preventive treatment is suggested when the daily dose exceeds 5 to 7.5 mg of prednisone or its equivalent for at least three months [22].

3 EVIDENCE ON DOSE AND BONE OUTCOMES IN SLE

3.1 Studies showing a dose-response

Al Sawah and colleagues studied 2,199 patients from the Hopkins Lupus Cohort using time-dependent Cox models, with damage measured by the SLICC/ACR Damage Index. Demographic factors such as age and race, baseline damage, SLE disease activity, and the use of immunosuppressants and antimalarials were controlled for. Results showed that a mean prednisone dose of 20 mg/day or higher carried a hazard ratio (HR) of 2.51 for any new organ damage compared with doses below 7.5 mg/day, with each additional 1 mg/day raising the risk by 2.8%. For individual organs, a mean dose of 7.5 mg/day or greater was associated with an increased risk of osteoporotic fractures (HR 2.16) and cataracts (HR 2.41) [28].

A more recent analysis from the same Hopkins cohort, published in Arthritis Care & Research in 2026, looked at bone density rather than fractures. In 1,003 patients with repeated spine DXA results, a mean prednisone dose above 5 mg/day (averaged over all earlier visits) was an independent predictor of osteoporosis, defined as a T-score of −2.5 or lower. Older age, Black race, lower body mass index and lower mean 25-hydroxyvitamin D were also independent predictors. A mean dose below 5 mg/day gave a raised but non-significant estimate (adjusted odds ratio 1.35). Patients whose prednisone was stopped in the year before the next BMD measurement had higher mean spine T-scores, suggesting that some of the loss is reversible [29]. Fractures were not the outcome, and because both Hopkins analyses draw on the same cohort, they are not independent.

In another study, Ugarte-Gil and colleagues conducted a systematic review and meta-regression analysis of 49 observational studies involving 16,224 patients with SLE in 2021 [11]. Their results showed that the overall rate of developing osteoporosis with fractures was 1.14 per 100 patient-years (95% CI 0.82 to 1.60). A dose-response association was observed, with higher average daily GC doses directly associated with the onset of osteoporosis with fractures and higher cumulative doses with osteonecrosis.

Supporting this, a 2014 study of the Cruces Lupus Cohort by Ruiz-Arruza et al. followed 230 patients over five years and found that those who developed permanent organ damage had received a higher mean daily prednisone dose than those who did not (10.4 vs 6.0 mg/day, $P < 0.001$) [10]. Compared with patients taking no prednisone, those on medium-to-high doses (>7.5 mg/day) had a substantially increased risk of accumulating global damage (adjusted odds ratio [OR] 5.39, 95% CI 1.59 to 18.27) and of glucocorticoid-related damage, defined as osteonecrosis, osteoporotic fractures, diabetes mellitus or cataracts (adjusted OR 9.9, 95% CI 1.1 to 84.0). Notably, the study found that neither low daily doses (≤7.5 mg/day) nor brief intravenous methylprednisolone pulses given to treat flares were associated with damage accrual [10].

3.2 Studies finding no clear dose association

While many large cohorts show a dose-response relationship, several small-scale studies and meta-analyses have found no significant association between GC dose and bone outcomes in SLE [30,31]. This is most likely due to confounding variables, such as traditional risk factors or underlying disease activity, outweighing the steroid effect.

Garelick and colleagues conducted a retrospective study of 250 patients at University College Hospital, London, with a median follow-up of 17 years. Fragility fractures occurred in 28 patients (11.2%). Patients with fractures had a lower average daily dose than those without (5.36 vs 6.23 mg/day, P = 0.127) and a higher median cumulative dose (25.19 vs 20.96 g, P = 0.229), but neither difference was significant. Instead, established risk factors such as older age at diagnosis, baseline osteoporosis and secondary hyperparathyroidism were significantly linked with fractures. The authors emphasised that, because 94% of the population had received glucocorticoids, comparing users and non-users was problematic [30].

Mendoza-Pinto et al. conducted a major systematic review and meta-regression of 38 publications involving 3,442 patients with SLE and 6,198 controls [31]. While the study demonstrated that patients with SLE have considerably lower BMD than healthy controls (mean difference −0.057, 95% CI −0.071 to −0.044), there was no significant difference in BMD between patients who had received glucocorticoids and those who had not. The study found that glucocorticoids had no statistically significant independent effect on BMD, implying that the systemic inflammation of lupus, together with age and body mass, may be the main cause of bone loss [31].

3.3 Fracture incidence compared with the general population

In a UK Clinical Practice Research Datalink cohort of 4,343 patients with SLE and 21,780 matched controls, SLE had an adjusted relative risk of clinical fracture of 1.22 (95% CI 1.05 to 1.42), and GC use in the previous 6 months increased fracture risk (adjusted RR 1.27, 95% CI 1.02 to 1.58) [32]. A meta-analysis of population-based studies found an unadjusted RR of 2.07 and an adjusted RR of 1.22 for fractures at all sites [14,33]. Tertiary referral centres reported higher relative risks, up to 4.7, suggesting that they may overstate risk by selecting patients with more severe disease [14,15]. Two larger prospective BMD studies found that bone loss occurs mostly in people using at least 7.5 mg/day of prednisone [14].

3.4 Summary of key studies

The key studies are summarised in Table 4.

Table 4: Key SLE studies of glucocorticoid dose and bone outcomes

Study	Design and population	Dose measure	Outcome	Main finding
Ruiz-Arruza 2014 [10]	Cruces Lupus Cohort, n = 230, 5 years	Mean daily prednisone dose	Permanent organ damage, including osteoporotic fractures within a composite	Medium-to-high dose (>7.5 mg/day) vs none: global damage adjusted OR 5.39, GC-related damage adjusted OR 9.9; low doses and IV pulses not associated with damage
Ugarte-Gil 2021 [11]	Systematic review and meta-regression, 49 observational studies, n = 16,224	Average daily and cumulative dose	Osteoporosis with fractures	1.14 per 100 patient-years; higher average daily dose associated with osteoporosis with fractures
Al Sawah 2015 [28]	Prospective cohort (Hopkins), n = 2,199	Mean prior prednisone dose, time-dependent	New damage on SLICC/ACR Damage Index, by organ	7.5 mg/day or more vs below: osteoporotic fracture HR 2.16; 20 mg/day or more vs below 7.5: any damage HR 2.51
Madanchi 2026 [29]	Hopkins Lupus Cohort, n = 1,003, repeated spine DXA	Mean prednisone dose across prior visits	Osteoporosis (spine T-score −2.5 or lower)	Mean dose above 5 mg/day an independent predictor; below 5 mg/day non-significant (adjusted OR 1.35); stopping prednisone linked to higher T-scores

Garelick 2021 [30]	Retrospective, London, n = 250, median 17 years	Average daily and cumulative dose	Fragility fracture	28 fractures (11.2%); no significant association with dose
Mendoza-Pinto 2018 [31]	Systematic review and meta-regression, 38 articles	GC therapy yes or no	BMD, vertebral fracture	Lower BMD in SLE; no BMD difference by GC use
Bultink 2014 [32]	UK primary-care cohort, 4,343 SLE vs 21,780 controls	GC use in previous 6 months	Clinical fracture	SLE RR 1.22; recent GC use RR 1.27
Wang 2016 [33]	Meta-analysis of population-based studies	SLE vs general population (dose not compared)	Fractures at all sites	Unadjusted RR 2.07; adjusted RR 1.22
Gu 2019 [34]	Meta-analysis of cross-sectional and case-control studies	Daily dose, cumulative dose, duration	Osteoporosis on DXA	Prevalence 16%; cumulative dose and duration differed, daily dose did not
Xia 2019 [35]	Meta-analysis, 71 reports, 33,527 patients	Not detailed in abstract	Low BMD, osteopenia, osteoporosis	45%, 38% and 13% prevalence at any site

4 WHY THE STUDIES DISAGREE, AND WHAT ELSE MATTERS

4.1 How dose is measured

Different dose metrics are used in studies, such as average daily and cumulative dose [30] or mean past dose [28,29]. They cannot be interpreted in the same way and are not interchangeable. The difference between BMD-based studies [29,31,34] and fracture-based cohorts [28,30] may be explained by this methodological variance as well as by the biological processes of steroid-induced damage. Glucocorticoids cause myopathy and quickly deteriorate internal bone microarchitecture, which raises the risk of falls. As a result, the immediate fracture risk is tightly related to current or daily doses [36], and patients typically experience fragility fractures at higher BMD T-scores before total bone mineral loss is seen on a scan [22]. In contrast, overall BMD reduction indicates long-term cumulative exposure and is frequently masked in meta-analyses by the severe baseline bone loss caused by lupus inflammation. However, the metric chosen does not entirely explain why some smaller cohorts yield null results. Cut-offs also differ with the 2015 Hopkins analysis used 7.5 and 20 mg/day [28], the 2026 analysis used 5 mg/day [29], and the London cohort compared average daily and cumulative doses between patients with and without fractures [30].

4.2 Confounding by disease activity and indication

Confounding by indication makes it difficult to isolate the specific skeletal toxicity of glucocorticoids (GCs) in observational research. Because clinicians prescribe greater GC doses to patients with severe lupus flares, medication dose and illness severity become inextricably linked [14]. As a result, it is impossible to tell whether a fracture was caused by the high-dose steroid or by the strong inflammatory flare that prompted it.

Advanced statistical models used in the Hopkins study try to account for this by correcting for disease activity (for example, time-varying SLEDAI scores), but they still show an independent GC dose-response [28]. However, residual confounding is difficult to eliminate in observational studies. Clinical disease activity scores may not reflect the complete severity of the inflammation, raising the possibility that some of the harm attributed to GCs results from unmeasured illness severity.

Furthermore, cohort studies often lack appropriate control groups. In the London cohort, for example, 94% of patients had received GC therapy, leaving only a small unexposed group for comparison [30]. The study's statistical power was significantly limited by the low number of events (just 28 fragility fractures). There is a high risk of type II error, in which a meaningful dose-response relationship exists but the study lacks the statistical power to detect it [30].

Finally, GCs also pose a dual-mechanism problem. On the one hand, GCs cause osteoblast and osteocyte death, degrade internal bone microarchitecture and reduce intestinal calcium absorption. On the other hand, by actively inhibiting the immune system, GCs quickly shut down the systemic inflammatory cytokines that cause osteoclast hyperactivity [14]. In individuals with extremely active SLE, timely use of GCs may have a net protective effect on bone in the short term by preventing inflammatory bone loss, complicating the precise assessment of net harm.

4.3 Other risk factors

Beyond dose, several factors modify bone risk in SLE:

- **Lupus nephritis and renal impairment.** Few lupus studies have looked at secondary hyperparathyroidism and low 1,25-dihydroxyvitamin D caused by severe renal failure, since many excluded individuals with impaired renal function [14]. In the London cohort, fractures were linked to secondary hyperparathyroidism [30].
- **Age, race, body mass index, vitamin D, stroke and falls.** Older age [29] and older age at SLE diagnosis [30], Black race and lower body mass index [29], and stroke or seizures [32] were linked to osteoporosis or fractures. Low mean 25-hydroxyvitamin D also independently predicted osteoporosis in the 2026 Hopkins analysis [29]. About 20% of women with SLE have been reported to be frail, and a history of stroke may indicate an increased risk of falls [14].

5 CLINICAL IMPLICATIONS AND CONCLUSION

At the beginning of GC therapy, the risk of fracture for all patients should be evaluated. The ACR advises a clinical risk assessment, DXA with vertebral fracture assessment or spine radiography, and FRAX if the patient is 40 years of age or older, ideally within 6 months of starting, for persons anticipated to take 2.5 mg/day or more for more than three months [17]. Clinical judgement and vertebral imaging remain crucial in SLE because FRAX has limitations: it does not account for cumulative GC exposure, falls or prevalent vertebral abnormalities, it is not validated before age 40, and it may underestimate risk [14,17]. Patients who continue GCs should be reassessed every one to two years [17].

EULAR advises lowering maintenance GCs to 5 mg/day or less and stopping them when feasible [9,19]. The target should be viewed as a ceiling to move below rather than as a safe dose, because the 2026 Hopkins analysis found a significant osteoporosis risk above 5 mg/day and a raised, though non-significant, estimate below it [29]. Its finding that stopping prednisone was followed by higher spine T-scores [29] is consistent with a benefit from tapering.

The ACR conditionally suggests increasing dietary and supplemental calcium intake (up to a total of 1,000 to 1,200 mg/day) and vitamin D (with a target 25-hydroxyvitamin D level of at least 30 to 50 ng/mL, which generally requires 600 to 800 IU/day or more), along with quitting smoking, limiting alcohol consumption to no more than two drinks per day, and weight-bearing exercise, although the evidence supporting these recommendations is of low certainty [17]. Pharmacological intervention is advised for adults at moderate, high or very high fracture risk. Oral bisphosphonates are strongly recommended in place of no treatment for those at high and very high risk, while anabolic therapy is conditionally preferred for those at very high risk. Adults at low risk should not be prescribed osteoporosis medications. Younger adults typically fall into the low-risk category, and treatment for those under 40 years is conditionally recommended only for individuals at moderate or very high risk, as specified by the guideline [17].

A limitation of this review is that the studies included vary in their dose metrics, outcomes and populations, which prevents them from being combined. Among the studies examined here, none was a prospective trial of bone protection with a fracture endpoint in SLE, and the ACR points out that much of the evidence for glucocorticoid-induced osteoporosis (GIOP) is downgraded because it relies on BMD or on fracture data from the general osteoporosis population [17]. Prospective studies with standardised dose measures, a larger number of patients who have not been exposed to GCs, and broader ethnic and geographic representation are needed.

To conclude, there has been no recorded long-term GC dose that has proven safe for bone health in patients with lupus. The evidence for a dose-response relationship is clearest at doses of 7.5 mg/day and higher, with osteoporosis risk in one cohort significant above 5 mg/day and uncertain below it; however, not all studies agree, and variations in how doses are measured, together with confounding, outcome differences and the selection of study cohorts, likely account for much of the inconsistency. In clinical practice, the goal is to use the lowest effective dose, coupled with steroid-sparing treatment to achieve and maintain a dose below 5 mg/day, together with early assessment of fracture risk including vertebral imaging, and bone protection tailored to the identified risk.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

The authors gratefully acknowledge Universitas Airlangga for its resources and facilities, the supervising faculty and Dr Soetomo General Academic Hospital for their guidance and academic support throughout the writing of this paper.

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this review.

REFERENCES

[1] Fava A, Petri M. Systemic lupus erythematosus: diagnosis and clinical management. J Autoimmun. 2019;96:1-13. doi:10.1016/j.jaut.2018.11.001

[2] Tsokos GC. Systemic lupus erythematosus. N Engl J Med. 2011;365(22):2110-21. doi:10.1056/NEJMra1100359

[3] Tian J, Zhang D, Yao X, Huang Y, Lu Q. Global epidemiology of systemic lupus erythematosus: a comprehensive systematic analysis and modelling study. Ann Rheum Dis. 2023;82(3):351-6. doi:10.1136/ard-2022-223035

[4] Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI: a disease activity index for lupus patients. Arthritis Rheum. 1992;35(6):630-40. doi:10.1002/art.1780350606

[5] Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002;29(2):288-91.

[6] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997;40(9):1725. doi:10.1002/art.1780400928

[7] Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Arthritis Rheumatol. 2019;71(9):1400-12. doi:10.1002/art.40930

[8] Martin-Iglesias D, Paredes-Ruiz D, Ruiz-Irastorza G. Use of glucocorticoids in SLE: a clinical approach. Mediterr J Rheumatol. 2024;35(Suppl 2):342-53. doi:10.31138/mjr.230124.uos

[9] Fanouriakis A, Kostopoulou M, Andersen J, Aringer M, Arnaud L, Bae SC, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis. 2024;83(1):15-29. doi:10.1136/ard-2023-224762

[10] Ruiz-Arruza I, Ugarte A, Cabezas-Rodriguez I, Medina JA, Moran MA, Ruiz-Irastorza G. Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus. Rheumatology (Oxford). 2014;53(8):1470-6. doi:10.1093/rheumatology/keu148

[11] Ugarte-Gil MF, Mak A, Leong J, Dharmadhikari B, Kow NY, Reátegui-Sokolova C, et al. Impact of glucocorticoids on the incidence of lupus-related major organ damage: a systematic literature review and meta-regression analysis of longitudinal observational studies. Lupus Sci Med. 2021;8(1):e000590. doi:10.1136/lupus-2021-000590

[12] Hayes KN, Baschant U, Hauser B, Burden AM, Winter EM. When to start and stop bone-protecting medication for preventing glucocorticoid-induced osteoporosis. Front Endocrinol (Lausanne). 2021;12:782118. doi:10.3389/fendo.2021.782118

[13] Florez H, Carrasco JL, Barberá M, Hernández-Rodríguez J, Muxi A, Mocritcaia A, et al. Risk factors for glucocorticoid induced osteoporosis in young adults. Front Endocrinol (Lausanne). 2025;16:1528962. doi:10.3389/fendo.2025.1528962

[14] Bultink IEM. Bone disease in connective tissue disease/systemic lupus erythematosus. Calcif Tissue Int. 2018;102(5):575-91. doi:10.1007/s00223-017-0322-z

[15] Bultink IEM, Lems WF. Lupus and fractures. Curr Opin Rheumatol. 2016;28(4):426-32. doi:10.1097/BOR.0000000000000290

[16] Canalis E. Mechanisms of glucocorticoid-induced osteoporosis. Curr Opin Rheumatol. 2003;15(4):454-7. doi:10.1097/00002281-200307000-00013

[17] Humphrey MB, Russell L, Danila MI, Fink HA, Guyatt G, Cannon M, et al. 2022 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Rheumatol. 2023;75(12):2088-102. doi:10.1002/art.42646

[18] Chotiyarnwong P, McCloskey EV. Pathogenesis of glucocorticoid-induced osteoporosis and options for treatment. Nat Rev Endocrinol. 2020;16(8):437-47. doi:10.1038/s41574-020-0341-0

[19] Moysidou GS, Fanouriakis A. EULAR 2023 recommendations for the management of systemic lupus erythematosus: one step forward. Mediterr J Rheumatol. 2024;35(1):63-5. doi:10.31138/mjr.130124.erm

[20] Buttgereit F, da Silva JA, Boers M, Burmester GR, Cutolo M, Jacobs J, et al. Standardised nomenclature for glucocorticoid dosages and glucocorticoid treatment regimens: current questions and tentative answers in rheumatology. Ann Rheum Dis. 2002;61(8):718-22. doi:10.1136/ard.61.8.718

[21] Fangtham M, Petri M. 2013 update: Hopkins lupus cohort. Curr Rheumatol Rep. 2013;15(9):360. doi:10.1007/s11926-013-0360-8

[22] Cho SK, Sung YK. Update on glucocorticoid induced osteoporosis. Endocrinol Metab (Seoul). 2021;36(3):536-43. doi:10.3803/EnM.2021.1021

[23] van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Oral corticosteroids and fracture risk: relationship to daily and cumulative doses. Rheumatology (Oxford). 2000;39(12):1383-9. doi:10.1093/rheumatology/39.12.1383

[24] Krugh M, Langaker MD. Dual-energy x-ray absorptiometry. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Nov 9]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519042/

[25] Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res. 1994;9(8):1137-41. doi:10.1002/jbmr.5650090802

[26] International Society for Clinical Densitometry. 2023 ISCD official positions - adult [Internet]. Middletown (CT): ISCD; 2023 [cited 2026 Nov 9]. Available from: https://iscd.org/wp-content/uploads/2024/03/2023-ISCD-Adult-Positions.pdf

[27] Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int. 2008;19(4):385-97. doi:10.1007/s00198-007-0543-5

[28] Al Sawah S, Zhang X, Zhu B, Magder LS, Foster SA, Iikuni N, et al. Effect of corticosteroid use by dose on the risk of developing organ damage over time in systemic lupus erythematosus - the Hopkins Lupus Cohort. Lupus Sci Med. 2015;2(1):e000066. doi:10.1136/lupus-2014-000066

[29] Madanchi N, Fava A, Goldman DW, Magder LS, Petri M. Role of prednisone and 25-hydroxyvitamin D on bone mineral density and osteoporosis in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2026;78(6):743-8. doi:10.1002/acr.25701

[30] Garelick D, Pinto SM, Farinha F, Pires T, Khan E, Isenberg D. Fracture risk in systemic lupus erythematosus patients over 28 years. Rheumatology (Oxford). 2021;60(6):2765-72. doi:10.1093/rheumatology/keaa705

[31] Mendoza-Pinto C, Rojas-Villarraga A, Molano-González N, Jiménez-Herrera EA, León-Vázquez ML, Montiel-Jarquín A, et al. Bone mineral density and vertebral fractures in patients with systemic lupus erythematosus: a systematic review and meta-regression. PLoS One. 2018;13(6):e0196113. doi:10.1371/journal.pone.0196113

[32] Bultink IEM, 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(4):1275-83. doi:10.1007/s00198-013-2587-z

[33] Wang X, Yan S, Liu C, Xu Y, Wan L, Wang Y, et al. Fracture risk and bone mineral density levels in patients with systemic lupus erythematosus: a systematic review and meta-analysis. Osteoporos Int. 2016;27(4):1413-23. doi:10.1007/s00198-015-3449-7

[34] Gu C, Zhao R, Zhang X, Gu Z, Zhou W, Wang Y, et al. A meta-analysis of secondary osteoporosis in systemic lupus erythematosus: prevalence and risk factors. Arch Osteoporos. 2019;15(1):1. doi:10.1007/s11657-019-0667-1

[35] Xia J, Luo R, Guo S, Yang Y, Ge S, Xu G, et al. Prevalence and risk factors of reduced bone mineral density in systemic lupus erythematosus patients: a meta-analysis. Biomed Res Int. 2019;2019:3731648. doi:10.1155/2019/3731648

[36] Van Staa TP, Leufkens HGM, Cooper C. The epidemiology of corticosteroid-induced osteoporosis: a meta-analysis. Osteoporos Int. 2002;13(10):777-87. doi:10.1007/s001980200108