Haugeberg et al recently published clinical decision rules to identify patients with rheumatoid arthritis (RA) at risk for osteoporosis. Included were patients treated with glucocorticoids, a subject that has been for a long time the interest of rheumatologists.

For example, the Dutch Society for Rheumatology has recently published guidelines for the prevention of glucocorticoid induced osteoporosis (GIOP). This document was prepared by a group of rheumatologists of the society and other experts to mark the occasion of the publication of the 3rd Osteoporosis Guideline, (the “CBO consensus”) which was, in turn, prepared at the request of the Dutch authorities by a multidisciplinary group who examined evidence based medicine.

Figure 1 is a stream diagram showing the diagnostic and therapeutic steps in making decisions for the prevention of GIOP. Factors that influence this decision include the dose of glucocorticoids and the presence of other risk factors such as age, sex, previous fracture, and bone mineral density (BMD). The main message is that treatment with bisphosphonates should be started immediately in patients at high risk (high dose of glucocorticoids, prevalent fracture, postmenopausal women, and elderly men).

The recommendations cover some uncertainties. Firstly, it is unclear what is the threshold value of BMD below which prevention is indicated if the intake of glucocorticoids is 7.5 mg prednisone equivalents/day in the absence of other risk factors. The CBO consensus suggested a T score ≤ −2.5 or a Z score ≤ −1. However, other groups have suggested different thresholds. The UK consensus group suggested a T score ≤ −1.5 and the American College of Rheumatology suggested a T score ≤ −1. The main reason for the absence of consensus is the uncertainty that the risk for osteoporosis is increased in a low risk group treated with low dose glucocorticoids, that fractures can be prevented in this group and, perhaps most relevant, that the fracture threshold is altered in GIOP. Indeed, bone loss is limited in patients chronically treated with low dose glucocorticoids if calcium and vitamin D supplements are given.

Secondly, it is still unclear if these patients should have an x ray examination of the spine to document vertebral deformities. Although only one in three vertebral deformities is accompanied by acute symptoms of fractures, it has been recently shown that non-clinically manifest vertebral deformities also result in increased morbidity and an increased risk for new fractures. Introducing a new risk factor is a reason for increasing awareness: starting glucocorticoid treatment should be accompanied by treatment with bisphosphonates in high risk patients and by dual energy x ray absorptiometry (DXA) measurement in others.

Thirdly, specific risk factors of bone loss in conditions such as RA were not considered. Accelerated bone loss has been documented in patients with RA with high disease activity, immobility, and low body weight. However, no studies are available on the prevention of osteoporosis in patients with RA with these risk factors, and, thus, this information was lacking in the guidelines.

Figure 1 Stream diagram for osteoporosis prevention in GIOP.
Does long term treatment with azathioprine predispose to malignancy and death in patients with systemic lupus erythematosus?

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The treatment of patients with rheumatic diseases with second line agents has expanded in the past three decades. However, such drugs have been linked with the development of malignancy, particularly in patients with rheumatoid arthritis. Azathioprine is used to treat patients with systemic lupus erythematosus (SLE) with renal disease, or as a steroid-sparing agent. We have assessed the risk that azathioprine treatment predisposes to the development of malignancies and death in patients with SLE.

We carefully reviewed the case notes of 358 patients with SLE receiving long term follow up in the Lupus Clinic at University College London, between 1978 and 2002, and assessed their treatment. Three hundred and twenty six (91.1%) patients were female and 32 (8.9%) male. One hundred and forty eight (41.3%) were treated at any time with azathioprine, while 210 (58.7%) never used this second line agent. The mean (SD) ages of the users and non-users were similar (40.5 (12.7) v 45.3 (13.2), respectively, which is not significant by $\chi^2$ test with 95% confidence intervals). The mean (SD) duration of azathioprine treatment was 3.8 (3.9) years (minimum of 6 months and maximum of 18 years). Most patients are alive (83.2%) and only a minority were lost to follow up (3.1%). Forty nine (13.7%) of our patients have died: 27/148 (18%) had received azathioprine and 22/210 (10%) had not. Eight of our patients prescribed azathioprine developed a malignancy (none had a lymphoma), whereas 14 not given azathioprine have done so (three had lymphomas: one non-Hodgkin and two Hodgkin). These differences are not statistically significant ($\chi^2$ test). However, the number of deaths in the azathioprine group which is almost double that in the other group does raise concerns, although it may simply be identifying a subgroup with more serious disease.

Table 1 shows the number of malignancies and death in patients with SLE treated with azathioprine, according to the duration of treatment.

Five of the patients who died were receiving azathioprine for <1 year, 10 for between 1 and 4 years, 11 for between 5 and 9 years, and 1 for >10 years. Five patients who developed malignancy were receiving azathioprine for...