

Letter to the Editor (Matters arising from published papers)

Rheumatology Advances in Practice 2022;00:1–2
<https://doi.org/10.1093/rap/rkac011>
Advance Access Publication 21 February 2022

Comment on: Paradoxically protective effect of glucocorticoids on bone mass and fragility fracture in a large cohort: a cross-sectional study. Reply

DEAR EDITOR, We thank Hayes *et al.* [1] for their interest in our report [2]. Many of their points are well taken. They expand on the scenario of selection bias that can explain why, in our cross-sectional observation, patients on glucocorticoids (GC) had higher bone mass than patients not on GC. Indeed, our observations are controversial, ‘...given that the vast majority of ... studies show that GC increase fracture risk by a multitude of mechanisms, including BMD loss’.

Their main arguments focus on the following points: the idea that GC users are referred for DXA scan at an early stage of exposure, in contrast to other patients who are referred because of classic risk factors; the idea that GC users with a fracture are preferentially not referred for a DXA scan because guidelines suggest starting therapy without a scan and because the relationship between fracture and low BMD is less strong in GC users; and the idea that GC users referred for a scan are healthier and under better treatment than those not referred. We agree that all these mechanisms might be at work.

One counter-argument we would like to make is that many studies show that adherence to guidelines for screening and treatment of osteoporosis is low, also in GC-treated patients.

Another counter-argument is that all these worries about selection bias are never levelled at that vast majority of studies that do find a relationship between GC exposure, BMD loss and fracture. As we have stated repeatedly in the past, observational studies on the adverse effects of GC are hopelessly confounded by indication [3], and there is a strong publication bias at work favouring studies that confirm detrimental effects of GC. Our report is but one example of this mechanism at work; it took us well over a year to get this report accepted.

And as an aside, the widely quoted study of Van Staa *et al.* [4] on the higher fracture risk of GC-treated patients with relatively high bone mass rests on a model that has vanishingly few cases, and it is a single study >20 years old that has never been replicated. Nevertheless, there is a growing body of literature, also in observational studies, to suggest the effects are not as bad as many think, such as our systematic review of prospective studies of bone loss [5].




We are happy to agree with Hayes *et al.* [1] that we need the results of the GLORIA trial, NCT 02585258. M.B. is lead author, and he is confident that the results (which are looking good for bone health) will appear in the literature in the coming months.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work on this manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

Marwan Bukhari ¹, **Nicola Goodson** ² and **Maarten Boers** ^{3,4}

¹Department of Rheumatology, University Hospitals of Morecambe Bay Foundation NHS Trust, Royal Lancaster Infirmary, Lancaster, ²Department of Rheumatology, Aintree University Hospitals NHS Trust, Liverpool, UK, ³Department of Epidemiology and Biostatistics and ⁴Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, The Netherlands
Accepted 7 February 2022

Correspondence to: Marwan Bukhari, University Hospitals of Morecambe Bay Foundation NHS Trust, Royal Lancaster Infirmary, Ashton Road, Lancaster LA1 4RP, UK. E-mail: marwan.bukhari@mbht.nhs.uk

References

- Hayes KN, Burden AM, Winter EM, Hauser B. Comment on: Paradoxically protective effect of glucocorticoids on bone mass and fragility fracture in a large cohort: a cross-sectional study. *Rheumatol Adv Pract* 2021; 2022-003
- Bukhari M, Goodson N, Boers M. Paradoxically protective effect of glucocorticoids on bone mass and fragility fracture in a large cohort: a cross-sectional study. *Rheumatol Adv Pract* 2021;<https://doi.org/10.1093/rap/rkab089>.
- Boers M. Observational studies on glucocorticoids are harmful! *Lupus Sci Med* 2017;4:e000219.

4 Van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Use of oral corticosteroids and risk of fractures. *J Bone Miner Res* 2000;15:993–1000.

5 Lems WF, Baak MM, van Tuyl LH *et al.* One-year effects of glucocorticoids on bone density: a meta-analysis in cohorts on high and low-dose therapy. *RMD Open* 2016;2:e000313.