Background

Glucocorticoids are used due to their anti-inflammatory and immuno-suppressive effects and are part of the treatment of numerous inflammatory conditions (1). However, glucocorticoids also have several unwanted side effects, including the risk of secondary osteoporosis (2).

This study uses a DXA-scanned cohort of 64000 individuals from OUH, combined with registry data from Statistics Denmark, to study the association between glucocorticoid dose and bone loss.

The aim of this register-based study is to quantify the short- and long-term bone loss in treatment-naive and unopposed men and women during glucocorticoid treatment.

Methods

Individuals with prescriptions for glucocorticoids within five years of their first DXA scan were excluded, to ensure glucocorticoid exposed individuals were treatment-naive. Individuals with no exposure in the study period, were used as a control population. Receiving a prescription for anti-osteoporotic medication censored you from that date forward. Individuals were required two or more DXA scans on record, to calculate at least one difference in BMD for each individual.

Short-term bone loss: Annualized percentage difference in total left hip BMD between the first two DXA scans

Long-term bone loss: Percentage difference in total left hip BMD from first DXA scan and six years forward

The short- and long-term bone losses were stratified by tertiles of glucocorticoid exposure and the unexposed group.

Cooperations & Presentations

Benjamin Bakke Hansen, Katrine Rubin, Pernille Hermann, Morten Frost Munk Nielsen, Bo Abrahamsen. *Biological heterogeneity in skeletal susceptibility to glucocorticoid induced bone loss: Short- and long-term BMD trajectories during unopposed GC treatment in adults.*
Oral Presentation at Society for Endocrinology BES 2023, Glasgow, Scotland. Endocrine Abstracts (2023) 94

Benjamin Bakke Hansen**,** Katrine Rubin, Pernille Hermann, Morten Frost Munk Nielsen, Catharina Vind Nielsen, Bo Abrahamsen.
Modelling the initial effects of systemic glucocorticoids (GCs) on absolute changes in total left hip BMD in GC treatment-naïve and unopposed adults using linear regression.
Oral and Poster Presentation at European Calcified Tissue Society Congress (May 2024), Marseille, France.

Results

Short-term Bone Loss

	LOWER TERTILE		MIDDLE TERTILE		UPPER TERTILE		UNEXPOSED	
	Men: 90	Women: 429	Men: 143	Women: 376	Men: 263	Women: 256	Men: 1224	Women: 5025
Baseline Age, mean (SD)								
Age At First DXA	64.0 (14.3)	64.3 (12.0)	63.5 (13.3)	62.8 (14.0)	63.6 (14.5)	60.5 (15.8)	58.2 (15.6)	61.8 (13.2)
Glucocorticoid Usage, median (IQR)								
Glucocorticoids (avg. mg per day)	0.2 (0.2)	0.1 (0.1)	1.6 (1.9)	1.3 (1.6)	10.9 (7.8)	10.9 (7.7)	0	0
Change in BMD, median (IQR)								
% Annualized BMD Change	-0.3 (1.5)	-0.9 (1.2)	-0.7 (1.5)	-1.1 (1.7)	-1.2 (2.4)	-1.4 (3.0)	-0.3 (1.8)	-0.8 (1.6)
Nominally Losing/Gaining BMD, % of group								
Nominal Bone Loss	71,1	84,8	77,6	82,7	78,3	77,7	59,6	75,5
Nominal Bone Gain	28,9	15,2	22,4	17,3	21,7	22,3	40,4	24,5

Table 1) Overview of the age at first DXA, average daily glucocorticoid exposure between first two DXA and the change in percentage annualized BMD for the tertiles and unexposed group

Unsurprisingly, the median annualized BMD loss is the greatest for the upper tertile, whereas the unexposed group is comparable to the lower tertile. However the change in BMD has the largest observed variance in the upper tertile group. The proportion of people with nominal bone loss or gain, is approximately stable across the tertile groups. Roughly one in five experienced no nominal bone loss in the upper tertile. This indicates a large heterogeneity in how treatment-naive individuals respond to increasingly higher dosages of glucocorticoids, supporting the notion that there are unexplained factors that predispose to bone loss.

Long-term Bone Loss

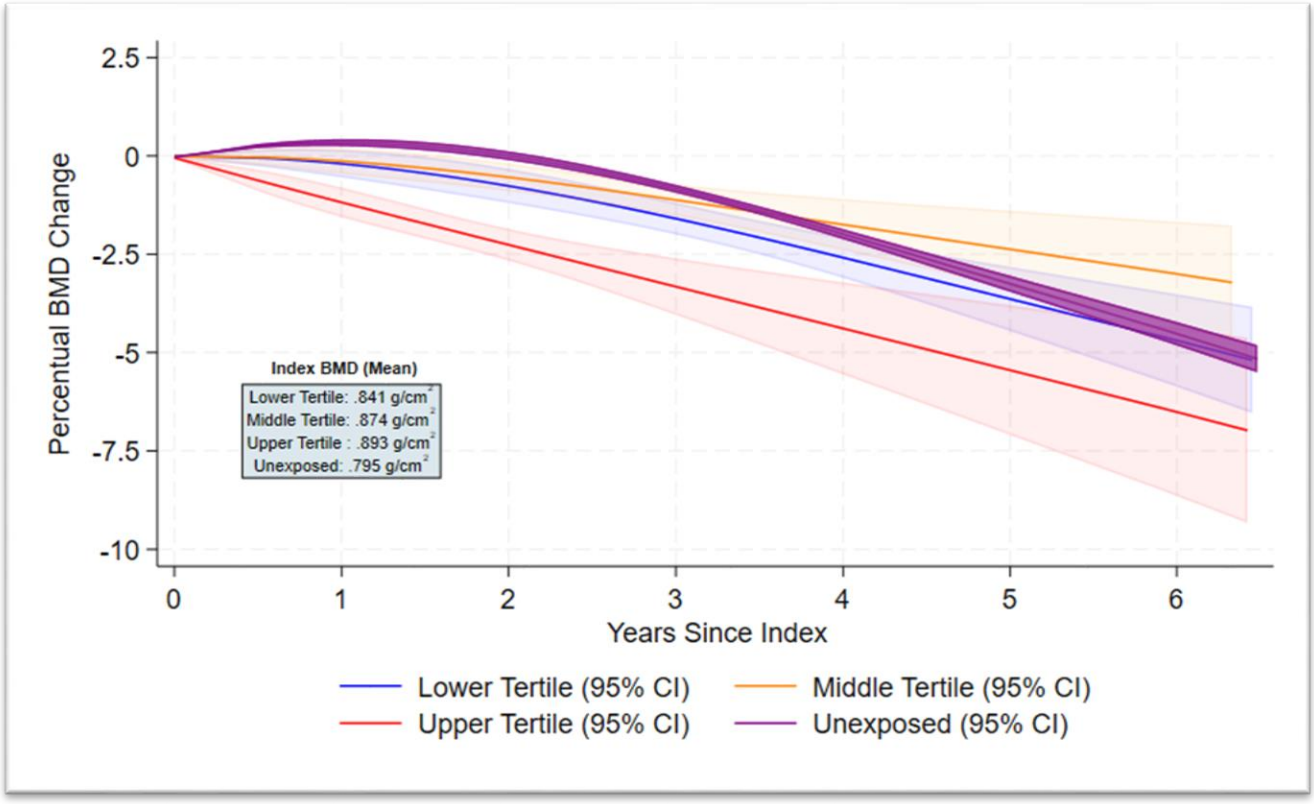

Figure 1) Cubic Spline Regression of the six year change in BMD from baseline measurement with 95% confidence interval bands for glucocorticoid tertiles and the unexposed group

The long-term bone loss appears to support the same findings from the short-term bone loss (Table 1). The upper tertile experiences a faster and steeper bone loss. The lower and middle tertile, as well as the unexposed group regress towards roughly the same expected loss.

These long-term findings are preliminary and could be explained by the fact that a smaller proportion of the groups contribute with data at the later years. Individuals who start anti-osteoporotic medication get censored out of the analysis from the day they initiate treatment, potentially creating a biased projection where people with large bone loss are left out of the analysis. More nuanced investigations of the long-term bone loss that account for this potential issue, are currently being conducted.

Perspectives

This initial exploration is focused on quantifying and describing the association between bone loss and glucocorticoids, at different tertiles of glucocorticoid exposure.
Future studies will focus on a deeper investigation of identifying which factors predispose to accelerated bone loss, in order to better understand the observed heterogenic response to glucocorticoids in the short- and long-term. Lastly, we want to explore ideas for better estimation of fracture thresholds during glucocorticoid treatment.

References

1. Chourpiliadis C, Aeddula NR**.** Physiology, Glucocorticoids. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC.; 2023.
2. Chotiyarnwong P, McCloskey EV**.** Pathogenesis of glucocorticoid-induced osteoporosis and options for treatment. Nat Rev Endocrinol. 2020;16(8):437-47.