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THE LIMITATIONS OF USING SIMPLE DEFINITIONS OF GLUCOCORTICOID EXPOSURE ON THE PREDICTION OF FRACTURE RISK

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Objective: To evaluate the effects of different definitions of glucocorticoid (GC) exposure on the magnitude and pattern of fracture risk using the same dataset.

Material and methods: Data from patients with rheumatoid arthritis (RA) were extracted from the Clinical Practice Research Datalink, a primary care database with electronic health records in the United Kingdom. Patients exposed to oral GCs were matched to up to two unexposed patients by age, gender and location. The first osteoporotic fracture (locations: vertebral, hip, forearm, humerus, pelvis or rib) was identified with adjusted and unadjusted cox proportional hazard ratios (HR) and 95% confidence intervals (CI) produced for fracture risk following GC therapy using different

models of risk attribution. These models included current daily dose (categories 0.1 – 4.9, 5 - 9.9, 10 – 14.9, 15 – 19.9, 20 – 24.9, 25+ mg prednisolone equivalent dose (PEQ)/day), cumulative dose (categories 0.1 – 0.9, 1 – 2.4, 2.4 – 4.9, 5 – 7.4, 7.5 – 10, >10g PEQ) and times since discontinuation of GCs (categories current use, 1 day – 1 month, 1-3 months, 3 – 6 months, 6 months – 1 year, > 1 year ago). Unexposed was the comparator for all models.

Results: There were 16,507 patients included of which 8,357 contributed time to the exposed category. Approximately 70% of all patients were female and patients were followed for four years on average. Exposed patients were older, with higher body mass index and more comorbidities. There were three key results. 1. Risk of fracture increases with current daily dose 1.44 (1.17, 1.77) for 5 to 9.9mg PEQ to 3.02 (1.77, 5.15) for 15 to 19.9mg PEQ. 2. Risk of fracture increases with cumulative dose, from 1.22 (1.03, 1.44) (0.1 to 0.9g) to 1.83 (1.35, 2.48) (7.5 to 10g), however the individual effects of dose and duration in this model were unclear. 3. Risk of fracture increased during the first month after discontinuation of GCs from HR (95% CI) 1.43 (1.21, 1.68) for current users to 1.66 (1.27, 2.16) before decreasing to non-significant levels 1.11 (0.79, 1.57) for those exposed between 1 and 3 months prior.

Conclusion: GC exposure was associated with excess fracture risk, but effect size differed according to definition of exposure, highlighting the need to incorporate multiple exposure dimensions in assessments of fracture risk in patients with RA using oral GCs.