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RISK OF INCIDENT FRACTURE IS ASSOCIATED WITH DOSE, DURATION AND RECENCY OF ORAL GLUCOCORTICOID EXPOSURE

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Objective: To evaluate how oral glucocorticoids (GCs) affect the risk of fracture in patients with rheumatoid arthritis (RA) using a statistical method incorporating dose, duration and recency of exposure in one model.

Material and methods: Patients with RA were identified from the Clinical Practice Research Datalink, a primary care, electronic medical record database in the United Kingdom. Patients exposed to GCs were matched to up to two unexposed patients by age, gender and geographic location. First osteoporotic fracture was

identified for each patient. A novel method, the weighted cumulative exposure (WCE) was used to assess the effect of oral GCs on fracture risk. A data defined weight function (WF) was produced using flexible spline curves. This WF was applied to theoretical patterns of GC use to estimate the risk of fracture compared to non-use with hazard ratios (HR) and 95% confidence intervals (CI) produced using bootstrapping.

Results: 16,507 patients were included of which 8,357 were exposed to oral GCs. Average follow up was 4 years with 70% of patients female. The exposed patients were older, had higher BMI and more comorbidities. The most appropriate WF was 3 years in duration. The WF showed an increased risk for the first year after GC use; risk decreased with time. Comparing different patterns of GC exposure there were 3 key results: 1. Risk of fracture increased with duration of use: HR (95%CI) 1.09 (1.13, 1.05) to 1.25 (1.16, 1.35) to 1.42 (1.30, 1.55) for 5mg/day for 1, 3 and 6 months respectively. 2. A low dose, long term treatment (5mg/day for 6 months) has a lower cumulative risk than a high dose, short term treatment (30mg/day for 1 month) HR (95% CI) 1.42 (1.30, 1.55) v 1.70 (1.37, 2.09). 3. Discontinuation of oral GCs decreased the risk of fracture; risk returned to baseline between 6 months and 1 year. HR (95% CI) 1.06 (0.97, 1.15) (5mg for 6 months stopped 6 months ago) v 0.99 (0.92, 1.06) (30mg for 1 months stopped 1 year ago).

Conclusion: A novel method was used to assess the association between oral GCs use and fracture risk. Doses of oral GCs taken in the past year increase the risk of fracture. Risk increased with duration of use. Long term low dose treatments have a lower cumulative risk than high dose, short term treatments with equal total dose. Risk of fracture returns to baseline 6 months to 1 year after discontinuation.