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Impact of rheumatoid arthritis patient eligibility for Tumour Necrosis Factor inhibitor therapy (as per NICE guidance concerning disease activity) on need for joint replacement: a regression discontinuity study

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Background: Data are lacking on the comparative effectiveness of tumour necrosis factor inhibitor (TNFi) therapy compared to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) on the need for total hip (THR) or knee replacement (TKR).

Objective: NICE guidance restricts TNFi use to patients with a disease activity score (DAS) >5.1. We aimed to estimate the effect of meeting the DAS eligibility criteria on the incidence of THR and TKR in rheumatoid arthritis (RA).

Methods: We obtained data from the British Society for Rheumatology Biologics Registry for RA (BSRBR-RA) (2001 - 2016). Prior THR/TKR and prevalent TNFi users were excluded. Baseline characteristics of patients "just below" (5.0≤5.1) the DAS treatment threshold were compared to those "just above" (5.2≤5.3). Patients were followed from date of registration to earliest of: outcome, death, loss-to-follow-up or change of TNFi exposure status (stopping, switching or starting). Incidence of THR and TKR was estimated per 0.1 increment of the DAS score. A regression discontinuity design (RDD) was used to estimate the impact of the DAS 5.1 threshold for TNFi treatment eligibility (rather than treatment allocation per se). Specifically, segmented linear regression was used to estimate the difference in incidence of THR and TKR (analysed separately) at the DAS threshold, taking into account trends within different bandwidths around the cut-off: +/- 0.3, +/- 0.5 and +/- 0.7.

Results: Patients with a DAS "just below" or "just above" the DAS treatment threshold were similar in baseline characteristics, although small differences were found in age, health activity score (HAQ) and pain (SF-36). In analyses using a bandwidth of +/- 0.3 around the DAS threshold for TNFi eligibility, there was a non-significant reduction in THR incidence of -6.88 [95% CI: -22.48 to 8.72; p=0.20] per 1,000 PYs associated with being above the threshold. In analyses using a bandwidth of +/- 0.5 there was a reduction in THR of -5.69 [-10.98 to -0.39; p=0.039] per 1,000 PYs, and when using a bandwidth of +/- 0.7 there was a reduction in THR of -4.37 [-7.91 to -0.84; p=0.020] per 1,000 PYs associated with being above the DAS threshold. There was no effect on TKR incidence.

Conclusion: Our findings suggest that RA patients with a DAS "just above" vs. "just below" the NICE criteria for TNFi eligibility had a reduced risk of THR but not TKR. Further work is needed to confirm these findings.