Response to: 'Correspondence on 'Warfarin use and risk of knee and hip replacements" by Cheng and Zhang

We thank the authors for their interest in our work.[1] As the authors point out, we reported that paracetamol prescriptions were higher among the cases (ie, those with knee or hip replacements) than the controls, as would be expected.[2] To address the authors' question regarding timing of paracetamol in relation to warfarin, we evaluated a 90-day window around the time of the first warfarin prescription. We found that 59.4% of warfarin users had no prescription for paracetamol, 32.4% had a paracetamol prescription prior to their warfarin prescription, 6.3% had a paracetamol prescription after their warfarin prescription and 1.9% had the same date for both. A very similar pattern existed for direct oral anticoagulant (DOAC) prescriptions. We do not think there is a biological rationale for warfarin or DOAC prescription leading to a paracetamol prescription. To address the author's question regarding potential interaction between the anticoagulant exposure (warfarin vs DOAC), we conducted an analysis with an interaction term between the exposure variable and paracetamol. We found that the interaction term was not statistically significant (p=0.8), and the effect estimate did not change materially from the main results reported. Thus, paracetamol does not appear to have an impact on the relation of warfarin versus DOAC to risk of end-stage osteoarthritis as defined by knee or hip replacement. Similarly, no impact of paracetamol was noted in the Rotterdam study, which also reported on the relation of the vitamin K antagonist acenocoumarol to osteoarthritis progression.[3] These findings are consistent with a previous study that did not find a clinically relevant interaction between vitamin K antagonist anticoagulants and acetaminophen.[4]

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