

## Response to: 'Association between bisphosphonate use and risk of undergoing knee replacement in osteoarthritis patients' by Chen *et al*

We thank Dr Chen and colleagues for their interest in our paper.<sup>1</sup> As outlined in our paper,<sup>2</sup> the definition of knee osteoarthritis (OA) was based on diagnosis by the patient's general practitioner (GP), which is recorded as a read code in The Health Improvement Network (THIN). Because these are patients who are being seen by their GP, the diagnosis of knee OA is typically for symptomatic knee OA. While it is true that knee replacement surgery is not the only relevant longer term knee OA outcome, we were unable to assess other facets of knee OA outcomes due to the nature of the database used; for example, The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores are not available in this GP database. Nonetheless, knee replacement surgery is considered an important symptomatic endpoint for knee OA. We excluded individuals who had prior knee replacement surgery but not prior knee injuries or other surgeries that were unlikely to be confounders. We were able to adjust for socioeconomic status (Townsend deprivation index). The SD for the mean follow-up time were 2.43 and 2.36 years for the bisphosphonate initiators and the comparator group, respectively. Any medications that were prescribed after the initiation of bisphosphonates and after these subjects' newly diagnosed knee OA would be considered intermediates along the causal pathway in the scenario proposed by Dr Chen and colleagues; adjustment for those types of medication use would induce bias. The potential mechanisms by

which bisphosphonates may confer the noted effects was beyond the scope of this paper.

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