**TITLE: TRENDS IN GABAPENTINOID PRESCRIBING IN OSTEOARTHRITIS IN THE UNITED KINGDOM: COHORT STUDY IN PRIMARY CARE**

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**Background:** A recent report on dependence-forming medicines has highlighted a sharp rise in the use of gabapentinoids in the United Kingdom, reinforcing concerns over their increasing off-label use and potential for misuse and diversion. Despite little clinical trial evidence of their effectiveness for pain control in osteoarthritis (OA), there are anecdotal reports of unlicensed (off-label) gabapentinoid use for OA. We sought to estimate the trend in incidence rate of gabapentinoid prescribing in patients with OA (irrespective of indication) and the proportion where OA is the likely indication.

**Methods:** We conducted a descriptive analysis using data from the Clinical Practice Research Datalink (CPRD). Patients aged 40 years and over with a new diagnosis of OA recorded between 1995 and 2015 were identified and followed to their first prescription of gabapentin or pregabalin, or other censoring event (transfer out date, death date, last collection date of practice data, study end). Using Lexis expansion of attained age and calendar year at date of prescription, we estimated the crude and age-standardised incidence rates of gabapentinoid prescribing in this population of patients with OA. We further stratified annual crude incidence rates by patient sex, geographical region, and time since OA diagnosis. A series of analyses based on proximity of diagnostic codes in the patient record to the first gabapentinoid prescription were used to estimate the proportion of prescriptions attributable to OA versus licensed indications.

**Results:** Of 383,680 newly diagnosed OA cases, followed for a median of 6.1 years, 35,031 received at least one gabapentinoid prescription. The annual age-standardised incidence rate of first gabapentinoid prescriptions among patients with OA increased throughout the course of the study period, rising from 1.6 (95% CI: 1.3, 2.0) per 1,000 personyears in 2000, to 27.6 (26.7, 28.4) in 2015. This trend was seen across all ages and was not explained by longer duration of follow-up. Higher rates of gabapentinoid prescribing were seen among women, younger ages, and in Northern Ireland, Scotland and the North of England. Approximately 9-10% of first prescriptions could be attributed to OA, with a further 11-12% of first prescriptions associated with use for a licensed indication. A large proportion of first gabapentinoid prescriptions were issued without a recorded diagnostic code and could therefore not be attributed.

**Conclusion:** Patients with OA have become increasingly likely to receive a gabapentinoid in the past decade. In this patient group, offlabel use for control of OA pain appears almost as common as for comorbidities that are licensed indications, although this is subject to uncertainty since the majority of first gabapentinoid prescriptions do not have an accompanying diagnostic code in the primary care record. The effect of reclassifying gabapentinoids as class C drugs on OA care and outcomes should be investigated.