

Independent associations of incident epilepsy, enzyme-inducing, and non-enzyme- inducing antiseizure medications with the development of osteoporosis: a population-based analysis

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Purpose: Both epilepsy and enzyme- inducing antiseizure medications (eiASM) having varying reports of association with increased risks for osteoporosis. The purpose of this study was to quantify and model the independent hazards of epilepsy and ASMs for osteoporosis. **Method:** Population- based linked primary care and hospital electronic health records cohort study that included all cases of incident adult- onset (≥ 18 years) epilepsy. Exposure to an eiASM was defined as those whose first four consecutive ASMs were for enzyme- inducers. The outcome was incident osteoporosis. Hazard was assessed using accelerated failure time models and incident epilepsy was treated as a time- varying covariate. All analyses controlled for age, sex, socioeconomic status, cancer, 1+ years of corticosteroid use, body mass index, bariatric surgery, eating disorders, hyperthyroidism, inflammatory bowel disease, rheumatoid arthritis, smoking status, falls, fragility fractures, and osteoporosis screening tests. Additional analyses included propensity matching for receipt of an eiASM, restricted analyses to only those with incident onset epilepsy, and restricted analyses to the cohort of people that developed epilepsy at age ≥ 65 . **Results:** Of 8,095,441 adults, we identified 6,275 people with incident adult- onset epilepsy (incidence rate 62 per 100,000 person- years) with a median age of 56 (inter-quartile range 38- 73) and 3,220 (51%) were female. When controlling for osteoporosis risk factors, incident epilepsy was independently associated with an increased risk for osteoporosis (time ratio [TR] 0.59, 95% confidence interval [95%CI] 0.52- 0.67; $p < 0.001$) as were eiASMs (TR 0.91, 95%CI 0.87- 0.95; $p < 0.001$) and non- eiASMs (TR 0.77, 95%CI 0.76- 0.78; $p < 0.001$). The independent associations between epilepsy, eiASMs, and non- eiASMs remained consistent in propensity matched analyses, cohorts restricted to adult- onset epilepsy, and cohorts restricted to late- onset epilepsy. **Conclusion:** Epilepsy is independently associated with a clinically meaningful increase in the risk for osteoporosis, as are both eiASMs and non- eiASMs. Routine screening and prophylaxis should be considered in all people with epilepsy.