34th ICPE (2018) ABSTRACTS

ABSTRACT TEMPLATE

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TITLE: Negative Control Time Window To Identify Residual Confounding In Comparative Effectiveness Study: An Example Of Bisphosphonate Use And risk Of Fracture.

BACKGROUND

Negative controls are often used in pharmaco-epidemiology to identify residual confounding although their use is limited. Time windows of no drug activity (negative control time windows) have been identified from preclinical/RCT data for most preventative therapies: bisphosphonates have no effect on fracture risk for the first 6+ months after initiation, providing an opportunity to test the method.

OBJECTIVES

To identify whether early treatment windows can be used as a negative control in a study assessing fracture risk after bisphosphonate (BP) use in patients with chronic kidney disease (CKD).

METHODS

Patients with stage 3B+ CKD (eGFR<45), aged ≥40 were extracted from UK primary care records (CPRD). Main outcome was major osteoporotic fracture. BP users were matched to up to 5 non-users using propensity scores. Fracture rates were calculated per 1,000 person years for both groups. Hazard ratios were calculated using cox proportional hazards (CPH) models for the full models and censoring at 180 days and 360 days.

RESULTS

10,694 bisphosphonate users were matched to 42,445 non users with CKD. Risk of fracture was increased in bisphosphonate users HR (95% CI) 1.38 (1.28, 1.49) with rates of 36.3 (34.0, 38.9) and 26.2 (25.3, 27.0) in the exposed and unexposed patients respectively. Risk of fracture in the first 6 months (180 days) was considerably higher HR 2.00 (1.69, 2.36). At this time, rates of fracture in users were considerably higher than later 56.1 (49.8, 63.2), but stable over time in the non-users 28.2 (25.9, 30.7). By the first year risk of fracture had decreased to HR 1.78 (1.57, 2.01) with rates of 47.5 (43.2, 52.2) and 26.7 (25.1, 28.5) in the exposed and unexposed patients respectively, suggesting residual confounding by indication.

CONCLUSIONS

Risk of fracture in the first 6 months may be suitable for use as a proxy for a negative control time window. Risk of fracture was 2 fold in the first 6 months compared to 1.4 times throughout follow-up suggesting the risk calculated throughout follow-up is biased by the initial increased risk. More research is needed to explore the usefulness of this method to estimate actual (un-biased) treatment effect/s.