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Title: Self controlled case series in surgical epidemiology: checking the underlying assumptions in an empirical example

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Background: The self controlled case series (SCCS) is a within person study design which controls for all time fixed confounding. It has previously been shown to be useful for vaccine and drug safety studies, however its use in surgical safety has not been investigated. One key question is whether the assumptions underlying SCCS are likely to hold in surgical epidemiology.

Objectives: Demonstrate the checking of assumptions of the SCCS in a surgical safety setting.

Methods: Patients undergoing bariatric surgery who experienced an osteoporotic fracture within 5 years prior or post-surgery were identified in the clinical practice research datalink (CPRD) linked to hospital episode statistics (HES). The outcome, osteoporotic fracture, included all locations except skull and digits. An SCCS model, using a Poisson model, compared the 5 year risk of fracture post surgery to the 5 year risk pre-surgery. Three assumptions of the SCCS were tested in separate models: (I) The independence of the outcome and probability of further exposure (surgery); (II) the independence of recurring events; and (III) the lack of association between outcome and early departure from study. These assumptions were tested by comparing the incidence rate ratio (IRR) produced in the initial model to (I) a model with an 8 week wash out period prior to surgery, and (II) a model of each patient's first fracture. Assumption (III) was checked with a likelihood ratio test comparing models with and without an interaction with early departure. A histogram of the time between fracture and surgery was also used to check assumption (I).

Results: Of 5,492 patients undergoing bariatric surgery, 252 patients had 272 osteoporotic fractures within 5 years either side of surgery. Risk of osteoporotic fracture was not increased after bariatric surgery (IRR (95% confidence interval, CI) 1.17 (0.86, 1.60)). The histogram was uniformly distributed, suggesting fractures didn't affect the likelihood of surgery. 12 fractures occurred in the

wash out period, and 20 were subsequent fractures within patient and 145 patients departed early. The two adjustments to the dataset gave IRRs (95% CIs) of 1.14 (0.78, 1.50), and 1.10 (0.76, 1.61) for assumptions (I) and (II) respectively. The result of the LRT (assumption III) was 0.46. These results suggest no assumption was invalid.

Conclusions: The SCCS appears to be suitable for use in surgical safety settings in this specific example. The same assumption checks used for vaccine/drug safety studies can be used for surgical safety studies using the SCCS. Different settings/surgical procedures would require further testing.