

Title (15/15 words)

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

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Context: The self controlled cases series (SCCS) method, a within person study design, has been proven effective for both vaccine and drug safety studies. However, its validity for surgical safety research has not been proven.

Objective: To demonstrate the underlying assumptions of the SCCS in a clinical example of surgical safety observational research using routinely collected data.

Method: Patients identified from the CPRD linked to HES who underwent bariatric surgery and experienced a fracture at any location except skull and digits within 5 years either side of surgery were included. An SCCS Poisson model was fit to assess the risk of fracture comparing the 5 years post- to the 5 years pre-surgery. Three key assumptions of the SCCS were assessed: (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. Assumption (I) was tested using a histogram of the time between fracture and surgery. Assumptions (I) and (II) were tested by comparing the incidence rate ratio (IRR) between the original model and (I) a model with an 8 week wash out period and (II) a model with only each patients first fracture included. Assumption (III) was assessed using a likelihood ratio test comparing the fit of models with and without an interaction for early departure.

Results: Of 5,492 patients undergoing bariatric surgery, 252 fractured (272 fractures). Risk of fracture was not increased after bariatric surgery (IRR (95% confidence interval), 1.17 (0.86, 1.60)). (I) The likelihood of surgery was not found to be affected by fracture (IRR of 1.14 (0.78, 1.50)) The histogram produce a uniform distribution. (II) Recurrent events were sufficiently independent (IRR, 1.10 (0.76, 1.61)). (III) And there was no association between fracture and early departure, p-value 0.46.

Conclusion: This empirical example demonstrates the suitability of SCCS methods for use in surgical safety settings. The same assumption checks used for vaccine/drug safety studies can be used for surgical epidemiology applications. Further research is needed in different settings/procedures.