Methods: Age and gender adjusted CSSP and GP were compared under three alpha spending functions (O'Brien-Fleming, Pocock, Uniform) with three alpha levels (0.01, 0.05, 0.10), using Optum, a US claims database between 2005 to 2010 split into 6 time periods. Concordance was assessed for the OMOP reference set of 50 drug-outcome pairs for true associations (9 positive pairs and 41 negative controls). Four comparator groups defined by OMOP were used.

Results: Overall, GP had higher/comparable sensitivity and slightly lower/comparable specificity than CSSP, varying by setting of comparator drug definition, alpha spending function and alpha level. The setting for best sensitivity in GP (56%) resulted in a specificity of 59% while the same setting for CSSP resulted in a sensitivity of 33% and specificity of 66%; the setting for best sensitivity in CSSP (44%) resulted in a specificity of 83% while the same setting for GP resulted in a sensitivity of 44% and specificity of 80%. Across all settings, GP tends to pick up signals faster than CSSP: 60-100% pairs in CSSP were picked up at a later period compared with GP. Computation time for both methods are comparable.

Conclusions: Our results suggest that GP performance is comparable to CSSP and both methods showed potential for safety surveillance. With the features of flexible confounding control and fewer assumptions, GP may be a strong alternative to CSSP. Further study to understand the capacity of GP to handle rare events and assess the generalizability of our findings is needed.

757. Considerations for Using Electronic Medical Record Data for Pharmacoepidemiology

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Background: A recent article in *Medical Care* provides a list of caveats for using electronic health record (EHR) data in comparative effectiveness research (CER), including EHRs may contain inaccurate data, often do not tell a complete patient story, and have been collected or coded for purposes other than research and clinical care. Many researchers are not closely involved in patient care or may conduct studies spanning multiple clinical disciplines. Especially in these cases, understanding the caveats of using EHR data can be a challenge.

Objectives: To describe a 3-step process that helps ensure the availability, accuracy, and representativeness of EHR data used in studies.

Methods: The first step in the process is to *investigate the target study population*. It includes gathering information about the common demographic profile affected, the ways the disease commonly manifests itself, and diagnostic tests and treatments given. This provides a baseline of the data that can be expected. Institution-specific numbers should be compared with national estimates and previous publications so any differences can be explored and explained. The second step is to *discover the care workflow*. It usually involves discussing with care providers the types of interactions patients in the target population have with the health care system. Medical record data reflects these interactions, so the goal is to ensure all points of data entry are identified and understood. The third is to *understand the underlying data*. It requires iteratively pulling and validating data to ensure the study population is represented, that all relevant data are available, and that the medical record data adequately represents the real-world interactions of patients with providers. Any deviations can be identified and addressed to ensure not only the data, but the study results are complete, accurate, and reflective of clinical practice.

Results: This process has been tested and adopted by our research team as we've performed studies in health domains ranging from mental health to oncology to cardiovascular health to surgery.

Conclusions: This 3-step process allows research teams to confidently conduct CER studies using EHR data.

758. Impact of Varying Control Moment Selection in a Case-Crossover (CCO) Study on Antidepressant Drug (AD) Use and Hip/Femur Fracture (HFF) in PROTECT

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Background: The CCO design is appealing because it eliminates time-invariant person related confounding. A prerequisite is that exposure in real life drug use is sufficiently transient to allow for independence of exposure states. The impact of variation in time of control moment selection is relatively unknown.

Objectives: To assess the influence of selection of control moments at different times in a CCO study of AD and HFF on variation in effect estimates.

Methods: Adult patients with HFF who received an AD prescription during 2001-2009 were identified from the Dutch Mondriaan GP database. For each patient, a case moment (the date of HFF) and four control moments at 3, 6, 9, and 12 months before the HFF (M3, M6, M9, M12) were defined. Each AD prescription had a pre-defined duration of 90 days. AD treatment episodes were constructed and divided into current, recent (0-2 months following current use) and past use (>2 months follow current use). We used conditional logistic regression to compute odds ratios (ORs) and 95% confidence intervals CI between AD use and HFF.

Results: Pairwise (1:1) comparisons of 82 case moments to varied control moments for current versus no use resulted in ORs for HFF-M3 of 16.3 (95%CI: 2.2-123), M6: 7.8 (2.3-26), M9: 5.9 (2.1-16.1), and M12: 4.1 (1.8-9.4). Including all (1:4), M3-M12, resulted in OR 7.0 (3.2-15.2). For recent use even higher ORs were found; M3: 49.7 (3.9-637), M6: 17.6 (2.5-136), M9: 2.6 (0.7-9.5), M12: 3.7 (0.7-20), All 8.6 (2.7-27).

Discordancy of exposure and thus number of strata contributing to the analyses increased from 32% in M3 to 50% in M12.

Conclusions: Selection of control moments at different times in CCO has considerable impact on effect estimates in this particular setting. CCO studies should be designed with sufficient time between case and control moments to allow for sufficient discordancy in exposure to get reliable estimates.

759. Study Designs in Pharmacoepidemiologic Studies on Electronic Healthcare Databases: A Systematic Review

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Background: Observational studies are widely used in the real life pharmacoepidemiologic studies. Several designs are available, such as cohort (C), case-control (CC), or self-controlled (SC) designs, of which case-crossover (CCO), case-time-control (CTC) and self-controlled case-series (SCCS). Recommendations on their use in medical products (MP) safety monitoring on electronic healthcare databases (EHDB) have been recently published.

Objectives: We aimed at describing which designs are used in pharmacoepidemiologic studies on EHDB, whether they fit the recent recommendations, and how frequent are the situations in which CO could have been applied.

Methods: We searched Medline for articles published in the second part of 2011. Terms referring to 1) EHDB, 2) effect of MP, and 3) observational designs, were combined. More SC were added after enlarging the search between 01-2011 and 12-2012. Data focusing on designs, exposures (EXP) and events (EV) characteristics were collected using a standardized extraction form by two independent readers. In papers reporting more than one design, the SC was considered. 15% of papers were read by both readers. SC could be applied in case of abrupt onset and rare or recurrent event, and intermittent or acute exposure. Specific assumptions for CCO and SCCS were explored in papers using each design respectively.

Results: In the initial search, 94 papers were analysed. Of these, 48 (51%) used data of administrative DB, 19 (20%) of pharmacy records, 16 (17%) of primary care records, other DB were less common. Safety was assessed in 49 (52%) papers, effectiveness in others. Study designs used were 67 C, 25 CC, and 2 SC. Basic assumptions for SC use were met in 18% of papers using a different design. The enlarged search found 13 CCO and 5 SCCS. The formers were always used adequately concerning specific assumptions, except 1 article. Specific assumptions for SCCS use were less often fulfilled.

Conclusions: SC designs have advantages, but their use is subjected to key assumptions fulfilment. When they are used, key assumptions are often fulfilled. However, they could be employed more frequently and their use should be encouraged.