Propensity Score Modeling to Reduce Channeling Bias when Exposure is Rare

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Background & Objective

- Channeling bias in post-marketing surveillance of treatments introduces challenges in contextualizing rates of adverse events, particularly with rare treatments indicated for a small subset of patients with a common disease, or when treatment is first-in-class.
- Methodology is needed to quantify the baseline risks of adverse events in the treatment-indicated population.

Objective: Within a relevant case study, use retrospective, real-world data to generate a counterfactual (CF) group consisting of patients who were demographically and clinically similar to the treatment initiators, but did not receive treatment. Leverage CF group to contextualize risk of adverse events in the treatment-indicated population.

Case Study: Initiation of elagolix among patients with endometriosis.

Methods

Study Population

- Women aged 15-55 with endometriosis (EM) or an elagolix prescription identified within the IBM MarketScan insurance claims database during the index period, starting July 1, 2018 and ending July 1, 2019.

Exposure

- New initiation of elagolix, a product to treat EM-associated pain. New initiation was defined as the first elagolix prescription in the index period described above, with no prior use looking back over all data.

Study Design

- The baseline period was defined as the 365 days prior to and including index date.
- Index date was new initiation of elagolix for exposed patients, and an EM diagnosis for unexposed patients.
- Patients were followed until the earliest of disenrollment, death, outcome event, one year maximum follow-up reached, or end of data (Sep 30, 2020).

Methods and Statistical Analyses

- Patients from the overall EM cohort were sorted into those exposed and unexposed to elagolix.
- Univariable regression models quantified the association between baseline demographics, comorbidities, medication and symptoms, and initiation of elagolix.
- Variables with a p-value <0.25 were included in a the propensity score (PS). Conditions of interest over follow-up were assessed over baseline and forced into PS score, regardless of p-value.
- Women with EM unexposed to elagolix (general EM group) were PS-matched 1:1 with a 1% caliper to elagolix exposed patients, to generate an unexposed counterfactual group of patients with a similar distribution of characteristics (CF group).
- PS distribution and matching performance were assessed using standardized mean differences of covariates (Fig 2a) and Kernel density plots of PS overlap (Fig 2b-c), pre- and post-PS matching.
- Baseline prevalence of adverse events was quantified among the general EM and CF group, as well as follow-up risk (per 1,000 patients) of adverse events, stratified by baseline prevalence yes/no.
- Significance of baseline prevalence and follow-up risk for all adverse events was assessed using Chi-squared and Fisher's exact tests.
- The overall relative risk (RR) (95%CI) of adverse events during follow-up, comparing the counterfactual group and general EM group, was also estimated.
- Data were analyzed using the Aetion Evidence Platform (AEP)®.

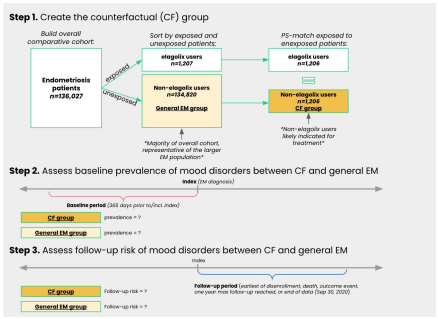

Figure 1. *Illustration for building of counterfactual (CF) group and study design.*

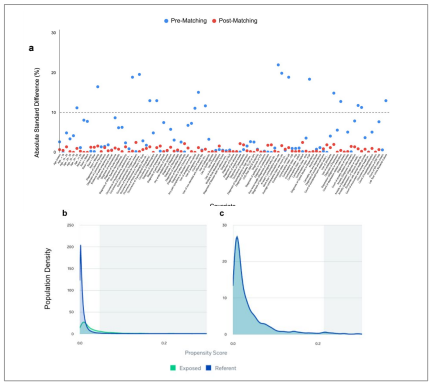

Figure 2a-c. *Covariate balance (a) and propensity score overlap between the counterfactual and general endometriosis groups before (b) and after (c) propensity score matching.*

Results

Counterfactual group generated

- 136,027 women with EM were identified; 1,207 (0.9%) had a prescription claim for elagolix.
- Among 121 baseline covariates considered, 83 were included in the PS model.
- Due to the low frequency of elagolix use, the PS were low (mean 0.04 in the exposed group); yet, matching was robust due to a large referent group with EM and a wide range of baseline covariate distribution profiles.
- There were no significant differences in baseline covariate distribution between the two groups after matching (Fig 2a).
- The exposure and counterfactual groups demonstrated significant heterogeneity from the general EM population
- For many adverse events, higher baseline risk was significantly correlated with higher follow-up risk (Fig 3).

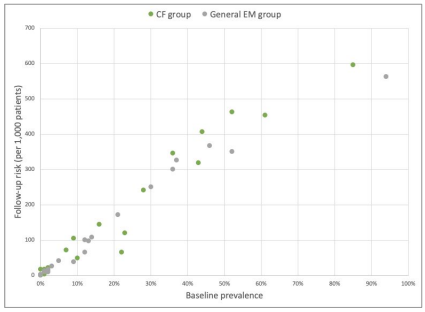

Figure 3. *Correlation between baseline prevalence and follow-up risk of safety events. Each marker represents one of 23 outcomes examined.*

Conclusions

Propensity score matching generated a counterfactual drug group that may be a suitable comparator to quantify baseline adverse event rates in the indicated population for post-market surveillance. These methods can inform the benefit-risk profile of the treated population prior to initiating a comparative safety analysis, and can account for differences in comorbidities and disease severity in patients with the same disease who initiate treatment compared to those who do not.

Disclosure

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