Oral Presentation Methods in Pharmacoepidemiology

Session: Pharmacoepidemiologic Methods and SARS-CoV-2

Evaluating the Comparative Effectiveness and Safety of Repurposed Drugs for COVID-19

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Background: There is a multitude of studies investigating drug interventions for COVID-19. Trials are limited by the inability to include multiple treatment comparisons in a single study and also the lack of representativeness due to restrictive inclusion criteria.

Objectives: 1. To empirically evaluate the robustness of simultaneous head-to-head analyses of multiple treatments and outcomes in real world data (RWD)
2. To estimate the effectiveness and safety of repurposed drugs that satisfied study diagnostics

Methods: We conducted a multinational, distributed network cohort study, using a new user, active comparator design and applied study diagnostics (covariate balance, equipoise, and power) to assess the validity of our findings. We included 9 health databases from the United States and Spain mapped to the OMOP common data model. We considered 650 treatment comparisons and 31 outcomes in patients with a COVID-19 diagnosis or positive test in 4 outpatient and inpatient treatment initiation settings. The study period started on 1 January 2020 and ended at the last available date for all data sources (range 23 April to 31 October 2020). We employed variable-ratio propensity score matching and Cox proportional hazard models for each target-comparator-outcome combination that passed diagnostics with 30-day time-at-risk to estimate the hazard ratio (HR).

Results: Of 725,400 potential comparisons, 304 had sufficient size and populations that could be matched, passing diagnostics. Each target-comparator cohort had a median of 7,488 (range: 2,261-160,133) patients. Of those comparison-outcome scenarios that satisfied diagnostic criteria, we found a lower risk of cardiovascular events [HR (95% confidence interval) = 0.77 (0.66 — 0.89)] in hospitalised patients treated with heparin versus aspirin, whereas compared to prednisone, dexamethasone treatment in the outpatient setting had higher risk of complications (requiring intensive services [1.34 (1.04 — 1.73)], mechanical ventilation [1.32 (1.02 — 1.71)], and pneumonia [1.30 (1.20 — 1.40)]).

Conclusions: We investigated a large set of drug exposures and outcomes using multi-national RWD for repurposed therapies in COVID-19 diagnosed patients and found a small proportion of comparisons could generate effectiveness and safety evidence. We found a lower risk of cardiovascular events among hospitalised patients treated with heparin versus

aspirin, and higher rates of complications among outpatients for dexamethasone compared to prednisone. The evidence generated could focus resources for future studies on drug pairs with signals on effectiveness and safety outcomes.

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