MSR93

Patient Cloning for Assessing Dynamic Treatment Protocols: A Novel Approach for Observational Data Analysis Using Real-World Data (RWD)

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Objectives

Traditional approaches for analyzing real-world data are often ill-equipped to handle the complexity of clinical decision-making.

Methods such as propensity score matching were designed to mimic static treatments at a single timepoint; they cannot tackle situations in which treatment decisions are made over time in response to changing patient characteristics.

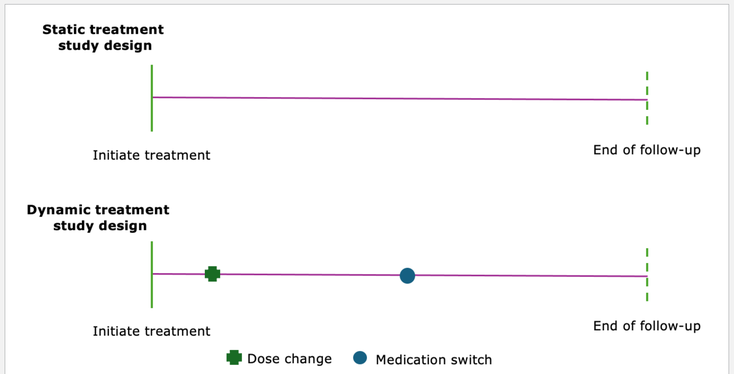

Figure 1. Illustration of a static treatment assignment compared with a treatment protocol responding to time-varying patient characteristics.

Examples of dynamic treatment regimes:

- Doses adjusted to achieve desired biomarker levels
- Treatment stopped when adverse events occur
- Switch or add medications to improve treatment response
- Insurance coverage disruptions causing uninsurance, delayed care, and unfilled prescriptions

We describe a novel approach to evaluate complex questions around optimal disease management over time.

Methods

Below is hypothetical cohort data for patients hospitalized with COVID-19 infections. This data will be used to demonstrate the clone-censor-weight methodology in an analysis of the real-world comparative effectiveness of remdesivir for treating COVID-19.

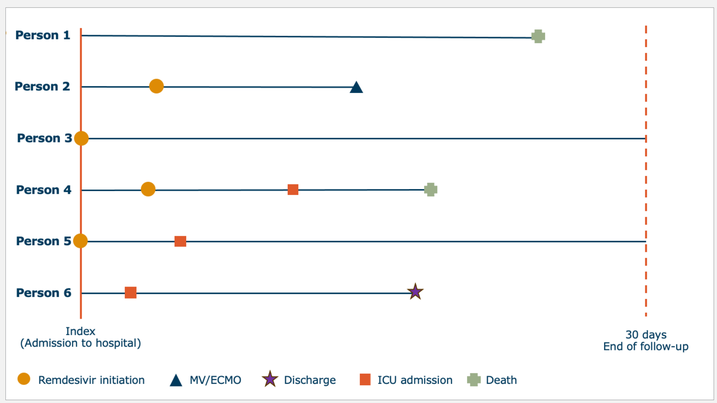

Figure 2. Hypothetical cohort data for patients admitted to hospital with COVID-19.

Step 1: In the **clone-censor-weight** design, patients are "cloned" into one cohort per treatment protocol, allowing for comparison of specific treatment sequences observed in the real world.

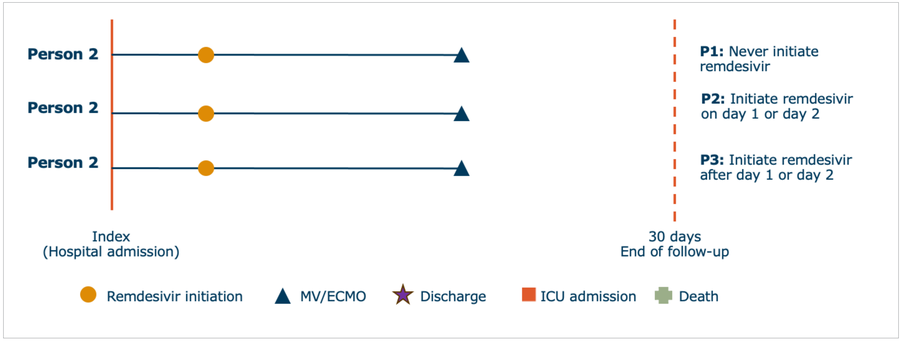

Figure 3. Each participant's data is copied once for each protocol specified in the study design. In this example there are 3 remdesivir protocols: never initiate remdesivir, initiate remdesivir on day of or day after hospital admission, or initiate remdesivir after day 2 following hospital admission.

Step 2: In each cloned cohort, patients are artificially censored upon deviation from the treatment sequence associated with that cohort.

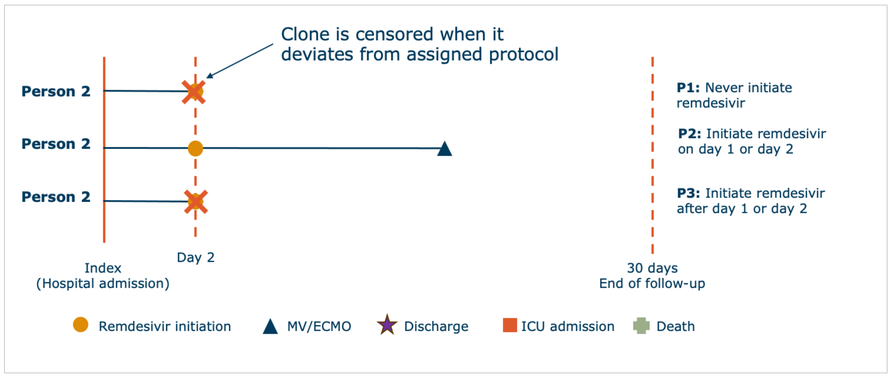

Figure 4. Each clone is censored at the point which they deviate from their assigned protocol, experience an outcome, or reach the end of the follow-up period.

Step 3: To account for the artificial censoring, patients are reweighted using inverse probability of censoring weights to reflect the original target population.

Results

This approach has been successfully implemented across multiple therapeutic areas and patient populations.

We recently used clone-censor-weighting to examine effectiveness of various remdesivir treatment protocols for preventing disease progression among patients hospitalized with COVID-19.

We demonstrated that failure to account for complex, time-varying patient characteristics underestimated the real-world effectiveness of remdesivir.

Results for in-hospital mortality under each remdesivir protocol: overall and by level of oxygen supplementation.

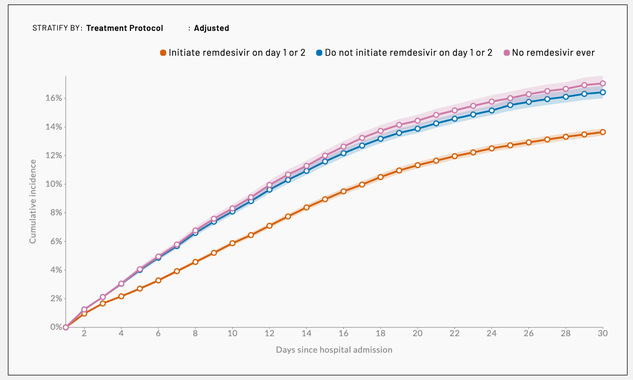

Figure 5. Cumulative incidence of in-hospital mortality under remdesivir-based treatment protocols among patients hospitalized with COVID-19.

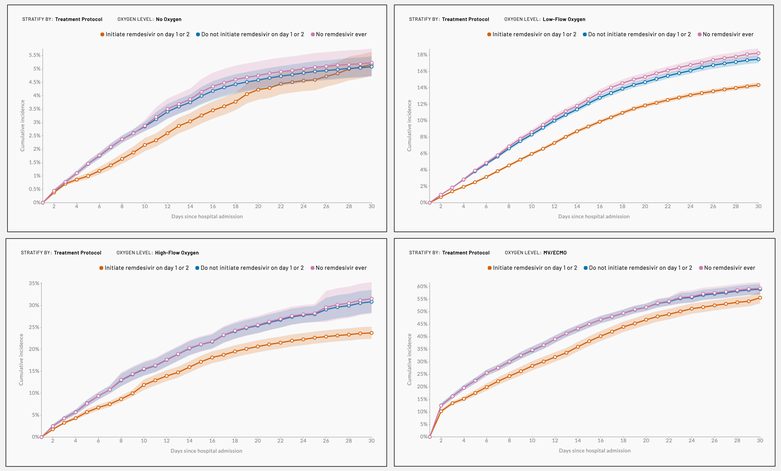

Figure 6. Cumulative incidence of in-hospital mortality under remdesivir-based treatment protocols among patients hospitalized with COVID-19 by level of oxygen supplementation at admission.

Conclusions

As pharmaceutical therapies advance, and as access to data about real-world use of those therapies grows, we must update our analytic methods accordingly.

Randomized controlled trials are too costly and time-consuming to answer every treatment question.

The clone-censor-weight approach bridges this evidence gap between clinical trials and real-world practice.

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