Marginal Structural Model for studying the causal effect between vaso-occlusive crises and occurrence of death or complications in sickle-cell disease patients

Context
Sickle-cell disease (SCD) is one of the most prevalent inherited diseases. Previous research suggests a relationship between Vaso-Occlusive Crises (VOC) and death or complications. However, the time-varying effect of VOC on these outcomes presents the establishment of a causal relationship using classically adjusted models. The number of VOC in the previous year could instead only imply the occurrence of acute complications and death.

Objective
This study aimed to assess the effect of the number of VOCs experienced in the previous year on occurrence of death and common disease-related complications using an inverse Probability Weighted Marginal Structural Model (MSM-IPW).

Dataset
Prevalent patients with SCD between 2008 and 2018 were identified using ICD-10 diagnosis codes (D57.0, D57.1, D57.2) recorded in NHS England's Hospital Episode Statistics database linked to the Office for National Statistics Mortality Data. The database included information on patient demographics (sex, age, ethnicity), death and complications experienced through ICD-10 codes. The 20 most common complications were defined into three groups, 0 VOCs, 1-2 VOCs and 3+ VOCs. These categories are consistent with a previous study (Platt 1991) which showed that patients experiencing an average of 0, 1-2 and 3+ VOCs each year had different survival trajectories. These time-varying VOC categories were aggregated at a one-year time scale to allow maximum follow-up in the dataset.

Discussion and limitations
The patients with more than 3 VOC during the previous 12 months had an estimated causal risk of death multiplied by 4.50 [2.91;6.97] and of ACS multiplied by 5.51 [3.67;8.27] compared to the patients without VOC during the previous 12 months.

Conclusion
The IPW analysis is an interesting tool in case of dynamic time-varying exposure. In this illustration having more than one VOC in the previous 12 months was associated with a higher risk of death and complications. Preventing or reducing the number of VOCs experienced each year may significantly reduce the occurrence of death and some common complications.

REFERENCES