Trajectories in diabetes mellitus type II treatment intensification with massive observational data

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Abstract
Well-established protocols anchor clinical treatment approaches for diabetes mellitus type II. However, characterizing typical treatment in practice is more elusive. To our knowledge, little research has illustrated how patients progress through treatment regimens and how critical clinical tests alter these trajectories. We take a step toward addressing these shortcomings by examining the medical claims data tracking 1.3 million diabetic patients from the MarketScan Lab Results database and modeling the number of diabetes drugs patients consume as a continuously observed birth-death process. We advance our model by incorporating hemoglobin A1c (HbA1c), the critical lab value for motivating treatment intensification. In general, we see that adding treatments decreases the transition rate from high HbA1c to low HbA1c. We further use these models to show that patients with high HbA1c on fewer than 6 medications are more likely to intensify treatment to another oral medication than use insulin.

Introduction
The impact of diabetes mellitus type 2 (DM2) on public health reverberates from individual patients to the national economy. The American Association of Clinical Endocrinologists has produced a standard protocol for treatment intensification [American Association of Clinical Endocrinologists, 2015]. Identifying how treatment intensification evolves in practice is more elusive. Due to the natural history of the disease and the ever increasing number of treatments, many patients will have different pathways through the choice of treatments. In an effort to quantify this, Hripcsak et al. designed and implemented an observational study to map out the treatment pathways for diabetes within the Observational Health Data Sciences and Informatics (OHDSI) collaborative.

Methods
While Hripcsak et al. quantify the diversity of diabetic treatment pathways, they fail to capture the time component of the pathways. To address this, we elect to model the number of oral anti-hyperglycemic medication a patient consumes as a birth-death process. We advance this model by incorporating HbA1c. We use these models to learn the average time to first use of the \( k \)th oral anti-hyperglycemic medication, the expected time spent using \( k \) oral anti-hyperglycemic medication, and the time to first use of insulin. From these models we learn how HbA1c level changes these important clinical quantities.

Conclusion
This research produces the first known full depiction of a patient trajectory through DM2 treatment (Figure 1). In doing so, we open the floor to the host of questions that we can now ask about patient trajectories. Although many patients use more than two treatments, the actual time spent in greater than dual therapy is surprisingly small. We see that adding treatments decreases the transition rate from high HbA1c to low
Figure 1: Birth-death process including high and low HbA1c state and insulin initiation for the diabetic patients in MSLR dataset. The size of the nodes is proportional to the time spent in each state, the edge widths are proportional to the MLE estimated transition rates, and the transparency is proportional to the standard error.

HbA1c. Additionally, patients with high HbA1c on fewer than 6 medications are more likely to intensify treatment to another oral medication than use insulin.

REFERENCES
