An artificial-intelligent (AI) and big data approach to prevent statin-associated symptoms and improve adherence

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Introduction

An estimated 47% of Americans at age 65+ take statins, which are highly effective in lowering low-density lipoprotein cholesterol, preventing atherosclerotic cardiovascular disease, and reducing all-cause mortality. Unfortunately, ~50% of patients prescribed statins do not obtain these benefits because they discontinue use within 1 year of treatment initiation. Thus, statin discontinuation has been identified as a major public-health concern due to increased morbidity, mortality, and healthcare costs. Statin-associated symptoms (SAS) often result in dose reduction or discontinuation of these drugs. Currently, physicians reactively manage SAS after they manifest, such as alter treatment plan (e.g., changing medication and dosage) or a ‘statin holiday’. To prevent SAS and increase adherence, we propose a proactive strategy using AI and big data to personalize treatment plan (statin agent + dosage) employed prior to statin initiation or rechallenge.

Methods

In this proof-of-concept study, we develop a machine-learning model trained with big data (OptumLabs® Data Warehouse) to produce the proactive strategy. Specifically, we develop a 2-step Personalized Statin Treatment Plan (PSTP) platform including: (1) Prediction: Deep learning model simultaneously estimate an individual’s risks of SAS and discontinuation for each treatment plan. (2) Optimization: Multi-objective optimization actively identifies treatment plans with the lowest risks (proactive strategy).

Results

![Comparison between human with machine to produce the proactive strategy.](image)

In practical settings, a prescribing physician usually take a few important characteristics of an individual into account when prescribing statin therapy to reduce SAS and increase benefit. Therefore, the concept of proactive strategy has been widely considered in practice, but the implementation is usually limited to a few characteristics. Simultaneously taking many characteristics and interactions into account may further improve the implementation, but that becomes
a huge burden for human and infeasible in practice. As a result, we develop a machine-learning algorithm that takes multiple individual characteristics and interactions into account aimed at empowering physicians to implement this concept and more accurately make the proactive decisions.

Figure 1 demonstrates comparison of performances between human and machine. In general, performance of the proactive strategy when taking a few important characteristics (three sets of columns to the left; represent proactive strategy by only human) is in the range between 40% and 60%. On the other hand, with the machine’s support (that take over 70 variables and complex interactions into account), the performances of the proactive strategy are improved to the range between 60% and 95% (two sets of columns to the right). In other words, we have a large space to improve the implementation of proactive strategy using machine learning and AI approaches.

Figure 2 shows a visual example of the proactive strategy (produced by the proposed PSTP platform) that helps to distinguish the best treatment plan (low risks of discontinuation and SAS) for a patient. Each dot represents a possible treatment plan (specific statin agent + dosage) for an individual. For example, the dot RO40 (one of the proactive strategy in Figure 2) represents Rosuvastatin 40 mg. The treatment plan RO40 is most likely to prevent future SAS. Consequently, the proposed method will create a new precision-medicine tool to empower the treating physicians.

Figure 2. A visual example of the proactive strategy produced by the Personalized Statin Treatment Plan (PSTP) platform for an individual. Each dot represents a possible treatment plan (statin agent+particular dosage).

Conclusions

In this study, we have tested feasibility to create the proactive strategies using big-data and AI approaches for patients who were initially diagnosed with cardiovascular disease. Meanwhile, we are intensively working on expanding our work to include various patient subgroups. The most important and challenging lesson learned so far is to explore the process of translational research (data-science discovery to clinical implementation). Although we can develop AI methods to discover proactive strategy in the data, in other words, that mean no one had used the AI tools before. As a result, it is a challenge to have evidence to support the subsequent clinical trial, which is a gold-standard and important step in the translational research. In the near future, we plan to evaluate, validate, add practical components, and add another dimension of LDL reduction to improve our translational-research agenda.

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