DYNAMIC TREATMENT REGIME

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ABSTRACT

Physicians must be able to make numerous healthcare decisions during the course of a patient's illness by monitoring both the individual's medical history and the evolution of the disease together with its possible consequences. Dynamic Treatment Regime (DTR) is a treatment design where a set of decision rules aim to find the optimal regime that, if followed by the individual, would yield the best results on average.

***K*eywords** Personalized Medicine · Data Treatment Regime

1 Introduction

Not all clinical treatments work the same on different patients and this has always been clear, and surely it is impossible to predict which drug or procedure will be safe and effective for each person. In health sciences Personalized Medicine[1] (PM) is an area of increasing interest that tries to solve this problems by defining a set of medical decisions and therapies adapted to each patient based on his/her clinical history and individual characteristics reducing margin for error as much as possible. The information available on the patient may include genetic, physiologic, demographic, and other clinical variables based on the type of conducted study.

Patients can react differently to a particular treatment both in terms of side effects and primary clinical results. PM wants to optimize health care by maximizing clinical outcomes in the long run also managing to reduce costs, for example by avoiding treatments when not necessary. In contrast with PM, traditional drug therapy typically considers immense patient populations to be moderately homogeneous. This is the case of the *one-size-fits-all* approach which is a description for a solution that would fit in all cases. Every person receive the same treatment providing little to no individualized care [1]. We are now more interested in creating more evidence-based personalized treatments using the systematic use of individual information. The goals of personalized medicine can be summarized as follows: stratify populations to identify those who benefit most from a given treatment finding an ideal treatment plan, and decrease the number of patients unnecessarily treated.

One of the main needs in this area is the ability to identify subgroups of the population that react in a similar way to treatments, especially those for whom some treatments may be particularly risky. The main challenge in identifying these patients is to select them from a lot of plausible subgroups and this selection ends up being a subjective choice made by the researcher. It is also important to acknowledge which are the most influential characteristics of an individual related to treatment, in order to have solid information on which to base an optimal treatment plan.

In conclusion, personalized medicine aims to define a therapy and a dosage for an individual patient considering intrinsic factors such as genetic, risk of failure or relapse. The various interventions must therefore be adjusted over time to the needs of the patient and his/her new clinical conditions that may evolve.

As well explained in the book of Chakraborty and Moodie [2], two types of problems may arise in personalized medicine:

1. Single-Stage decision problems
2. Multi-Stage decision problems

[1] Also called precision medicine, stratified medicine, and P4 medicine.

The first type of problems implies that the physician decides the optimal treatment for an individual patient evaluating an utility function. The second type of problems implies that decisions taken at one stage may influence those of the later stages. We will focus on multi-stage decision problems defining a way to determine how to adapt treatment over time making a sequence of decision rules. In this context it is possible to place the dynamic treatment regime.

2 Dynamic Treatment Regime

Dynamic Treatment Regime (DTR)[2] takes into account the patient's previous history up to that time by defining a series of decision-making rules or actions (e.g., treatment type, drug dosage), one for each stage of the study. The goal is estimating the optimal regime, that, if followed by the patient population, would yield the most favorable outcome on average improving long-term benefits. This may be achieved using data from a clinical trial or observational study which are hardly available due especially to privacy. The term "dynamic" refers to the fact that decisions are made sequentially to optimize patient outcomes given the too many variations in a patient's response to treatment that may evolve over time.

DTRs are an emerging methodological area in health research where the input is a set of clinical observations and assessments of a patient. The outputs are the treatment options for every stage. In the case of multi-stage problems the optimal DTR should be found by comparing several preconceived DTRs with each other and evaluating them in terms of utility choosing the most efficient one.

Following the syntaxis of Anastasios A. et al's work [3] we can define a finite number $K \geq 1$ decision points and let $\mathcal{A}_k$ be the set of feasible treatment options at Decision k with $k = 1, ..., K$. A single option in $\mathcal{A}_k$ is represented by a_k. Let x_k now denote the additional information available on an individual arising between Decisions $k-1$ and k after receiving the option $a_k \in \mathcal{A}_k$. The available *history* h_k on an individual is defined as

$$h_1 = x_1$$
$$h_k = (x_1, a_1, ..., x_{k-1}, a_{k-1}, x_k),\ k = 2, ..., K,$$

and Let $\mathcal{H}_k$ denote the support of h_k. A decision rule $d_k(h_k)$ is a function which maps an individual's history to an appropriate treatment option as

$$d_k : \mathcal{H}_k \longrightarrow \mathcal{A}_k,\ k = 1, ..., K.$$

A DTR is a collection of these decision rules.

The main challenges in this area are conceptual rather than methodological. In particular, they concern the ability to properly define the information of interest and, as specified in the book of Anastasios A. et al, to understand how to characterize the contribution provided by a treatment option to a global regime. how to use the "contribution" of this option to a global scheme.

References

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[3] Anastasios A. Tsiatis, Marie Davidian, Shannon T. Holloway, and Eric B. Laber. Dynamic treatment regimes: Statistical methods for precision medicine. Chapman and Hall/CRC, 2019.

[2] Also called treatment strategies, adaptive treatment strategies, treatment policies.