Optimization of Treatment Initiation Decision for Patients with Alzheimer’s Disease

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Abstract

As societies age, Alzheimer’s disease (AD) is an increasingly critical public health concern due to its high incidence in the elderly. Although current treatments are shown to temporarily slow the development of symptoms, they are associated with major drawbacks. First, none of them stops or reverses the underlying disease progression. Second, more effective treatments are potentially more toxic which raises questions about the tradeoff between prolonging the time in better health states and reduced quality of life due to adverse side-effects. The unique nature of the disease, and risks associated with treatments pose challenges for physicians and patients making decisions about initiating the therapies. We develop a Markov Decision Process model to investigate the optimal time to initiate treatment following an AD diagnosis. We use sensitivity analysis for treatment effectiveness to evaluate the impact of a new treatment on quality of life, and to identify optimal treatment policies. This research incorporates the dynamic nature of a chronic life-long disease on treatment decision making capturing both the uncertainty related to disease progression and treatment outcomes. To the best of our knowledge, our model is the first dynamic post-diagnosis Alzheimer’s disease treatment model.

Keywords
Markov decision processes, Alzheimer’s disease, optimization of treatment, decision analytical modeling.

1. Introduction

Alzheimer’s disease (AD) is a progressive neurodegenerative brain disease which impacts brain regions involved in learning and memory processes. As a result, patients suffer from weakening cognitive functions, and control of thinking, judgment and behavior. AD exacts significant social and economic burden on individuals, families and health care systems. The total estimated worldwide costs of dementia were US$604 billion in 2010 [1]. Based on predicted increases in the numbers of people with AD, it is estimated that there will be an 85% increase in costs to 2030 [2].

There is no known cure for AD, but a number of treatments are shown to temporarily slow worsening of symptoms. Currently, five drugs are approved by the U.S. Food and Drug Administration (FDA) for the symptomatic treatment [3]. They are classified in two classes: Acetylcholinesterase (AChE) inhibitors and N-Methyl-D-Aspartate (NMDA) antagonists. The AChE inhibitors are used for the treatment of mild and moderate stages and aim to improve mental functions such as memory, attention, reasoning and language abilities. NMDA antagonists are used for the treatment of moderate to severe AD.