Mathematical Biosciences 282 (2016) 191–203

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Analysis of depression trajectory patterns using collaborative learning

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ARTICLE INFO

Article history:
Received 28 March 2016
Revised 19 October 2016
Accepted 23 October 2016
Available online 24 October 2016

Keywords:
Depression
Trajectory pattern
Statistical learning
Mental health
Clustering
Classification

ABSTRACT

Background: Depression is a common, complex, and dynamic mental disorder. Mitigating depression has become a national health priority as it affects 1 out of 10 American adults and is the most common mental illness seen in primary care. The emerging use of electronic health record (EHR) provides an unprecedented information infrastructure to understand depression trajectories.
Objective: We aim to effectively analyze patterns in the collected depression trajectories of a treatment population and compare several methods to predict individual trajectories for monitoring treatment outcomes.
Methods: Our data includes longitudinal Patient Health Questionnaire (PHQ)-9 scores over 4 years for assessing depression severity from the Mental Health Research Network. We analyzed $>3{,}000$ patients with at least six PHQ-9 observations who have ongoing treatment. We used smoothing splines to model individual depression trajectories. We then used K-means clustering and collaborative modeling (CM) to identify subgroup patterns. We further predicted the individuals' PHQ-9 scores based on depression trajectories learnt from individual growth model (IGM), mixed effect model (MEM), CM, and similarity-based CM (SCM), and compared their predictive performances.
Results: We found five broad trajectory patterns in the ongoing treatment population: stable high, stable low, fluctuating moderate, an increasing and a decreasing group. For prediction, the root mean square error (rMSE) in the testing set for IGM, MEM, CM, and SCM are 12.53, 5.91, 5.18, and 3.21.
Limitations: Our EHR data provide limited information on patients' demographic, socioeconomic, and other clinical factors that may be relevant to improve model performances.
Conclusion: We established a trajectory-based framework for depression assessment and prognosis that is adaptable to model population heterogeneity using EHR data. Collaborative modeling outperformed other established methods.

1. Introduction

Depression is a common, complex and dynamic mental disorder characterized by sad mood, loss of interest in activities, weight gain or loss, psychomotor agitation or retardation, fatigue, inappropriate guilt, difficulties concentrating, and recurrent thoughts of death [1]. Depression related mortality and morbidity have been rising in recent decades [2]. Suicide recently became the number one violent cause of death and the 10th leading cause of death in the U.S. [3,4]. The economic burden of depression is estimated at billions of dollars each year [5]. Consequently, mitigating depression has become a national health priority as it affects 1 out of 10 American adults and is the most common mental illness seen in primary care [1]. Treatment for depression includes psychotherapy and antidepressants. The goals of treatment are to achieve complete remission and prevent relapse of depression. Due to potential side effects of the medication, the Food and Drug Administration (FDA) emphasizes that patients taking antidepressants should be closely monitored [6]. While depression is essentially a heterogeneous dynamic process, monitoring needs a quantitative understanding of the progression patterns. Understanding trajectories of depression is essential when health care providers and health systems want to allocate attention and resources to those who need them most. We need more sophisticated approaches for monitoring outcomes and identifying those likely to need more intensive treatment.

Hence, empirically-based monitoring strategies are critical for diagnosis, prognosis and evaluation of treatment outcome of depression. The emerging use of electronic health record (EHR) in health care systems provides an abundance of data that contains

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http://dx.doi.org/10.1016/j.mbs.2016.10.008
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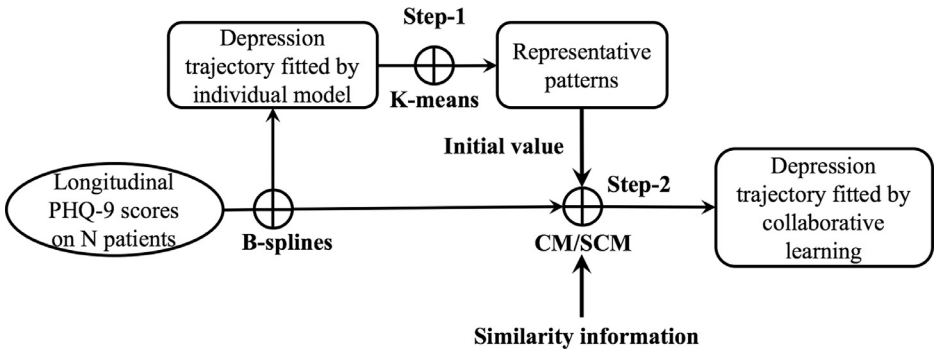

Fig. 1. A flow chart that summarizes the analysis procedure. Trajectory patterns found from step-1 is used to initialize the CM/SCM model in step-2, and the individual trajectories and latent patterns can be obtained from step-2 simultaneously.

the disease trajectories of many individuals. Thus, statistical analysis of these trajectories could lead to a quantitative understanding of the progression patterns, providing useful knowledge for guiding the clinical actions for depression monitoring. However, knowledge of how depression progress over time is still limited. Much previous research on depressive symptom trajectories has examined average effects. For example, longitudinal study of depressive trajectory across adult lifespan has found a quadratic pattern (U-shaped), in which depression is highest among young and older adults [7]. Research regarding individual trajectories is more limited. One investigation found a five−class trajectory patterns in a cohort of Australian family practice [8]. To the best of our knowledge, there is no research on individual depression trajectories for the intermediate timeframe (2–5 years) using large U.S. EHR data. Understanding depression progression in the 2–5 years' time window is clinically relevant for designing monitoring and treatment follow-up strategies.

One common tool to assess depression level is the Patient Health Questionnaire (PHQ)−9, a self-administered questionnaire that includes 9 multiple-choice questions [9]. The Mental Health Research Network (MHRN) provides one of the largest depression datasets of longitudinal PHQ-9 observations in the U.S. for this study [10]. The objective is to design a modeling framework to effectively analyze patterns in the collected depression trajectories of a treatment population and predict individual level trajectories for monitoring treatment outcomes. We first apply clustering algorithm to identify representative subgroup patterns in a treatment population (Step-1); we then use these patterns as prior knowledge to discover and predict depression trajectory for individual patient using the collaborative modeling approach (CM) and similarity-based collaborative modeling (SCM), which incorporate the similarity between individuals and latent structure in the population (Step-2). The overall process of analysis is summarized by the flow chart in Fig. 1. We compare the prediction performances of CM and SCM with the method that predicts individual trajectories independently (IGM) and the mixed effects model (MEM) which does not exploit the latent structure in population. We find that EHR may show few and/or incomplete records that only cover a segment of the trajectory (i.e., sparsity), and observations may be discrete and irregular (i.e. irregularity). Existing methods of disease trajectory analysis came from diverse disciplines such as statistics, machine learning, and engineering prognostics [11–15]. However challenges remain for processing the heterogeneous and irregular depression trajectory data: depression has complex dynamics embedded in individual's disease trajectory that is further complicated by the widely reported heterogeneity of the dynamics in the population [7,8]. Thus, we assemble a good combination of statistical tools, tailored for the data challenges that we encounter in the depression EHR dataset, to discover the representative patterns for the heterogeneous depression dynamics and predict individual depression trajectories. We will show that they are effective in discovering progression patterns of depression and more powerful than other statistical models that are commonly used for analyzing individual trajectories in the literature.

2. Methods

2.1. Data

The MHRN dataset contains depression monitoring outcome data with approximately 1.2 million observations from a diverse and representative sample of outpatients in five states (California, Colorado, Minnesota, Washington and Idaho). Using the conventional classification of total scores in PHQ-9, depression was minimal (score 0–4) in 262,841 (35%), mild (score 5–9) in 184,448 (25%), moderate (score 10–14) in 138,184 (18%), moderately severe (score 15–19) in 96,624 (13%), and severe (20 or greater) in 65,217 (9%) [16]. The dataset includes person-level longitudinal depression measures (total scores and item 9′s scores) in EHR between years 2007 and 2012 and are linked to relative time between measures, diagnosis and treatment status, type of providers (primary care, mental health specialist) where the questionnaires were conducted, individuals' age, sex, and the Charlson Comorbidity Score (a standard indicator of medical disease burden). In mental health specialty clinics (the majority of this sample), questionnaires were typically completed in waiting areas, and results were delivered to providers at the beginning of the visit. In primary care clinics (the minority of this sample), questionnaires could be completed prior to the visits (if depression was the reason for visit) or during the visit (when the provider identified depression as a concern).

Our study sample was limited to 9306 individuals receiving onging treatment (defined as mental health diagnosis, mental health medication, or mental health specialty visit within the prior 180 days, excluding those completing the PHQ-9 for depression screening). The basic statistics of this group is summarized in Appendix Table A.1. The majority are older than age 45 and female (70%). The average follow-up duration is 2.2 years. The average time to the next PHQ-9 measurement is 5.2 months, with a range from one day to 6.6 years. Since the PHQ-9 assesses the patients' depression levels in the past two weeks, we transformed the time unit to two weeks (biweekly) and averaged the measurements within each biweekly window. In the ongoing group, 3159 (33.9%) of them are frequently measured individuals that have at least six biweekly measurements. We conduct analysis on this group to discover the representative patterns in their trajectories and do trajectory prediction.