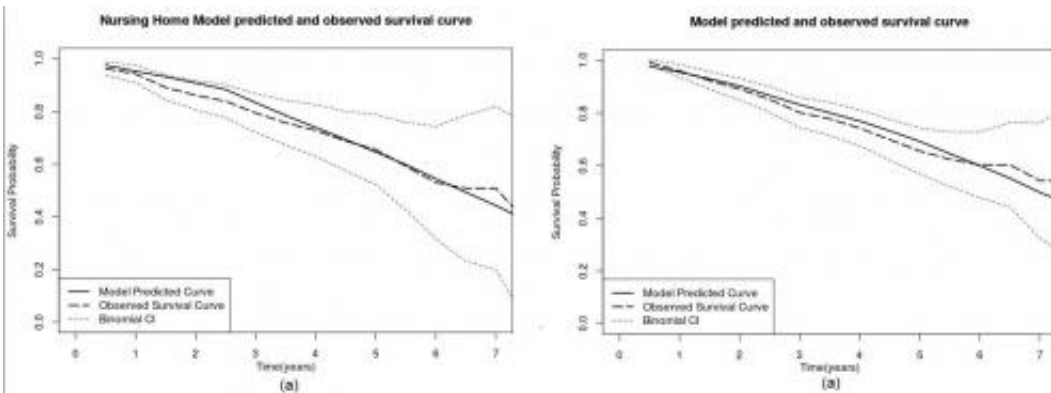


New method predicts time from Alzheimer's onset to nursing home, death

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These graphs compare predictions made with the L-GoM (used to validate the model for predicting time to Alzheimer's disease endpoints) with the actual outcomes. The left graph shows time to nursing home, and the right graph shows time to death. The solid black line shows the predicted timeframe; the dotted black line shows the actual timeframe. The dotted light blue lines indicate the range (confidence interval) of the actual outcomes. Credit: Drs. Ray Razlighi/Yaakov Stern, Columbia University Medical Center

A Columbia University Medical Center-led research team has clinically validated a new method for predicting time to full-time care, nursing home residence, or death for patients with Alzheimer's disease. The method, which uses data gathered from a single patient visit, is based on a complex model of Alzheimer's disease progression that the researchers developed by consecutively following two sets of Alzheimer's patients for 10 years each. The results were published online ahead of print in the

Journal of Alzheimer's Disease.

"Predicting Alzheimer's progression has been a challenge because the disease varies significantly from one person to another—two Alzheimer's patients may both appear to have mild forms of the disease, yet one may progress rapidly, while the other progresses much more slowly," said senior author Yaakov Stern, PhD, professor of neuropsychology (in neurology, psychiatry, and psychology and in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain and the Gertrude H. Sergievsky Center) at CUMC. "Our method enables clinicians to predict the disease path with great specificity."

"Until now, some methods of predicting the course of Alzheimer's have required data not obtained in routine clinical practice, such as specific neuropsychological or other measurements, and have been relatively inaccurate. This method is more practical for routine use," said Nikolaos Scarmeas, MD, a study co-author and associate professor of neurology, in the Taub Institute and the Sergievsky Center. "It may become a valuable tool for both physicians and patients' families."

The new method also may be used in clinical trials—to ensure that patient cohorts are balanced between those with faster-progressing Alzheimer's and those with slower-progressing disease—and by health economists to predict the economic impact of Alzheimer's disease.

The prediction method is based on a Longitudinal Grade of Membership (L-GoM) model, developed by a research team also led by Dr. Stern and published in 2010.

The L-GoM includes 16 sets of variables, such as ability to participate in routine day-to-day activities; mental status; motor skills; estimated time of symptom onset; and duration of tremor, rigidity, or other neurological symptoms. It also includes data obtained postmortem (time and cause of

death).

"The benefit of the L-GoM model is that it takes into account the complexity of Alzheimer's disease. Patients don't typically fall neatly into mild, moderate, or severe disease categories. For example, a patient may be able to live independently yet have hallucinations or behavioral outbursts," said Dr. Stern, who also directs the Cognitive Neuroscience Division at CUMC. "Our method is flexible enough to handle missing data. Not all 16 variables are needed for accurate predictions—just as many as are available."

Results can be presented as expected time to a particular outcome. Two 68-year-old Alzheimer's patients, for example, had similar mental status scores (one a mini-mental status score (mMMS) of 38/54, the other of 39/54) at initial visit. The first patient was more dependent on his caregiver and had psychiatric symptoms (delusions). These and other subtle differences in the initial presentation of the two patients resulted in different predictions of time until death. The method accurately predicted that the first patient would die within three years, while the other would survive more than 10 years.

"In addition to time to nursing home residence or death, our method can be used to predict time to assisted living or other levels of care, such as needing help with eating or dressing, or time to incontinence," said first author Ray Razlighi, PhD, assistant professor of neurology at CUMC and adjunct assistant professor of biomedical engineering at Columbia University.

Development of the method began in 1989, when Dr. Stern received a grant from the National Institutes of Health to begin the Predictors of Severity in Alzheimer's Disease study. "The fact that work on this prediction method began nearly 25 years ago underlines the difficulties

of studying Alzheimer's disease," said Richard Mayeux, MD, MS, neurology chair, the Gertrude H. Sergievsky Professor of Neurology, Psychiatry and Epidemiology and co-director of the Taub Institute and the Sergievsky Center.

Dr. Stern and colleagues at Massachusetts General Hospital and Johns Hopkins first followed 252 non-familial Alzheimer's patients every six months for 10 years. Eric Stallard, an actuary at Duke and a co-author of the paper, used the resultant data to create an L-GoM model of Alzheimer's progression. They published their results in 2010 in *Medical Decision Making*. The researchers then followed a separate group of 254 patients and used data from only a single patient visit to predict outcomes for this group.

Dr. Stern and his team are now developing a computer program that would allow clinicians to input the variables and receive a report. They expect the program to become available within the next two years. Eventually, such a program might be incorporated into electronic health records. "At our Alzheimer's center, patients are already filling out much of their clinical information electronically," said Dr. Stern.

The researchers are also testing the method with a third cohort. While the first two sets of [patients](#) were primarily white, educated, and of high socioeconomic status, the new cohort follows a diverse group of participants from CUMC's Washington Heights-Inwood Columbia Aging Project (WHICAP), an ongoing, community-based study of aging and dementia comprising elderly, urban-dwelling residents. Because participants may be dementia-free when they join the study, the researchers are able to capture the age of dementia onset and track symptom development over time.

More information: The paper is titled, "A New Algorithm for Predicting Time to Disease Endpoints in Alzheimer's Disease Patients."

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Provided by Columbia University Medical Center

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