The Predictors study: Development and baseline characteristics of the Predictors 3 cohort

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Abstract

Introduction: The Predictors study was designed to predict the length of time to major disease outcomes in Alzheimer’s disease (AD) patients. Here, we describe the development of a new, Predictors 3, cohort.

Methods: Patients with prevalent or incident AD and individuals at-risk for developing AD were selected from the North Manhattan community and followed annually with instruments comparable to those used in the original two Predictors cohorts.

Results: The original Predictors cohorts were clinic based and racially/ethnically homogenous (94% white, 6% black; 3% Hispanic). In contrast, the 274 elders in this cohort are community-based and ethnically diverse (39% white, 40% black, 21% other; 78% Hispanic). Confirming previous observations, psychotic features were associated with poorer function and mental status and extrapyramidal signs with poorer function.

Discussion: This new cohort will allow us to test observations made in our original clinic-based cohorts in patients that may be more representative of the general community.

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Keywords: MCI; ADL; Cognitive function; Extrapyramidal signs; Psychotic features; Pharmacoeconomics; Prediction algorithms

1. Introduction

The ability to predict the length of time from disease onset to major disease outcomes such as the need for nursing home care or death in individual patients with Alzheimer’s disease (AD) has implications for patient care, the development of interventions and public health. The major aim of the Predictors study has been to further the understanding of the natural history of AD to develop predictor algorithms that can accurately make these predictions.

The first two Predictors cohorts consisted of a total of 506 patients with mild AD drawn from memory disorder clinics at three AD research centers: Columbia University College of Physicians and Surgeons, Johns Hopkins University School of Medicine, and the Massachusetts General Hospital. Although relatively small by epidemiologic standards, the primary value of these cohorts has been the long-term acquisition of data at short intervals.

Data from the first two cohorts of the Predictors study have led to advances in clarifying the natural history of the disease [1–7] with regard to motor signs [8–11], psychiatric manifestations [12–17], imaging [18,19], function, and quality of life [20–27], genotype [28–30], medication use [31], economic burden [32–38], and clinico-pathologic relationships [39–42]. We have also developed several assessment tools that are in general use in clinical assessment and drug studies [21,22,43].

Most notably, we recently developed [44] and validated [45] a new model of AD progression, which can be used to predict time to multiple disease endpoints. The analyses used a longitudinal form of the Grade of Membership (GoM) model [46,47], which allows large amounts of data on individual patients collected over multiple visits to be efficiently and accurately summarized using a small number of distinct
variables that represent the most salient characteristics of the AD process as it develops over time [48,49].

Despite the Predictors study’s impact on our understanding of AD and its progression, the two patient cohorts were clinic-based and racially/ethnically homogenous (94% white, 3% Hispanic). As clinical cohorts are not representative of the true distribution of the disease in the population, these studies are necessarily biased by the nature of the referral and recruitment patterns particular to the clinical setting. Furthermore, it is not known what proportion of patients with AD actually is seen in clinical settings. There have been very few studies examining the progression of AD in community populations or in patients where the date of disease onset is known.

The current article introduces a new Predictors 3 cohort, which was designed to remediate these drawbacks by recruiting a population-based, ethnically diverse cohort of patients, with an emphasis on those with incident AD. Recruitment of this cohort took advantage of the existing Washington Heights-Hamilton Heights-Inwood Columbia Aging Project (WHICAP), which for many years has followed random samples of elders in North Manhattan. From WHICAP, we identified elders with recent incident AD and recently identified prevalent AD, as well as individuals at-risk for AD. At this point, we have recruited 274 elders into the Predictors 3 cohort and are following them annually with many of the same instruments included in the two original Predictors cohorts, as well as additional evaluations. This culturally and experientially diverse population provides a unique opportunity to assess a range of medical and sociocultural factors that may contribute to differential disease progression and specific outcomes.

This report is intended to describe the design and implementation of the Predictors 3 cohort and describe baseline subject population demographics. We also include some early cross-sectional observations that replicate observations in the previous two cohorts.

2. Methods

2.1. Participant recruitment

Our source of community-based subjects was the WHICAP cohort. All WHICAP participants were first identified from a random sample of elderly Medicare recipients residing in the designated areas of Washington Heights, Hamilton Heights, and Inwood in North Manhattan, NY. Potential participants were excluded at the time of recruitment if they did not speak English or Spanish. Prior analyses of the demographic characteristics indicate that WHICAP study participants are matched to U.S. Census data of older adults living in northern Manhattan with respect to age, years of education, race/ethnicity, and sex. The WHICAP participants were evaluated approximately every 18 months. WHICAP follows a combination of remaining participants from cohorts originally recruited in 1992 (N = 2332), between 1999 and 2001 (N = 2776), and 2009–2015 (N = 2088). Recruitment of the Predictors 3 cohort began in 2011.

2.1.1. AD dementia

Our primary goal was to recruit patients from WHICAP who were diagnosed with incident AD no earlier than 2 years before the start of the recruitment or at any subsequent time. To be considered an incident case or case with known onset, subjects had to have one or more initial WHICAP assessments in which they did not meet criteria for dementia followed by a subsequent assessment in which they met criteria for AD. That visit when AD was first diagnosed constituted their initial Predictors 3 assessment. We also included patients with prevalent AD. These were WHICAP participants diagnosed with AD at their initial visit, which occurred within 2 years before the start of Predictors 3 recruitment. The diagnoses of AD are based on the recent 2011 criteria [50], and the Clinical Dementia Rating Scale (CDR) [51] is used to rate dementia severity.

2.1.2. At-risk for AD

We also enrolled subjects with a high probability of converting to AD over time as they were followed. This includes those participants with the diagnoses of mild cognitive impairment (MCI), which was based on the recent 2011 criteria [52]. In addition, we identified at-risk individuals the WHICAP algorithm for evaluating neuropsychological test scores. This algorithm uses a set of cut scores applied to the neuropsychological battery that are not norms based to determine whether an individual has sufficient cognitive deficit to meet criteria for dementia [53]. To do so, the individual must score below cut scores on two of three memory domains (immediate and delayed verbal recall and nonverbal recognition) as well as below cut scores on at least one test from two of the four other cognitive domains (orientation, language, reasoning, and visuospatial function). Individuals who algorithmically come close to meeting these cutpoints (e.g., meet only three of the four required cutpoints, or score close to the cutpoint on the fourth) are also flagged as at-risk for AD, even if they do not meet formal criteria for MCI. These individuals have a high probability of converting to AD. Our reason for following at-risk individuals is to eventually enrich our pool of patient with incident dementia on subsequent visits, and then follow AD progression from its initial diagnosis. In addition, we eventually hope to extend our GoM model to individuals at-risk for developing AD.

Once a subject is included in the Predictors 3 cohort, they are followed annually. Participants’ data at each assessment wave are reviewed in a consensus conference, where a new working diagnosis is established. Thus, we can ascertain if and when any of these at-risk individuals convert to AD.

2.2. Schedule of assessments

The following procedures are completed annually. A subset of the assessments is or can be conducted via informants.
All assessment instruments are administered by bilingual psychometricians. The assessment battery is conducted in English and Spanish by balanced bilingual research staff. At baseline, participants are asked their opinion of which language would yield their best performance, and this language is used to administer the battery throughout all follow-up visits. All interview questions, test instructions, and stimuli have been translated into Spanish by a committee of Spanish speakers from Cuba, Puerto Rico, Spain, and the Dominican Republic, and then back-translated to ensure accuracy. Where necessary, scoring criteria are modified so that credit is given for responses that reflect regional idioms.

2.2.1. Informant questionnaires
Each participant in the Predictors study is required to have an informant. Informants are generally family members or home care paraprofessionals. For patients in nursing homes, clinical staff who have worked closely with the patient for at least 3 months are acceptable.

2.2.2. Medical and neurological evaluation
A semi-structured medical and neurological examination is administered. We collect a measure of body mass index (weight in kilogram/height in meter$^2$) [54]. We document all past and current medical conditions, medical procedures, assistive devices obtained, and hospitalizations. The Rosen modification of the Hachinski Ischemic Scale score [55] is included as a measure of cerebrovascular disease and a potential predictive sign. Selected items from the Unified Parkinson’s Disease Rating Scale [56–59] are used, comprising ratings of voice, facial immobility, resting tremor, rigidity (neck and each limb), brady/hypokinesia, posture, and gait. Severity of each sign is rated as either absent (0), slight (1), mild-moderate (2), marked (3), or severe (4). Having a moderate severity of at least one of these symptoms is considered as having moderate extrapyramidal signs (EPS). Reliability of this instrument has been established [9]. Signs are coded as idiopathic, probably induced by current neuroleptic medication use or possibly induced by previous use of neuroleptic medication. If signs are possibly or probably drug induced, then we consider them separately for analytic purposes. The presence and severity of myoclonus and other dyskinesias are also recorded.

A semi-structured interview captures nine key criteria for Lewy Body Dementia, which includes questions and probes regarding fluctuating cognition with pronounced variations in attention and alertness, visual hallucinations, parkinsonism, auditory, olfactory, or tactile hallucinations, repeated falls, syncope, transient alteration of consciousness, neuroleptic sensitivity, and systematized delusions. We include it to explore the predictive utility of these features in AD.

Comorbidities are systematically queried in the interview. We have typically summarized these with the Charlson index [60]. Now using cost linkage data, we can make use of the Elixhauser index [61], as it performs better in predicting health outcomes (e.g., mortality) with administrative claims data than the Deyo-Charlson method [61–64].

A standardized form is used to record medications, including medications prescribed or supplements taken for AD as well as vitamins. It records the medication name (which is subsequently coded), number of days the medication was taken during the study interval, total dose/day, and number of pills/day. Alcohol tobacco use is also recorded.

2.2.3. MMSE and mMMS
Global cognitive function is examined using the (Folstein) mini-mental state examination (MMSE) [65] as well as our 57-point version, the modified MMSE (mMMS) [66].

2.2.4. Test for severe impairment
To better assess cognition in the severe stages of dementia, patients scoring 30 points or less on the mMMS also receive the test for severe impairment [43,67]. It assesses six cognitive domains and presents tasks using simple one-step commands and nonverbal gestures.

2.2.5. The clinical dementia rating scale
The CDR is used to evaluate the patient at each measurement point to provide a global assessment of the severity of dementia [68].

2.2.6. Functional assessment
Functional capacity is rated using the Blessed Dementia Rating Scale (Part 1) (BDRS [69]). We consider a score of 15 an endpoint for analysis. We have also developed subscores for the BDRS based on factor analysis [20]. The disability and functional limitation instrument is also administered [70,71].

2.2.7. Neuropsychological test battery
The neuropsychological test battery includes the following tests: Orientation: The 10 orientation items from the Mini-Mental State Examination [65]. Memory: Two tests are used: (1) Selective reminding test [72], (2) Benton visual retention test (BVRT) [73], Recognition Memory Multiple Choice version. Visuospatial ability: (1) Rosen Drawing Test [74], 5 selected items. (2) BVRT Matching, multiple-choice version. Language: (1) Naming. Boston Naming Test [75], 15 selected items. (2) Verbal fluency. The Controlled Word Association Test [76] and category naming: Animals, food, and clothing. (3) Comprehension. Complex ideational material subtest of the Boston Diagnostic Aphasia Evaluation (BDAE) [77]: first 6 items. (4) Repetition. High frequency items from the BDAE repetition of phrases subtest. Psychomotor speed: The Color Trails test [78] part 1 is administered. Executive functioning: (1) WAIS-R similarities [79], (2) Color trails part 2. Raw scores and demographically corrected T-scores (age, years of education, sex, and ethnicity) are available. However, the primary measures we use in our analyses are...
neuropsychological factor scores derived from WHICAP data. The structure of the four-factor model and the magnitude of the relationship between the observed variables and the latent constructs are invariant across English and Spanish speakers [80]. The factors include memory, language, processing speed, and visual-spatial ability.

2.2.8. Dependence scale
This scale assesses the amount of assistance required by patients [21]. We typically use the sum of item scores for analysis. A dependence level can be derived from these items, ranging from 0, totally independent, to 5, totally dependent.

2.2.9. Equivalent institutional care rating
This rating records the rater’s impression of the level of institutional care received by the patient, irrespective of the patient’s actual location. Categories include limited home care, adult home (a supervised setting with regular assistance in most activities), and health-related facility [21].

2.2.10. Psychiatric and behavioral changes
We administer the neuropsychiatric interview [81]. In addition, the Columbia University Scale for Psychopathology in Alzheimer’s Disease [12] is used to elicit information about symptoms of delusions, hallucinations, illusions, depressed mood, and other behavioral signs (wandering, verbal outbursts, physical threats and/or violence, agitation or restlessness, and nighttime confusion) occurring during the month before assessment.

Patient-related past and current depressive symptoms are assessed. We use modified versions of the Patient Health Questionnaire-2 (PHQ) [82] and PHQ-9 [83] relating to past and current depression consistent with DSM-IV criteria. Informant-related depressive symptoms, relative to caregiving burden experienced within the past week, are assessed using the 10-item CES-D [84].

2.2.11. Quality of life ratings
We use our modified version of the Pleasant Events Schedule-AD [85] and the Apparent Emotion Scale to assess aspects of quality of life [22].

2.2.12. Life-extending measures
After a subject death, we record life-extending measures that caregivers may have chosen to request or withhold. These include administration of IV antibiotics or fluids, feeding tubes, or ventilatory support. We also note whether advanced care directives existed, or if a do not resuscitate order had been issued.

2.2.13. Informal care
In dementia, up to two-thirds of care is delivered by informal caregivers. The cost value of these services depends on both the amount of time caregivers provide services and the type of services provided. We have developed an instrument that captures “hands-on help” (help with the activities of daily living) as well as time spent supervising, cuing, or managing patient behavioral disturbances. We also have developed methodology to convert time to costs [36].

2.2.14. Medicare and Medicaid claims data
We obtained Medicare and Medicaid data (1999–2010) for the entire WHICAP cohort and the Predictors 3 cohort subset through the Research Data Assistance Center (ResDAC), a Center for Medicare and Medicaid Services contractor housed at the University of Minnesota. We currently plan to obtain SAFs and outpatient drug benefit (Part D) claims that are available for 2011–2013. A limitation to be kept in mind is that data from Medicare advantage participants are not available.

3. Results
The cohort consists of 274 community-based participants that represent all the incident and recent identified prevalent cases of AD, and individuals at-risk of developing AD that were available over the present study period. Although we continue to recruit, we expect very few new participants. Demographics for each of the three subject groups are summarized in Table 1. The participants self-identify as 39% white, 40% black or African American, and 21% other; 78.4% are Hispanic/Latino. Educational attainment ranges from 0 to 20 years, but the mean for the cohort is 6.9 years of schooling.

Clinical features of Alzheimer’s disease for each of the cohort subgroups are presented in Table 2. In general, the at-risk group shows the least severity or prevalence of each clinical feature, followed by the incident group and then the prevalent group. For example, mean MMSE was 15.6 in the prevalent group, 19.1 in the incident group and 22.7 in the at-risk group. Similarly, mean CDR was 1.23, 1.06, and .43 respectively across the prevalent, incident, and at-

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic features of the Predictors 3 cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevalent AD</td>
</tr>
<tr>
<td>N</td>
<td>46</td>
</tr>
<tr>
<td>Age</td>
<td>85.6 (7.2)</td>
</tr>
<tr>
<td>White/black/other, n (%)</td>
<td>16/17/13 (35/37/28)</td>
</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>41 (91.1)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>37 (80.4)</td>
</tr>
<tr>
<td>Education (y)</td>
<td>5.6 (4.5)</td>
</tr>
</tbody>
</table>
Table 2
Clinical features of Alzheimer’s disease in the three subject groups

<table>
<thead>
<tr>
<th></th>
<th>Prevalent AD</th>
<th>Incident AD</th>
<th>At-risk AD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>46</td>
<td>109</td>
<td>119</td>
<td></td>
</tr>
<tr>
<td>Modified MMSE, mean (SD)</td>
<td>25.2 (6.9)</td>
<td>30.8 (7.3)</td>
<td>38.1 (6.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Folstein MMSE score, mean (SD)</td>
<td>15.6 (4.3)</td>
<td>19.1 (4.5)</td>
<td>22.7 (3.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>CES-D, mean (SD)</td>
<td>3.6 (2.1)</td>
<td>3.0 (1.5)</td>
<td>3.4 (1.6)</td>
<td>.092</td>
</tr>
<tr>
<td>Dependence sum, mean (SD)</td>
<td>8 (3.1)</td>
<td>6.7 (3.2)</td>
<td>3.8 (3.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Dependence level, mean (SD)</td>
<td>3.6 (1.3)</td>
<td>3.6 (1.4)</td>
<td>2.5 (1.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Equivalent institutional care, n (%)</td>
<td>6 (13.6)</td>
<td>31 (29.8)</td>
<td>76 (65.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Limited home care</td>
<td>24 (54.5)</td>
<td>57 (54.8)</td>
<td>35 (30.2)</td>
<td></td>
</tr>
<tr>
<td>Adult home</td>
<td>14 (31.8)</td>
<td>16 (15.4)</td>
<td>5 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Health-related facility</td>
<td>4.2 (2.1)</td>
<td>3.3 (1.8)</td>
<td>1.7 (1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>IADL, mean (SD)</td>
<td>2.3 (2)</td>
<td>1.8 (2.1)</td>
<td>1.1 (1.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Delusion, n (%)</td>
<td>28 (60.9)</td>
<td>59 (57.3)</td>
<td>35 (30.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hallucination, n (%)</td>
<td>15 (32.6)</td>
<td>27 (26.2)</td>
<td>18 (15.5)</td>
<td>.035</td>
</tr>
<tr>
<td>Illusion, n (%)</td>
<td>3 (6.5)</td>
<td>2 (1.9)</td>
<td>3 (2.6)</td>
<td>.305</td>
</tr>
<tr>
<td>Any psychiatric symptom, n (%)</td>
<td>30 (65.2)</td>
<td>61 (59.2)</td>
<td>41 (35.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Moderate EPS, n (%)</td>
<td>14 (31.1)</td>
<td>25 (23.1)</td>
<td>22 (18.5)</td>
<td>.218</td>
</tr>
<tr>
<td>CDR, mean (SD)</td>
<td>1.23 (0.49)</td>
<td>1.06 (0.4)</td>
<td>0.43 (0.18)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; MMSE, mini-mental state examination; SD, standard deviation; EPS, extrapyramidal signs; CDR, Clinical Dementia Rating Scale.

risk groups. As two original Predictors cohorts used a strict MMSE cutpoint as one of the criteria for admission; here, we sought out as many incident and prevalent cases as we could identify within the 2 years before the initiation study and going forward. This resulted in patients who were primarily in the mild range of the disease, but some patients had a CDR score greater than one: 10 patients (21.8%) in the prevalent group and seven patients (6.4%) in the incident group.

Depressive affect, as measured by the PHQ or CES-D, was relatively low in all groups. Although all these participants lived at home at the baseline visit, a notable percentage of the patients with AD were reported to be receiving the equivalent of health-related facility care (i.e., an amount of care similar to that in a nursing home). As we have reported previously [12], simple delusions were quite prevalent in the AD patients with hallucinations and delusions less so.

We then investigated cross sectional associations with two clinical risk factors that have been reliably associated with poorer clinical outcomes: the presence of psychotic features and of moderate EPS. Here, we evaluated their association with cognition, measured by the MMSE and function as measured by the sum of IADL and BADL scores from the BDRS. As summarized in Table 3, in all three subgroups, the presence of psychotic features was associated with poorer ADL scores. Psychotic features were associated with poorer MMSE scores in the incident AD and at-risk groups; the difference was in the same direction but nonsignificant in the prevalent AD group. As summarized in Table 4, the presence of moderate EPS was associated with poorer ADL scores in the two AD groups but not in the at-risk individuals. No significant differences were noted for MMSE scores in patients with and without EPS.

4. Discussion

Here, we present the design and implementation of the new Predictors 3 cohort and describe the baseline subject population demographics and some early cross-sectional observations. This cohort differs from the previous two Predictors study cohorts in that it is community-based and strongly multiethnic. In addition, although the previous two cohorts consisted of patients who had mild-prevalent AD at baseline, this cohort also includes individuals at-risk for AD, as well as incident cases where the date of onset is relatively fixed. Despite these differences, we have retained most of the evaluation instruments from the previous two cohorts. This should allow us to determine whether the observations that we have made on these clinic-based cohorts remain valid.

We believe that the Predictors 3 cohort is more representative of the larger population of individuals with AD because it is drawn from the community and clinic based as were the initial two cohorts. On the other hand, the Washington Heights–Inwood community of Northern Manhattan is predominantly Hispanic, and 70% of the cohort has 8 or fewer years of schooling. It therefore may not be representative of community-based AD patients in general. Long-term
follow-up of this cohort will provide important data about the natural history of Alzheimer’s disease this understudied group.

We required that each participant in the study have an informant. This could impact on generalizability. The “workload” for each study participant is relatively comparable to that in our previous studies. A large degree of the evaluation is completed by the informant, reducing burden on the patient. We continue using the quality of life instruments from the first two Predictors cohorts. We are aware that these instruments do not correspond to those used in current clinical trials, but they provide important quality of life information.

Despite the differences between the current and previous cohorts, preliminary baseline analyses showed a relationship between the presence or absence of extrapyramidal signs and psychotic features and severity of the disease as measured by either a mental status test or functional scale, as we have previously reported in the earlier cohorts [14]. In the clinic-based cohorts, we have shown that these disease features are predictive of the future course of the disease [2,5]. These features are also components of the grade of membership model of AD progression that was developed based on patients in the Predictors 1 cohort [44]. When applied to the Predictors 2 cohort data, a prediction algorithm based on this model showed excellent accuracy in predicting time to nursing home admission, equivalent nursing home care or death [45].

As mentioned above, the Predictors study is developing algorithms to predict time until important disease endpoints.

Table 4
Relation of presence or absence of moderate extrapyramidal signs to cognition (MMSE) and function (ADL)

<table>
<thead>
<tr>
<th></th>
<th>Moderate EPS</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>P</td>
</tr>
<tr>
<td>Prevalent AD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>31</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>15.3 (4.5)</td>
<td>16.4 (3.9)</td>
<td>.440</td>
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<tr>
<td>ADL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>31</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.8 (3.2)</td>
<td>8.1 (3.5)</td>
<td>.036</td>
</tr>
<tr>
<td>Incident AD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>80</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>19.1 (4.5)</td>
<td>19.1 (4.5)</td>
<td>.978</td>
</tr>
<tr>
<td>ADL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>83</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>4.8 (2.9)</td>
<td>6.6 (4.4)</td>
<td>.016</td>
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<td>At-risk</td>
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<td>MMSE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>95</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>22.5 (3.6)</td>
<td>23.7 (2.9)</td>
<td>.137</td>
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<tr>
<td>ADL</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Number</td>
<td>95</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.8 (2.7)</td>
<td>2.6 (2.7)</td>
<td>.753</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; MMSE, mini-mental state examination; SD, standard deviation.

To date, we have considered nursing home entry, the need for nursing home care, and death, as well as cut scores on both the MMSE and BDRS. The grade of membership model that we have developed is capable of predicting time until any value of any of the measures in the model, such as time until a specific score on the scale, or until a specific item on the scale is endorsed. Accurate prediction of time until endpoints provides a service to patients, families, and physicians. It also could aid in the assignment of patients to arms of clinical trials and in economic modeling of the disease.

One of our goals is to extend the present grade of membership model to this community-based population to determine whether it truly models the progression of AD in non-clinic-based patients. Presence of at-risk subjects will eventually allow us to extend the model to the preclinical stage. The availability of Medicare/Medicaid linkage data will allow us to generate important observations about the relationship between various aspects of the disease and cost. We hope that over time analyses of follow-up data from this cohort will contribute to the understanding of the natural history and risk factors for progression of AD to the same level as the previous two Predictors cohorts.

Acknowledgments

This work was supported by R01 AG07370 from the National Institute on Aging (PI, Dr Stern).

RESEARCH IN CONTEXT

1. Systematic review: Data from the first two cohorts of the Predictors study has led to advances in our understanding of the natural history of Alzheimer’s disease (AD) and has resulted in algorithms for predicting time to important disease endpoints in individual patients. However, the patients in these studies were clinic-based and almost all White.

2. Interpretation: We therefore have recruited a new, Predictors 3 cohort that is population-based and ethnically diverse. Our aim is to attempt to replicate and expand on our previous observations in a cohort that may be more representative of AD in the community. Already in our baseline data, we replicate our previous observation that two clinical features, extrapyramidal signs and psychotic features are associated with more severe disease presentation.

3. Future direction: Our hope is that analysis of follow-up data will increase our understanding of the natural history and risk factors for the progression of AD in this ethnically diverse, population-based cohort.
References


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