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Objective: To examine dementia severity as determined by the Clinical Dementia Rating (CDR) over time.

Design: Secondary analysis of data from longitudinal studies of aging and dementia.

Setting: Alzheimer’s Disease Research Center, where a variety of clinicians contributed CDR ratings during the study.

Participants: Adults aged 63 to 83 years with no (CDR 0), very mild (CDR 0.5), or mild (CDR 1) dementia enrolled in the Alzheimer’s Disease Research Center at any time from August 13, 1979, through May 30, 2007.

Main Outcome Measures: Within each CDR group, changes in scores on standardized psychometric tests with time were examined using multiple linear regression analyses. These tests included the Mini-Mental State Examination, Short Blessed Test, Logical Memory IIA-Immediate from the Wechsler Memory Scale–Revised, and Blessed Dementia Scale, and a psychometric composite score.

Results: A total of 1768 participants met the inclusion criteria. With time, participants were older, more educated, and more likely to be nonwhite and less likely to be men. Statistically significant change in psychometric test performance with time occurred only within the CDR 1 group for Logical Memory and the psychometric composite, but the degree of change was minimal.

Conclusion: Despite changes in participant characteristics, the CDR demonstrates general stability for assessment of dementia for almost 3 decades.

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D I A G N O S T I C  D R I F T  D E S C R I B E S change in diagnosis and diagnostic classification with time. It can influence assessment methods and diagnostic algorithms. Consequently, diagnostic drift is important to consider in longitudinal studies that depend on the accurate and reliable identification of disease and staging of disease severity. Precise comparison of the prevalence and incidence of dementia with time is particularly important given the projected increase in the number of individuals with dementia of the Alzheimer type (DAT) for the next several decades.

The Clinical Dementia Rating (CDR) has been used for nearly 3 decades in the evaluation and staging of dementia. The CDR was developed at Washington University in St Louis for use in longitudinal studies of aging and dementia. The validity and reliability of the CDR have been demonstrated, including in multicenter studies. A literature review conducted in November 2008 revealed 708 references since 1982 for the CDR, which has been translated into 60 languages and dialects.

Changes have been made to the CDR and its scoring rules in response to growing knowledge of dementia symptoms. With increasing clinical and research interest in early stages of dementia, a relevant issue is whether improvements in diagnostic precision caused “drift” in the CDR with time such that the average level of cognitive impairment within a particular CDR rating has decreased. The question of CDR drift is the focus of the present study.

METHODS

Data from the initial clinical assessments of newly enrolled participants during our longitudinal studies from August 13, 1979, through May 30, 2007, were used. Participant inclusion criteria were age at the first assessment between 63 and 83 years (the age range of the original sample recruited in 1979) and a CDR indicating no (0), very mild (0.5), or mild (1) dementia at the initial assessment. We excluded participants with moderate (CDR 2) or severe (CDR 3) dementia because we anticipated that any occurrence of drift would be toward earlier dementia detection.

EVALUATION

Experienced clinicians (neurologist, psychiatrist, geriatrician, or clinical nurse specialist) conducted a clinical assessment to evaluate features indicative of a dementing disorder. Clinicians interviewed the participant and a knowledgeable collateral source (typically a spouse, an adult child, or another relative) and

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completed a detailed neurologic examination of each participant. The assessment protocol evaluated intradividual cognitive change, and the clinician determined whether memory and thinking difficulties consistent with decline from an individual's baseline level of cognitive function were present. The clinical assessment also included the Blessed Dementia Scale (BDS) as a means to assess decline in function in daily activities and 2 brief cognitive screening instruments: the Mini-Mental State Examination (MMSE) and the Short Blessed Test (SBT). In determining the CDR and clinical diagnosis, the clinician was unaware of the results of psychometric testing.

The CDR quantifies decline in cognitive function from an earlier level and ascertains consequent impairment in routine activities. The clinician synthesized information obtained from the clinical assessment to use the CDR to rate cognitive function in 6 domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The CDR describes 5 levels of impairment—0 (none), 0.5 (very mild or questionable), 1 (mild), 2 (moderate), and 3 (severe)—for each of these 6 domains, with the exception of personal care, for which scores of 0, 1, 2, and 3 are described. A global CDR score was derived from individual domain scores as delineated by a standard scoring algorithm. The clinician also diagnosed the presumed cause of the dementia for all participants with a CDR of 0.5 or greater, in accord with standard clinical diagnostic criteria as previously described. The clinical diagnostic criteria for DAT in our sample, even for individuals at the prodromal stage, is verified by the neuropathologic diagnosis of DAT in our sample, even for individuals at the Boston Naming Test. Additional psychometric tests were Wechsler Memory Scale Mental Control, word fluency for S and P with 60 seconds permitted for each letter, Digits (forward and backward), and copying Form D of the Benton Visual Retention Test, an untimed visuospatial test. Details of the scoring algorithm have been described previously. Scores from the tests in the psychometric battery were combined in a composite factor score using the weights obtained from a principal components analysis of 81 participants without dementia that produced a single factor that accounted for 34% of the variance.

HUMAN RESEARCH PROTECTION

The Washington University Human Studies Committee approved all procedures. Informed consent was obtained from participants and collateral sources after the study was described fully.

STANDARDIZED TESTS EXAMINED

Within each CDR stratum and for the period that each test was administered, changes in scores with time on a subset of standardized tests from the clinical and psychometric assessments were examined. These tests were the BDS, MMSE, SBT, and Logical Memory IA-Immediate from the Wechsler Memory Scale–Revised, and the psychometric composite score. Logical Memory was selected because it is a commonly used measure of episodic memory. Higher scores on the SBT and BDS and lower scores on the MMSE, Logical Memory, and psychometric composite score indicate greater cognitive impairment. During the research program, certain tests were administered at some times and not at other times. The dates over which data for each test were available are as follows: BDS, August 13, 1979, through May 30, 2007; Logical Memory and the psychometric composite, August 13, 1979, through September 8, 2005; SBT, April 10, 1984, through November 29, 2005; and MMSE, October 7, 1996, through May 30, 2007.

STATISTICAL ANALYSES

Time was treated as a continuous variable using 1-day increments with the time scale converted to years after dividing by 365.25. Because inspection of scatterplots indicated that the relationship, if any, between time and scores on each of the tests examined was linear, Pearson product moment correlations were used to examine the unadjusted association of scores on each test with time. Multiple linear regression was used to examine whether scores on each test were associated with time of testing after adjustment for age, sex, race/ethnicity (white vs nonwhite), and educational level. Although for the initial years of the study only individuals with dementia who were thought on the basis of clinical grounds to have DAT were enrolled, on August 22, 1990, the clinical diagnostic criteria were expanded to include individuals with non-DAT causes of dementia. For participants with a CDR of 0.5 or 1, the multiple regression analyses were repeated using data collected beginning August 22, 1990, with adjustment for receipt of a DAT diagnosis (yes vs no), as well as the other demographic variables.

To examine change in test scores across time graphically, least squares means scores for each test per year, adjusting for the demographic variables, were calculated and plotted for years in which that test was administered for the entire year.

Changes in participant demographics with time were tested using Pearson product moment correlations for age and educational level and using logistic regression for sex, race/
ethnicity, and receipt of a DAT diagnosis. Additional subgroup analyses examined participants with dementia who had a DAT diagnosis only.

RESULTS

A total of 1768 participants met the inclusion criteria, including 580 individuals with a CDR of 0, 684 individuals with a CDR of 0.5, and 504 individuals with a CDR of 1. Many individuals with a CDR of 0.5 (499 [72.9%]) or 1 (473 [93.8%]) were diagnosed as having DAT, and the remainder had non-DAT diagnoses, including dementia with Lewy bodies, frontotemporal dementia, and vascular dementia. Figure 1 provides the distribution of the initial assessments for these participants during the study years. Fluctuations in the number of initial assessments during the early years of the study are explained by differing emphases for recruiting efforts during those years; enrollment for 2007 is through May 2007.

Demographic information for study participants is presented in Table 1. The demographic characteristics of the sample changed through the years. With time, participants enrolling for initial assessments had more years of education (r = 0.12, P < .001) and were older (r = 0.10, P < .001), even though the age range was restricted by the present study’s inclusion criteria. In addition, participants were less likely to be men (odds ratio, 0.985; 95% confidence interval, 0.972-0.998; P = .02) and more likely to be nonwhite (1.111; 1.080-1.143; P < .001). For CDR 0.5 and CDR 1 participants with a first assessment in August 1990 or later, the likelihood of having a DAT diagnosis decreased (0.950; 0.916-0.985; P = .005). This trend is probably because enrollment in the initial years of the studies was restricted to individuals with DAT.

UNADJUSTED ANALYSES

Significant unadjusted correlations of test scores with time were found for the MMSE (r = 0.13, P = .01) and the psychometric composite (r = 0.10, P = .01) within the CDR 0.5 group and for the BDS (r = 0.12, P = .01) and Logical Memory test (r = 0.13, P = .01) within the CDR 1 group, such that scores on each test increased with time.

ADJUSTED ANALYSES

There were no significant changes in test scores with time for the CDR 0 group in the adjusted analyses. Within the CDR 0.5 group, there was a statistically significant increase in scores on the psychometric composite.
ite (b=0.03, P=.002) with time when adjusted for age, sex, race/ethnicity, and educational level, but this effect was no longer significant after adjustment for receipt of a DAT diagnosis (Table 2). For the CDR 1 group, scores on the SBT (b=–0.13, P=.045), Logical Memory (b=0.04, P=.007), and the psychometric composite (b=0.03, P=.004) changed significantly with time in the direction of less cognitive impairment. After adjustment for DAT diagnosis in this group, only Logical Memory and the psychometric composite showed significant effects of small magnitude (Table 2).

Figure 2 shows the least squares mean test scores at each year within each CDR group, adjusted for age, sex, race/ethnicity, and educational level, for periods when the test was administered the entire year. Analyses conducted for the subset of participants with DAT demonstrated comparable results.

As evidenced by stability of performance on standardized psychometric tests with time, the CDR generally reflects the same level of impairment now as it did nearly 30 years ago. The exceptions are for Logical Memory performance and the psychometric composite score that showed statistically significant effects for less impairment with time, but these effects were limited to the CDR
1 group and were of such slight magnitude that they likely are not clinically meaningful (Figure 2). The CDR has remained stable even as the typical participant is older, more highly educated, more likely to be nonwhite, and more likely to be a woman compared with the early participants and with turnover in the individual clinicians. The generalizability of the findings to other research groups is suggested by studies that demonstrate the reliability of the CDR in multicenter trials.26

This study demonstrates the general stability of the CDR and emphasizes the usefulness of ascertainment of cognitive change as operationalized by the CDR.27 The literature examining diagnostic drift in dementia assessment is limited. The present study has a number of strengths. The participants are well characterized, and the study duration is 28 years. As the sample has become increasingly diverse in terms of race/ethnicity, dementia diagnosis, and clinician staff (initially neurologists and psychiatrists and now neurologists, psychiatrists, geriatricians, and clinical nurse specialists), the CDR demonstrated continued stability.

The study has some limitations. Our sample is a convenience sample, which may limit the generalizability of the findings. The stability of the CDR was assessed at the research center that developed the CDR and clinicians were trained at the center. Additional studies conducted at other centers that use the CDR could help to establish further that the CDR demonstrates no substantive evidence of diagnostic drift.

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Author Contributions: Drs Williams, Roe, and Morris had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Williams, Roe, and Morris. Acquisition of data: Williams, Roe, and Morris. Analysis and interpretation of data: Williams, Roe, and Morris. Drafting of the manuscript: Williams and Roe. Critical revision of the manuscript for important intellectual content: Williams, Roe, and Morris. Statistical analysis: Roe. Obtained funding: Morris. Administrative, technical, and material support: Morris. Study supervision: Morris.

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