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Short Communication

Use of the Quick Dementia Rating System (QDRS) as an Initial Screening Measure in a Longitudinal Cohort at Risk for Alzheimer's Disease

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Abstract. The Quick Dementia Rating System (QDRS) and Clinical Dementia Rating Scale (CDR) assess global cognitive and functional decline. We evaluated whether the shorter QDRS was a valid screen for problems identified by the CDR in individuals with minimal clinical abnormalities. Agreement between QDRS-Global and CDR-Global was assessed for 54 participants from the Wisconsin Registry for Alzheimer's Prevention. Resource-savings achieved by adopting an "administer CDR-only-if-QDRS-Global>0" approach were estimated based on 238 subsequent participants. Agreement statistics (concordance = 88.9%) supported use of the QDRS as an initial informant report and modifying center protocol to administer CDRs only when QDRS>0 reduced CDR assessments by 79.8%.

Keywords: Alzheimer's disease, cognition, memory, neuropsychological test

INTRODUCTION

The Clinical Dementia Rating Scale (CDR) is a staging metric to detail the nature and severity of global cognitive and functional impairment in Alzheimer's disease (AD) and other dementia syndromes. It is a semi-structured interview administered to a participant or patient and an informant, with scores greater than 0 indicating impairment [1]. Although the CDR is a rigorous tool commonly used in clinical trials and longitudinal cohort studies [2–6], the length and complexities of its administration and interpretation have led to efforts to develop a comparable rating system that is less resource-intensive.

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The Quick Dementia Rating System (QDRS) is a 10-item questionnaire that is completed by the participant's informant/caregiver, and has been shown to yield comparable results to the CDR in 267 patient-caregiver dyads [7]. In contrast to the CDR, the QDRS does not require face-time with the participant or direct interaction with a clinician, takes only 3–5 minutes to complete, and may be completed prior to an appointment by a participant's informant. The QDRS includes 10 domains representing multiple facets of cognitive capacity: memory and recall, orientation, decision making and problem solving abilities, activities outside the home, function at home and hobby activities, toileting and personal hygiene, behavior and personality changes, language and communication abilities, mood, and attention and concentration. The first six domains are comparable to those assessed in the CDR [7].

Longitudinal cohorts that look to study the earliest signs of AD, such as the Wisconsin Registry for Alzheimer's Prevention (WRAP) [8], Biomarkers for Older Controls at Risk for Dementia (BIOCARD) [9], and the Adult Children Study (ACS) [10], among others, often employ global screening measures as part of their testing batteries. Given the potential advantages of the QDRS, the primary aim of this study was to compare how the QDRS and CDR performed in WRAP, a longitudinal middle-aged cohort enriched for parental history of AD [8]. Our secondary aim was to evaluate resource-savings achieved by adopting a two-stage approach to use of the QDRS and CDR.

METHODS

All consecutive WRAP participants were approached to complete both the QDRS and CDR; fifty-four participants had complete data for both assessments and were included in the initial analysis. The overall WRAP study, including the present assessments, is IRB approved by the University of Wisconsin School of Medicine and Public Health Institutional Review Board. In WRAP, an informant is defined as a spouse, friend or family member that knows the subject well, and can answer informant-based questionnaires and interviews; the same informant provided data for the QDRS and the CDR. After this initial validation cohort of 54 subjects (for whom data was collected over approximately 3.5 months time), subsequent consecutive participants ($N = 238$) were administered the QDRS, and the CDR was only given to subjects who scored greater than 0 (positively, indicating impairment) on the QDRS-derived CDR global (QDRS-global), as well as an equal number of participants with a non-impaired QDRS-global to avoid tester bias.

The QDRS-global was calculated using the same algorithmic procedure as the CDR-Global score [7]. The QDRS-derived Sum of Boxes (QDRS-SB) equivalent score was calculated by adding the scores from the first six domains of the QDRS [7]. As the personal care category of the CDR does not allow for a score of 0.5, subjects with a score of 0.5 in the toileting and personal hygiene QDRS category were marked as receiving a 0 in this category for scoring equivalence purposes.

Statistical analyses were conducted in IBM-SPSS version 22 (Armonk, NY). True positive (TP), true negative (TN), false positive (FP), and false negative (FN) rates for the QDRS-global were calculated, compared to the CDR-global. The concordance rate is defined as the TP rate+ the TN rate. Agreement between the QDRS-Global and the CDR-Global was assessed using McNemar's test and the SB correspondence was assessed using a two-way mixed intra-class correlation. We also evaluated whether the QDRS FN group would have been flagged as showing signs of abnormality by other methods currently in place in the WRAP study besides a positive CDR, such as lower than expected cognitive performance [11, 12] or other abnormal informant ratings (Informant Questionnaire on Cognitive Decline in the Elderly-Short Form, (IQCODE) [13] or modified Lawton Instrumental Activities of Daily Living scale (Lawton-IADL)) [14].

To evaluate the resource-savings achieved by incorporating QDRS in our informant reports, we calculated the reduction in number of CDRs administered due to the tiered QDRS/CDR approach for the $N = 238$ subsequent participants. The number of CDRs that were required after a positive QDRS screening of these 238 subjects was calculated.

RESULTS

In the 54 subjects (demographics, Table 1) who received both the CDR and QDRS, the FN rate (i.e., QDRS-Global = 0, CDR-Global = 0.5) was 9.26% ($N = 5$). The FP rate (i.e., QDRS-Global = 0.5, CDR-Global = 0) was 1.85% ($N = 1$). The concordance rate between the QDRS-Global and CDR-Global was 88.89% (TN, $N = 44$; TP, $N = 4$). McNemar's test indicated that the proportion of QDRS and CDR positives

Table 1
Participant Characteristics

	All Subjects ($N=54$)	True Negatives ($N=44$)	True Positives ($N=4$)	False Negatives ($N=5$)	False Positives ($N=1$)
Age, *mean (SD)*	64.7 (5.29)	64.4 (5.53)	67.8 (2.36)	63.6 (4.72)	69
Sex, *percent females*	57.4% ($N=31$)	63.6% ($N=28$)	25% ($N=1$)	20% ($N=1$)	100% ($N=1$)
APOE ε4, *percent positive*	44.4% ($N=24$)	45.5% ($N=20$)	50% ($N=2$)	40% ($N=2$)	0% ($N=0$)
Family History, *percent positive*	66.7% ($N=36$)	63.6% ($N=28$)	50% ($N=2$)	100% ($N=5$)	100% ($N=1$)
CDR-global, *median (range)*	0 (0.5)	0 (0)	0.5 (0)	0.5 (0)	0
QDRS-global, *median (range)*	0 (0.5)	0 (0)	0.5 (0)	0 (0)	0.5
CDR-Sum of Boxes, *median (range)*	0 (2)	0 (0.5)	0.75 (1.5)	0.5 (1.5)	0
QDRS-Sum of Boxes, *median (range)*	0 (2)	0 (0.5)	1.25 (1)	0.5 (0.5)	0.5
Number of Comorbid Conditions, *median (range)*	1 (5)	1(5)	1 (2)	0 (4)	3
WRAT Reading Standard Score, *mean* (SD)	105.7 (9.60)	105.0 (9.94)	110.8 (9.88)	106.8 (6.87)	111
Trails B raw score sec, *mean (SD)*	59.54 (21.63)	56.5 (18.80)	65.5 (38.07)	74.4 (23.37)	97
Logical Memory Immediate, *mean (SD)*/ Logical Memory Delayed, *mean (SD)*	28.6 (6.38)/25.9 (7.05)	29.2 (6.13)/26.7 (6.74)	30.75 (7.85)/26.25 (10.72)	24.4 (4.45)/21.0 (4.18)	16/15
RAVLT Total Learning Trials 1–5, *mean (SD)*/ RAVLT Long Delay, *mean (SD)*	49.6 (9.83)/9.9 (3.43)	50.9 (9.75)/10.07(3.53)	43.3 (6.18)/9.5 (1.73)	45.0 (10.77)/8.4 (4.04)	39/9
MMSE, *median (range)*	30 (4)	30 (4)	30 (1)	29 (1)	30
CES-D, *mean (SD)*	5.3 (5.57)	4.9 (5.48)	7.3 (3.77)	7.0 (8.22)	6

Conditions included in the comorbid conditions assessment: epilepsy, meningitis, stroke, multiple sclerosis (MS), Parkinson's disease, hypertension, diabetes, hypercholesteremia, liver disease, kidney disease – no subjects report liver disease, meningitis or MS; CES-D, center for epidemiological studies depression scale; RAVLT, Rey Auditory Verbal Learning Test; WRAT, Wide Range Achievement Test. *Post-hoc* analyses comparing the true negative, true positive, false negative and false positive groups on demographic and cognitive variables were not performed due to insufficient sample sizes.

did not differ significantly ($p = 0.219$). The QDRS and CDR SB scores displayed a moderate correlation, with a two-way mixed intra-class correlation coefficient of 0.606 ($p < 0.001$). All 5 FN subjects were flagged by at least one of the other methods in place in WRAP to trigger further review; all 5 had abnormal informant reports (IQCODE or Lawton-IADL), 2 had cognitive performance below internally developed norms [11, 12], and 1 subject had cognitive performance below published norms.

In the post-validation sample ($N = 238$), 24 subjects had QDRS-global>0 (impaired QDRS). Per the modified protocol, only the informants for these 24 plus 24 participants with QDRS = 0 were administered the CDR resulting in a 79.8% reduction in CDR administration (i.e., (238–48)/238).

DISCUSSION

Although the CDR is a well-validated screening measure for functional impairments in dementia, it requires substantial resources including clinician training, personnel time, a lengthy interview, availability of an observant informant, as well as face-time with the patient or study participant [1, 7]. Since most CDR-Global scores will be zero in predominantly cognitively healthy cohorts, such as WRAP (which enrolled individuals who were cognitively normal at baseline, but is enriched with persons at risk for AD), a less time- and resource-intensive instrument may be advantageous.

In the participants of the initial validation series that were administered both instruments ($N = 54$), we observed good agreement between the two measures (88.89%) and a marginally acceptable false negative rate such that 9.26% of CDR-positive cases were undetected with the QDRS. As all participant-study partner dyads were requested to complete both the QDRS and the CDR, this subset of 54 participants was used to examine the statistical agreement between the two clinical rating scales. The overall accuracy (combined with the additional flagging mechanisms that "caught" the $N = 5$ FNs and appropriately triggered further review) was deemed sufficient to switch to the collection paradigm by which all participant informants complete the QDRS, and every participant scoring greater than or equal to 0.5 (global) and a corresponding negative case are administered the CDR. The use and importance of the flagging mechanisms, however, should not be underscored, given the ~10% FN rate. This procedure represents how we intend to use the QDRS in practice in this preclinical-AD research setting.

Out of 238 complete QDRS administrations there were only 24 positive scores, leading to a decline in CDR administration by 79.83%, a significant reduction in time and resources. We estimate that the average CDR, including pre and post activities, takes 90 minutes to complete. Assuming ~600 visits per year, and a 79.8% reduction in CDR's given, this results in savings equivalent to approximately one-third of a technician's yearly salary (600 visits at 1.5 hours per visit * $21.60 per hour*0.798) and over 700 person-hours (600 visits at 1.5 hours per visit*0.798). Furthermore, in addition to the reduction in time spent and associated financial costs with the administration of each CDR, there are also savings upfront, in that in contrast to the CDR, the QDRS does not require extensive training before personnel can administer the test.

Interestingly, there were $N = 8$ out of 54 cases in the initial validation series where the QDRS and CDR were in agreement but were contradicted by consensus conference diagnosis. There were $N = 4$ instances where participants were deemed cognitively normal by both the QDRS and CDR, but were diagnosed as having mild cognitive impairment after consensus conference review of neuropsychological data. There were also $N = 4$ subjects that were diagnosed as cognitively normal by clinical consensus conference, but who scored 0.5 on both the CDR and QDRS global assessments. As the goal of the paper was to evaluate the performance of the QDRS compared to the CDR and determine the utility/time savings achieved by using the QDRS, these subjects were kept in the analysis unmodified.

For the global rating, these data suggest that in a majority of cases, the QDRS can substitute for the CDR measure in a mostly cognitively healthy cohort. It is important to note, however, that the QDRS does not entirely recapitulate the CDR. Quantitative analysis to determine the reason for the FNs and FPs on the QDRS was not sufficiently powered–possibly because the rate of FNs and FPs was overall quite low.

Compared to the subjects analyzed by Galvin [7], the current sample comprises a more restricted range, as WRAP is focused on the preclinical stage of AD. This limits the applicability of the SB metric; the largest SB value in our validation sample was 2 for both the CDR and QDRS. It is likely that the SB metric would be more useful for assessing cognitive decline in subjects with more clinically apparent disease [1, 7].

The QDRS is administered via a written questionnaire and does not require administering personnel to be extensively trained. The original validation of the QDRS [7] examined its performance in a cohort spanning a greater severity of and various types of dementia. The current study extends the previous work to suggest that the QDRS has utility as a screening measure in a risk population that is not yet experiencing clinically significant cognitive decline. In older populations that are at higher risk for cognitive decline simply due to advancing age, additional testing to the QDRS, such as the flagging mechanisms used in WRAP, is important. While the accuracy rates for the QDRS were reported relative to the CDR as a reference, it is important to recognize that the CDR itself is bounded by a degree of measurement error and thus accuracy rates can only be approximate. Both instruments possess intrinsic informant variability and response bias that may have affected the accuracy rates we observed. Despite these limitations, this study suggests that the QDRS is an efficient alternative to the CDR in this preclinical AD research context.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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