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CORRECTION

Correction to: Staging Disease Severity Using the Alzheimer's Disease Composite Score (ADCOMS): A Retrospective Data Analysis

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Following the publication of this article, the calculation of ADCOMS estimates in this publication were found to be incorrect as a result of a programming error. Resultantly, values presented in the paper text, tables and figures have been corrected in addition to estimated cut point values for the ADCOMS. This correction does not impact upon the study conclusion; the basic structure of the paper or the discussion. For completeness for this correction, the programming used to derive the ADCOMS variable has been independently checked by two analysts. The complete programming code for the whole analysis has been independently checked by one analyst. No errors or bugs were identified. Additionally, the data output file was checked against the corrected manuscript by a separate researcher.

The corrected values are given below:

ABSTRACT, Results: The following ADCOMS value ranges for the total population and Aβ + population were identified: < 0.11 indicative of normal cognition, 0.11 to < 0.31 indicative of MCI, 0.31–0.77 indicative of mild AD, and > 0.77 indicative of at least moderate AD.

Results

Sample Overview

The demographic characteristics of the study population are provided in Table 5. Scores on all the assessment measures at baseline were indicative of significantly greater impairment among the AD-related dementia group versus the MCI group, and significantly greater impairment among the MCI group versus the cognitively normal group. Among participants who were cognitively normal at both baseline and the 24-month visit, change scores on all the assessment measures were small (e.g., no change in ADCOMS values and an increase of 0.04 in CDR-SB scores). However, cognitively normal participants who progressed to MCI or AD at the 24-month visit had larger change

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scores (e.g., an increase of 0.12 in ADCOMS values and 1.31 in CDR-SB scores). The same was true for participants diagnosed with MCI (e.g., ADCOMS change scores of 0.04 and CDR-SB change scores of 1.50 among those who remained diagnosed with MCI versus 0.34 and 2.97, respectively, among those who progressed to AD). The same pattern of findings was observed among the subset of the population with positive amyloid β confirmation (Table 5). This suggests that the measures have reasonable known-groups validity and are sensitive to changes in disease severity, regardless of predisposition for developing AD.

In the following subsections, the results from the ROC curves based on the published cut

Table 3 ADCOMS items and weighting. Source: Wang et al. [7]

Scale	Item		PLS coefficient (weighting factor)
	Name	Possible score	
ADAS-Cog	Delayed word recall	0–10	0.008
	Orientation	0–8	0.017
	Word recognition	0–12	0.004
	Word-finding difficulty	0–5	0.016
MMSE	Orientation to time	0–5	0.042
	Drawing	0–1	0.038
CDR-SB	Personal care	0–3	0.054
	Community affairs	0–3	0.109
	Home and hobbies	0–3	0.089
	Judgement and problem solving	0–3	0.069
	Memory	0–3	0.059
	Orientation	0–3	0.078

To score the ADCOMS, each item is weighted according to the partial least-squares regression coefficients. Total ADCOMS values range from 0 to 1.97

ADAS-Cog Alzheimer's Disease Assessment Scale-Cognition, *ADCOMS* Alzheimer's Disease Composite Score; *CDR-SB* Clinical Dementia Rating Scale-Sum of Boxes, *MMSE* Mini-Mental State Examination, *PLS* partial least-squares

Table 5 Participant characteristics

	Total population			Positive amyloid β confirmation		
	Cognitively normal Baseline (*n* = 777)	**MCI Baseline (*n* = 938)**	**AD Dementia (any) Baseline (*n* = 358)**	**Cognitively normal Baseline (*n* = 191)**	**MCI Baseline (*n* = 441)**	**AD Dementia (any) Baseline (*n* = 224)**
Age at baseline, years						
Mean (SD)	73.1 (6.1)	73.0 (7.6)	74.9 (7.9)*	74.5 (6.2)	73.3 (7.2)	73.9 (8.1)
Range	56 to 90	54 to 91	55 to 91	57 to 90	54 to 91	55 to 90
Female gender identity, *n* (%)	428 (55.1)*	381 (40.6)	159 (44.4)	109 (57.1)*	176 (39.9)	99 (44.2)
Education level, years						
Mean (SD)	16.6 (2.6)*	15.9 (2.8)	15.2 (3.0)*	16.5 (2.7)	16.1 (2.8)	15.5 (2.8)
Range	6 to 20	4 to 20	4 to 20	6 to 20	6 to 20	8 to 20
ADCOMS (0 to 1.97)[a]						
Baseline	*n* = 777	*n* = 938	*n* = 358	*n* = 191	*n* = 441	*n* = 224
Mean (SD)	0.05 (0.03)*	0.20 (0.10)	0.57 (0.19)*	0.05 (0.03)*	0.21 (0.10)	0.58 (0.19)*
Range	0 to 0.20	0.03 to 0.58	0.15 to 1.17	0 to 0.20	0.04 to 0.57	0.17 to 1.10
Change from baseline at month 24						
Same baseline diagnosis	*n* = 406	*n* = 452	*n* = 159	*n* = 112	*n* = 207	*n* = 94
Mean (SD)	0.01 (0.05)	0.04 (0.11)	0.37 (0.27)	0.01 (0.05)	0.05 (0.11)	0.38 (0.29)
Range	− 0.15 to 0.31	− 0.27 to 0.56	− 0.21 to 1.10	− 0.15 to 0.26	− 0.19 to 0.43	− 0.21 to 1.10
Progressed to another diagnosis	*n* = 31	*n* = 177	–	*n* = 20	*n* = 113	–
Mean (SD)	0.12 (0.16)	0.34 (0.19)	–	0.10 (0.14)	0.33 (0.19)	–
Range	− 0.03 to 0.59	− 0.19 to 1.25	–	− 0.03 to 0.51	− 0.19 to 1.25	–
CDR global score (0 to 3)[a]						
Baseline	*n* = 777	*n* = 938	*n* = 358	*n* = 191	*n* = 441	*n* = 224

Table 5 continued

	Total population			Positive amyloid β confirmation		
	Cognitively normalBaseline (*n* = 777)	**MCIBaseline (*n* = 938)**	**AD Dementia (any)Baseline (*n* = 358)**	**Cognitively normalBaseline (*n* = 191)**	**MCIBaseline (*n* = 441)**	**AD Dementia (any)Baseline (*n* = 224)**
Mean (SD)	0.00 (0.03) *	0.50 (0.04)	0.76 (0.26) *	0 (0)a	0.50 (0.04)	0.77 (0.26)*
Range	0 to 0.5	0 to 1	0.5 to 2	0	0 to 1	0.5 to 2
Change from baseline at month 24						
Same baseline diagnosis	*n* = 406	*n* = 453	*n* = 159	*n* = 112	*n* = 207	*n* = 94
Mean (SD)	0.04 (0.13)	− 0.02 (0.14)	0.48 (0.56)	0.07 (0.18)	− 0.01 (0.15)	0.47 (0.56)
Range	0 to 0.5	− 0.5 to 0.5	− 0.5 to 2	0 to 0.5	− 0.5 to 0.5	− 0.5 to 2
Progressed to another diagnosis	*n* = 31	*n* = 177	–	*n* = 20	*n* = 113	–
Mean (SD)	0.45 (0.24)	0.34 (0.36)	–	0.43 (0.18)	0.32 (0.32)	–
Range	0 to 1	− 0.5 to 1.5	–	0 to 0.5	− 0.5 to 1.5	–
CDR-SB (0 to 18)[a]						
Baseline	*n* = 779	*n* = 939	*n* = 360	*n* = 191	*n* = 441	*n* = 224
Mean (SD)	0.04 (0.13) *	1.50 (0.88)	4.40 (1.68) *	0.05 (0.16)*	1.56 (0.9)	4.44 (1.61)*
Range	0 to 1	0 to 5.5	1 to 10	0 to 1	0 to 5.5	1 to 10
Change from baseline at month 24						
Same baseline diagnosis	*n* = 406	*n* = 453	*n* = 159	*n* = 112	*n* = 207	*n* = 94
Mean (SD)	0.08 (0.38)	0.27 (0.98)	3.17 (2.58)	0.12 (0.42)	0.36 (0.99)	3.23 (2.71)
Range	− 1 to 3.5	− 3 to 5.5	− 2 to 11	− 1 to 2	− 2 to 3.5	− 2 to 11
Progressed to another diagnosis	*n* = 31	*n* = 177	–	*n* = 20	*n* = 113	–
Mean (SD)	1.31 (1.41)	2.97 (1.82)	–	1.08 (1.05)	2.88 (1.80)	–
Range	0 to 5	− 3 to 10	–	0 to 4	− 3 to 10	–

Table 5 continued

	Total population			Positive amyloid β confirmation		
	Cognitively normalBaseline (*n* = 777)	**MCIBaseline (*n* = 938)**	**AD Dementia (any)Baseline (*n* = 358)**	**Cognitively normalBaseline (*n* = 191)**	**MCIBaseline (*n* = 441)**	**AD Dementia (any)Baseline (*n* = 224)**
ADAS-Cog (0 to 70)[a]						
Baseline	*n* = 776	*n* = 938	*n* = 358	*n* = 191	*n* = 441	*n* = 224
Mean (SD)	6.85 (3.13)*	10.42 (4.59)	19.70 (6.72)*	6.52 (3.09)*	11.05 (4.70)	20.25 (6.97)*
Range	0 to 19.33	1 to 27.67	7.3 to 42.67	0 to 16.33	1.00 to 27.00	8.67 to 42.67
Change from baseline at month 24						
Same baseline diagnosis	*n* = 405	*n* = 453	*n* = 159	*n* = 112	*n* = 207	*n* = 94
Mean (SD)	− 0.31 (2.83)	0.45 (3.88)	9.10 (8.24)	− 0.34 (2.65)	0.75 (4.41)	9.01 (7.97)
Range	− 9.7 to 10.3	− 11 to 20.7	− 6 to 32.3	− 7 to 6.7	− 11 to 20.7	− 6 to 31
Progressed to another diagnosis	*n* = 31	*n* = 177	–	*n* = 20	*n* = 113	–
Mean (SD)	0.82 (3.48)	5.69 (6.10)	–	0.63 (3.52)	5.55 (5.86)	–
Range	− 5 to 7	− 7 to 39	–	− 5 to 7	− 5.3 to 32.3	–
MMSE (0 to 30)[a]						
Baseline	*n* = 778	*n* = 939	*n* = 360	*n* = 191	*n* = 441	*n* = 224
Mean (SD)	29.08 (1.10)*	27.62 (1.83)	23.20 (2.09)*	29.08 (1.14)*	27.49 (1.86)	23.17 (2.03)*
Range	24 to 30	19 to 30	18 to 29	24 to 30	23 to 30	19 to 27
Change from baseline at month 24						
Same baseline diagnosis	*n* = 406	*n* = 453	*n* = 159	*n* = 112	*n* = 207	*n* = 94
Mean (SD)	− 0.05 (1.36)	− 0.42 (2.26)	− 4.24 (4.81)	− 0.33 (1.43)	− 0.87 (2.54)	− 4.34 (4.67)
Range	− 4 to 4	− 17 to 6	− 21 to 5	− 4 to 3	− 17 to 6	− 21 to 4
Progressed to another diagnosis	*n* = 31	*n* = 177	–	*n* = 20	*n* = 113	–

Table 5 continued

	Total population			Positive amyloid β confirmation		
	Cognitively normalBaseline (*n* = 777)	**MCIBaseline (*n* = 938)**	**AD Dementia (any)Baseline (*n* = 358)**	**Cognitively normalBaseline (*n* = 191)**	**MCIBaseline (*n* = 441)**	**AD Dementia (any)Baseline (*n* = 224)**
Mean (SD)	− 1.29 (1.78)	− 3.89 (3.40)	–	− 1.20 (1.58)	− 3.45 (3.31)	–
Range	− 4 to 2	− 19 to 5	–	− 4 to 2	− 19 to 5	–

AD Alzheimer's disease, *ADAS-Cog* Alzheimer's Disease Assessment Scale-Cognition, *ADCOMS* Alzheimer's Disease Composite Score, *CDR* Clinical Dementia Rating Scale, *CDR-SB* Clinical Dementia Rating Scale-Sum of Boxes, *MCI* mild cognitive impairment, *MMSE* Mini-Mental State Examination, *SD* standard deviation, –, missing data

*$P < 0.001$

[a]Parenthetical numbers next to each assessment measure refer to the possible score range on the measure. All statistical comparisons are based on MCI as the reference group and the χ^2 statistic (categorical data) or analysis of variance (continuous data)

Table 6 ROC curve baseline results: optimal ADCOMS values

	Optimal cut point score	Area under the curve	χ^2 test of equality, p value	Correctly classified, %
Total population				
Cognitively normal and MCI[a]				
CDR global (0 and 0.5)	0.10	0.976	0.157	91
CDR-SB (0 and 0.5–4.0)	0.08	0.976	0.360	93
ADAS-Cog (< 8 and 8–15)	0.11	0.811	0.210	72
MCI and mild AD				
CDR global (0.5 and 1)	0.44–0.47[b]	0.993	0.037	91–96[c]
CDR-SB (0.5–4.0 and 4.5–9.0)	0.47	0.995	0.046	96
ADAS-Cog (8–15 and 16–32)	0.27–0.31[b]	0.871	0.013	81–82[c]
MMSE (≥ 26 and 21–25)	0.23	0.912	0.638	82
Mild AD and moderate AD[d]				
ADAS-Cog (16–32 and ≥ 33)	0.69	0.913	0.606	82
MMSE (21–25 and 11–20)	0.62	0.864	0.536	79
Confirmed positive amyloid β population				
Cognitively normal and MCI[a]				
CDR global (0 and 0.5)	0.10	0.976	0.468	91
CDR-SB (0 and 0.5–4.0)	0.08	0.980	0.494	93
ADAS-Cog (< 8 and 8–15)	0.11	0.826	0.809	76
MCI and mild AD				
CDR global (0.5 and 1)	0.47	0.995	0.048	95
CDR-SB (0.5–4.0 and 4.5–9.0)	0.47	0.995	0.093	96
ADAS-Cog (8–15 and 16–32)	0.33	0.872	0.620	81
MMSE (≥ 26 and 21–25)	0.34	0.907	0.428	87
Mild AD and moderate AD[d]				
ADAS-Cog (16–32 and ≥ 33)	0.69	0.881	0.981	79

Table 6 continued

	Optimal cut point score	Area under the curve	χ^2 test of equality, *p* value	Correctly classified, %
MMSE (21–25 and 11–20)	0.62	0.823	0.606	75

AD Alzheimer's disease, *ADAS-Cog* Alzheimer's Disease Assessment Scale-Cognition, *ADCOMS* Alzheimer's Disease Composite Score, *CDR* Clinical Dementia Rating Scale, *CDR-SB* Clinical Dementia Rating Scale-Sum of Boxes, *MCI* mild cognitive impairment, *MMSE* Mini-Mental State Examination, *ROC* receiver operating characteristic

[a]The MMSE is not sensitive to distinguishing between normal cognition and MCI; thus no results based on the MMSE are reported for the cognitively normal and MCI comparison

[b]Between the validation ROC and the derivation ROC

[c]In both the derivation and validation sets

[d]No patients had CDR or CDR-SB scores indicative of moderate AD at baseline; thus, no results based on these measures are reported for the mild AD and moderate AD comparison

Table 7 ROC curve 24-month visit results: optimal ADCOMS values

	Optimal cut point score	Area under the curve	χ^2 test of equality, *p* value	Correctly classified, %
Total population				
Cognitively normal and MCI[a]				
CDR global (0 and 0.5)	0.08	0.942	0.114	86
CDR-SB (0 and 0.5–4.0)	0.08	0.936	0.017	85
ADAS-Cog (< 8 and 8–15)	0.10	0.871	0.782	79
MCI and mild AD				
CDR global (0.5 and 1)	0.49	0.986	0.391	94
CDR-SB (0.5–4.0 and 4.5–9.0)	0.49	0.992	0.111	94
ADAS-Cog (8–15 and 16–32)	0.46	0.913	0.379	85
MMSE (≥ 26 and 21–25)	0.29	0.920	0.854	88
Mild AD and moderate AD				
CDR global (1 and 2)	0.97	0.986	0.811	91
CDR-SB (4.5–9.0 and 9.5–15.5)	1.03	0.984	0.862	92
ADAS-Cog (16–32 and ≥ 33)	0.91	0.917	0.337	81
MMSE (21–25 and 11–20)	0.77	0.871	0.377	79

Table 7 continued

	Optimal cut point score	Area under the curve	χ^2 test of equality, p value	Correctly classified, %
Confirmed positive amyloid β population				
Cognitively normal and MCI[a]				
CDR global (0 and 0.5)	0.09	0.947	0.395	87
CDR-SB (0 and 0.5–4.0)	0.08	0.939	0.057	87
ADAS-Cog (< 8 and 8–15)	0.11	0.869	0.393	81
MCI and mild AD				
CDR global (0.5 and 1)	0.49	0.975	0.819	92
CDR-SB (0.5–4.0 and 4.5–9.0)	0.49	0.988	0.418	93
ADAS-Cog (8–15 and 16–32)	0.46	0.893	0.893	84
MMSE (≥ 26 and 21–25)	0.29	0.884	0.285	82
Mild AD and moderate AD				
CDR global (1 and 2)	1.13	0.997	0.374	98
CDR-SB (4.5–9.0 and 9.5–15.5)	1.13	0.995	0.914	96
ADAS-Cog (16–32 and ≥ 33)	0.98	0.942	0.095	87
MMSE (21–25 and 11–20)	0.69	0.883	0.204	79

AD Alzheimer's disease, *ADAS-Cog* Alzheimer's Disease Assessment Scale-Cognition, *ADCOMS* Alzheimer's Disease Composite Score, *CDR* Clinical Dementia Rating Scale, *CDR-SB* Clinical Dementia Rating Scale-Sum of Boxes, *MCI* mild cognitive impairment, *MMSE* Mini-Mental State Examination, *ROC* receiver operating characteristic

[a]The MMSE is not sensitive to distinguishing between normal cognition and MCI; thus, no results based on the MMSE are reported for the cognitively normal and MCI comparison

Table 8 Biomarker values and APOE4 genotype according to ADCOMS staging score group

	Normal cognition (ADCOMS < 0.11) *N* = 946	**MCI (ADCOMS > 0.11 and < 0.31) *N* = 679**	**Mild AD (ADCOMS ≥ 0.31 and < 0.77 *N* = 412**	**Moderate/severe AD ADCOMS ≥ 0.77) *N* = 59**
CSF Tau (pg/ml)				
N	491	431	251	40
Mean (SD)	237.7 (96.0)[a]	290.8 (128.6)[a]	361.1 (154.5)[b]	391.0 (142.1)
CSF P-tau$_{181}$ (pg/ml)				
N	491	431	251	40
Mean (SD)	21.9 (10.0)[a]	28.3 (14.6)[a]	36.2 (16.8)[b]	37.9 (14.2)
CSF Amyloid β_{1-42} (pg/ml)				
N	491	431	251	40
Mean (SD)	1181.9 (440.6)[a]	964.0 (439.3)[a]	670.1 (303.5)[b]	622.7 (288.4)
APOE4 carrier				
N	671	614	381	56
Yes: *n* (%)	19 (2.8)[a]	73 (11.9)[a]	68 (17.9)[c]	11 (19.6)

Statistical significance was assessed using a one-way analysis of variance for continuous measures (tau, ptau$_{181}$, amyloid β_{1-42}) with Bonferonni correction for multiple comparisons, and a χ^2 goodness of fit test for APOE4

AD Alzheimer's disease, *ADCOMS* Alzheimer's Disease Composite Score, *APOE4* apolipoprotein ε4 allele, *CSF* cerebrospinal fluid, *MCI* mild cognitive impairment

[a] $P < 0.001$ compared with all other ADCOMS staging subgroups

[b] $P < 0.001$ compared with all other ADCOMS staging subgroups except the ADCOMS ≥ 0.77 (moderate/severe AD) subgroup

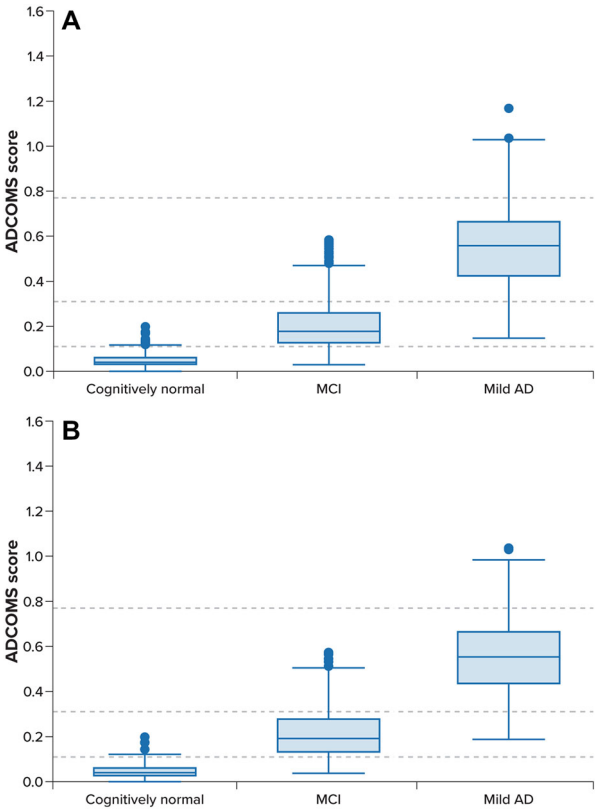

Fig. 1 Box plot of ADCOMS values at baseline by diagnosis for the total and confirmed amyloid β-positive populations[a]. **a** Total population. **b** Confirmed amyloid β-positive population. *AD* Alzheimer's disease, *ADCOMS* Alzheimer's Disease Composite Score, *MCI* mild cognitive impairment. [a]Horizontal dashed lines represent the selected ADCOMS cut point scores (i.e., 0.11, 0.31, and 0.77). Whiskers represent the minimum and maximum values excluding outliers; the horizontal line within the box represents the median; the upper and lower portions of the box represent the upper and lower quartiles; circles represent outliers

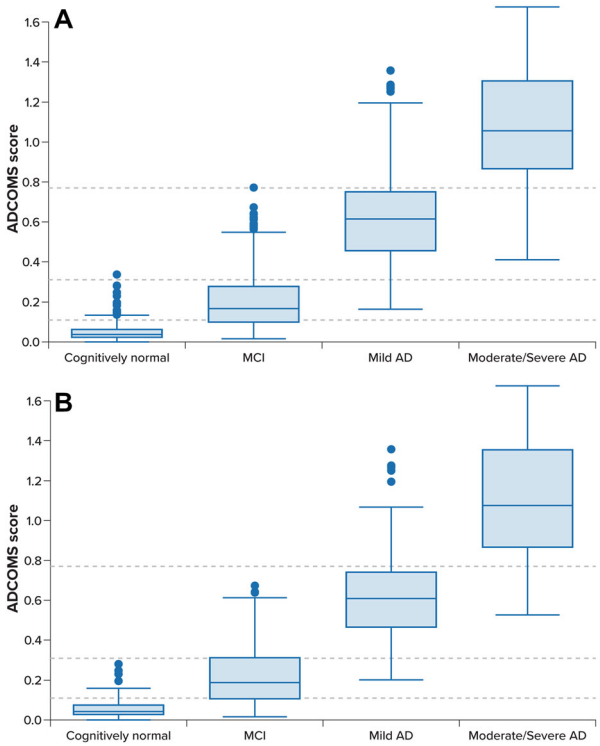

Fig. 2 Box plot of ADCOMS values at 24-month visit by diagnosis for the total and confirmed amyloid β-positive populations[a]. **a** Total population. **b** Confirmed amyloid β-positive population. *AD* Alzheimer's disease, *ADCOMS* Alzheimer's Disease Composite Score, *MCI* mild cognitive impairment. [a]Horizontal dashed lines represent the selected ADCOMS cut point scores (i.e., 0.11, 0.31, and 0.77). Whiskers represent the minimum and maximum values excluding outliers; the horizontal line within the box represents the median; the upper and lower portions of the box represent the upper and lower quartiles; circles represent outliers

point scores for the reference assessment measures are presented for the baseline and the 24-month visit data. The diagnostic accuracy test results are then presented, followed by a summary and examination of the selected ADCOMS cut scores.

ROC Curves

Baseline Data

The results of the ROC curves of ADCOMS values generated using the baseline data for both the total population and the amyloid β–positive population are presented in Table 6. The ROC curves primarily suggested an optimal ADCOMS cut point score of between 0.08 to 0.11 for normal cognition versus MCI. Of note, there is no threshold on the MMSE that distinguishes between normal cognition and MCI; thus,

MMSE scores could not be used for this determination. The optimal ADCOMS cut point score to distinguish between MCI and mild AD varied across the different assessment measures (Table 6). There were too few patients at baseline with a CDR or CDR-SB score indicative of moderate AD; thus, ROC curves could not be generated for differentiating mild from moderate AD using these measures. On the ADAS-Cog and MMSE, optimal scores for distinguishing between mild and moderate AD also varied (Table 6). The tests of equality between the derivation and the validation sample confirmed the results (Table 6).

Twenty-Four-Month Visit Data

The results of the ROC curves of ADCOMS values generated using the 24-month visit data for both the total population and the amyloid β-positive population are presented in Table 7. These results confirmed the finding that an optimal ADCOMS cut score of 0.08 to 0.11 distinguishes between normal cognition and MCI. For MCI and mild AD and for mild AD and moderate AD, the suggested cut score varied across the different assessment measures (Table 7). The tests of equality between the derivation and validation samples confirmed the results (Table 7).

Diagnostic Accuracy

Analyses were restricted to patients with a CDR score of 0.5 at baseline (MCI, $n = 471$; AD, $n = 84$) to determine the cut point for the ADCOMS value that differentiated between ADNI-defined clinical diagnoses of MCI or mild AD. The ROC curve demonstrated that an ADCOMS cut score of 0.31 (sensitivity = 90.5%, specificity = 86.6%) best discriminated between patients with MCI versus mild AD: 87% of patients were correctly classified. The area under the ROC curve was 0.933.

When restricting the analysis to patients with a CDR score of 1.0 at month 24 (mild AD, $n = 70$; moderate or severe AD, $n = 24$), the ROC curve demonstrated that an ADCOMS cut score of 0.77 (sensitivity = 79.2%, specificity = 68.6%) best discriminated between patients with mild AD versus moderate/severe AD: 71% of patients were correctly classified. The area under the ROC curve was 0.821.

Derived ADCOMS Staging Scores

The results from all ROC curve analyses suggested that an ADCOMS value < 0.11 is indicative of normal cognition. Correspondingly, the mean (standard deviation [SD]) ADCOMS at baseline for cognitively normal participants was 0.05 (0.03) for the total population and the population with positive amyloid β confirmation (Table 5). When the cut point scores were applied to the 24-month visit data, we found that 73% of participants from the total population (65% of patients with positive amyloid β confirmation) with an ADCOMS value less than 0.11 had a diagnosis of normal cognition rather than MCI.

For MCI, the ROC results suggested the ADCOMS value should be less than a value somewhere between 0.23 and 0.49, while the diagnostic accuracy checks suggested a score of 0.31. Therefore, an ADCOMS value of less than 0.31 was selected as the optimal score to distinguish MCI from mild AD; thus, an ADCOMS value between 0.11 and less than 0.31 is considered to be indicative of MCI. Correspondingly, the mean (SD) ADCOMS value at baseline for participants diagnosed with MCI was 0.20 (0.10) for the total population and 0.21 (0.10) for the population with positive amyloid β confirmation (Table 5). When the cut point scores were applied to the 24-month visit data, we found that 94% of participants from the total population (93% of patients from the amyloid β population) with an ADCOMS value between 0.11 and less than 0.31 had a diagnosis of MCI rather than mild AD.

The results from all ROC curve analyses suggested that the ADCOMS value should be less than somewhere between 0.62 to 1.03 for mild AD. However, the diagnostic accuracy checks suggest a score of 0.77. Therefore, an ADCOMS value less than 0.77 was selected as the optimal score to distinguish mild AD from moderate/severe AD; thus, an ADCOMS value between 0.31 and less than 0.77 is indicative of

mild AD. Correspondingly, the mean (SD) ADCOMS value for participants diagnosed with mild AD at baseline in both the total population (n = 327) and population with positive amyloid β confirmation (n = 203) was 0.56 (0.18). When the cut point scores were applied to the 24-month visit data, we found that 91% of participants from the total population (93% of the population with positive amyloid β confirmation) with an ADCOMS value between 0.31 and less than 0.77 had a diagnosis of mild AD rather than moderate/severe AD.

Based on the results above, an ADCOMS value of 0.77 or greater was considered to be indicative of moderate/severe AD. Few patients were diagnosed with moderate AD at baseline; the mean (SD) ADCOMS value for participants diagnosed with moderate/severe AD at the 24-month visit was 1.07 (0.29) for the total population (n = 102) and 1.10 (0.31) for population with positive amyloid β confirmation (n = 58). When the cut point scores were applied to the 24-month visit data, we found that 62% of participants in the total population and 63% of participants with positive amyloid β confirmation with an ADCOMS value of 0.77 or greater had a diagnosis of moderate/severe AD rather than mild AD.

Figure 1a, b presents a box plot of ADCOMS values by diagnosis at baseline for the total population and amyloid β population, with horizontal lines representing the selected ADCOMS cut point scores. Figure 2a, b presents ADCOMS values at the 24-month visit, which shows that within each diagnosis, the interquartile range of ADCOMS values fell within the selected cut point range.

Table 8 presents values of the biomarkers total tau, tau phosphorylated at threonine 181 (p-tau$_{181}$), and amyloid $\beta_{1–42}$ as measured in CSF at baseline and the number of patients carrying the apolipoprotein ε4 allele (APOE4) gene according to ADCOMS staging groups. People staged as having normal cognition using the ADCOMS have significantly lower mean tau and p-tau$_{181}$ levels and significantly higher mean amyloid $\beta_{1–42}$ values than those staged as having early AD (soluble amyloid $\beta_{1–42}$ is known to decrease as patients progress [21]). Additionally, the likelihood of being an APOE4 carrier increased across the ADCOMS staging groups, such that people staged as having moderate/severe AD had the highest likelihood of carrying this gene.

DISCUSSION

Using a large sample of participants from the North American ADNI study, we derived the following severity scoring ranges for the ADCOMS measure: a score of < 0.11 is indicative of normal cognition; a score of 0.11 to < 0.31 is indicative of MCI; a score of 0.31 to 0.77 is indicative of mild AD; and a score of > 0.77 is indicative of at least moderate AD.

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The original article has been corrected.

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