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
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                                             | Possible score | PLS coefficient (weighting factor) |
| 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
|                          | 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) *     |                  |                                 |                          |
| 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) * |                  |                                 |                          |
| Baseline                 | n = 777          | n = 938                         | n = 358                  | n = 191          | n = 441          | n = 224          |
|                          | Total population | Positive amyloid β confirmation |
|--------------------------|------------------|---------------------------------|
|                          | Cognitively normal Baseline (n = 777) | MCIBaseline (n = 938) | AD Dementia (any) Baseline (n = 358) | Cognitively normal Baseline (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)*        | n = 779          | n = 939                     | n = 360                    | n = 191                                | n = 441                   | n = 224                     |
| Baseline                 |                  |                              |                          |                                       |                          |                           |
| 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 | MCIBaseline (n = 938) | AD Dementia (any)Baseline | Cognitively normalBaseline | MCIBaseline | AD Dementia (any)Baseline |
|                          | (n = 777)        | (n = 358) | (n = 191) | (n = 441) | (n = 224) |
| ADAS-Cog (0 to 70)       |                  |                  |                  |                  |                  |
| 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)           |                  |                  |                  |                  |                  |
| 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 normal Baseline | MCIBaseline (n = 938) | AD Dementia (any) Baseline (n = 358) | Cognitively normal Baseline | 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

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 χ² 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 | \( \chi^2 \) 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 \( \beta \) 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 |

\( \Delta \) Adis
**Table 6** continued

| Optimal cut point score | Area under the curve | χ² 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

aThe 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

bBetween the validation ROC and the derivation ROC

cIn both the derivation and validation sets

dNo 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

| Total population | Optimal cut point score | Area under the curve | χ² test of equality, p value | Correctly classified, % |
|------------------|-------------------------|----------------------|-----------------------------|------------------------|
| Cognitively normal and MCIa | 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                 | 0.391                       | 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                 | 0.811                       | 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                     |
|                          | Optimal cut point score | Area under the curve | $\chi^2$ test of equality, $p$ value | Correctly classified, % |
|--------------------------|-------------------------|----------------------|--------------------------------------|-------------------------|
| Confirmed positive amyloid β population |                         |                      |                                      |                         |
| Cognitively normal and MCI<sup>a</sup> |                         |                      |                                      |                         |
| 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                     |

<sup>a</sup>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.

<sup>AD</sup> Alzheimer’s disease, <sup>ADAS-Cog</sup> Alzheimer’s Disease Assessment Scale-Cognition, <sup>ADCOMS</sup> Alzheimer’s Disease Composite Score, <sup>CDR</sup> Clinical Dementia Rating Scale, <sup>CDR-SB</sup> Clinical Dementia Rating Scale-Sum of Boxes, <sup>MCI</sup> mild cognitive impairment, <sup>MMSE</sup> Mini-Mental State Examination, <sup>ROC</sup> receiver operating characteristic.
Table 8 Biomarker values and APOE4 genotype according to ADCOMS staging score group

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

Statistical significance was assessed using a one-way analysis of variance for continuous measures (tau, ptau<sub>181</sub>, amyloid β<sub>1–42</sub>) with Bonferonni correction for multiple comparisons, and a χ² goodness of fit test for APOE4

AD Alzheimer’s disease, ADCOMS Alzheimer’s Disease Composite Score, APOE4 apolipoprotein e4 allele, CSF cerebrospinal fluid, MCI mild cognitive impairment

<sup>a</sup>P < 0.001 compared with all other ADCOMS staging subgroups

<sup>b</sup>P < 0.001 compared with all other ADCOMS staging subgroups except the ADCOMS ≥ 0.77 (moderate/severe AD) subgroup
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 \(\beta\) 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 \(\beta\) 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 \(\beta\) 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 \(\beta\) 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 \(\beta\) 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 \((p\text{-tau}_{181})\), and amyloid \(\beta_{1–42}\) as measured in CSF at baseline and the number of patients carrying the apolipoprotein \(e4\) allele \((APOE4)\) gene according to ADCOMS staging groups. People staged as having normal cognition using the ADCOMS have significantly lower mean tau and \(p\text{-tau}_{181}\) 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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