Cognitive Trajectories of Alzheimer's Disease Patients Receiving Lecanemab Using Monthly Remote Assessment

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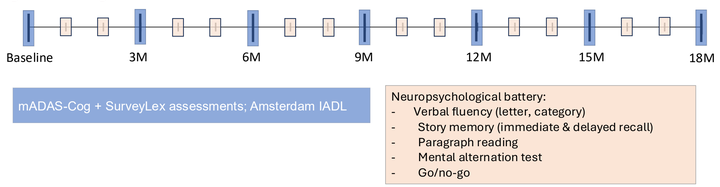
BACKGROUND

- Disease-modifying therapies (DMTs) for Alzheimer's disease (lecanemab, donanemab) are increasingly prescribed in clinical practice, including for patients with atypical AD phenotypes (Posterior Cortical Atrophy, Primary Progressive Aphasia) who were excluded from pivotal trials[1].
- No standard exists for how clinicians should monitor individual treatment response outside the trial setting.
- Pivotal trials assessed cognition quarterly, an interval that may obscure within-person fluctuation relevant to real-world clinical decisions such as dose modification or continued treatment.
- We developed a brief remote neuropsychological battery to enable frequent, low-burden monitoring of individual cognitive trajectories in patients receiving DMTs.

METHODS

- 33 participants with early-stage AD (including atypical clinical phenotypes) receiving a DMT were enrolled in REAL outcomes AD (REmote Assessment of cLinical outcomes in AD), a prospective observational study at MGH.
- All assessments were conducted remotely via secure videoconference by a trained study coordinator. Responses were collected using SurveyLex, a novel web-based platform designed to capture and analyze voice data.
- Participants completed a modified AD Assessment Scale-Cognitive (m-ADAS-Cog) and battery of five neuropsychological assessments according to the following schedule:

Figure 1. Testing schedule



- Neuropsychological test scores were normalized and averaged to yield a composite.
- Individual cognitive slopes were calculated via linear regression across all available timepoints.

Table 1. Participant Demographics

	Typical AD (N=22)	PCA (N=5)	PPA (N=6)
Mean age, years (SD)	70.54 (7.75)	65.89(5.51)	63.69 (7.27)
Sex (F/M)	(8/14)	(4/1)	(5/1)
Mean education, years (SD)	18.09 (2.38)	16.8 (1.10)	18 (1.79)
Race, white - N (%)	21 (95.4)	5 (100)	6 (100)
CDR Global	CDR= 0 (N=1)		CDR=0 (N=1)
	CDR= 0.5 (N=14)	CDR=0.5 (N=3)	CDR=0.5 (N=3)
	CDR=1 (N=5)	CDR=1.0 (N=2)	CDR=1.0 (N=1)
Mean MoCA (SD)	22.48 (4.76)	15.6 (3.91)	19.83 (6.85)
Mean mADAS-Cog (SD)	20.41 (8.68)	30.60 (5.94)	28.11 (26.15)
Mean informant Amsterdam IADL (SD)	28.19 (28.49)	50.24 (20.80)	23.79 (26.18)

RESULTS

- Group-level mADAS-Cog scores showed modest worsening over follow-up.

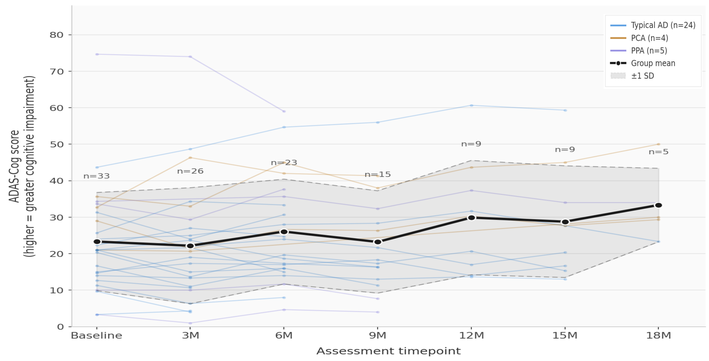


Figure 2. mADAS-Cog scores (0-80), assessed quarterly. N at each timepoint reflects participants who have reached that visit (ongoing enrollment). Error band=+/- 1 SD.

- Individual trajectories differed markedly from the group mean. Group-level summary obscures substantial individual heterogeneity (change from baseline to final available mADAS-Cog assessment across the sample ranged from −6.0 to +15.7 points).

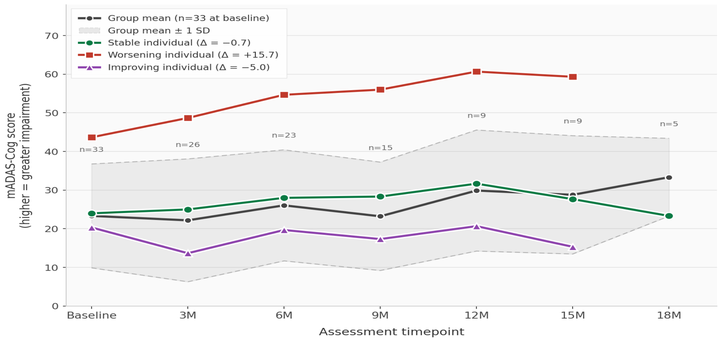


Figure 3. mADAS-Cog score trajectories (0-80) for three patients.

- Monthly neuropsychological composite scores showed considerable variability both within and across participants throughout follow-up.

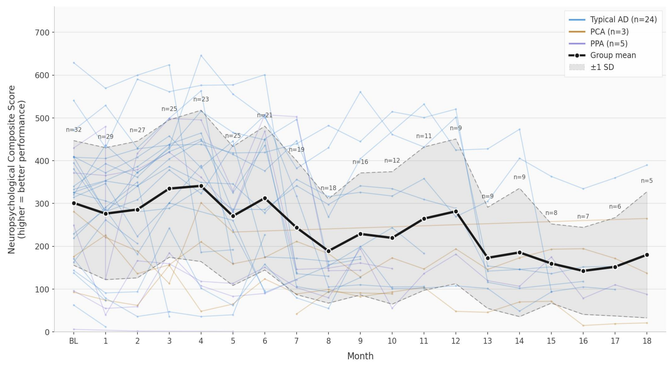


Figure 4. Monthly performance on neuropsychological battery. Individual lines=monthly composite scores for each participant. Composite score=normalized sum of five subtests (letter & category fluency; story immediate and delayed recall; paragraph reading; mental alternation; and go/no-go) administered.

- Patients show substantial fluctuation month-to-month (Individual coefficient of variation averaged 33%, range 7.7%–68.8%), a pattern undetectable with quarterly assessment alone.

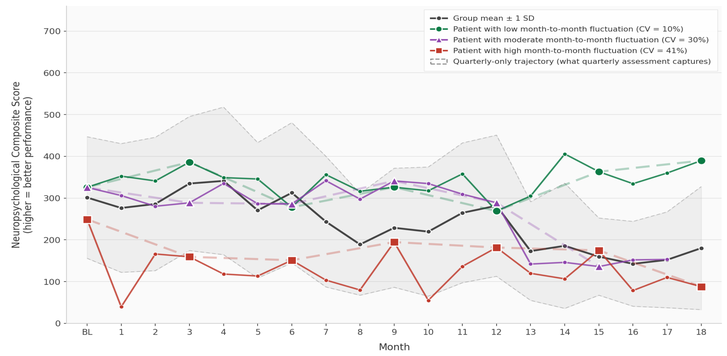


Figure 5. Monthly performance on neuropsychological battery for three patients. Dashed lines connect only the quarterly timepoints (large markers), illustrating what quarterly-only assessment would capture and what it would miss.

CONCLUSIONS

- Monthly remote neuropsychological monitoring of lecanemab-treated AD patients is feasible over 18 months with high retention across typical and atypical phenotypes.
- Quarterly assessment alone obscures substantial within-person cognitive fluctuation — a pattern invisible at standard monitoring intervals but detectable with monthly sampling.
- Group-level trajectories mask marked individual heterogeneity, underscoring that population averages are insufficient for monitoring individual treatment response.
- These findings provide a framework for individualized DMT monitoring in real-world clinical practice, where no such standard currently exists.

REFERENCES

1. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023;388(1):9–21.

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