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Drivers of Increased Healthcare Utilization and Medicare Payments During Cognitively Unimpaired (Preclinical) Alzheimer's Disease Progression



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OBJECTIVE

- To describe Medicare payment trends across the pre- and post-progression year and characterize the types of payments during the progression month (month of first documented progression).

CONCLUSION

- Medicare payments increased significantly during the progression-month compared with the pre-progression year for both Alzheimer’s disease (AD) and cognitive impairment (CI) groups.
- Progression-month payments were primarily driven by non-AD-related procedures corresponding with participants’ comorbidities.
- The observed payment pattern suggests that CI may remain unrecognized within the healthcare system until patients incur costly hospitalizations or procedures for other conditions, reflecting a broader lack of routine cognitive monitoring in usual care, even for these participants in an AD clinical trial.
- Future studies should seek to further contextualize these findings in a larger non-trial population, which might better represent the real-world heterogeneity of individuals with cognitively unimpaired AD.

Limitations

- The A4 cohort is a highly selected clinical trial population, which may limit generalizability to broader real-world cognitively unimpaired AD populations.
- Payment analyses were restricted to Medicare FFS enrollees, excluding Medicare Advantage participants.
- AD and CI diagnoses in claims data may be underreported, potentially underestimating progression events, and lack clinical detail on the magnitude and persistence of disease progression

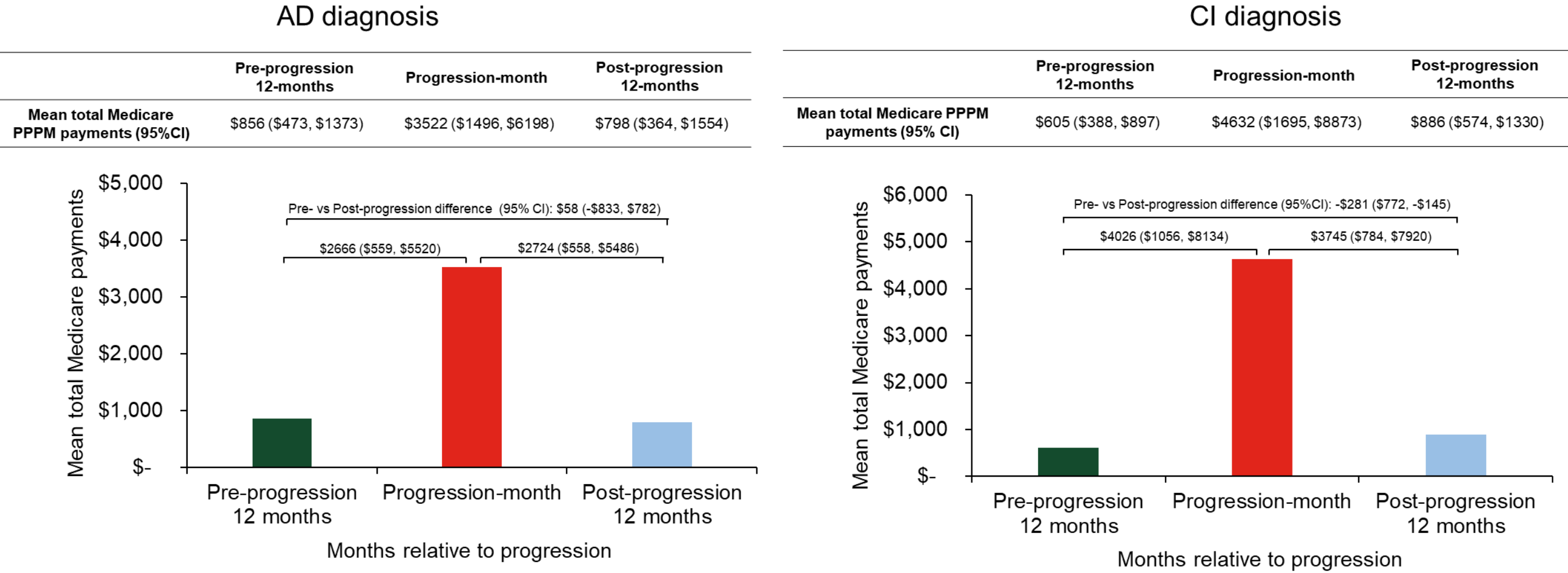
BACKGROUND

- Individuals who are cognitively unimpaired and show evidence of AD pathology (cognitively unimpaired AD) represent a critical yet understudied population in terms of healthcare resource utilization and costs.
- Prior analyses from this study have shown that progression from cognitively unimpaired to later stages of AD is linked with significantly increased Medicare payments¹, yet the specific drivers of these cost increases—and whether increased costs persist, stabilize, or return to pre-progression levels—remain poorly understood.

KEY RESULT

Medicare payments significantly increased during the progression month

- Medicare payments for the FFS cohort with AD diagnosis and CI diagnosis were significantly higher during progression month compared with pre- and post-progression months.
- Pre- and post-progression payments were not significantly different from each other.



Demographics at trial entry

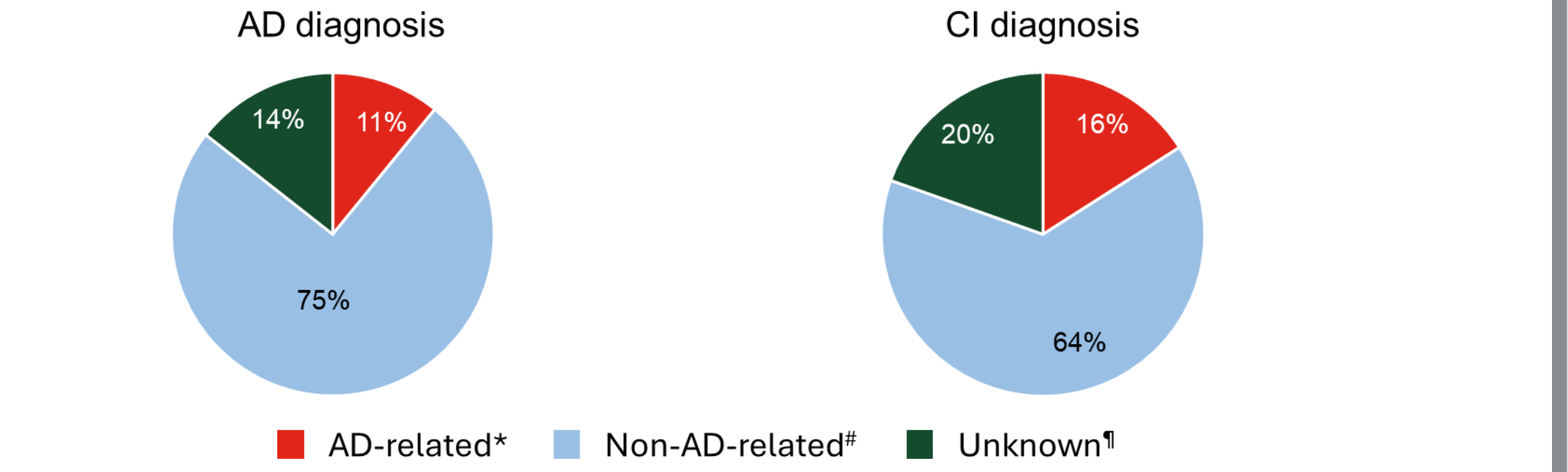
- Demographics were similar between AD and CI progressors, with both groups predominantly female and a mean age of ~72–73 at trial entry and concentrated in the Northeast.

	AD diagnosis	CI diagnosis
Gender		
Female	58%	64%
Male	42%	36%
Age in year of trial entry, mean, (SE)	71.67 (0.73)	73.24 (0.58)
Region in US		
Northeast	47%	39%
South	28%	27%
Midwest/West	25%	34%
CDR-Global, mean, (SE)*	0.22 (0.05)	0.11 (0.03)
Mini-Mental State Exam, mean, (SE)*	27.25 (0.87)	28.33 (0.45)

*Scores at time of AD or CI progression.
Abbreviations: AD, Alzheimer’s disease; CDR, Clinical Dementia Rating; CI, cognitive impairment; SE, standard error.

Progression-month payments were primarily for non-AD-related procedures

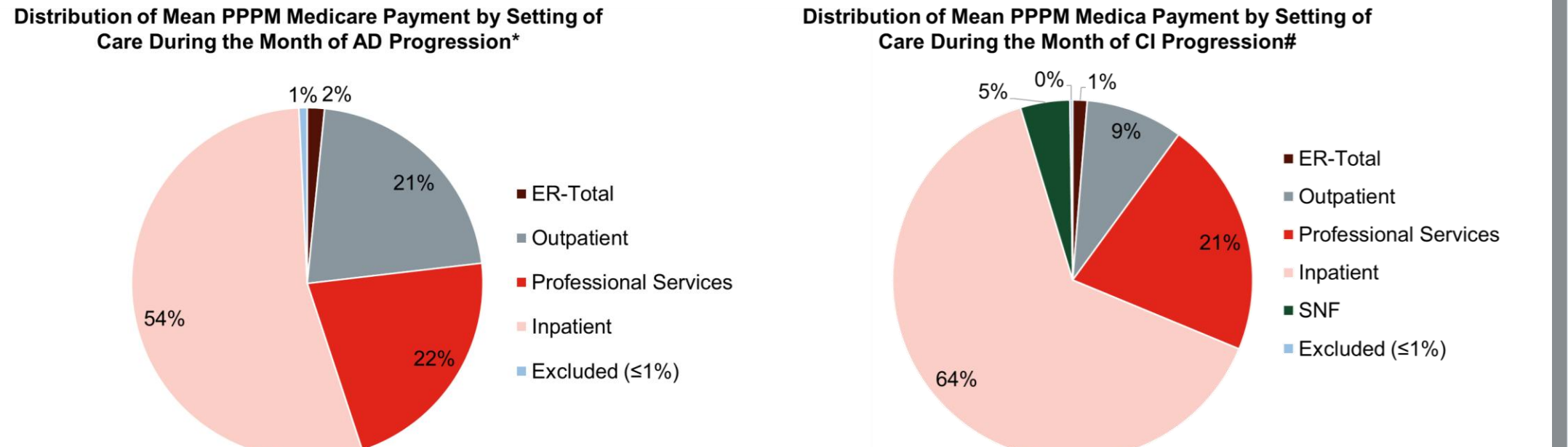
- The majority of Medicare expenditure during the progression-month was for non-AD procedures.



*AD-related procedures included neuropsychological/psychological/cognitive testing and brain imaging.
#Non-AD-related procedures accounting for 10% or more payments in the month of progression (either AD or CI diagnosis) were cancer treatment, cardiovascular procedures, emergency care/services, musculoskeletal procedures/surgery, and other surgical procedures.
†Procedures with an unknown relationship with AD, accounting for 10% or more payments in the month of progression (either AD or CI diagnosis), were evaluating and management/screening services and sleep studies.

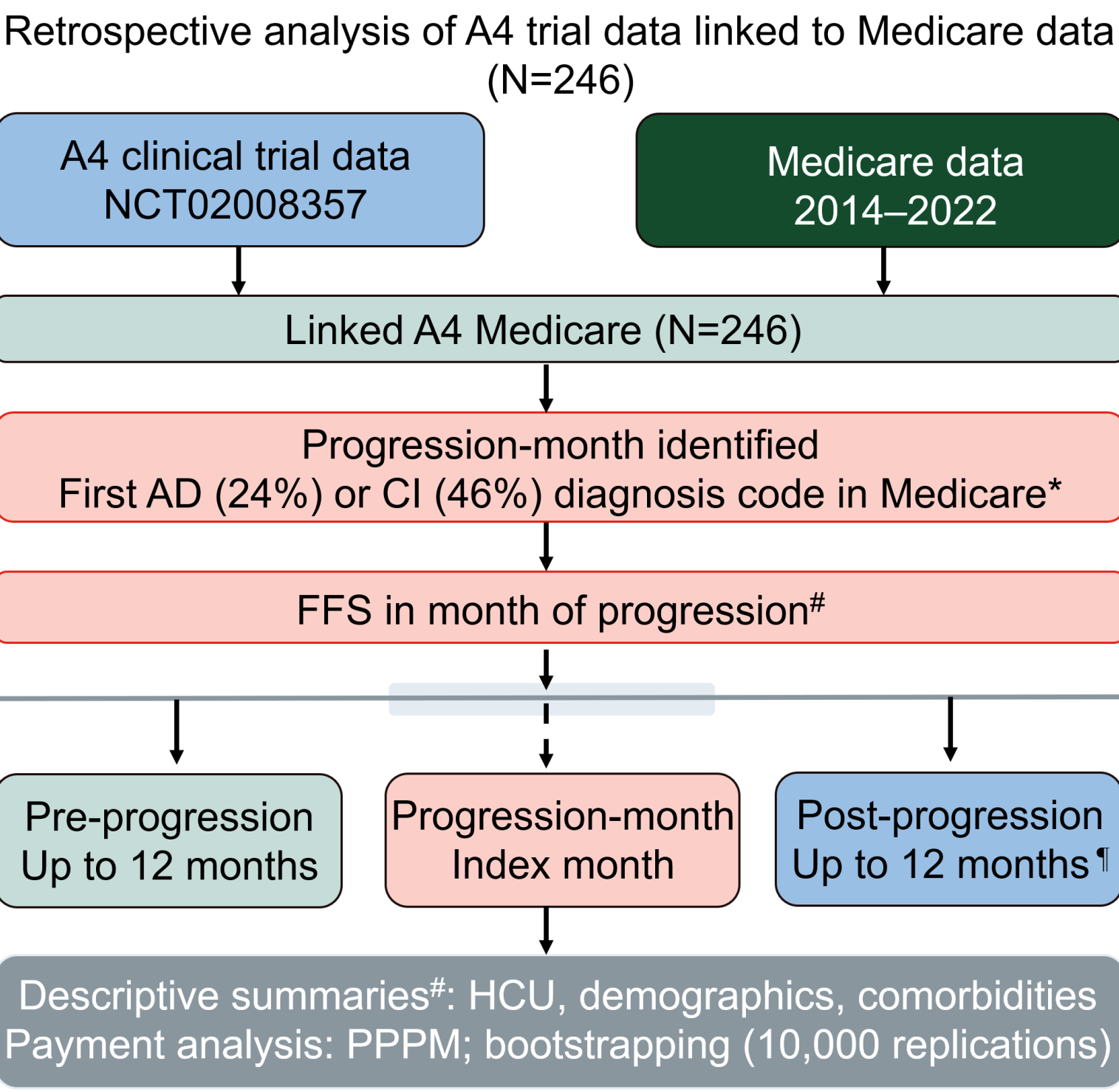
Progression-month payments were primarily in the inpatient setting

- Inpatient services accounted for the largest proportion of PPM payments during the progression-month (AD: \$1913, 95% CI: \$183, \$4323; Cognitive impairment: \$2968, 95% CI: \$386, \$6733).



*The following cost categories were excluded as each comprised 1% or less of total costs: DME (0.48%), Home Health (0.28%), Hospice (0.00%), SNF (0.00%), Other (0.00%).
#The following cost categories were excluded as each comprised 1% or less of total costs: DME (0.14%), Home Health (0.11%), Hospice (0.00%), Other (0.00%).

STUDY DESIGN

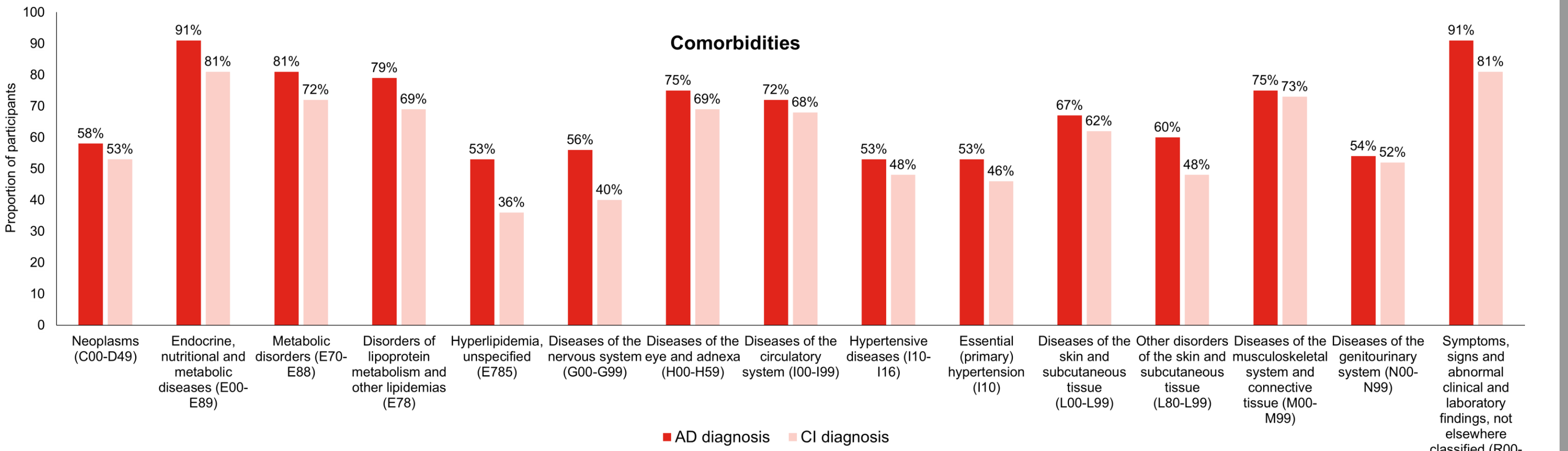


*Progression (evidence of cognitive and/or functional decline) was identified by AD or CI diagnosis codes in Medicare
#Denominators are purposefully not reported as a strategy for complying with the CMS cell suppression policy
†Pre/post-progression 12 months does not include the month of progression

RESULT

Pre-progression comorbidities

- Common pre-progression comorbidities included endocrine and metabolic disorders, lipid disorders, musculoskeletal and circulatory diseases (including hypertension), skin disorders, and nonspecific signs and symptoms, each affecting more than half of participants in both the AD and CI progression groups.



Abbreviations: A4, Anti-Amyloid Treatment in Asymptomatic Alzheimer’s Disease; AD, Alzheimer’s disease; CI, cognitive impairment; 95% CI, 95% confidence interval; CMS, cell suppression policy; DME, durable medical equipment; FFS, fee-for-service; HCU, healthcare utilization; PPM, per person per month; SE, standard error; SNF, skilled nursing facility.
References: Beyrer J, Sheff Z, Payakachat N, et al. J Prev Alzheimers Dis. April 1, 2026. doi:10.1016/j.tpad.2026.100547
Disclosures: Julie Beyrer, Zachary Sheff, Nalin Payakachat, Yun-Fei Chen, Karen C. Holdridge, and Roy Yaari are employees and shareholders of Eli Lilly and Company. Joanna Kubisiak and Angelina Lee are employees of Westat. Paul Aisen: Grants: Eli Lilly, Eisai; Consulting fees: Merck, Roche, Genentech, Abbvie, Biogen, Arrowhead, ImmunoBrain Checkpoint, AltPep, Bristol Myers Squibb, Johnson&Johnson, New Amsterdam. Michael S. Rafii: grants/contracts-Eli Lilly, Eisai; consulting fee: AC Immune, Positrgo, Aerska, Recall Therapeutics, Ainylam, Sumitomo Pharmaceutical, Lonis. Reisa A. Sperling: Grants: A4 NIH, GHR Foundation, Eli Lilly, Alzheimer’s Association, NIA, GHR Foundation, Eisai; Consulting fees: AbbVie, AC Immune, Acumen, Alector, Apellis, Biogen, Biohaven, Bristol Myers Squibb, Genentech, Ionis, Immunobrain, Janssen, Novo Nordisk, Oligomerix, Prothena, Roche, Therini, Vaxxinity, Eli Lilly, Roche. Travel and meeting support: Alzheimer’s Association, Clinical Trials in Alzheimer’s Disease, Janssen.
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