

Impact of Biomarker Modalities in the Diagnostic Evaluation of Patients with Suspected Alzheimer’s Disease: A US Retrospective Study

OBJECTIVE

- The objective of this study was to assess how amyloid biomarker modality (PET, CSF, or BBM) influences time from initial cognitive concern and initial biomarker assessment to initiation of AAT among patients undergoing evaluation for AD in a real-world US setting.

CONCLUSIONS

- This retrospective study provides real-world insights into diagnostic and therapeutic pathways for US patients with AD or MCI.
- Clinical diagnosis often occurred ahead of amyloid biomarker testing, while initiation of AATs remained limited and delayed.
- Despite a greater likelihood of subsequent confirmatory testing prior to treatment initiation, patients initially evaluated with BBMs were associated with the shortest time from initial cognitive concern to AAT initiation, suggesting BBMs may support earlier pathway entry and more efficient triage.
- CSF and PET biomarkers were associated with more frequent initiation of AATs than BBMs, highlighting opportunities to optimize diagnostic pathways and streamline patient access to therapy.
- Findings should be interpreted in the context of a retrospective analysis of administrative claims data, which lack detailed clinical information.

LIMITATIONS

- ### Data Limitations
- Omissions or miscoding may lead to misclassification of events.
 - Biomarker results were unavailable and analyses relied on procedure codes.
 - Medication codes do not confirm treatment use as prescribed.
 - Uninsured patients were not captured.

- ### Design Limitations
- The multivariate Cox model was adjusted only for observable confounders (e.g., socioeconomic status could not be quantified).
 - First events recorded may not reflect true symptom onset (e.g., amnesia may precede the first recorded visit by months or years), particularly for cognitive concern.



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Introduction

- Accurate and timely diagnosis of Alzheimer’s disease (AD) remains challenging in routine clinical practice,¹ partly due to the variability in access to and use of amyloid biomarkers such as cerebrospinal fluid (CSF) assays, positron emission tomography (PET) imaging, and blood-based biomarkers (BBMs).²
- Differences in biomarker modalities may influence time to confirmed diagnosis and subsequent treatment decisions, including care planning and initiation of anti-amyloid therapy (AAT).^{3,4}
- Real-world analyses using healthcare claims data can provide insights to streamline processes and optimize patient access to appropriate care and therapies.⁵

Methods

- This retrospective, observational study identified patients in the Optum Market Clarity Database with documented cognitive concerns (reported or observed issues in cognitive function prompting clinical evaluation) and ≥2 International Classification of Diseases (ICD) codes for AD or mild cognitive impairment (MCI) between Jan 2022 and Jun 2025.
- Eligible patients received amyloid biomarker testing by PET, CSF, or BBM and had continuous health insurance eligibility for ≥12 months prior to the initial documented cognitive concern through initiation of AAT or censoring.

Results

Time to Event Analysis

Overall Population

- The overall cohort comprised 4,001 patients who underwent initial amyloid biomarker testing using BBM (n=1,710), CSF (n=629), or PET (n=1,662) (**Table 1**).
- Mean time from initial cognitive concern to AD or MCI diagnosis and initial biomarker test was 6.8 months and 11.9 months, respectively, with most patients clinically diagnosed before biomarker testing (76.1%) (**Table 2**).

Patients Treated with AAT

- AAT was initiated in 11.9% of the overall patient population (n=475); among these, initial biomarker testing was most often PET (61.3%), followed by BBMs (20.2%) and CSF (18.5%).
- Mean time to each clinical milestone, by biomarker modality, in patients treated with AAT are summarized in **Table 3**.
- Patients treated with AATs were more likely to repeat biomarker testing after an initial BBM test (79.2%) compared with CSF (17.0%) or PET (4.1%).

Time to AAT Treatment or Censoring From Initial Amyloid Biomarker

- CSF and PET tests were associated with a higher likelihood of AAT initiation compared with BBM tests (**Figure 2**).
- In a multivariate Cox model, higher likelihood of AAT initiation was also associated with female sex, White race, and practices in southern regions (**Figure 3**).

Table 1. Overall Patient Characteristics Stratified by Initial Biomarker Modality

	Overall (n=4,001)	BBM (n=1,710)	CSF (n=629)	Amyloid PET (n=1,662)
Age, mean ±SD years	74.3 ± 8.2	75.4 ± 8.2	70.7 ± 8.6	74.6 ± 7.6
Female, n (%)	2,231 (55.8)	985 (57.6)	346 (55.0)	900 (54.2)
White, n (%)	3,094 (77.3)	1,324 (77.4)	500 (79.5)	1,270 (76.4)
Quan-CCI Score, mean ± SD (median)	2.5 ± 2.0 (2.0)	2.5 ± 2.1 (2.0)	2.3 ± 1.9 (2.0)	2.6 ± 1.9 (2)
AD or MCI diagnosis relative to biomarker, n (%)				
Before initial biomarker	3,044 (76.1)	1,134 (66.3)	471 (74.9)	1,439 (86.6)
On or after initial biomarker	957 (23.9)	576 (33.7)	158 (25.1)	223 (13.4)
Patients prescribed AAT, n (%)				
Donanemab, n (%)	131 (3.3)	32 (33.3)	13 (4.8)	86 (29.6)
Lecanemab, n (%)	344 (8.6)	64 (66.7)	75 (85.2)	205 (70.4)

AAT = anti-amyloid therapy; AD = Alzheimer’s disease; BBM = blood-based biomarker; CSF = cerebrospinal fluid; MCI = mild cognitive impairment; PET = positron emission tomography; Quan-CCI = Quan adaptation of the Charlson Comorbidity Index; SD = standard deviation

Table 2. Overall Time to Event Analysis

	Overall (n=4,001)	BBM (n=1,710)	CSF (n=629)	Amyloid PET (n=1,662)
Time from initial cognitive concern, mean ± SD months				
To initial AD or MCI diagnosis	6.8 ± 7.4	6.7 ± 7.7	6.7 ± 6.6	6.9 ± 7.4
To initial biomarker	11.9 ± 9.4	10.8 ± 9.8	10.5 ± 7.9	13.5 ± 9.4
Time from initial biomarker, mean ± SD months				
To initial AD or MCI diagnosis*	1.8 ± 3.2	1.9 ± 3.3	2.8 ± 4.1	0.9 ± 1.8
Time from initial AD or MCI diagnosis, mean ± SD months				
To initial biomarker	7.3 ± 7.8	7.1 ± 8.2	6.0 ± 6.1	7.8 ± 7.8

AAT = anti-amyloid therapy; AD = Alzheimer’s disease; BBM, blood-based biomarker; CSF = cerebrospinal fluid; MCI = mild cognitive impairment; PET = positron emission tomography; SD = standard deviation
*AD or MCI diagnosis on or after biomarker test
References 1. Atri A, et al. *Alzheimers Dement*. 2025;21(1):e14335. 2. Schindler SE, et al. *Nat Rev Neurol*. 2024;20(7):426-439. 3. Largent EA, et al. *Neurology*. 2023;100(21):1010-1019. 4. VandeVrede L, Schindler SE. *Alzheimers Dement*. 2025;21(1):e14201. 5. Unukade RP. *JCST*. 2025;7(8):223-229. **Disclosures** AH and AHM: paid consultants for Biogen; SES: unpaid consultant for Biogen; LW, KF, and NB: employees of Biogen. **Acknowledgments** This study was funded by Biogen. Medical writing support was provided by Panacea85 Ltd supported by Biogen.

- Cohort assignment (PET, CSF, or BBM) was based on the initial amyloid biomarker assessment. The preceding 12 months were used to assess baseline characteristics, and patient follow-up extended until AAT initiation or censoring (**Figure 1**).
- Among biomarker-tested patients, the primary outcome was time from initial cognitive concern to initial AAT infusion. Secondary objectives included time from initial biomarker test to AAT initiation, and time from initial cognitive concern to biomarker testing.

Figure 1. Study Design

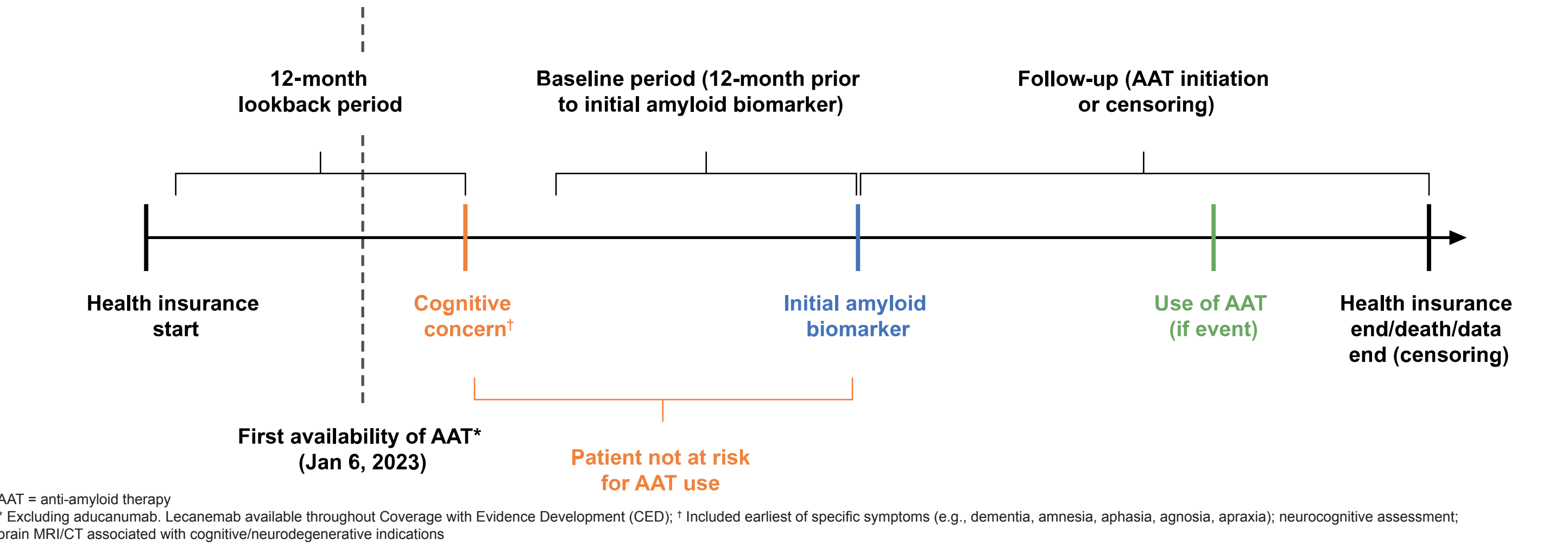


Table 3. Time to Event Analysis in Patients Treated With AAT

	Overall (N=475)	BBM (n=96)	CSF (n=88)	Amyloid PET (n=291)
Time from initial cognitive concern, mean ± SD months				
To initial AD or MCI diagnosis	6.2 ± 6.4	6.3 ± 6.0	5.9 ± 6.0	6.3 ± 6.7
To initial biomarker	11.0 ± 8.6	8.8 ± 8.7	10.4 ± 7.2	11.9 ± 8.8
To initial AAT infusion	15.5 ± 9.0	15.1 ± 9.1	15.9 ± 8.1	15.6 ± 9.2
Time from initial biomarker, mean ± SD months				
To initial AD or MCI diagnosis*	1.2 ± 2.0	1.7 ± 2.5	1.1 ± 1.4	0.8 ± 1.5
To initial AAT infusion	4.6 ± 3.3	6.3 ± 4.2	5.5 ± 3.8	3.7 ± 2.3
Time from initial AD or MCI diagnosis, mean ± SD months				
To initial biomarker	6.7 ± 7.2	6.7 ± 8.2	5.3 ± 5.2	7.1 ± 7.5
To initial AAT infusion	9.3 ± 7.5	8.8 ± 7.5	10.0 ± 6.3	9.3 ± 7.9

AAT = anti-amyloid therapy; AD = Alzheimer’s disease; BBM, blood-based biomarker; CSF = cerebrospinal fluid; MCI = mild cognitive impairment; PET = positron emission tomography; SD = standard deviation
*AD or MCI diagnosis on or after biomarker test

Figure 2. Overall Population Kaplan-Meier for Time From Initial Biomarker to AAT Infusion or Censoring

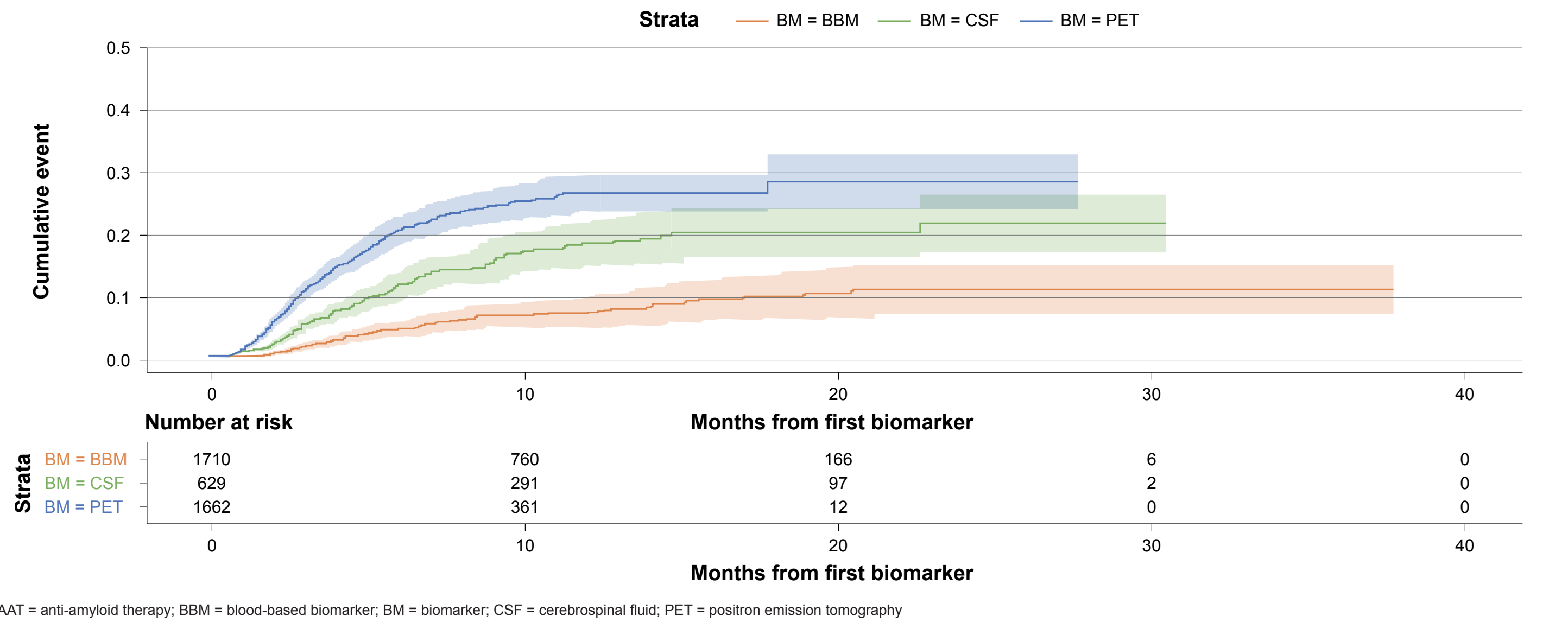
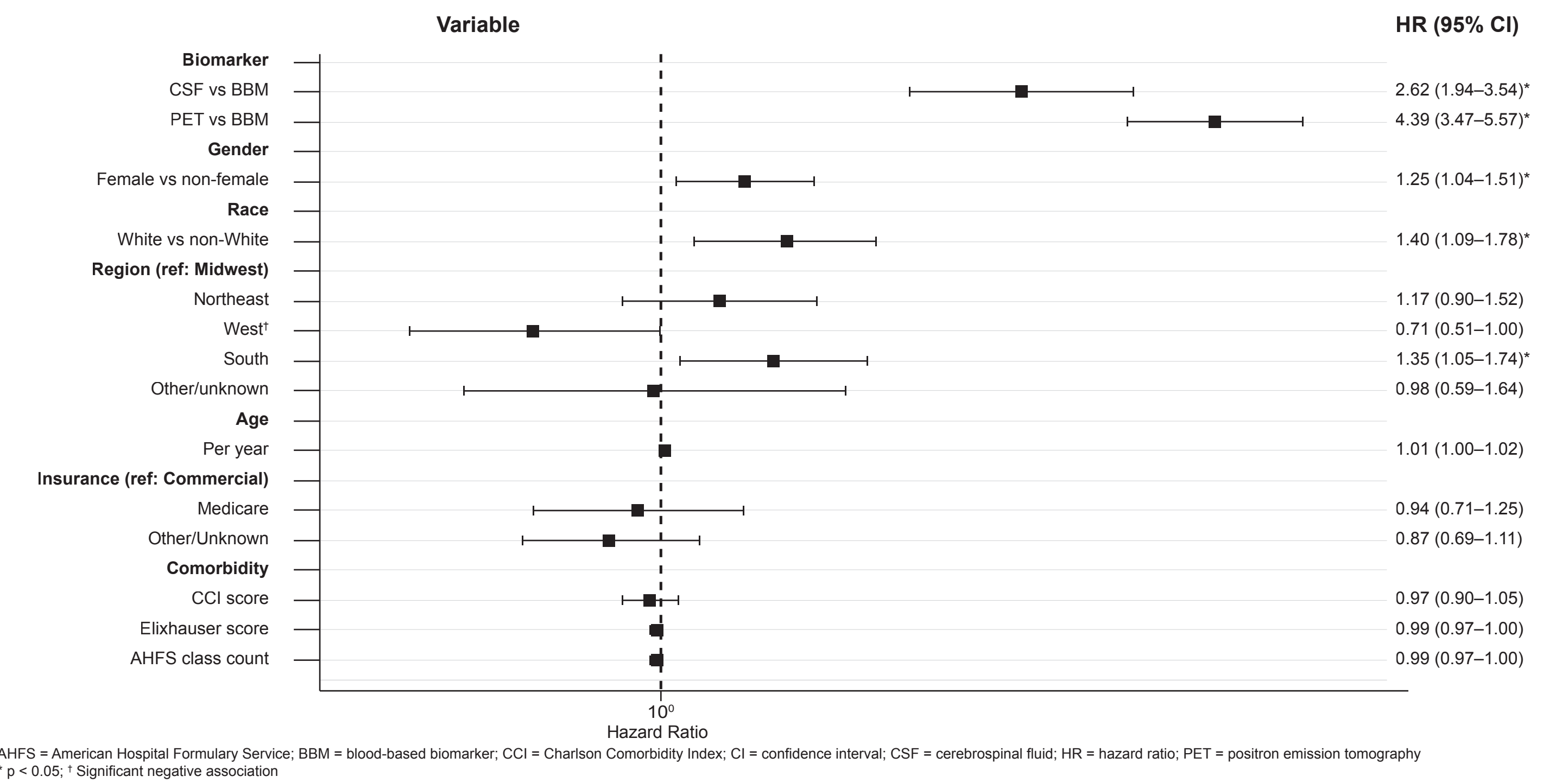


Figure 3. Overall Population Forest Plot for Time From Initial Biomarker to AAT Infusion or Censoring (Cox Model)



AHFS = American Hospital Formulary Service; BBM = blood-based biomarker; CCI = Charlson Comorbidity Index; CI = confidence interval; CSF = cerebrospinal fluid; HR = hazard ratio; PET = positron emission tomography
* p < 0.05; † Significant negative association