



Effects of neuropathology and sex on symptomatic pharmacological treatment of dementia of Alzheimer type

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BACKGROUND

Acetylcholinesterase inhibitors and memantine are recommended therapies for dementia of the Alzheimer type (DAT). However, many patients with the clinical diagnosis of DAT do not exhibit Alzheimer's disease (AD) pathology. It remains unclear whether these patients benefit from treatment with these drugs.

METHOD

This cohort study used longitudinal data from The National Alzheimer's Coordinating Center (NACC) Data Set. Eligibility criteria included clinical diagnosis of DAT, age 51-90 years, symptoms onset < 8 years, dementia diagnosis at baseline or during follow-up, start of symptomatic drug treatment within 15 months after baseline or no treatment, and available post-mortem neuropathology report. Eligible treated and untreated participants were matched on the propensity score for baseline characteristics and AD pathology. Mixed models with estimated marginal means were applied to assess the effect of treatment on trajectories of symptoms in the presence or absence of AD pathology. Sex effects were additionally analyzed.

RESULTS

Of the full Data Set, 427 participants met eligibility criteria of which 212 with a total of 840 data points were matched and included in the analyses. After follow-up of up to 48 months, no significant differences in symptomatic trajectories were observed between those with and without AD pathology in both treated and untreated groups. The decline was more pronounced in untreated male vs. female participants after 48 months. Treated male participants performed better than untreated male participants from the 24-month follow-up onward, a difference not observed in female participants. These sex effects were independent of the presence or absence of AD pathology. Sensitivity analyses confirmed the robustness of the results.

CONCLUSION

This study does not confirm effects of acetylcholinesterase inhibitors or memantine on the symptomatic course in individuals with the clinical diagnosis of DAT, irrespective of underlying AD pathology. The observed sex-specific treatment effects warrant further confirmatory studies.

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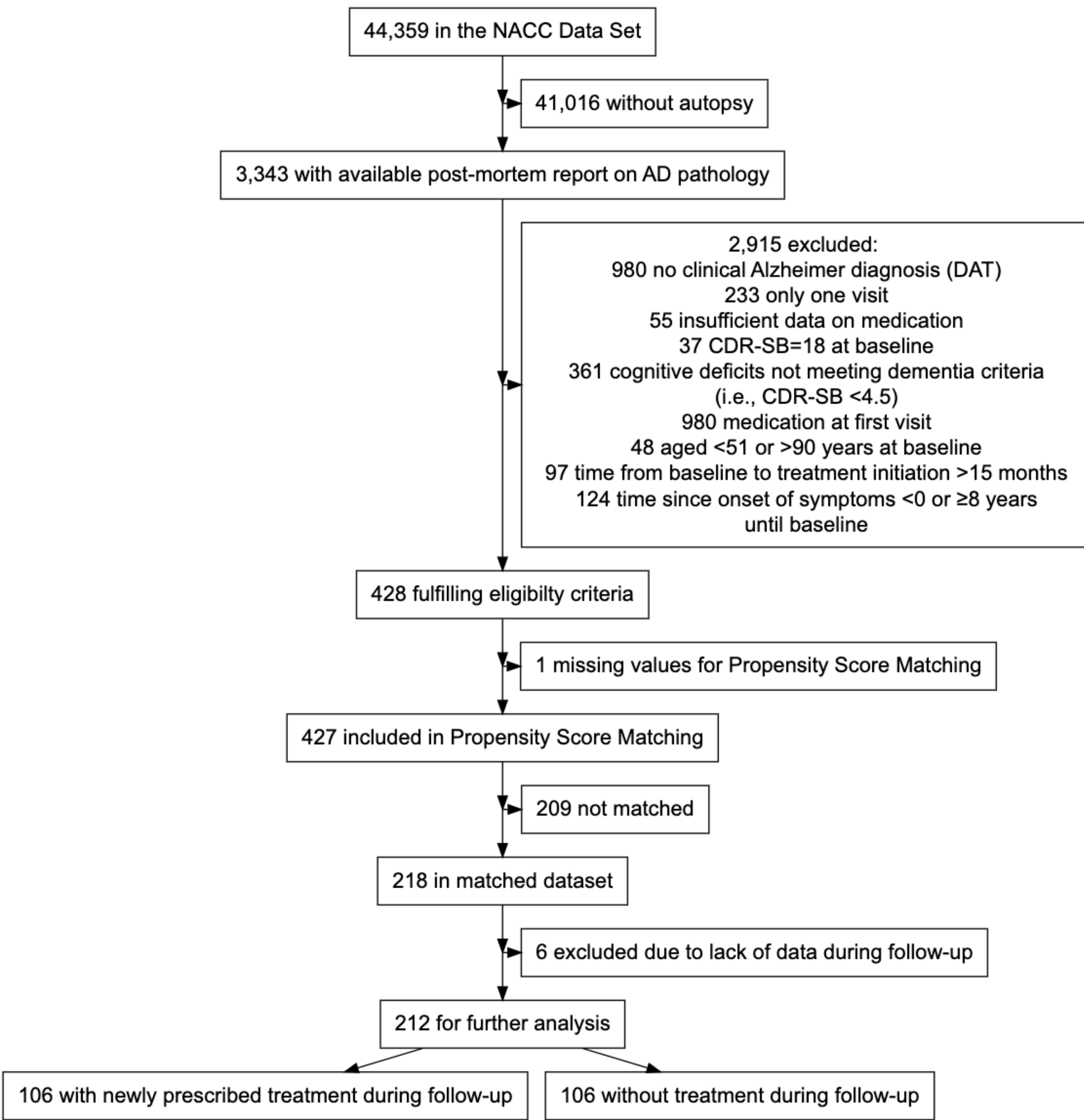


Figure 1. Selection of participants from NACC Data Set for data processing.

Characteristics of matched participants (N = 212)	Treated (N = 106)	Untreated (N = 106)
Age – yr		
at baseline	76.8 ± 8.9	77.0 ± 8.9
at death*	83.7 ± 8.8	83.4 ± 9.4
Sex (Female) – no. (%)	52 (49.1)	50 (47.2)
Race (White) – no. (%)	104 (98.1)	98 (92.5)
Education – yr*	15.6 ± 3.1	15.6 ± 2.9
Marriage status at baseline – no. (%)*		
Married or equivalent	76 (71.7)	70 (66.0)
Living alone or equivalent	30 (28.3)	36 (34.0)
Body mass index at baseline (kg/m ²)*	25.4 ± 4.2	25.5 ± 4.4
Time since onset of symptoms – yr	3.5 ± 1.9	3.4 ± 1.8
CDR-SB score at baseline		
Mean	3.5 ± 3.0	3.5 ± 3.0
Range	0.0 to 16.0	0.0 to 16.0
CDR-SB score at last visit*		
Mean	12.1 ± 4.5	11.9 ± 4.8
Range	4.5 to 18.0	4.5 to 18.0
Time interval (first visit to baseline, mo)*	17.7 ± 22.4	n.a.
Time interval (baseline to following visit, mo)*	12.5 ± 1.5	n.a.
Follow-up time (baseline to last visit) – mo*	61.3 ± 30.1	58.7 ± 34.2
AD pathology – no. (%)	83 (78.3)	83 (78.3)
Braak Stage* – no. (%)		
0	4 (3.8)	5 (4.7)
1	4 (3.8)	6 (5.7)
2	11 (10.4)	5 (4.7)
3	4 (3.8)	10 (9.4)
4	8 (7.5)	10 (9.4)
5	25 (23.6)	33 (31.1)
6	50 (47.2)	37 (34.9)

*Participants not matched on these variables

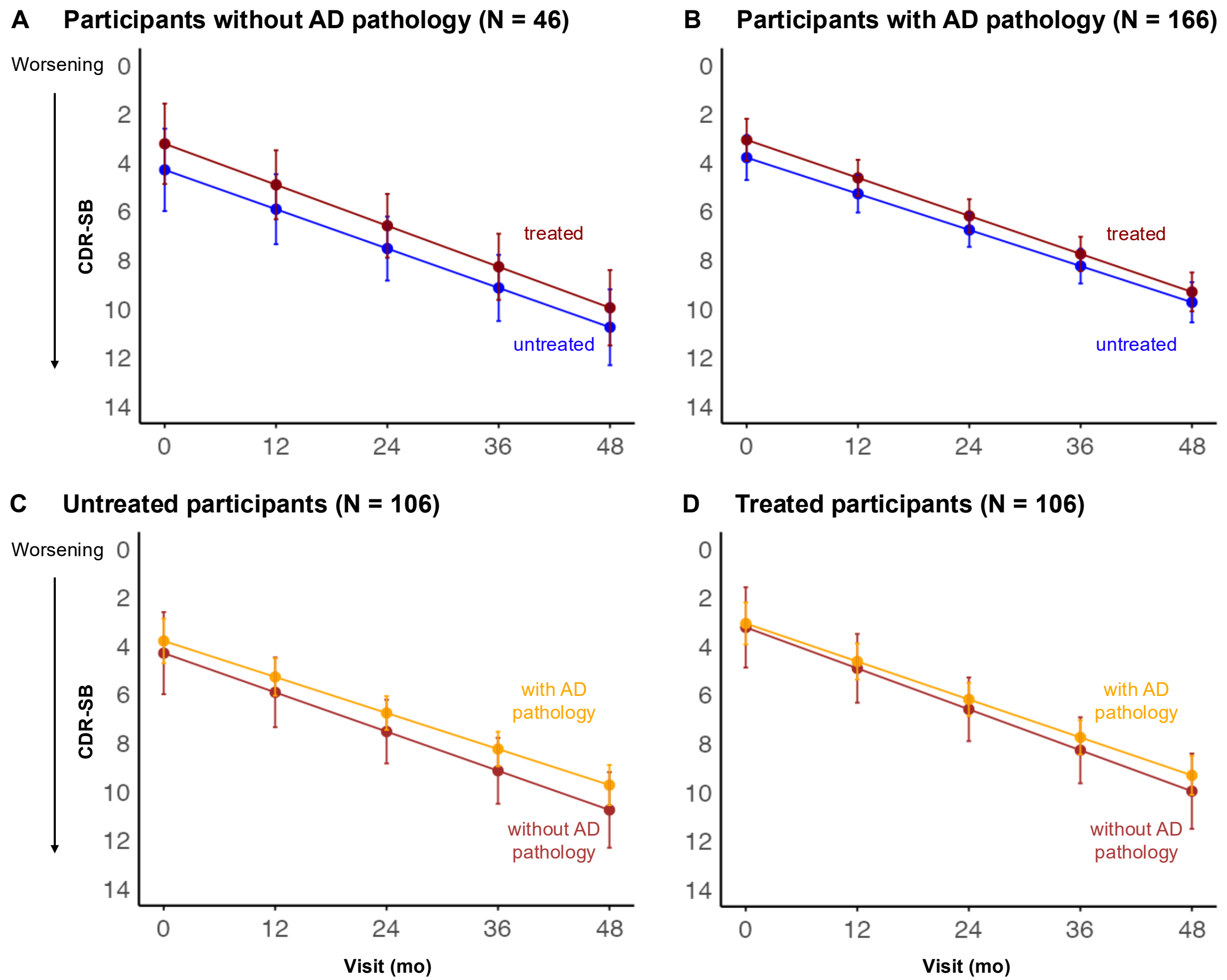


Figure 2: Symptomatic trajectories of matched participants stratified by AD pathology (A and B) and anti-dementia drug treatment (C and D). Points represent Estimated Marginal Means with 95% confidence intervals indicated by error bars, connected by solid lines to illustrate trends over time.

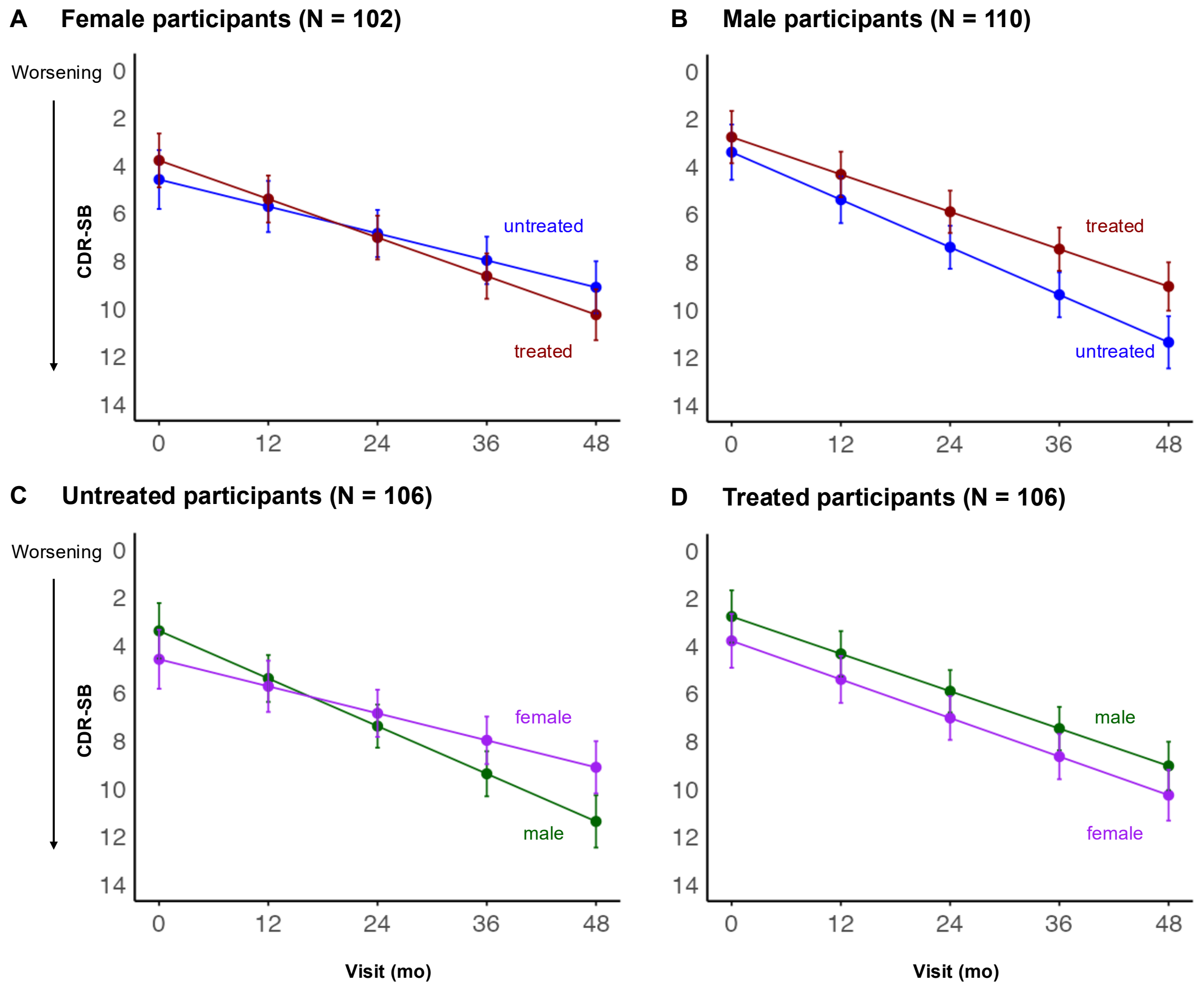


Figure 3: Symptomatic trajectories of matched participants stratified by sex (A and B) and anti-dementia drug treatment (C and D). Points represent Estimated Marginal Means with 95% confidence intervals indicated by error bars, connected by solid lines to illustrate trends over time.

Participants' co-pathologies – no. (%)*	Treated (N = 106)	Untreated (N = 106)
Lewy body pathology	52 (49.1)	36 (34.0)
Hippocampal sclerosis	25 (23.6)	14 (13.2)
Infarcts and lacunes	13 (12.3)	23 (21.7)
FTLD with tau pathology or other tauopathy	13 (12.3)	23 (21.7)
Single/multiple old hemorrhages	3 (2.8)	3 (2.8)
FTLD-tau subtype – Pick's disease	0 (0.0)	2 (1.9)

*P = 0.0148 (Fisher's Exact Test)