

BACKGROUND

- Alzheimer’s disease (AD) co-pathology is associated with faster cognitive decline and shorter survival in dementia with Lewy bodies^{1,2}
- The prevalence and prognostic significance of AD co-pathology in frontotemporal dementia (FTD) is largely unknown
- Prognostic biomarkers are needed to aid clinical management and trial design

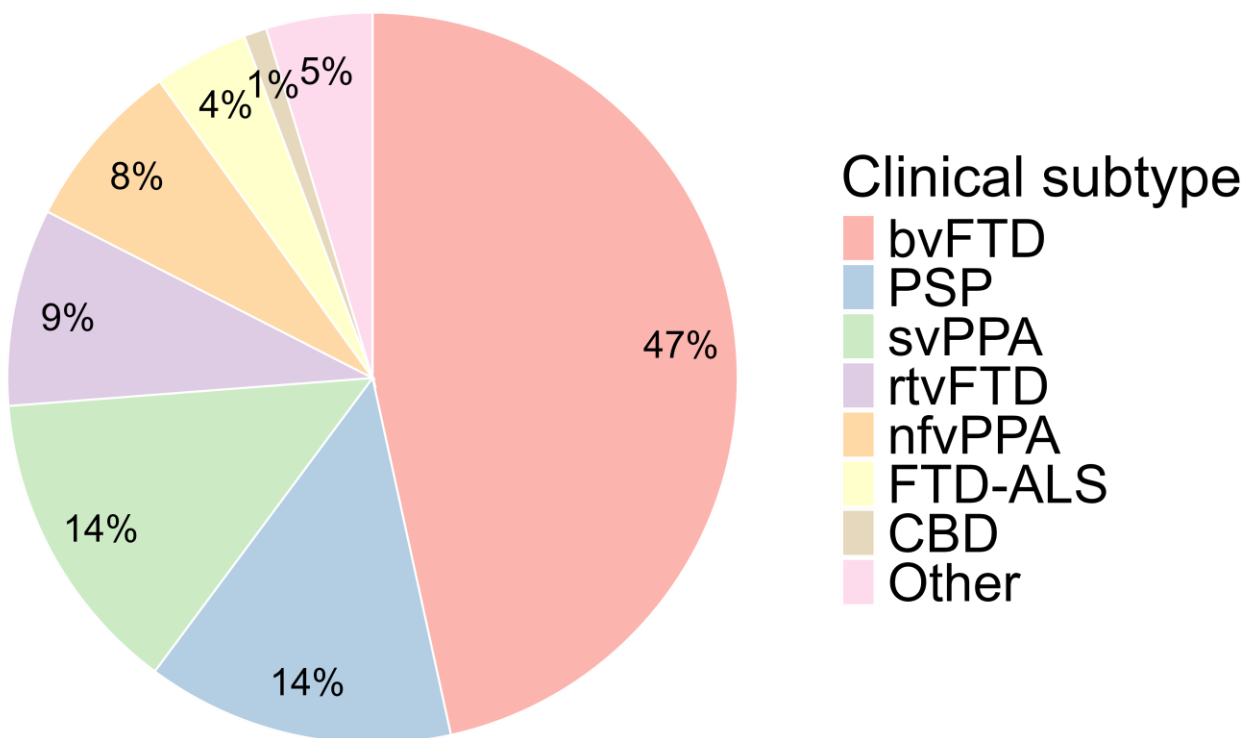
AIM

To assess the prevalence and impact of AD co-pathology, reflected by amyloid PET or cerebrospinal fluid biomarkers, on survival in FTD

METHODS

Population

- 590 patients from the Amsterdam Dementia Cohort with a clinical diagnosis in the frontotemporal lobar degeneration (FTLD) spectrum
- Subset of 54 patients with pathological confirmation of FTLD as the primary pathology



Biomarkers

- Amyloid status based on available biomarkers (hierarchical):
 - Amyloid PET, OR
 - CSF p-tau/Aβ42 ratio, OR
 - CSF Aβ42

Definitions

- Survival: interval from first memory clinic visit to death
- Censoring: at last clinical follow-up

Analysis

- Cox proportional hazards models: associations between amyloid status and survival
- Stratification by clinical subtype for the four largest subgroups

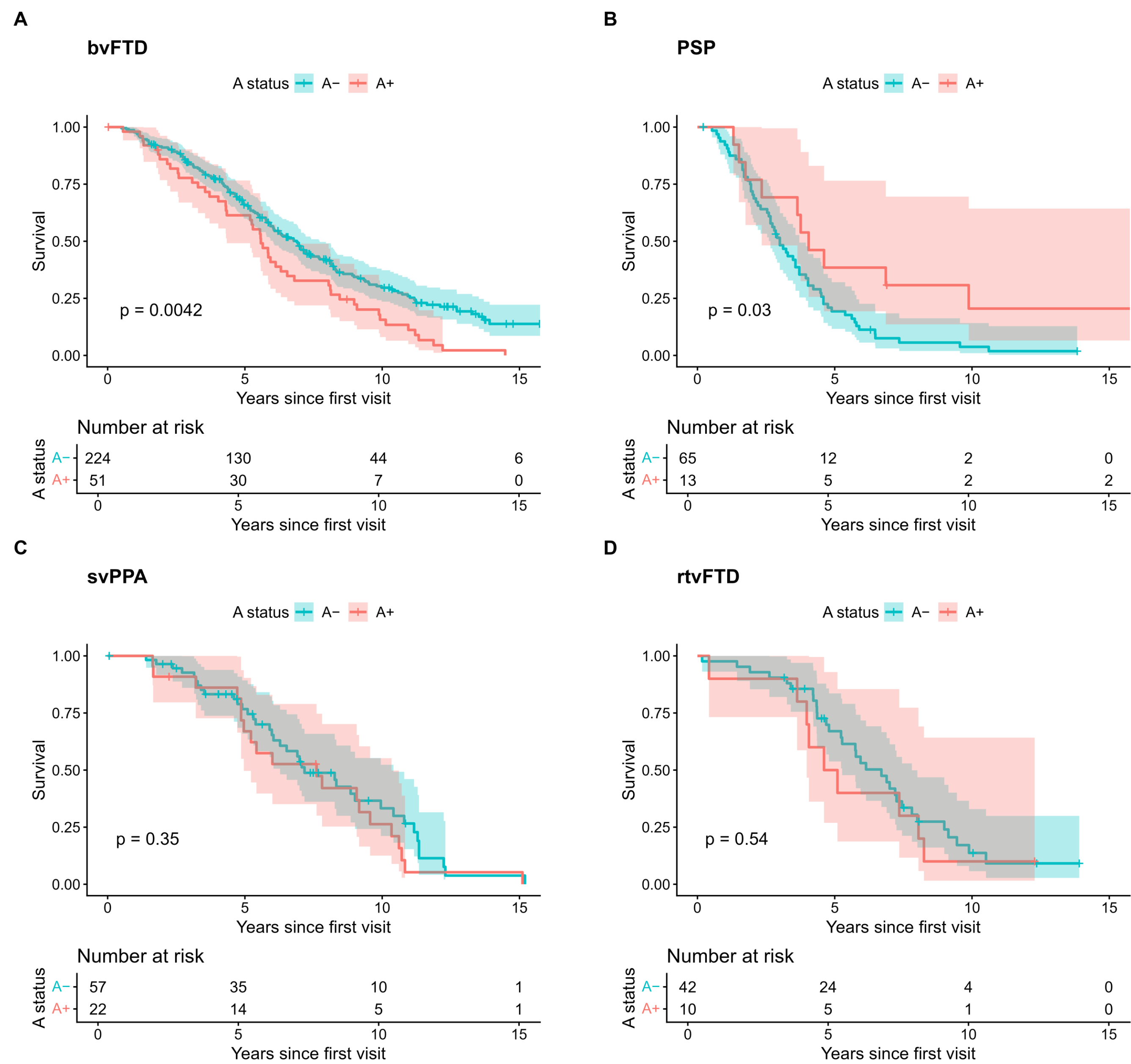
DEMOGRAPHICS AND PREVALENCE OF AD CO-PATHOLOGY

Variable	Total A-	Total A+	p	bvFTD A-	bvFTD A+	p	PSP A-	PSP A+	p	svPPA A-	svPPA A+	p	rtvFTD A-	rtvFTD A+	p
N	473	117 (25%)		224	52 (19%)		67	13 (16%)		57	23 (29%)		42	10 (19%)	
Female sex, n (%)	207 (43.8)	53 (45.3)		93 (41.5)	19 (36.5)		31 (46.3)	10 (76.9)		26 (45.6)	10 (43.5)		13 (31.0)	1 (10.0)	
Age (years), mean (sd)	63.2 (7.9)	65.3 (8.3)	*	61.9 (8.5)	64.2 (10.2)		66.8 (6.0)	68.1 (4.4)		61.3 (5.5)	65.0 (7.1)	*	64.5 (6.9)	64.3 (7.5)	
MMSE score, median [IQR]	25.0 [23.0, 27.0]	25.0 [21.0, 27.0]		25.0 [22.5, 27.0]	25.0 [20.0, 27.0]		25.0 [23.0, 28.0]	23.0 [21.8, 26.2]		25.0 [20.0, 28.0]	23.5 [18.8, 27.2]		26.0 [23.8, 28.0]	25.5 [23.5, 27.8]	
FAB score, median [IQR]	14 [11, 16]	13 [10, 16]		14 [11, 16]	12 [9, 16.5]		13 [11, 14]	13 [9, 14]		14 [13, 16]	13 [11, 15.5]		16 [13, 17]	16 [14.5, 17]	
APOE ε4 status, n (%)															
Homozygous ε4	7 (1.7)	6 (6.7)	***	1 (0.5)	3 (7.7)	**	1 (1.8)	0 (0.0)		3 (6.0)	0 (0.0)	*	0 (0.0)	2 (22.2)	**
Heterozygous ε4	109 (26.9)	37 (41.1)		56 (29.6)	18 (46.2)		16 (28.1)	5 (45.5)		9 (18.0)	8 (50.0)		10 (29.4)	4 (44.4)	
No ε4	289 (71.4)	47 (52.2)		132 (69.8)	18 (46.2)		40 (70.2)	6 (54.5)		38 (76.0)	8 (50.0)		24 (70.6)	3 (33.3)	

* ≤0.05; ** ≤0.01; *** ≤0.001

Amyloid status was determined using the following hierarchical approach based on data availability: amyloid PET (N = 94), CSF p-tau/Aβ42 ratio (N = 476), CSF Aβ42 levels alone (N = 17), or postmortem neuropathological assessment (N = 3). Amyloid status was defined as A- in case of absent ADNC (N = 2) or A+ in case of high ADNC (N = 1). Participants with low/intermediate ADNC (N = 3) or unscored ADNC due to incomplete ABC scores (N = 1) were excluded from analysis.

SURVIVAL ANALYSIS ACROSS FTLD SPECTRUM



OVERALL SURVIVAL

Overall median survival 4.7 [IQR 2.7-7.2] years

COX PROPORTIONAL HAZARDS

The association between Aβ status and survival differed significantly across clinical subtypes (p < 0.001)

Cohort	N	Events	Cox model	HR	95% CI	p
Total	586	456	Unadjusted	1.14	1.00-1.54	0.257
			Adjusted for clinical subtype, age and sex	1.07	0.85-1.34	0.581
bvFTD subgroup	275	203	Unadjusted	1.60	1.16-2.22	0.005
			Adjusted for age and sex	1.44	1.04-2.01	0.030
PSP subgroup	78	73	Unadjusted	0.48	0.24-0.94	0.033
			Adjusted for age and sex	0.46	0.23-0.91	0.026
svPPA subgroup	79	58	Unadjusted	1.29	0.75-2.24	0.356
			Adjusted for age and sex	1.09	0.60-1.96	0.775
rtvFTD subgroup	52	41	Unadjusted	1.26	0.60-2.66	0.536
			Adjusted for age and sex	1.48	0.70-3.13	0.310

CONCLUSION

- AD co-pathology was present in 25% of individuals with a clinical diagnosis of FTD
- AD co-pathology was associated with **shorter survival in bvFTD**, whereas it was associated with **longer survival in PSP**
- AD biomarker assessment may improve patient counselling in bvFTD and PSP
- These findings suggest potential benefit of combining amyloid-targeted with FTD-specific disease-modifying therapies, warranting investigation in future clinical trials