

# The combined impact of copathologies in dementia with Lewy bodies: a longitudinal study on survival and clinical outcomes

Juliette L. van Alphen<sup>1,2</sup>, Ezra Parsan<sup>3</sup>, Lyduine E. Collij<sup>2,4</sup>, Charlotte E. Teunissen<sup>2,5</sup>, Wiesje M. van der Flier<sup>2,6,7,8</sup>, Afina W. Lemstra<sup>1,2</sup>



j.l.vanalphen@amsterdamumc.nl



<sup>1</sup> Amsterdam Alzheimer Center, Amsterdam University Medical Centers, Amsterdam, The Netherlands.  
<sup>2</sup> Amsterdam Neuroscience, Neurodegeneration program, Amsterdam UMC, Amsterdam, The Netherlands.  
<sup>3</sup> Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.  
<sup>4</sup> Department of Radiology & Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands.  
<sup>5</sup> Neurochemistry Laboratory, Department of Laboratory Medicine, Amsterdam Neuroscience, Neurodegeneration, Amsterdam UMC, VU University Amsterdam, the Netherlands.  
<sup>6</sup> Department of Epidemiology & Biostatistics, Amsterdam Neuroscience, Amsterdam UMC, Amsterdam, The Netherlands.  
<sup>7</sup> Alzheimer Nederland, Amersfoort, the Netherlands.  
<sup>8</sup> Amsterdam Public Health, Amsterdam, the Netherlands.

## BACKGROUND

- Comorbid Alzheimer's disease (AD) and cerebral small vessel disease (CSVD) are common in DLB<sup>1,2</sup>
- Both AD and CSVD have been shown to **individually** affect clinical phenotype and prognosis<sup>3-5</sup>
- Little is known about their combined impact using ***in vivo* biomarkers**

## AIM

To investigate if comorbid Alzheimer's disease **and** cerebral small vessel disease have a **combined clinical impact** in dementia with Lewy bodies

## METHODS

### Amsterdam Dementia Cohort/DEVELOP-cohort (n=297)

- MCI-LB/DLB<sup>6-8</sup>
- Availability of CSF and/or amyloid-PET results
- Availability of MRI and/or CT results
- Availability of follow-up data

pure DLB  
(n=118)

DLB+AD  
(n=127)

DLB+CSVD  
(n=16)

DLB+AD+CSVD  
(n=36)

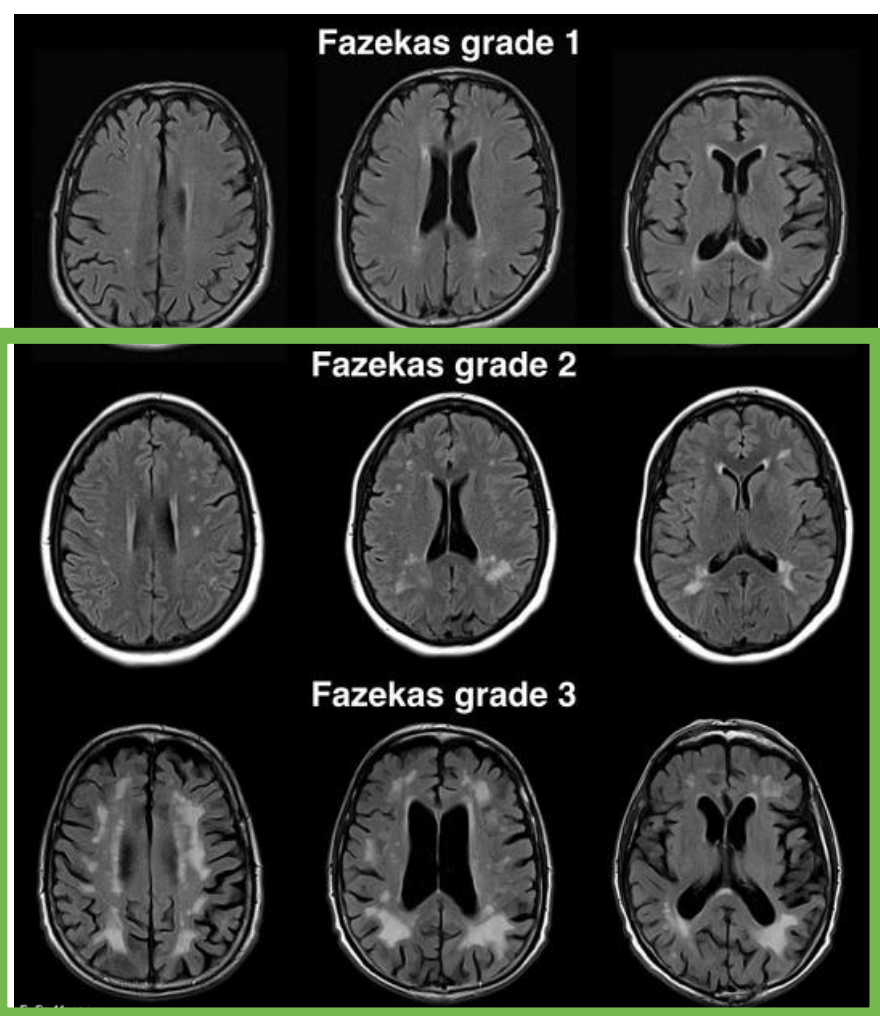
### Alzheimer's disease

abnormal CSF  
ptau181/Aβ<sub>42</sub>-ratio  
and/or  
positive amyloid PET-  
scan

### Outcome measures

global cognitive  
functioning  
MMSE

### Cerebral small vessel disease



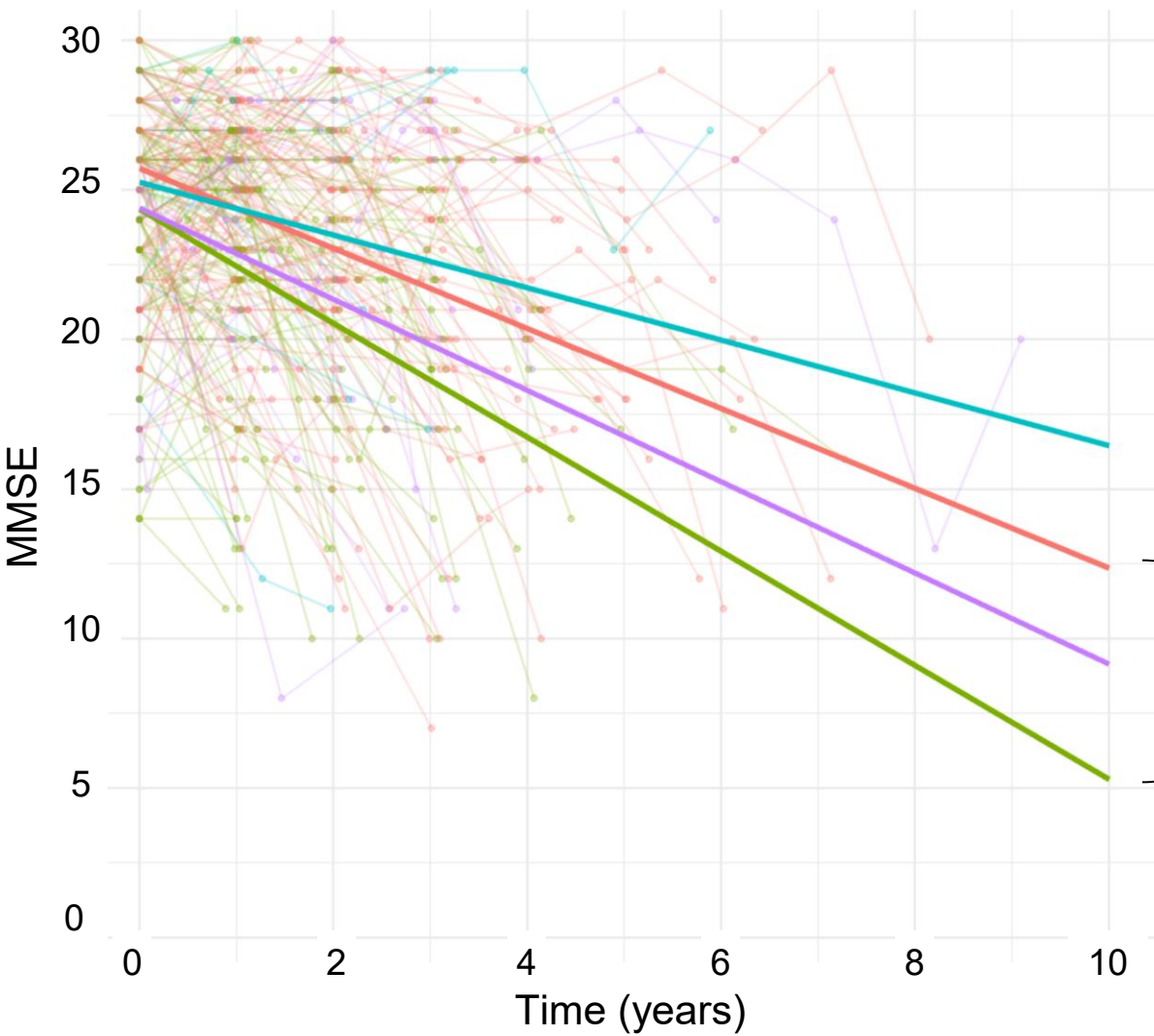
motor functioning  
MDS-UPDRS III



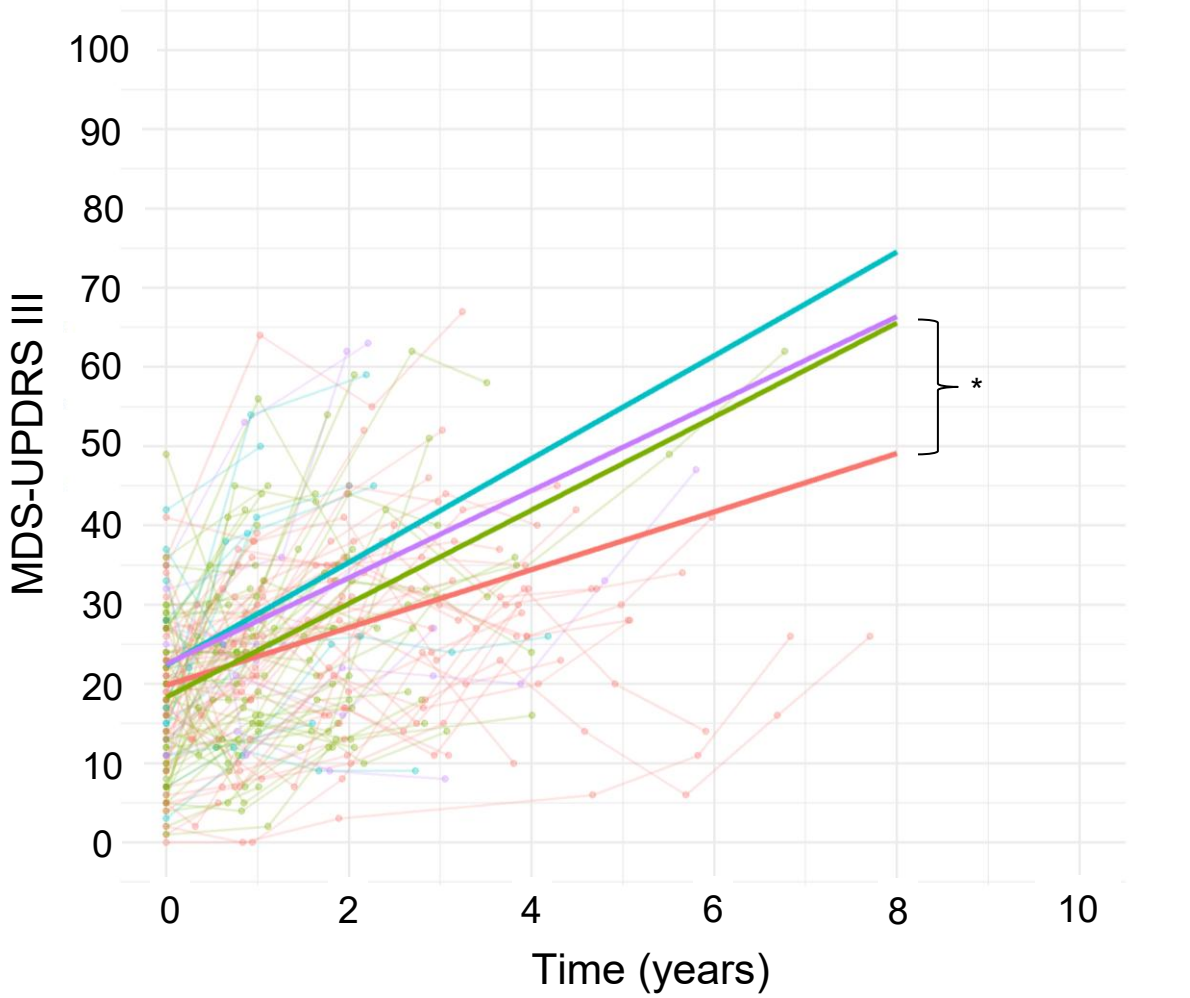
mortality

## RESULTS

|                               | full cohort<br>(n=297) | pure DLB<br>(n=118) | DLB+AD<br>(n=127) | DLB+CSVD<br>(n=16) | DLB+AD<br>+CSVD<br>(n=36) | p-value |
|-------------------------------|------------------------|---------------------|-------------------|--------------------|---------------------------|---------|
| <b>DEMOGRAPHIC</b>            |                        |                     |                   |                    |                           |         |
| Age                           | 68±6                   | 66±6                | 70±6              | 69±6               | 71±6                      | <.001   |
| Sex, female                   | 55/297 (19%)           | 11/118 (9%)         | 31/127 (24%)      | 4/16 (25%)         | 9/36 (25%)                | 0.012   |
| Years of education            | 12±3                   | 11±3                | 12±3              | 11±3               | 12±3                      | 0.154   |
| <b>BIOLOGICAL</b>             |                        |                     |                   |                    |                           |         |
| APOE-ε4 carrier               | 139/254 (55%)          | 41/110 (37%)        | 71/101 (70%)      | 5/13 (38%)         | 22/30 (73%)               | <.001   |
| Abnormal DAT-scan             | 134/158 (85%)          | 54/63 (86%)         | 54/66 (82%)       | 9/11 (82%)         | 17/18 (94%)               | 0.06    |
| <b>CLINICAL</b>               |                        |                     |                   |                    |                           |         |
| <b>core clinical features</b> |                        |                     |                   |                    |                           |         |
| CognFluc                      | 36/129 (28%)           | 8/49 (16%)          | 19/61 (31%)       | 4/8 (50%)          | 5/11 (45%)                | 0.20    |
| VisHall                       | 101/256 (39%)          | 31/102 (30%)        | 53/111 (48%)      | 3/16 (19%)         | 14/27 (52%)               | 0.04    |
| RBD                           | 92/124 (74%)           | 43/47 (91%)         | 38/58 (66%)       | 7/8 (88%)          | 4/11 (36%)                | <0.001  |
| parkinsonism                  | 194/237 (82%)          | 82/99 (83%)         | 80/97 (82%)       | 12/14 (86%)        | 20/27 (74%)               | 0.73    |
| MMSE                          | 23±4                   | 24±4                | 23±5              | 24±4               | 23±4                      | 0.644   |
| MoCA                          | 20±5                   | 21±4                | 20±5              | 21±5               | 18±6                      | 0.523   |
| MDS-UPDRS III                 | 19±11                  | 19±11               | 18±11             | 20±12              | 21±13                     | 0.952   |



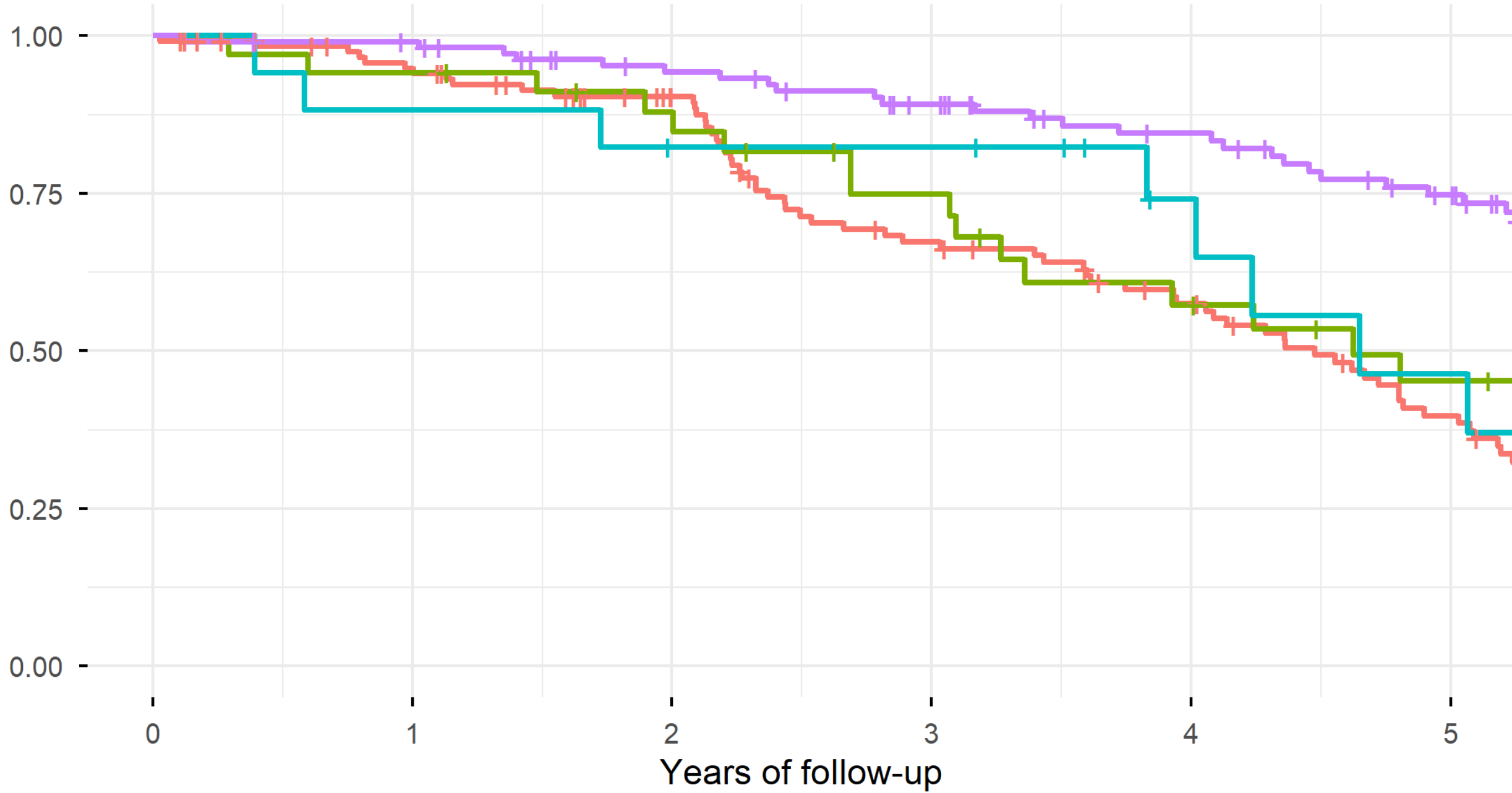
|                                      | MMSE β (SE),<br>p-value |
|--------------------------------------|-------------------------|
| pure DLB<br>(n=85, 353 obs)          | REF                     |
| DLB+AD * time<br>(n=81, 251 obs)     | -0.57 (0.26),<br>0.028* |
| DLB+CSVD * time<br>(n=9, 31 obs)     | 0.45 (0.56),<br>0.419   |
| DLB+AD+CSVD * time<br>(n=26, 99 obs) | -0.19 (0.35),<br>0.596  |



|                                    | MMSE β (SE),<br>p-value |
|------------------------------------|-------------------------|
| pure DLB<br>n=47, 199 obs          | REF                     |
| DLB+AD * time<br>n=50, 162 obs     | 2.251 (0.90),<br>0.015* |
| DLB+CSVD * time<br>n=7, 27 obs     | 1.838 (1.64),<br>0.266  |
| DLB+AD+CSVD * time<br>n=10, 31 obs | 2.873 (1.75),<br>0.103  |

|                  | Hazard Ratio<br>(confidence interval) | p-value |
|------------------|---------------------------------------|---------|
| pure DLB         | 1.00                                  |         |
| DLB+AD           | 2.15<br>(1.53-3.03)                   | <.001   |
| DLB+CSVD         | 0.96<br>(0.47-1.99)                   | 0.923   |
| DLB+AD+CSVD      | 2.19<br>(1.37-3.51)                   | 0.001   |
| Age at baseline  | 1.02<br>(1.00-1.04)                   | 0.081   |
| Sex              | 0.80<br>(0.55-1.18)                   | 0.268   |
| MMSE at baseline | 0.93<br>(0.90-0.96)                   | <.001   |

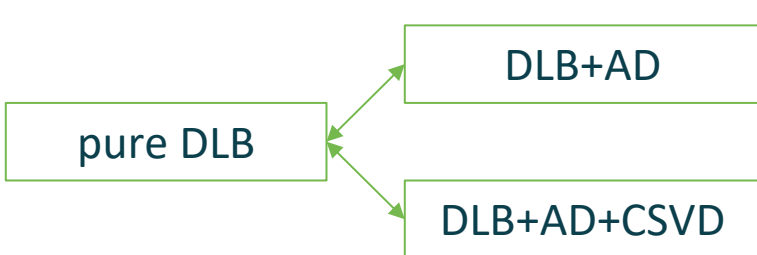
## RESULTS



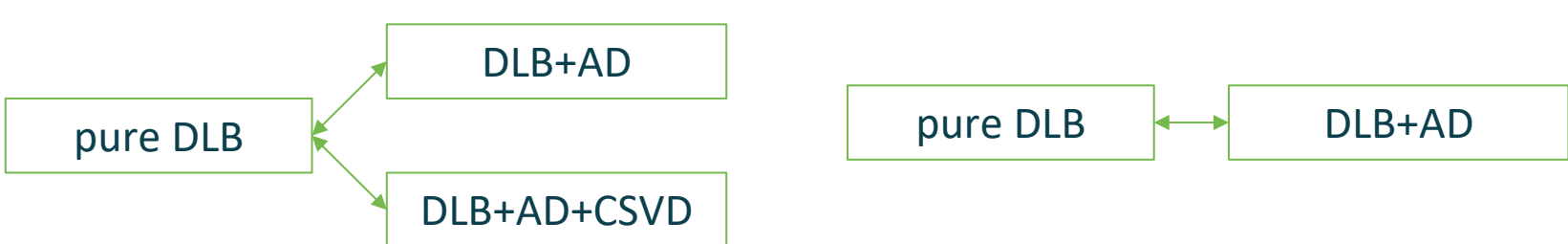
### Number at risk

|             | 0   | 1   | 2  | 3  | 4  | 5  |
|-------------|-----|-----|----|----|----|----|
| pure DLB    | 122 | 109 | 91 | 65 | 51 | 33 |
| DLB+AD      | 34  | 32  | 28 | 22 | 16 | 11 |
| DLB+CSVD    | 17  | 15  | 13 | 13 | 8  | 5  |
| DLB+AD+CSVD | 109 | 106 | 94 | 84 | 71 | 58 |

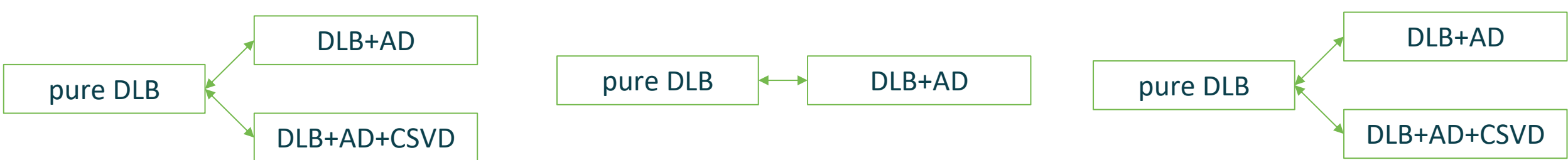
### baseline characteristics



### clinical decline



### mortality



**IN BOTH AD-GROUPS**

- ❖ older age
- ❖ more females
- ❖ more APOE ε4 carriers
- ❖ more VH, less RBD
- ❖ no difference in outcome measures

**IN DLB+AD GROUP ONLY**

steeper decline in both outcome measures

**IN BOTH AD-GROUPS**

significantly increased hazard ratio for mortality

## CONCLUSION

Our results suggest that **Alzheimer's disease copathology drives disease progression in dementia with Lewy bodies** with negligible additional impact of cerebral small vessel disease copathology