



## **Supplementary Material**

**Article Title:** The Clinical Picture of Alzheimer's Disease in the Decade Before Diagnosis: Clinical and Biomarker Trajectories

**Author(s):** Karen Ritchie, PhD; Isabelle Carrière, PhD; Claudine Berr, MD; Hélène Amieva, PhD; Jean-François Dartigues, MD; Marie-Laure Ancelin, PhD; and Craig W. Ritchie, MD

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### **Disclaimer**

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

## eAppendix 1

The SAS macro GMATCH (Division of Biostatistics, Mayo Clinic) results for each set of markers.

Set of variables	N° cases	N° controls	Age	Women
			Median (IQR)	%
Plasma Beta amyloids and CRP*	101	201	77 (73-81)	65.2
Cognitive tests and CES-D <sup>†</sup>	821	1640	78 (74-82)	63.5
Brain and white matter lesion volumes <sup>‡</sup>	44	87	74 (72-76)	54.2

\*The measurements of beta amyloids and CRP were available in 101 cases and 1221 controls. 100 cases were matched with two controls and one case was matched with only one control. The number of controls for this analysis is thus 201.

<sup>†</sup>For cognitive tests and CES-D scale 822 cases and 8211 controls had data, one case aged of 98 years could not be matched and two cases had only one controls in the age range the analysis is thus on 821 cases and 1640 controls.

<sup>‡</sup>Brain volumes and WMH data were available in only 44 cases and 638 controls. 43 cases were matched with 2 controls and one case was matched with only one control. The number of controls for this analysis is thus of 87.

### Abbreviations.

CES-D: Center for Epidemiological Studies-Depression Scale

CRP: C-reactive protein

## eAppendix 2

### Characteristics of cases and controls at inclusion

	Cases		Controls		
	N=821		N=1640		Chi2
Categorical variables	n	%	n	%	P value
Gender (male)	300	36.5	598	36.5	0.97*
Education $\leq$ 5 years, n=2452	337	41.3	437	26.7	<0.0001
CES-D $\geq$ 16, n=2392	248	31.4	380	23.5	<0.0001
APOE4, n=2407	227	30.7	265	17.7	<0.0001
Continuous variables					Wilcoxon
	Median	IQR	Median	IQR	test
Age (years)	78	74-82	78	74-82	0.95*
Isaac's test score, n=2426	39	32-45	45	39-52	<0.0001
Benton test score, n=2384	10	8-12	11	10-13	<0.0001
A $\beta$ n-40 (pg/ml), n=300	249	215-289	243	218-276	0.38
A $\beta$ n-42 (pg/ml), n=288	26	21-30	27	22-33	0.17
CRP (mg/l), n=300	2.01	1.11-4.14	2.13	1.21-4.86	0.32
Hippocampal volume/ICV (%), n=127	0.44	0.37-0.51	0.49	0.44-0.53	0.008
White matter lesions (ml), n=130	3.00	0.60-8.40	0.90	0.30-4.00	0.01

\* matched on gender, age and center

Of the 830 cases, 165 were prevalent at baseline. The mean, median and range of time to diagnosis for the remaining 665 incident cases were 4.68 years, 5.21 years and 0.76 to 9.07 years respectively. The time of diagnostic is defined as the mid-point between diagnosis and the prior examination.

Abbreviations. A $\beta$ n40: truncated amyloid-beta 40, A $\beta$ n42: truncated amyloid-beta 42  
APOE4: apolipoprotein E4, CES-D: Center for Epidemiological Studies-Depression Scale  
CRP: C-reactive protein, ICV: intracranial volume