Supplementary Data

Associations of Anti-Hypertensive Treatments with Alzheimer's Disease, Vascular Dementia, and Other Dementias

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Supplementary Table 1
Read/OXMIS codes used to define dementia

Read/OXMIS code	Read/OXMIS description	Diagnosis Code
Fyu3000	[X]Other Alzheimer's disease disease	Probable Alzheimer's disease
Eu00013	[X]Alzheimer's disease disease type 2	Probable Alzheimer's disease
Eu00011	[X]Presenile dementia, Alzheimer's disease type	Probable Alzheimer's disease
Eu00z00	[X]Dementia in Alzheimer's disease disease, unspecified	Probable Alzheimer's disease
Eu00.00	[X]Dementia in Alzheimer's disease disease	Probable Alzheimer's disease
F110100	Alzheimer's disease disease with late onset	Probable Alzheimer's disease
Eu00012	[X]Primary degen dementia, Alzheimer's disease type, presenile onset	Probable Alzheimer's disease
Eu00100	[X]Dementia in Alzheimer's disease disease with late onset	Probable Alzheimer's disease
Eu00111	[X]Alzheimer's disease disease type 1	Probable Alzheimer's disease
Eu00112	[X]Senile dementia,Alzheimer's disease type	Probable Alzheimer's disease
Eu00113	[X]Primary degenerative dementia of Alzheimer's disease type, senile onset	Probable Alzheimer's disease
Eu00z11	[X]Alzheimer's disease dementia unspec	Probable Alzheimer's disease
Eu00000	[X]Dementia in Alzheimer's disease disease with early onset	Probable Alzheimer's disease
F110.00	Alzheimer's disease disease	Probable Alzheimer's disease
F110000	Alzheimer's disease disease with early onset	Probable Alzheimer's disease
2901B	ALZHEIMER'S DISEASE DISEASE	Probable Alzheimer's disease
Eu00200	[X]Dementia in Alzheimer's disease dis, atypical or mixed type	Probable Alzheimer's disease
E000.00	Uncomplicated senile dementia	Possible Alzheimer's disease
Eu02z14	[X] Senile dementia NOS	Possible Alzheimer's disease
Eu02z11	[X] Presenile dementia NOS	Possible Alzheimer's disease
E001000	Uncomplicated presenile dementia	Possible Alzheimer's disease
E001100	Presenile dementia with delirium	Possible Alzheimer's disease
E001300	Presenile dementia with depression	Possible Alzheimer's disease
E002100	Senile dementia with depression	Possible Alzheimer's disease
E002z00	Senile dementia with depressive or paranoid features NOS	Possible Alzheimer's disease
Eu02z16	[X] Senile dementia, depressed or paranoid type	Possible Alzheimer's disease
E003.00	Senile dementia with delirium	Possible Alzheimer's disease
E00z.00	Senile or presenile psychoses NOS	Possible Alzheimer's disease
E00.00	Senile and presenile organic psychotic conditions	Possible Alzheimer's disease
E00.11	Senile dementia	Possible Alzheimer's disease
E001z00	Presenile dementia NOS	Possible Alzheimer's disease
E001200	Presenile dementia with paranoia	Possible Alzheimer's disease
E002000	Senile dementia with paranoia	Possible Alzheimer's disease
E00.12	Senile/presenile dementia	Possible Alzheimer's disease
E001.00	Presenile dementia	Possible Alzheimer's disease
E002.00	Senile dementia with depressive or paranoid features	Possible Alzheimer's disease
e000.00	Uncomplicated senile dementia	Possible Alzheimer's disease
2900	SENILE DEMENTIA	Possible Alzheimer's disease
2901A	PRESENILE DEMENTIA	Possible Alzheimer's disease
299 B	DEMENTIA	Non-specific dementia
299 G	DEMENTIA AGGRESSIVE	Non-specific dementia
Eu02.00	[X]Dementia in other diseases classified elsewhere	Non-specific dementia
E041.00	Dementia in conditions EC	Non-specific dementia
Eu02z00	[X] Unspecified dementia	Non-specific dementia
Eu02z13	[X] Primary degenerative dementia NOS	Non-specific dementia
E00y.00	Other senile and presenile organic psychoses	Non-specific dementia
Eu02y00	[X]Dementia in other specified diseases classif elsewhere	Non-specific dementia
F112.00	Senile degeneration of brain	Non-specific dementia
9hD1.00	Excepted from dementia quality indicators: Informed dissent	Non-specific dementia
9hD0.00	Excepted from dementia quality indicators: Patient unsuitable	Non-specific dementia
6AB.00	Dementia annual review	Non-specific dementia
E004100	Arteriosclerotic dementia with delirium	Vascular dementia
Eu01000	[X]Vascular dementia of acute onset	Vascular dementia
Eu01200	[X]Subcortical vascular dementia	Vascular dementia
Eu01100	[X]Multi-infarct dementia	Vascular dementia
E004.11	Multi infarct dementia	Vascular dementia
E004200	Arteriosclerotic dementia with paranoia	Vascular dementia
E004z00	Arteriosclerotic dementia NOS	Vascular dementia
Eu01z00	[X]Vascular dementia, unspecified	Vascular dementia

Supplementary Table 1
continued

Read/OXMIS code	Read/OXMIS description	Diagnosis Code
E004300	Arteriosclerotic dementia with depression	Vascular dementia
E004.00	Arteriosclerotic dementia	Vascular dementia
E004000	Uncomplicated arteriosclerotic dementia	Vascular dementia
Eu01.11	[X]Arteriosclerotic dementia	Vascular dementia
Eu01y00	[X]Other vascular dementia	Vascular dementia
Eu01.00	[X]Vascular dementia	Vascular dementia
Eu01300	[X]Mixed cortical and subcortical vascular dementia	Vascular dementia
2930	DEMENTIA ARTERIOSCLEROTIC	Vascular dementia
Eu01111	[X]Predominantly cortical dementia	Other dementia
Eu04100	[X]Delirium superimposed on dementia	Other dementia
Eu02500	[X]Lewy body dementia	Other dementia
F116.00	Lewy body disease	Other dementia
Eu02300	[X]Dementia in Parkinson's disease	Other dementia
342 CP	SENILE PARKINSONISM	Other dementia

Supplementary Table 2
Association of exposure to ACE-Is or ARBs with dementia additionally adjusted for index of multiple deprivation quintile

	Exposed		Unexposed		Fully adjusted[a]		Additionally adjusted for IMD[b]	
	Cases	Controls	Cases	Controls	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
ACE-Inhibitors versus other anti-hypertensives								
Probable Alzheimer's disease	304	6,909	622	9,871	0.70 (0.60–0.81)	<0.001	0.70 (0.60–0.81)	<0.001
Possible Alzheimer's disease	608	6,909	1,095	9,871	0.78 (0.70–0.87)	<0.001	0.78 (0.70–0.87)	<0.001
Probable vascular dementia	390	6,909	549	9,871	0.83 (0.72–0.96)	0.01	0.83 (0.72–0.96)	0.01
Unspecified or other dementia	206	6,909	290	9,871	0.93 (0.77–1.12)	0.42	0.93 (0.77–1.12)	0.43
Any dementia	1,508	6,909	2,556	9,871	0.79 (0.73–0.85)	<0.001	0.79 (0.73–0.85)	<0.001
Angiotensin II receptor blockers versus other anti–hypertensives								
Probable Alzheimer's disease	41	1,263	622	9,871	0.48 (0.34–0.66)	<0.001	0.48 (0.35–0.66)	<0.001
Possible Alzheimer's disease	63	1,263	1,095	9,871	0.44 (0.34–0.58)	<0.001	0.44 (0.34–0.58)	<0.001
Probable vascular dementia	57	1,263	549	9,871	0.70 (0.53–0.94)	0.02	0.70 (0.53–0.93)	0.02
Unspecified or other dementia	28	1,263	290	9,871	0.70 (0.47–1.03)	0.07	0.70 (0.47–1.04)	0.08
Any dementia	189	1,263	2,556	9,871	0.53 (0.45–0.63)	<0.001	0.53 (0.45–0.63)	<0.001

[a] *Adjusted for age at index date, gender and region, diabetes, stroke, coronary heart disease, number of consultations with GP prior to index date and blood pressure prior to index date;* [b]*additionally adjusted for IMD quintile. Odds-ratio (OR), 95% confidence interval (95% CI). The 27,564 patients from Table 2 with no records for IMD were dropped from this table.*

Supplementary Table 3
Association of exposure to ACE-Is or ARBs with dementia additionally adjusted for smoking status

	Exposed		Unexposed		Fully adjusted[a]		Additionally adjusted for smoking[b]	
	Cases	Controls	Cases	Controls	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
ACE-Inhibitors versus other anti-hypertensives								
Probable Alzheimer's disease	721	14,558	1,368	21,078	0.76 (0.69-0.84)	<0.001	0.76 (0.69-0.84)	<0.001
Possible Alzheimer's disease	1,199	14,558	2,085	21,078	0.82 (0.76-0.88)	<0.001	0.82 (0.76-0.89)	<0.001
Probable vascular dementia	834	14,558	1,187	21,078	0.83 (0.75-0.91)	<0.001	0.83 (0.75-0.92)	<0.001
Unspecified or other dementia	441	14,558	677	21,078	0.85 (0.75-0.97)	0.01	0.86 (0.75-0.97)	0.02
Any dementia	3,195	14,558	5,317	21,078	0.81 (0.77-0.85)	<0.001	0.81 (0.77-0.85)	<0.001
Angiotensin II receptor blockers versus other anti-hypertensives								
Probable Alzheimer's disease	89	2,728	1,368	21,078	0.47 (0.37-0.58)	<0.001	0.47 (0.37-0.58)	<0.001
Possible Alzheimer's disease	143	2,728	2,085	21,078	0.52 (0.44-0.62)	<0.001	0.52 (0.44-0.62)	<0.001
Probable vascular dementia	122	2,728	1,187	21,078	0.70 (0.57-0.85)	<0.001	0.70 (0.57-0.85)	<0.001
Unspecified or other dementia	60	2,728	677	21,078	0.63 (0.48-0.82)	0.001	0.63 (0.48-0.83)	0.001
Any dementia	414	2,728	5,317	21,078	0.56 (0.50-0.62)	<0.001	0.56 (0.50-0.62)	<0.001

[a]*Adjusted for age at index date, gender and region, diabetes, stroke, coronary heart disease, number of consultations with GP prior to index date and blood pressure prior to index date;* [b]*additionally adjusted for indicator variable equal to one if patient has any records indicating smoker or ex-smoker. Odds-ratio (OR), 95% confidence interval (95% CI). Patients were defined as ever smoking if they had a record indicating ex-smoker or current smoker at any time. The 1,274 patient included in Table 1 with no smoking status records were dropped from this table.*

Supplementary Table 4
Association of exposure to ACE-Is or ARBs sole-therapy with dementia

	Exposed		Unexposed		Basic adjusted[a]		Fully adjusted[b]	
	Cases	Controls	Cases	Controls	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
ACE-Inhibitors versus other anti-hypertensives								
Probable or possible Alzheimer's disease	534	3,150	3,606	21,628	1.03 (0.93-1.14)	0.55	1.01 (0.91-1.12)	0.86
Probable vascular dementia	184	3,150	1,222	21,628	0.99 (0.85-1.17)	0.93	0.91 (0.78-1.08)	0.29
Unspecified or other dementia	95	3,150	702	21,628	0.91 (0.73-1.14)	0.41	0.86 (0.69-1.07)	0.18
Any dementia	813	3,150	5,530	21,628	1.01 (0.93-1.09)	0.86	0.97 (0.89-1.06)	0.50
Angiotensin II receptor blockers vs other anti-hypertensives								
Probable or possible Alzheimer's disease	40	379	3,606	21,628	0.64 (0.46-0.89)	0.008	0.63 (0.45-0.88)	0.006
Probable vascular dementia	20	379	1,222	21,628	0.90 (0.57-1.41)	0.63	0.89 (0.56-1.41)	0.62
Unspecified or other dementia	9	379	702	21,628	0.70 (0.36-1.37)	0.30	0.67 (0.35-1.31)	0.25
Any dementia	69	379	5,530	21,628	0.71 (0.55-0.92)	0.009	0.69 (0.53-0.89)	0.005

[a]Adjusted for age at index date gender and region; [b] Adjusted as above and additionally indicator variables for records indicating, diabetes, stroke, or coronary heart disease, number of consultations with GP prior to index date and systolic blood pressure prior to diagnosis. Odds-ratio (OR), 95% confidence interval (95% CI).