Supplementary data on "Survival in memory clinic cohort is short, even in young onset dementia".

METHODS

Patients

We included 4495 subjects from the Amsterdam Dementia Cohort (ADC) with a baseline diagnosis of any type of dementia (n= 2625), MCI (n=739) or SCD (n=1131) who served as controls, and a baseline visit between 2000 and 2014, allowing a minimum follow-up duration of three years [1 ,2]. The group of patients with dementia included 1690 dementia due to AD, 399 FTD, 165 VaD and 192 DLB. There were 179 with more rare causes of dementia, summarized as 'other dementias' (48 CBD, 67 progressive supranuclear palsy (PSP), 9 CJD, 4 Huntington's disease and 51 with dementia of unspecified aetiology). At baseline, patients received a standardized and multi-disciplinary work-up, including medical history, physical, neurological examination, neuropsychological examination, mini mental state examination (MMSE) [3], laboratory tests and MRI. We offered all patients the possibility of lumbar puncture to collect CSF. Duration of complaints was defined as years since first symptoms by self-report. Diagnoses were made in a multidisciplinary consensus meeting, according to clinical or research consensus criteria: MCI was determined using Petersen's criteria; in addition all patients fulfilled the core clinical criteria of the National Institute on Aging-Alzheimer's Association for MCI from 2011 [4 ,5]. Patients were diagnosed with dementia due to AD using the criteria of the National Institute for Neurological and Communicative Diseases Alzheimer's Disease and Related Disorders Association; all patients also met the core clinical criteria of the National Institute on Aging-Alzheimer's Association for AD dementia from 2011 [6 ,7]. FTD was diagnosed using the Neary and Snowden criteria

until 2011, and after 2011, fulfilled the criteria from Rasckovsky [8 ,9]. VaD was diagnosed using the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l' Enseignement en Neurosciences criteria [10]. DLB was diagnosed using the McKeith criteria [11-13]. Subjects were labeled as SCD when the cognitive complaints could not be confirmed by cognitive testing and criteria for MCI, dementia or other neurological or psychiatric disorder known to cause cognitive complaints were not met.

Statistical analyses

Diagnostic groups were compared on baseline characteristics using parametric and nonparametric tests where appropriate. Next, we determined median survival time per diagnosis and across the total group of dementia (pooling dementia due to AD, FTD, VaD, DLB and other more rare causes of dementia) using Kaplan Meier curves. Analyses were repeated stratified for age (≤65 years and >65 years) and sex. Then, we assessed whether median survival had changed over time. For this, we derived median survival per year of baseline diagnosis pooling all patients with dementia, independent of age and stratified for age (≤65 years and >65 years), and used Cox proportional hazard models using year of baseline diagnosis as a continuous variable, adjusting for age, sex, MMSE and duration of complaints. Finally, for illustrative purposes, we compared median survival per decade for dementia due to AD and non-AD (pooling FTD, VaD, DLB and other more rare causes of dementia), with median survival in the general Dutch population in 2000 and 2010; for each decade we showed the median survival for the center age (e.g., 40 for 35-45) adjusted for the sex-distribution in the age bin of our study[14]. Statistical analyses were performed using SPSS version 22 (IBM, Armonk, NY, USA).

Supplementary table 1 Baseline characteristic of patients according to diagnosis.

	SCD n=1131	**MCI n=739**	**AD n=1690**	**FTD n=399**	**VaD n=165**	**DLB n=192**	**Other dementias n=179**	**Group differences p<0.05**
Female, n (%)	497 (44)	281 (38)	892 (53)	164 (41)	56 (34)	49 (26)	79 (44)	DLB,VaD<MCI,SCD,FTD,OD<AD
Age, years	60±10	68±9	68±9	63±8	70±9	71±8	66±9	SCD<FTD<MCI,AD,OD<VaD,DLB
MMSE	28±2	26±2	20±5	24±5	22±5	22±5	23±5	AD<DLB,VaD<FTD,OD<MCI<SCD
Duration of complaints, years	*NA*	3.0±2.9	3.2±2.4	3.8±3.3	3.3±3.3	3.1±22.2	3.2±2.7	MCI,AD,VaD,DLB,OD<FTD
Duration of follow-up, years	8.1±3.8	6.8±3.2	5.4±2.7	5.3±3.2	5.2±3.6	4.5±2.4	3.9±2.8	OD,DLB<AD,FTD,VaD,<MCI<SCD
Died, n(%)	134 (11)	288 (39)	1044 (62)	226 (57)	112 (68)	132 (69)	136 (76)	SCD<MCI<FTD<AD,VaD<DLB,OD

SCD= subjective cognitive decline, MCI= mild cognitive impairment, AD= Alzheimer's disease, FTD= frontotemporal dementia, VaD= vascular dementia, DLB= dementia with Lewy bodies, other dementias consist of more 'rare' causes of dementia=48 corticobasal degeneration, 67 progressive supranuclear palsy, 9 Creutzfeldt- Jacob's disease, 4 Huntington's disease and 51 with dementia of unspecified aetiology , MMSE= mini mental state examination (available in 4156 subjects), duration of complaints= by self-report, duration of follow-up= time to death or time to last known data alive, NA= not applicable. Data are presented as mean ± standard deviation, unless otherwise specified. Group differences were calculated using ANOVA with post-hoc Bonferroni for continuous variables. For categorical variables Chi-quadrate test were used.

Supplementary table 2 Mortality and median survival time in years according to baseline diagnosis, in total group and stratified for age and sex.

	Total			≤ 65 years			> 65 years			Female			Male		
Baseline diagnosis	**n total**	**n died (%)**	**Median survival time**	**n total**	**n died (%)**	**Median survival time**	**n total**	**n died (%)**	**Median survival time**	**n total**	**n died (%)**	**Median survival time**	**n total**	**n died (%)**	**Median survival time**
SCD	1131	134(12)	*NA*	790	40(5)	*NA*	341	94(28)	*NA*	549	53(10)	*NA*	673	81(12)	*NA*
MCI	739	288(39)	*NA*	256	43(17)	*NA*	483	245(51)	8.9(8.2-9.6)	296	119(40)	*NA*	506	170(34)	*NA*
Dementia	2625	1650(63)	6.0(5.8-6.2)	1020	546(53)	6.9(6.5-7.2)	1605	1104(69)	5.4(5.2-5.7)	1240	768(62)	6.3(6.0-6.6)	1385	882(64)	5.8(5.6-6.1)
AD	1690	1044(62)	6.2(6.0-6.5)	608	316(52)	7.0(6.6-7.6)	1082	728(67)	5.8(5.5-6.1)	978	535(55)	6.6(6.2-7.0)	874	522(60)	5.9(5.6-6.2)
FTD	399	226(57)	6.4(5.8-7.0)	246	132(54)	7.0(6.2-7.9)	153	94(61)	5.6(5.1-6.1)	180	105(58)	5.6(4.8-6.5)	259	123(48)	7.0(6.2-7.9)
VaD	165	112(68)	5.7(4.1-7.3)	44	19(43)	*NA*	121	93(77)	4.1(3.0-5.1)	60	34(57)	6.4(4.5-8.3)	118	80(68)	5.1(3.6-6.6)
DLB	195	132(69)	5.1(4.5-5.7)	46	26(57)	5.7(4.6-6.7)	143	106(73)	4.7(3.8-5.6)	54	41(76)	4.8(2.9-6.7)	459	94(59)	5.2(4.6-5.8)
Other Dementias	179	136(76)	3.6(3.2-4.0)	76	53(70)	4.5(3.0-6.0)	103	83(81)	3.5(3.0-4.0)	83	61(74)	3.6(2.5-4.8)	109	78(72)	3.6(3.1-4.0)

SCD= subjective cognitive decline, MCI= mild cognitive impairment, dementia= pooled data of Alzheimer's disease, vascular dementia, frontotemporal dementia, dementia with Lewy bodies and other dementia, AD= Alzheimer's disease, FTD= frontotemporal dementia, VaD= vascular dementia, DLB= dementia with Lewy bodies, other dementias consist of more 'rare' causes of dementia. Data are presented as median survival time in years (95% confidence interval), unless otherwise specified. Median survival time was calculated using Kaplan-Meier survival analyses. NA = not applicable, since <50% of the patients in this specific category had died, median survival time could not be derived.

Supplementary table 3 Mortality and median survival time per year of baseline diagnosis, for all patients with dementia (AD, VaD, DLB, FTD and other dementias), in total group and stratified for age.

	Total				≤ 65 years				> 65 years			
Year of baseline diagnosis	**n total**	**n died (%)**	**Median survival time (95%CI)**	**25-75 IQL in years**	**n total**	**n died (%)**	**Median survival time (95%CI)**	**25-75 IQL in years**	**n total**	**n died (%)**	**Median survival time (95%CI)**	**25-75 IQL in years**
2000	84	83 (99)	5.3 (4.8-5.7)	2.6-7.8	22	21 (96)	8.5 (4.9-12.1)	5.3-11.4	62	62 (100)	4.7 (3.7-5.7)	2.4-6.4
2001	96	94 (98)	5.0 (3.9-6.0)	2.5-7.6	26	24 (92)	6.1 (5.4-6.8)	4.5-8.0	70	70 (100)	4.1 (3.2-5.0)	2.4-7.5
2002	98	92 (94)	5.7 (4.7-6.7)	3.0-8.7	23	19 (83)	7.5 (4.1-11.0)	3.7-11.9	75	73 (97)	5.0 (3.5-6.5)	2.9-7.7
2003	122	110 (90)	5.9 (5.0-6.8)	3.5-8.7	35	27 (77)	7.7 (6.2-9.2)	5.1-12.5	87	83 (95)	5.3 (4.8-5.8)	3.3-8.1
2004	132	121 (92)	5.8 (4.8-6.8)	3.0-8.7	48	40 (83)	6.6 (5.6-7.6)	4.9-9.5	84	81 (96)	4.2 (3.1-5.4)	2.1-7.7
2005	137	123 (89)	5.7 (4.8-6.5)	3.0-8.6	47	37 (79)	7.1 (5.4-8.7)	4.1-11.2	90	86 (96)	5.2 (4.3-6.2)	2.7-8.1
2006	173	154 (89)	5.2 (4.3-6.1)	2.4-8.4	49	43 (88)	6.2 (5.0-7.4)	3.7-8.9	124	111 (90)	4.8 (3.8-5.8)	2.2-8.2
2007	194	155 (78)	6.3 (5.4-7.3)	3.7-9.5	73	54(74)	8.1 (6.9-9.4)	4.8-10.0	121	101 (84)	5.4 (4.9-5.9)	3.5-8.4
2008	209	150 (72)	6.1 (5.4-6.8)	-	80	49 (61)	7.1 (5.7-8.4)	-	129	101 (78)	5.5 (4.5-6.4)	3.5-8.3
2009	231	150 (65)	5.9 (5.3-6.5)	-	105	64 (61)	6.4 (5.6-7.3)	-	126	86 (68)	5.8 (5.2-6.4)	-
2010	184	106 (58)	6.4 (5.6-7.3)	-	93	54 (58)	6.2 (5.0-7.5)	-	91	52 (57)	6.7 (5.7-7.7)	-
2011	230	115 (50)	-	-	97	47 (49)	-	-	133	68 (51)	-	-
2012	238	96 (40)	-	-	101	32 (32)	-	-	137	64 (47)	-	-
2013	263	63 (24)	-	-	118	20 (17)	-	-	145	43 (30)	-	-
2014	234	38 (16)	-	-	103	15 (15)	-	-	131	23 (18)	-	-

Dementia= pooled data of AD= Alzheimer's disease, FTD= frontotemporal dementia, VaD= vascular dementia, DLB= dementia with Lewy bodies, other dementias consist of more 'rare' causes of dementia. Median survival time and 25-75 IQL were calculated using Kaplan-Meier survival analyses; median survival time and 25-75 IQL were only reported when they could be calculated. In case of too few endpoints, corresponding cells are left empty.

Cox proportional hazard models showed that a more recent year of baseline diagnosis was associated with longer disease duration (i.e. lower risk of mortality (HR .981(.966-.997), p.020)). When we stratified for age, we observed that this effect seemed to be specific for late onset patients (patients >65 years: HR .958(.940-.975), p.000), while in young onset patients this trend over time was not observed (patients ≤65 years: HR 1.005(.976-1.036), p.718).

Supplementary table 4 Median survival in Amsterdam dementia cohort, per decade, for dementia, compared with survival in general Dutch population.

	Median survival in years (95% CI) in ADC cohort				Median survival in years in general Dutch population	
	n	**AD dementia**	**n**	**non-AD dementia**	**2000**	**2010**
35-45	4	3.6 (2.6-4.6)	8	3.4 (2.2-4.6)	40.2	42.5
45-55	111	6.5 (5.6-7.5)	75	7.5 (5.9-9.0)	30.5	32.7
55-65	565	7.2 (6.7-7.8)	363	6.6 (5.9-7.4)	21.5	23.6
65-75	711	6.7 (6.2-7.2)	376	5.3 (4.8-5.8)	13.8	15.6
75-85	413	5.3 (5.0-5.6)	178	3.7 (3.4-4.0)	7.7	8.8
85-95	48	3.0 (1.6-4.4)	17	2.3 (0.0-6.0)	*NA*	*NA*

ADC= Amsterdam dementia cohort, AD= Alzheimer's disease, non-AD dementia= pooled data of VaD, FTD, DLB and other dementia, NA= survival data for this age group was not available.

Median survival for the ADC cohort was calculated using Kaplan-Meier survival curves for each decade and diagnostic group. Median survival in the general Dutch population in 2000 and 2010 is shown for illustrative purposes and derived from: https://opendata.cbs.nl/statline/portal.html?_la=nl&_catalog=CBS&tableId=71950ned&_theme=147. For each decade we show the median survival for the center age; so 40 for 35-45, adjusted for the sex-distribution in the age bin of our study.

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