Long-term Dementia Risk in Parkinson's Disease: Glass half-full?

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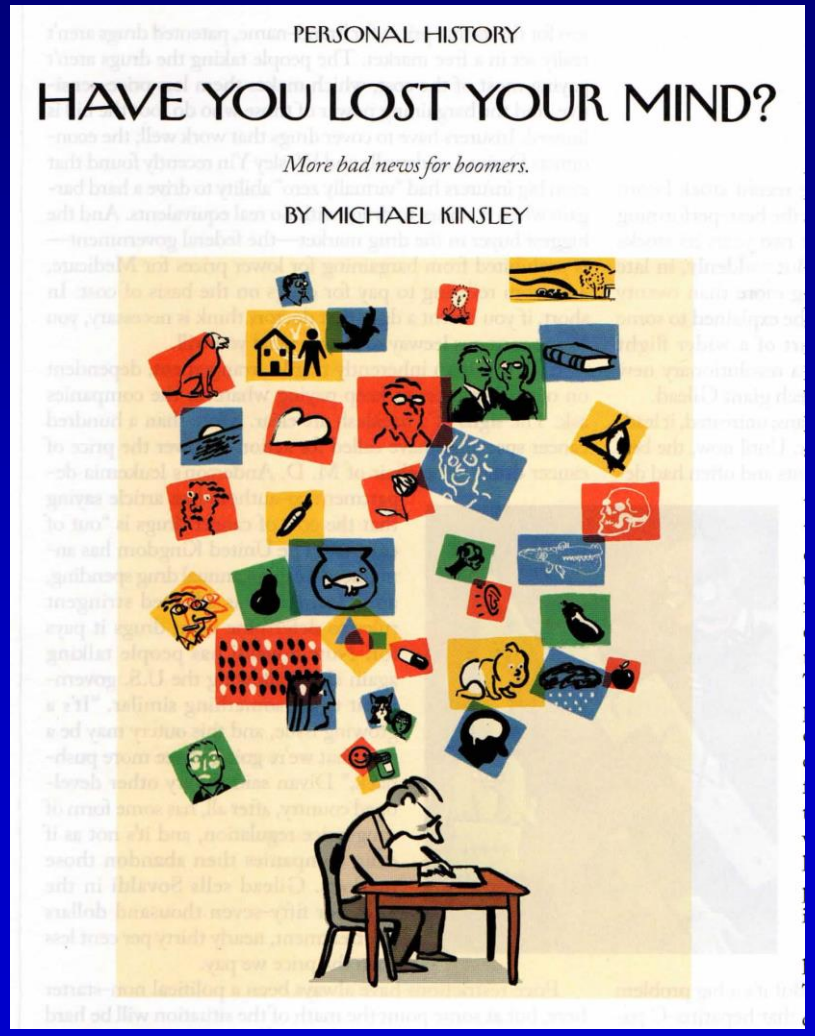
The Emerging Patient Voice

Patient's Perspective on "Mild" Cognitive Changes


PERSONAL HISTORY

HAVE YOU LOST YOUR MIND?

More bad news for boomers.

BY MICHAEL KINSLEY

- A
- R
- B
- M
- E
- P
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- A

ng Line

Slate

I knew that thinking was involved. I asked my neurologist at the time, and he answered carefully, "Well, after a few years you may lose your edge." Lose my edge? Lose my edge? Oh, [redacted]! I need my edge. My edge is how I make a living. More than that: My edge is my claim on the world. It's why people are my friends, why they invite me over for dinner, perhaps why they marry me. What am I worth to the world if I've lost my edge?

Patient Cognitive Complaint Predicts Future Cognitive Impairment in PD with Normal Cognition

TABLE 3. Longitudinal neuropsychological and functional assessments

Assessment*	Annual Change (SE) in –SCC Group	Annual Change (SE) in +SCC Group	*P* Value (Between-Group Difference in Annual Change)**
MoCA	–0.31 (0.10)	–0.45 (0.09)	0.28
MDRS-2 total score	–0.45 (0.15)	–0.94 (0.14)	0.02
HVLT-R immediate recall	0.10 (0.20)	–0.03 (0.18)	0.62
HLVT-R delayed recall	0.04 (0.13)	0.07 (0.12)	0.87
HVLT-R recognition discrimination	0.06 (0.08)	0.15 (0.08)	0.48
LNS	–0.22 (0.09)	–0.38 (0.08)	0.18
Phonemic verbal fluency, FAS	–1.01 (0.35)	–1.34 (0.33)	0.48
Animal fluency	–0.77 (0.17)	–0.88 (0.16)	0.65
Trail Making Test Part A, time	2.04 (0.64)	3.54 (0.61)	0.09
Trail Making Test Part B, time	6.10 (1.79)	11.31 (1.70)	0.04
SDMT	–1.32 (0.29)	–2.40 (0.27)	0.006
JOLO	–0.26 (0.18)	–0.47 (0.17)	0.41
Clock Drawing	–0.06 (0.05)	–0.01 (0.05)	0.46
BNT	–0.23 (0.08)	–0.18 (0.08)	0.64
ADCS-ADL total	–0.51 (0.33)	–2.16 (0.31)	<0.001
PDAQ KI total	–1.11 (0.32)	–1.50 (0.30)	0.38
PDAQ patient total	–0.62 (0.30)	–0.36 (0.30)	0.54

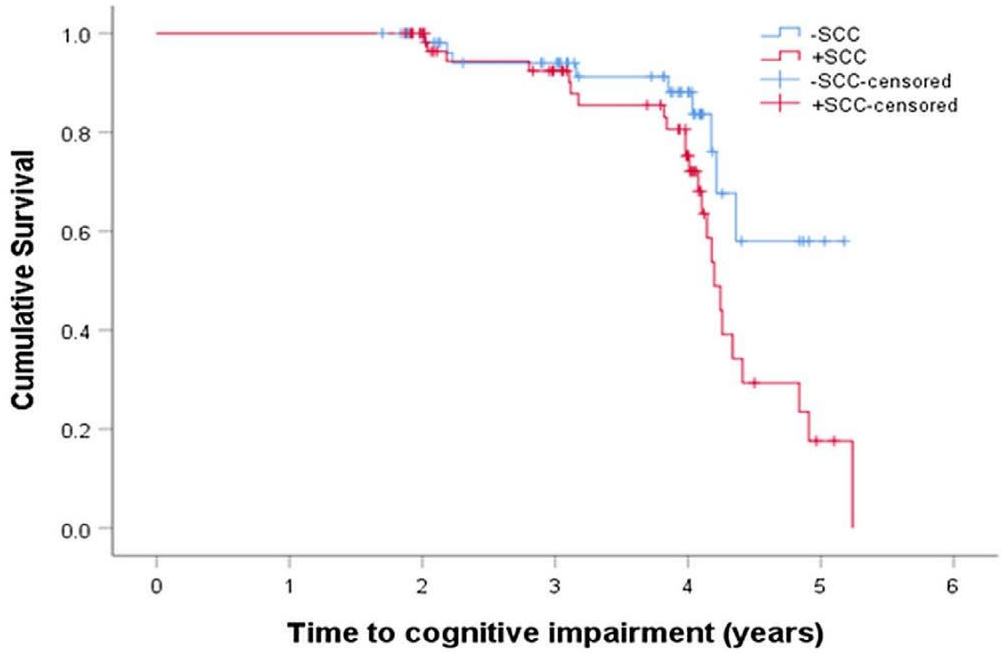
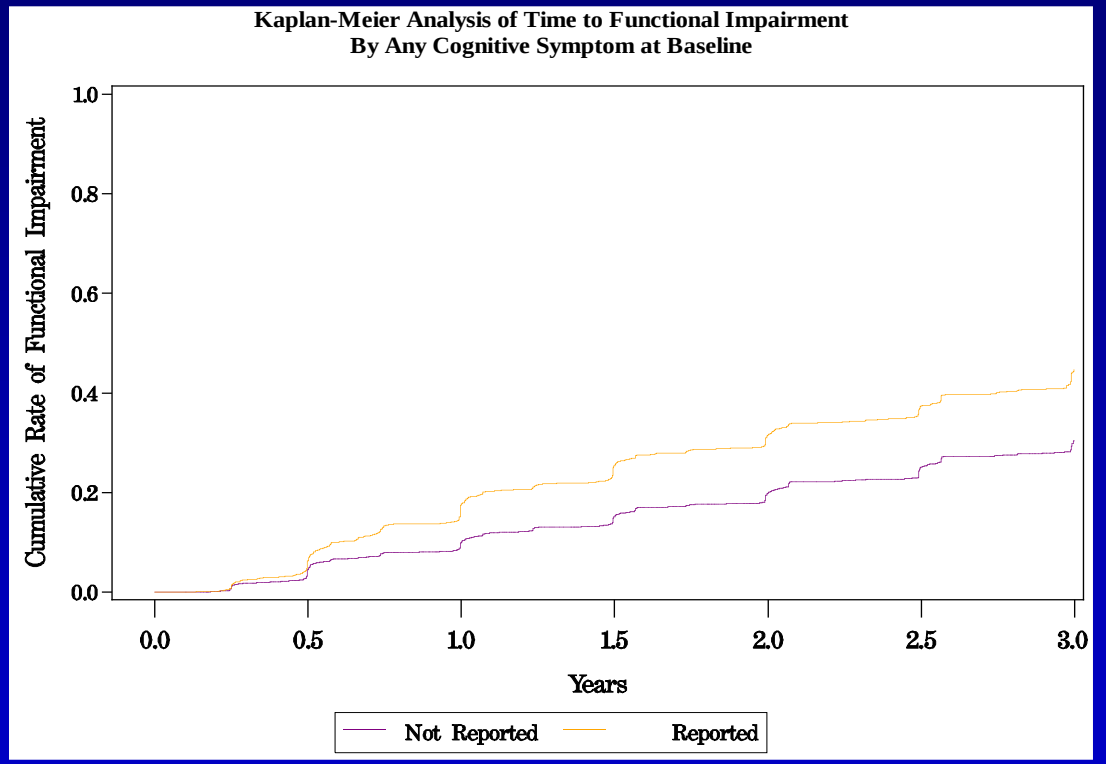


FIGURE 1. Kaplan-Meier survival curve for the progression from normal cognition to any cognitive impairment between groups. The presence of SCC at baseline predicted earlier onset of cognitive impairment (mild cognitive impairment or dementia) as determined by consensus. SCC, subjective cognitive complaint. [Color figure can be viewed at wileyonlinelibrary.com]

Purri et al. *Movement Disorders* 2020;35:1618-1625.

Fox Insight Patient Report of Problems (PD-PROP): Cognitive Complaint Predicts Incident Functional Impairment

Variable	Functional Impairment (N=7,332)	No Functional Impairment (N=13,828)	P value	Chi-Square or Cochran-Armitage Z score
Any cognitive complaint				
Not Reported	3675 (26%)	10735 (75%)	<0.001	1669.16
Reported	3657 (54%)	3093 (46%)		
Cognitive slowing				
Not Reported	6672 (33%)	13545 (67%)	<0.001	544.34
Reported	660 (70%)	283 (30%)		
Executive abilities				
Not Reported	6884 (34%)	13576 (66%)	<0.001	275.40
Reported	448 (64%)	252 (36%)		
Concentration/Attention				
Not Reported	6308 (33%)	12820 (67%)	<0.001	246.05
Reported	1024 (50%)	1008 (50%)		
Memory				
Not Reported	5570 (30%)	12789 (70%)	<0.001	1138.27
Reported	1762 (63%)	1039 (37%)		
Language/Word finding				
Not Reported	5893 (32%)	12628 (68%)	<0.001	526.12
Reported	1439 (55%)	1200 (45%)		
Mental alertness/awareness				
Not Reported	7009 (34%)	13521 (66%)	<0.001	79.21
Reported	323 (51%)	307 (49%)		
Visuospatial abilities				
Not Reported	7312 (35%)	13814 (65%)	0.003	8.79
Reported	20 (59%)	14 (41%)		
Cognitive impairment NOS				
Not Reported	7169 (34%)	13746 (66%)	<0.001	111.25
Reported	163 (67%)	82 (33%)		



Functional impairment based on PDAQ-15 cut-off score.

Weintraub et al. (in press).

Cognition in Early Disease

Cognitive Differences Detected in Prodromal PD

Table 3. Logistic regression models of cognitive domains predicting membership in the hyposmia+DAT reduction group (n=38) versus all others (n=187)[a]

Variable	Regression coefficient	Standard error	Wald chi-square	Odds ratio	95% CI	P-value
Global cognition	-0.68	0.24	8.30	0.51	0.32 – 0.81	0.004
Executive function / Working memory	-0.61	0.21	8.18	0.54	0.36 – 0.83	0.004
Language	-0.25	0.20	1.66	0.78	0.53 – 1.14	0.20
Memory	-0.50	0.21	5.52	0.61	0.40 – 0.92	0.02
Processing speed/Attention	-0.43	0.22	3.92	0.65	0.43 – 1.00	0.048
Visuospatial	-0.17	0.21	0.65	0.85	0.56 – 1.27	0.42

[a] Adjusting for age at testing, sex, and education

Chahine and Weintraub et al. *Movement Disorders* 2016;31:86-94.

Similar Story for Isolated RBD: Cognitive Impairment Predicts Conversion

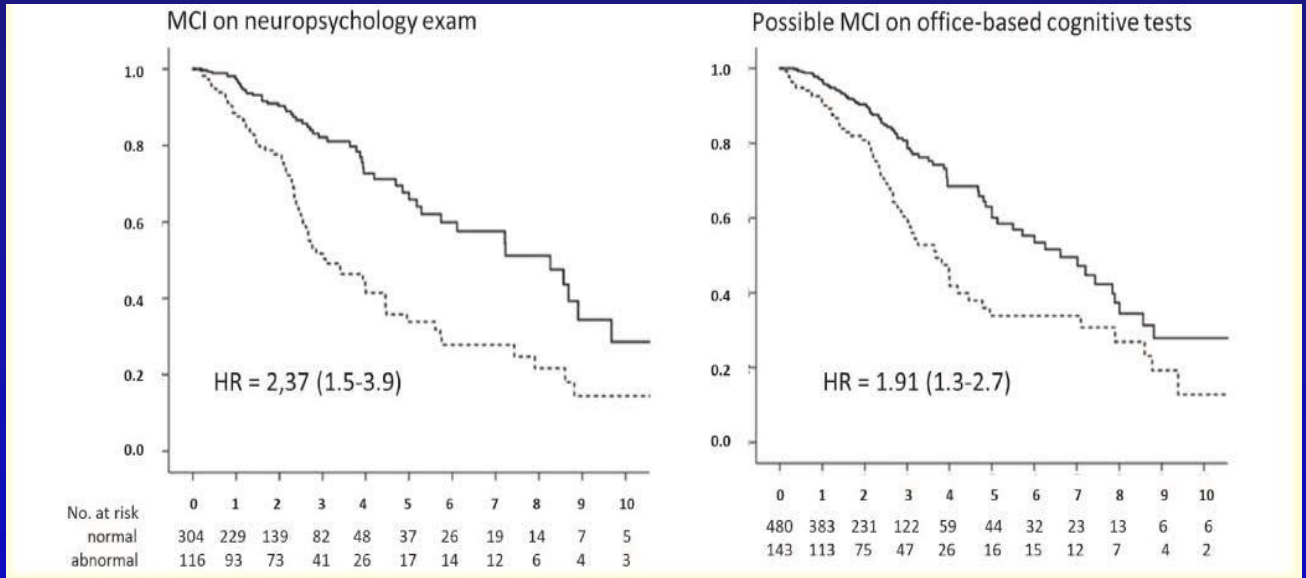


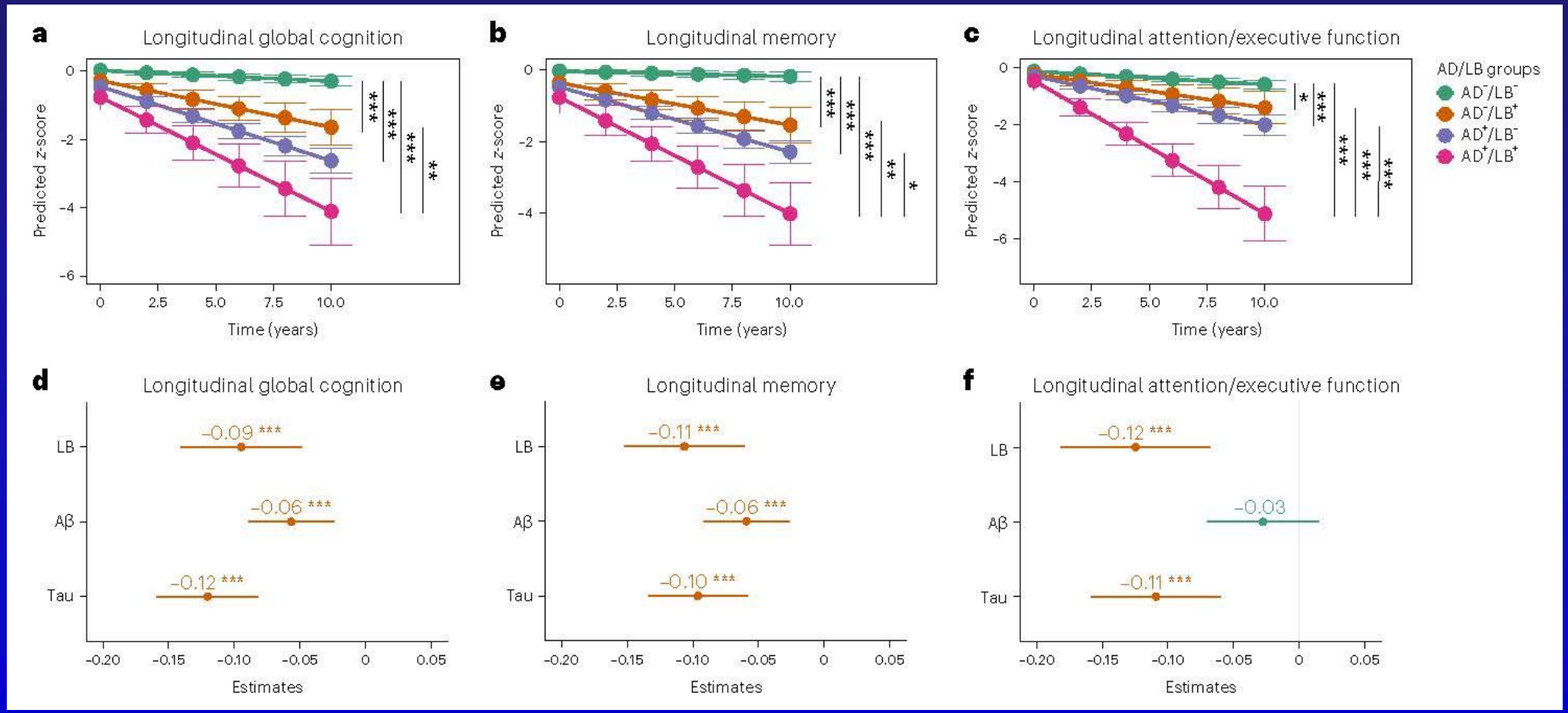
Figure 2 Kaplan-Meier plot of disease-free survival of patients with iRBD stratified according to presence of motor and cognitive markers. Results are presented according to baseline assessment (i.e. patients who develop a *de novo* marker abnormality over the course of the follow-up remain in the 'marker-free' group). Solid line indicates patients with normal values, dashed line abnormal values. Hazard ratios (HRs) are with Cox proportional hazards, adjusting for age, sex, and centre, with 95% confidence intervals in parentheses.

Table 3 Diagnosed Lewy body disease, divided into parkinsonism versus dementia-first

	Parkinsonism-first $n = 184$	Dementia-first $n = 146$	*P*-value
Age	67.4 ± 6.6	68.3 ± 7.1	0.23
Sex, % male	81.0	88.4	0.068
UPDRS Part III			
Combined: abnormal	60.4%	63.7%	0.64
1987 UPDRS	5.40 ± 4.38 ($n = 60$)	6.17 ± 4.96 ($n = 77$)	0.34
MDS-UPDRS	5.56 ± 5.08 ($n = 41$)	6.36 ± 3.69 ($n = 14$)	0.53
Quantitative Motor Abnormal	47.2% ($n = 36$)	82.4% ($n = 34$)	0.002
UPDRS Part II			
Combined, above mean	50.0%	61.7%	0.22
1987 UPDRS	1.44 ± 1.84 ($n = 35$)	1.10 ± 1.46 ($n = 34$)	0.51
MDS-UPDRS	2.38 ± 2.75 ($n = 34$)	5.60 ± 6.12 ($n = 15$)	0.27
Olfaction abnormal	75.7% ($n = 70$)	86.5% ($n = 52$)	0.13
Colour vision abnormal	30.3% ($n = 33$)	73.5% ($n = 34$)	<0.001
Insomnia	26.1% ($n = 46$)	32.1% ($n = 28$)	0.58
Daytime somnolence	28.6% ($n = 133$)	40.4% ($n = 114$)	0.051
Restless legs syndrome	21.1% ($n = 95$)	11.3% ($n = 62$)	0.11
Apnoea (AHI ⩾ 15)	26.8% ($n = 158$)	31.9% ($n = 94$)	0.98
REM %: above mean	57.4%	64.3%	0.47
Tonic REM % (MTL)	50.2 ± 28.1 ($n = 60$)	56.3 ± 31.6 ($n = 39$)	0.33
Phasic REM % (MTL)	29.8 ± 19.9 ($n = 42$)	35.8 ± 16.6 ($n = 34$)	0.16
% Any (SINBAR)	66.4 ± 19.9 ($n = 13$)	61.2 ± 26.0 ($n = 5$)	0.70
Constipation	56.8% ($n = 111$)	57.5% ($n = 80$)	0.92
Urinary dysfunction	29.4% ($n = 85$)	39.6% ($n = 53$)	0.22
Erectile dysfunction	52.8% ($n = 36$)	75.0% ($n = 28$)	0.069
Orthostatic symptoms	28.4% ($n = 67$)	39.1% ($n = 46$)	0.23
Systolic blood pressure drop	12.7 ± 15.7 ($n = 44$)	17.0 ± 21.9 ($n = 37$)	0.32
Abnormal office: cognitive test (regardless of complaint)	43.2%	65.2%	0.003
MoCA	25.8 ± 2.6 ($n = 49$)	22.6 ± 3.5 ($n = 30$)	<0.001
MMSE	27.8 ± 1.7 ($n = 57$)	26.4 ± 3.3 ($n = 70$)	0.002
Neuropsychological abnormal (regardless of complaint)	29.8% ($n = 57$)	86.8% ($n = 76$)	<0.001
Mild cognitive impairment			
Neuropsychological testing	25.9% ($n = 54$)	84.1% ($n = 63$)	<0.001
MoCA/MMSE	30.1% ($n = 73$)	56.9% ($n = 72$)	0.001
Depression	28.6% ($n = 119$)	32.6% ($n = 92$)	0.53
Anxiety	22.5% ($n = 71$)	28.2% ($n = 39$)	0.52
Substantia nigra ultrasound	60.0% ($n = 10$)	66.7% ($n = 3$)	0.84
DAT scan (putamen) abnormal	70.3% ($n = 37$)	71.4% ($n = 14$)	0.94

Postuma et al. *Brain* 2019;142:744-759.

Synuclein SAA+ Predicts Long-Term Cognitive Decline in *Unimpaired* Individuals in General Population



Palmqvist et al. *Nature Medicine* 2023;29:1971-1978.

PD Mild Cognitive Impairment (PD-MCI): Common and Heterogeneous

Mild cognitive impairment in Parkinson disease

A multicenter pooled analysis

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ABSTRACT

Background: In studies of mild cognitive impairment (MCI) in Parkinson disease (PD), patients without dementia have reported variable prevalences and profiles of MCI, likely to be due to methodologic differences between the studies.

Objective: The objective of this study was to determine frequency and the profile of MCI in a large, multicenter cohort of well-defined patients with PD using a standardized analytic method and a common definition of MCI.

Methods: A total of 1,346 patients with PD from 8 different cohorts were included. Standardized analysis of verbal memory, visuospatial, and attentional/executive abilities was performed. Subjects were classified as having MCI if their age- and education-corrected z score on one or more cognitive domains was at least 1.5 standard deviations below the mean of either control subjects or normative data.

Results: A total of 25.8% of subjects (95% confidence interval [CI] 23.5–28.2) were classified as having MCI. Memory impairment was most common (13.3%; 11.6–15.3), followed by visuospatial (11.0%; 9.4–13.0) and attention/executive ability impairment (10.1%; 8.6–11.9). Regarding cognitive profiles, 11.3% (9.7–13.1) were classified as nonamnestic single-domain MCI, 8.9% (7.0–9.9) as amnestic single-domain, 4.8% (3.8–6.1) as amnestic multiple-domain, and 1.3% (0.9–2.1) as nonamnestic multiple-domain MCI. Having MCI was associated with older age at assessment and at disease onset, male gender, depression, more severe motor symptoms, and advanced disease stage.

Conclusions: MCI is common in patients with PD without dementia, affecting a range of cognitive domains, including memory, visual-spatial, and attention/executive abilities. Future studies of patients with PD with MCI need to determine risk factors for ongoing cognitive decline and assess interventions at a predementia stage. *Neurology*® 2010;75:1062–1069

- PD-MCI prevalence in non-demented PD is 25-30%
- Cognitive changes occur broadly and variably in PD
  - Memory
  - Executive abilities
  - Attention
  - Visuospatial skills
  - Language

What About Dementia?

Is Dementia in PD Inevitable?

Results: We included 224 patients with PD (116 women). At baseline, 51 patients (26%) had dementia. Fifty-five patients died, and 10 refused follow-up without their dementia status known. Forty-three and 28 new cases of dementia were identified at the 4- and 8-year evaluations, respectively. The 4-year prevalence of dementia in PD was nearly 3 times higher than in the non-PD group. The 8-year prevalence in PD was 78.2% (95% confidence interval [CI], 71.1-84.0). Risk factors for dementia were hallucinations before baseline (odds ratio [OR]=3.1; 95% CI, 1.6-6.2) and akinetic-dominant or mixed tremor/akinetic PD (OR=3.3; 95% CI, 1.2-8.5).

Conclusions: More than three quarters of this representative PD cohort developed dementia during the 8-year study period. Early hallucinations and akinetic-dominant PD were associated with an increased risk of dementia.

Arch Neurol. 2003;60:387-392

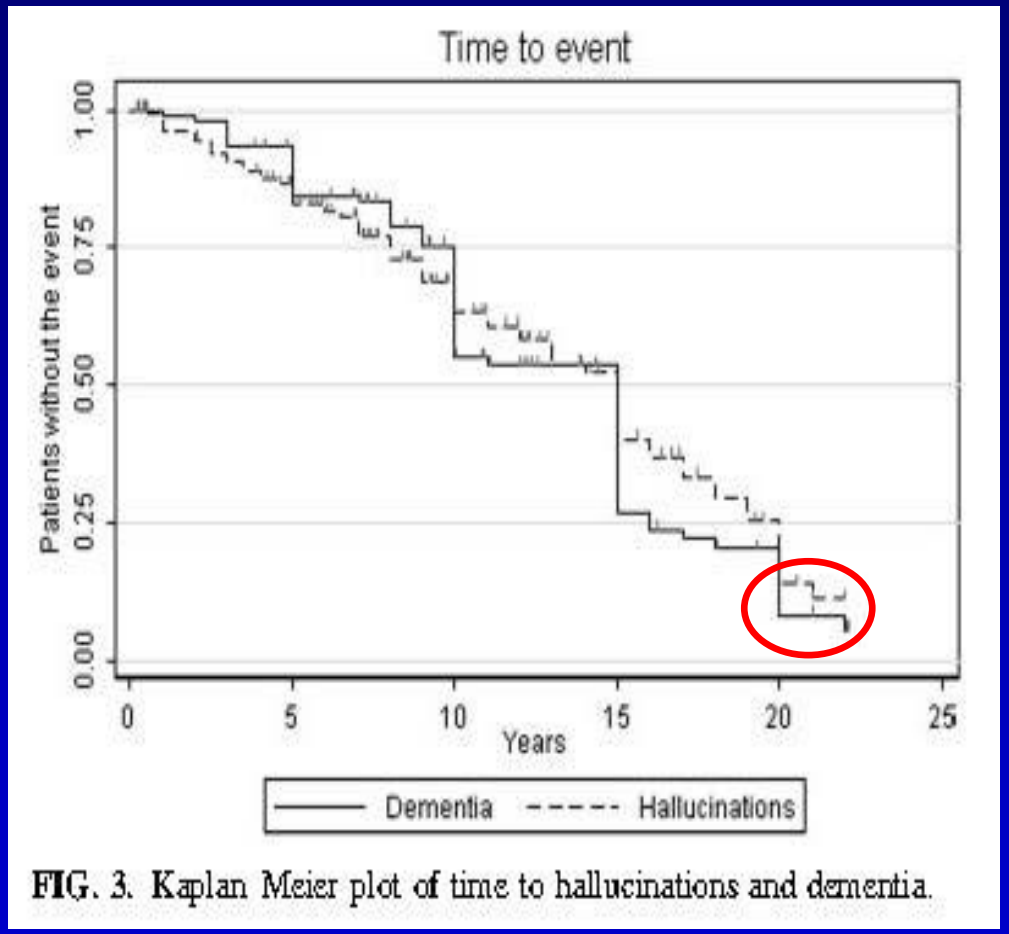


FIG. 3. Kaplan Meier plot of time to hallucinations and dementia.

Aarsland et al. *Archives of Neurology* 2003;60:387-392.
Hely et al. *Movement Disorders* 2008;23:837-844.

New Data:
University of Pennsylvania Cohort

Clinical Characteristics

Variable	Cohort	
	PPMI Cohort (N = 417)	Penn Cohort (N = 389)
Age at Baseline (Years)		
Mean (SD)	61.6 (9.8)	69.3 (8.0)
(Min, Max)	(33, 85)	(49, 94)
PD Duration at Baseline (Years)		
Mean (SD)	0.6 (0.5)	6.3 (5.3)
(Min, Max)	(0, 3)	(0, 32)
Age at PD Diagnosis Categories		
Age < 56	138 (33%)	89 (23%)
Age 56 - 70	212 (51%)	213 (55%)
Age > 70	59 (14%)	87 (22%)
Missing	8 (2%)	0
Sex		
Male	272 (65%)	261 (67%)
Female	145 (35%)	128 (33%)
Race		
White	385 (92%)	362 (93%)
Non-White	29 (7%)	27 (7%)
Missing	3 (1%)	0
Education (Years)		
Mean (SD)	15.6 (3.0)	16.0 (2.5)
(Min, Max)	(5, 26)	(8, 21)
MDS-UPDRS III Total Score		
Mean (SD)	20.9 (8.9)	28.2 (13.2)[a]
(Min, Max)	(4, 51)	(2, 85)
Missing	0	6
Hoehn & Yahr		
1	183 (44%)	33 (8%)
2	232 (56%)	151 (39%)
3	2 (<1%)	185 (48%)
4/5	0	16 (4%)
Missing	0	4 (1%)
MoCA		
Median	28	26
(Min, Max)	(17, 30)	(7, 30)
Missing	0	215[b]
LEDD		
Median	NA	600
(Min, Max)	NA	(0, 2960)

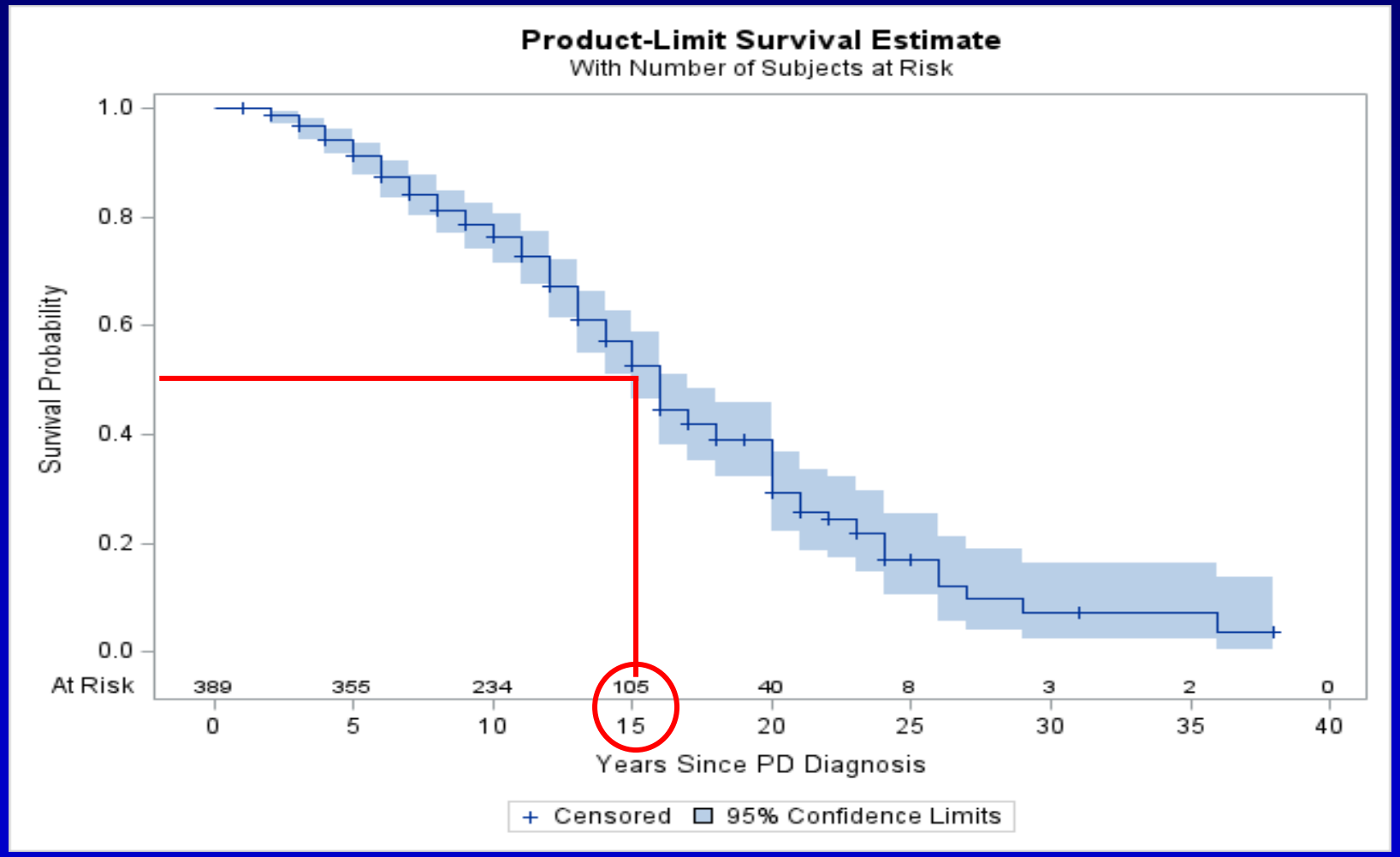
- N=389
- At each visit participants are administered detailed cognitive battery, including global tests (i.e., the Montreal Cognitive Assessment [MoCA] and Dementia Rating Scale-2) and 8 other domain-specific cognitive tests
- For each participant visit experts review cognitive test results, questionnaires assessing cognitive function, and clinician impression of cognitive status, then assign diagnosis of normal cognition, MCI or dementia
- At baseline mean (range) PD duration since diagnosis = 6.3 (0-32) years
- Mean number of follow-up visits (1-2 years apart) = 4.6

Unpublished data from Penn NIA U19 cohort.

Estimated Probability of Dementia

PD Duration	Dementia Diagnosis Probability 95% CL	Cumulative Dementia Diagnoses
Year 5	11.82% (8.8%, 15.77%)	27
Year 10	26.5% (22.15%, 31.51%)	74
Year 15	49.66% (44.42%, 55.15%)	133
Year 20	74.39% (69.76%, 78.8%)	167
Year 25	90.23% (86.57%, 93.25%)	178
Year 30	90.23% (86.57%, 93.25%)	183
Year 35* (24.756 - 34.693 years) (35.622 - 38.052 years)	 90.23% (86.57%, 93.25%) 95.12% (92.47%, 97.05%)	183

Dementia Survival Curve



About 50% at 15 years disease duration

Probability of Dementia by Age at PD Diagnosis

	<56 YEARS AT PD DIAGNOSIS		56-69 YEARS AT PD DIAGNOSIS		70+ YEARS AT PD DIAGNOSIS	
PD Duration	Dementia Diagnosis Probability (95% CL)	Cumulative Dementia Diagnoses	Dementia Diagnosis Probability (95% CL)	Cumulative Dementia Diagnoses	Dementia Diagnosis Probability (95% CL)	Cumulative Dementia Diagnoses
Year 5	1.79% (0.3%, 10.28%)	1	11.62% (7.78%, 17.19%)	11	23.53% (15.6%, 34.58%)	15
Year 10	3.85% (1.15%, 12.42%)	2	23.55% (18.05%, 30.39%)	35	59.27% (49.18%, 69.63%)	37
Year 15	18.79% (11.67%, 29.46%)	11	53.84% (46.42%, 61.63%)	71	85.85% (77.69%, 92.18%)	51
Year 20	55.71% (44.98%, 67.05%)	23	77.57% (71.4%, 83.21%)	91	-	53
Year 25	82.23% (73.08%, 89.72%)	30	-	95	-	53
Year 30	82.23% (73.08%, 89.72%)	35	-	95	-	53
Year 35* (24.756 – 34.693 years) (35.622 – 38.052 years)	82.23% (73.08%, 89.72%) 91.11% (83.87%, 95.97%)	35	-	95	-	53

Probability of Dementia by Sex

	FEMALE		MALE	
PD Duration	Dementia Diagnosis Probability (95% CL)	Cumulative Dementia Diagnoses	Dementia Diagnosis Probability (95% CL)	Cumulative Dementia Diagnoses
Year 5	5.11% (2.31%, 11.1%)	22	15.28% (11.13%, 20.8%)	5
Year 10	19.6% (13.65%, 27.7%)	54	29.77% (24.18%, 36.32%)	20
Year 15	32.89% (25.3%, 42.02%)	102	58.71% (52.37%, 65.18%)	31
Year 20	66.58% (58.31%, 74.66%)	126	78.38% (72.9%, 83.42%)	41
Year 25* (23.244 - 24.321 years) (25.66 - 34.693 years)	 73.86% (64.35%, 82.54%) 90.29% (84.04%, 94.84%)	132	90.16% (85.8%, 93.63%)	46
Year 30	90.29% (84.04%, 94.84%)	135	90.16% (85.8%, 93.63%)	48
Year 35	90.29% (84.04%, 94.84%)	135	90.16% (85.8%, 93.63%)	48

Probability of Dementia by Education Level

	< 13 Years		≥ 13 Years	
PD Duration	Dementia Dx Probability (95% CL)	Cumulative Dementia Diagnoses	Dementia Dx Probability (95% CL)	Cumulative Dementia Diagnoses
Year 5	24.24% (14.21%, 39.52%)	8	9.92% (6.97%, 14.02%)	19
Year 10	42.49% (29.71%, 58.03%)	16	24.25% (19.75%, 29.59%)	58
Year 15* (11.6 - 14.832 years) (15.797 - 17.855 years)	 58.18% (44.29%, 72.72%) 63.64% (49.57%, 77.57%)	21	49.38% (43.78%, 55.28%)	112
Year 20	85.52% (72.45%, 94.48%)	25	72.11% (67.1%, 76.93%)	142
Year 25	-	29	88.66% (84.68%, 92.01%)	149
Year 30	-	30	88.66% (84.68%, 92.01%)	153
Year 35* (24.756 - 34.693 years) (35.622 - 38.052 years)	-	30	 88.66% (84.68%, 92.01%) 94.33% (91.38%, 96.53%)	153

New Data:
Fox Foundation PPMI Study

Clinical Characteristics

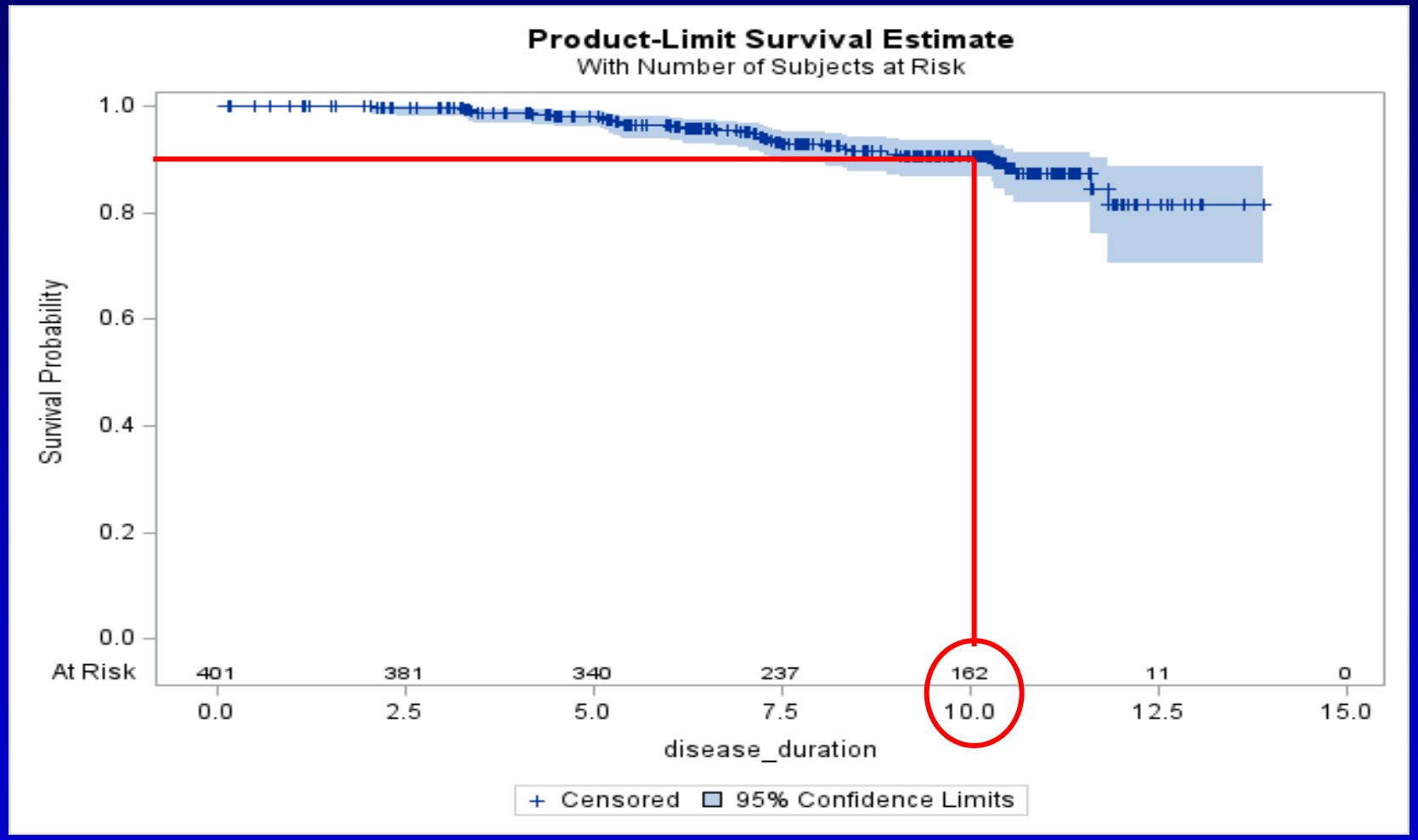
Variable	Cohort	
	PPMI Cohort (N = 417)	Penn Cohort (N = 389)
Age at Baseline (Years)		
Mean (SD)	61.6 (9.8)	69.3 (8.0)
(Min, Max)	(33, 85)	(49, 94)
PD Duration at Baseline (Years)		
Mean (SD)	0.6 (0.5)	6.3 (5.3)
(Min, Max)	(0, 3)	(0, 32)
Age at PD Diagnosis Categories		
Age < 56	138 (33%)	89 (23%)
Age 56 - 70	212 (51%)	213 (55%)
Age > 70	59 (14%)	87 (22%)
Missing	8 (2%)	0
Sex		
Male	272 (65%)	261 (67%)
Female	145 (35%)	128 (33%)
Race		
White	385 (92%)	362 (93%)
Non-White	29 (7%)	27 (7%)
Missing	3 (1%)	0
Education (Years)		
Mean (SD)	15.6 (3.0)	16.0 (2.5)
(Min, Max)	(5, 26)	(8, 21)
MDS-UPDRS III Total Score		
Mean (SD)	20.9 (8.9)	28.2 (13.2)[a]
(Min, Max)	(4, 51)	(2, 85)
Missing	0	6
Hoehn & Yahr		
1	183 (44%)	33 (8%)
2	232 (56%)	151 (39%)
3	2 (<1%)	185 (48%)
4/5	0	16 (4%)
Missing	0	4 (1%)
MoCA		
Median	28	26
(Min, Max)	(17, 30)	(7, 30)
Missing	0	215[b]
LEDD		
Median	NA	600
(Min, Max)	NA	(0, 2960)

- N=417
- Assignment of cognitive diagnosis (normal cognition, MCI or dementia) at each annual visit by site investigator
- Site investigator provided guidance document on how to assess for subjective cognitive change compared with pre-PD state, impairment in cognitive abilities, and functional impairment due to cognitive deficits
- Cognitive tests are MoCA, Hopkins Verbal Learning Test-Revised [HVLT-R], Benton Judgment of Line Orientation [JLO], Symbol-Digit Modalities Test [SDMT], Letter-Number Sequencing [LNS] and category [animal] fluency

Estimated Probability of Dementia

By site investigator diagnosis			By MoCA proxy definition			By UPDRS-I score		
PD Duration	Dementia Diagnosis Probability 95% CL	Cumulative Dementia Diagnoses	PD Duration	Dementia Diagnosis Probability 95% CL	Cumulative Dementia Events (MoCA <21)	PD Duration	Dementia Diagnosis Probability 95% CL	Cumulative Dementia Events (MDS-UPDRS 1 Cognition Score >2)
Year 1	0	0	Year 1** (0.21 - 0.97 years) (1.06 - 1.35 years)	0.43% (0.1%, 1.97%) 0.55% (0.14%, 2.12%)	1	Year 1	0	0
Year 2	0	0	Year 2	1% (0.35%, 2.86%)	3	Year 2** (0 - 1.77 years) (2.07 - 2.18 years)	0% 0.25% (0.04%, 1.69%)	0
Year 3	0.52% (0.13%, 2%)	2	Year 3	2.81% (1.59%, 4.93%)	10	Year 3	0.51% (0.13%, 1.94%)	2
Year 4	1.68% (0.78%, 3.6%)	5	Year 4	2.81% (1.59%, 4.93%)	11	Year 4	1.51% (0.64%, 3.54%)	4
Year 5	2.73% (1.44%, 5.12%)	7	Year 5	5.23% (3.39%, 8.02%)	17	Year 5	3.57% (2.12%, 5.99%)	10
Year 6	3.87% (2.37%, 6.29%)	13	Year 6	7.8% (5.59%, 10.83%)	26	Year 6	4.62% (2.93%, 7.24%)	14
Year 7	7.14% (4.99%, 10.17%)	17	Year 7	10.61% (8%, 14.01%)	32	Year 7	7.68% (5.46%, 10.76%)	18
Year 8	7.14% (4.99%, 10.17%)	23	Year 8	10.64% (8.03%, 14.05%)	37	Year 8	7.68% (5.46%, 10.76%)	24
Year 9	9.12% (6.66%, 12.43%)	27	Year 9	12.05% (9.24%, 15.63%)	40	Year 9	9.21% (6.8%, 12.42%)	29
Year 10	9.12% (6.66%, 12.43%)	28	Year 10	14.9% (11.67%, 18.92%)	41	Year 10	11.71% (8.9%, 15.34%)	31

PPMI Dementia Survival Curve



Only about 10% at 10 years disease duration

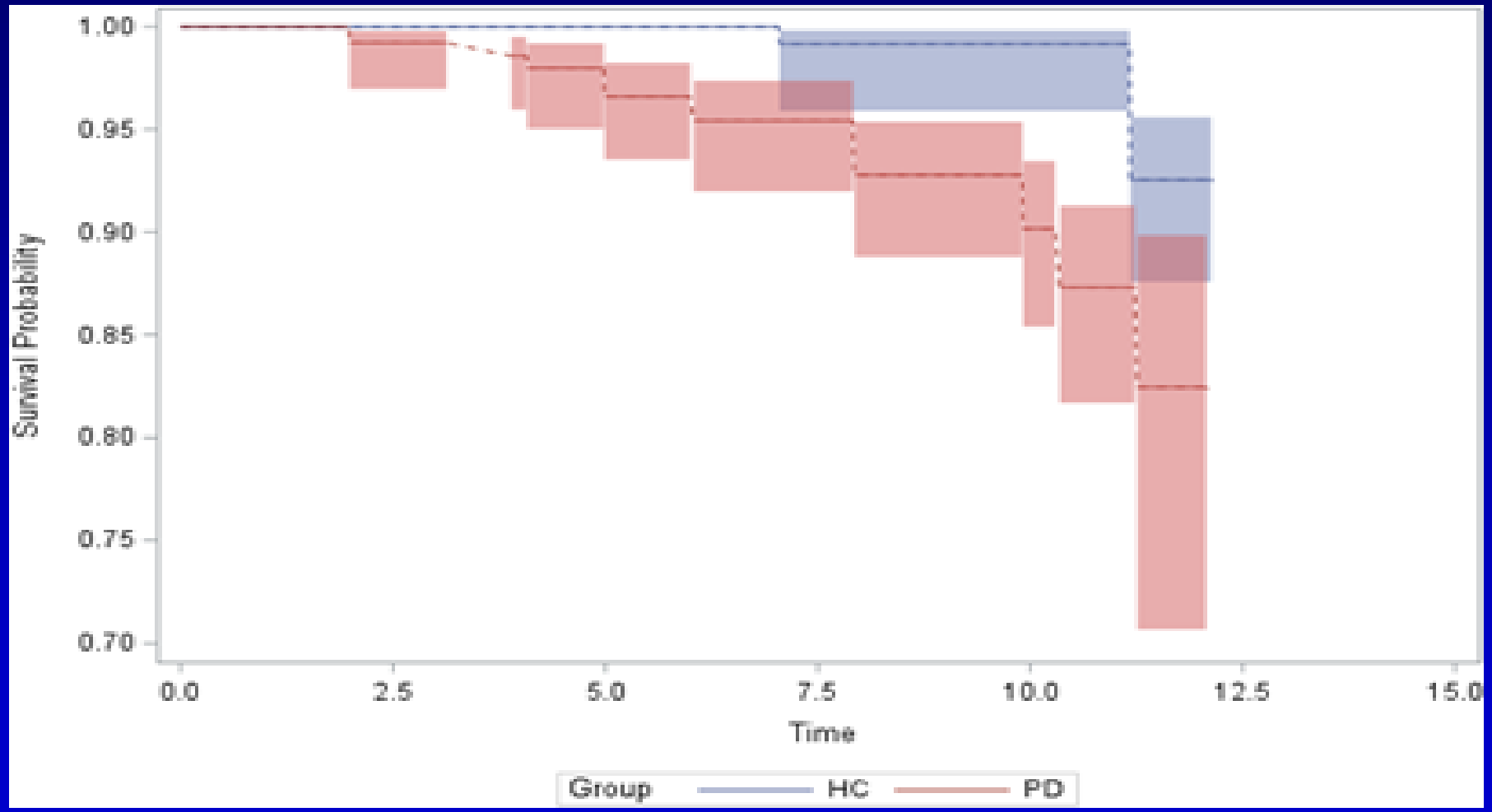
Unpublished data from PPMI study.

PD vs. Healthy Controls

Variable	Cohort	
	PD Participants (N = 280)	Healthy Controls (N = 192)
Age at Baseline (Years)		
Mean (SD)	60.5 (10.1)	60.6 (11.2)
(Min, Max)	(33, 82)	(31, 84)
Sex		
Male	177 (63%)	123 (64%)
Female	103 (37%)	69 (36%)
Race		
White	263 (94%)	176 (92%)
Non-White	15 (5%)	15 (8%)
Missing	2 (1%)	1 (1%)
Education (Years)		
Mean (SD)	15.7 (3.0)	16.0 (2.9)
(Min, Max)	(5, 26)	(8, 24)
MoCA		
Median	28.0	28.0
(Min, Max)	(27, 30)	(27, 30)

At baseline global cognition the same

Increased Dementia PD vs. Healthy Controls



Strengths and Limitations

- Strengths
  - Both studies current and ongoing
  - Relatively large compared with previous studies
  - Assess patients serially
  - Administer both global and detailed cognitive assessments across multiple domains
  - Have a site investigator or a consensus process to assign cognitive diagnosis at each study visit
  - Additionally, the PPMI study is multi-site and international
- Limitations
  - For PPMI study missing data in outlying years (partially due to COVID-19 pandemic)
  - For PPMI reliance on the site investigator to diagnose dementia without requiring consideration of cognitive test results
  - For both cohorts participants are relatively young at disease onset, highly educated, highly motivated, and overwhelmingly white, and were recruited specifically for participation in a research study

Conclusions

- Results from two large, ongoing prospective studies suggest that dementia in PD occurs less frequently, or at least later in the disease course, than oft-cited previous research studies have reported
  - Also must remember that dementia increasingly common in the general population as people age
- We also found that increasing age at disease diagnosis, male sex, and lower education level predicted development of dementia in PD, consistent with previous literature
  - This is not surprising as increasing age is also associated with an increased likelihood of comorbid Alzheimer's disease and vascular pathology, both of which are associated with cognitive impairment in PD
- This suggests a longer window to intervene to prevent or delay cognitive decline