



Supplementary Figure 1: Comparison of outcomes for a screening-adapted version of the PREDIGT Score (*Model 2*) to separate Parkinson’s patients from healthy controls in PPMI. Box plots illustrate the degree of classification, as depicted by AUC values for Step 1 (PREDIGT Questionnaire score only) and Step 2 (score for one of seven objective test results) and their combination, as color-coded in the inset). The box represents the median and the two middle quartiles (25–75%). Note, for GRS, the largest combined AUC value was equal to the corresponding AUCs of Step 1; and the largest combined AUC value when using UPSIT was the same as the corresponding AUC for the UPSIT test itself. Therefore, we placed extra green dots on top of the corresponding boxplots. Because of missing data, sample sizes in these tests were not identical. Therefore, AUC values of Step 1 (in black) were not identical. AUC, area under the ROC curve; UPSIT, University of Pennsylvania Smell Identification Test; GRS, genetic risk score; GDS, Geriatric Depression Scale; STAI-S, State-Trait Anxiety Inventory-State score; RBD, REM sleep behavior disorder Score Sheet; CSF, cerebrospinal fluid test.

1 **SUPPLEMENTARY TABLES**

2 **Supplementary Table 1:**

3 **Select variables and their previously assigned values within five categories that are entered**
 4 **into the PREDIGT Score formula [$P_R=(E+D+I) \times G \times T$].**

Factor	Assigned value	DeNoPa	PPMI	FOUND
Factor E: Exposome				
Metal exposure	0.5	Self-reported	n.a.	Self-reported
Pesticide exposure/Farm life	0.25	Self-reported	n.a.	Self-reported
Head trauma				
Concussive event(s)	1	Self-reported	MH	Self-reported
Subconcussive event(s)	0.5			
Constipation	0.5	MDS UPDRS: 1.11 SCOPA AUT: 05, 06 PD NMS: 05 PD NMSS: 21	MDS UPDRS: 1.11 SCOPA AUT: 05, 06	PPMI
Reduced olfaction		PD NMS 02		
Anosmia	1	PD NMSS 28		PPMI
Hyposmia	0.5	Sniffin' Sticks 16	UPSIT	
Smoking				
Current >= 20 years	-0.75			
Current 11-19 years	-0.5	Self-reported	n.a.	Self-reported
Past >= 20 years	-0.25			
Past 11-19 years	-0.125			
Any <= 10 years	-0.0625			
Caffeine intake				
>= 2 cups/day recent	-0.25	Self-reported	n.a.	Self-reported
>= 1 cups/day recent	-0.125			
Minimal risk score of 'E'				
Age of proband				
<= 50 years	0			
51-59 years	0.005			
60-69 years	0.0075			
70-79 years	0.02			
>= 80 years	0.03			
Factor D: DNA				
Family history of disease				
1st degree relative	0.5	Self-reported	Self-reported	PPMI
2nd degree relative	0.25			
3rd degree relative	0.125			

Minimal risk score of 'D'	0.01			
Factor I: Initiation of tissue response				
Presence of depression	0.25	MDS UPDRS: 1.3	MDS UPDRS: 1.3	PPMI
		PD NMS: 16		
		PD NMSS: 10		
		UPDRS 1: 3		
		PDQ39: 17		
		GDS; BDI; MADRS	GDS	
Presence of anxiety	0.25	MDS UPDRS: 1.4	MDS UPDRS: 1.4	PPMI
		PD NMS: 17		
		PD NMSS: 09		
		PDQ39: 21		
			STAI	
Presence of RBD	0.25	PD NMS: 25		PPMI
		RBD SQ	RBD SQ	
Minimal risk score of 'I'				
Age of proband				
<= 50 years	0			
51-59 years	0.001			
60-69 years	0.002			
70-79 years	0.003			
>= 80 years	0.004			
Factor G: Gender (Sex)				
Male	1.2	Sex	Sex	PPMI
Female	0.8			
Factor T: Time (Age)				
Age	Subject's age	Age at baseline visit	Age at baseline visit	PPMI

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6 Data collection in DeNoPa and PPMI+FOUND cohorts: most variables were collected using
7 self-reported questions. Additional instruments/assessments were highlighted in bold. DeNoPa =
8 *De Novo* Parkinson Study. PPMI = Parkinson's Progression Marker Initiative. FOUND = Follow
9 Up persons with Neurologic Disease Study. PD = Parkinson's disease. MH = Medical History.
10 MDS-UPDRS = Movement Disorder Society-Sponsored Revision of the Unified Parkinson's
11 Disease Rating Scale. Scopa-AUT = Scale for Outcomes in PD for Autonomic Symptoms. PD
12 NMS = Non-Movement Problems in Parkinson's. PD NMSS = Non-Motor Symptom assessment
13 scale for Parkinson's Disease. UPSIT = University of Pennsylvania Smell Identification Test.
14 UPDRS = Unified Parkinson's Disease Rating Scale. GDS = Geriatric Depression Scale (Short
15 Version). BDI = Beck's Depression Inventory. MADRS = Montgomery-Asberg Depression

- 16 Scale. STAI = State Trait Anxiety Inventory. RBD = REM Sleep Behavior Disorder. RBD SQ =
- 17 The REM Sleep Behavior Disorder Screening Questionnaire.

18 **Supplementary Table 2:**

19 **Questions used in DeNoPa and PPMI regarding five non-motor symptoms entered in the**
 20 **PREDIGT model.**

Variable	Question	DeNoPa		PPMI	
		OR (95% CI)	AUC (95% CI)	OR (95% CI)	AUC (95% CI)
Constipation	SCOPA.AUT.06	4.95 (2.79-8.95)	0.7 (0.64-0.76)	4.14 (2.76-6.31)	0.66 (0.63-0.7)
	SCOPA.AUT.05	4.75 (2.12-11.75)	0.61 (0.56-0.65)	3.53 (2.16-5.99)	0.61 (0.57-0.64)
	PD.NMS.05	6.48 (2.38-22.15)	0.6 (0.55-0.64)		
	MDS.UPDRS.1.11	5.96 (2.18-20.45)	0.59 (0.55-0.63)	3.51 (2.17-5.9)	0.61 (0.57-0.64)
	PD.NMSS.21.Severity	5.46 (1.78-22.44)	0.57 (0.53-0.6)		
	PD.NMSS.21.Frequency	5.46 (1.78-22.44)	0.57 (0.53-0.6)		
Hyposmia	PD.NMS.02	14.82 (6.94-34.78)	0.75 (0.71-0.8)		
	PD.NMSS.28.Severity	11.87 (5.56-27.83)	0.73 (0.68-0.78)		
	PD.NMSS.28.Frequency	14.23 (6.29-36.6)	0.74 (0.69-0.79)		
Depression	PDQ39.17	5.38 (3-9.86)	0.71 (0.65-0.77)		
	MDS.UPDRS.1.03	16.14 (6.13-54)	0.69 (0.65-0.74)	2.24 (1.36-3.8)	0.56 (0.53-0.59)
	PD.NMSS.10.Severity	8.69 (3.67-23.9)	0.66 (0.61-0.7)		
	PD.NMSS.10.Frequency	8.69 (3.67-23.9)	0.66 (0.61-0.7)		
	PD.NMS.16	4.35 (2.28-8.65)	0.64 (0.59-0.7)		
Anxiety	PDQ39.21	4.48 (2.45-8.43)	0.68 (0.62-0.74)		
	MDS.UPDRS.1.04	8.85 (2.61-46.91)	0.59 (0.55-0.62)	2.31 (1.52-3.57)	0.58 (0.55-0.62)
	PD.NMSS.09.Severity	4.35 (1.67-13.42)	0.58 (0.54-0.62)		
	PD.NMSS.09.Frequency	4.35 (1.67-13.42)	0.58 (0.54-0.62)		
	PD.NMS.17	4.44 (1.21-24.55)	0.54 (0.51-0.57)		
RBD	PD.NMS.25	3.35 (1.64-7.27)	0.6 (0.55-0.65)		
	RBD.SQ.06 sum 1-2	1.95 (1.09-3.53)	0.58 (0.52-0.64)	1.68 (1.16-2.43)	0.57 (0.53-0.61)
	RBD.SQ.06 sum 1-4	1.75 (0.99-3.12)	0.57 (0.51-0.63)	1.76 (1.22-2.55)	0.57 (0.53-0.62)

21 For each variable, the questions were ordered by their AUC values in the DeNoPa cohort. The
 22 most informative questions were also highlighted by bold.
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25 **Supplementary Table 3:**

26 **Questions included into Step 1 of Model 2 questionnaire.**

Factor	Variable	Questionnaire derived from DeNoPa	Questionnaire derived from PPMI
E	Metal exposure	Metal exposure? 0 = No 1 = Yes	Metal exposure? 0 = No 1 = Yes
	Pesticide exposure/ Farm life	Pesticide/herbicide and/or farm life? 0 = No 1 = Yes	Pesticide/herbicide and/or farm life? 0 = No 1 = Yes
	Head trauma	Severe Head Trauma? 0 = No 1 = Yes, didn't lose consciousness 2 = Yes, lost consciousness	Severe Head Trauma? 0 = No 1 = Yes, didn't lose consciousness 2 = Yes, lost consciousness
	Hyposmia	PD.NMS.02 Have you experienced any of the following in the last month? Loss or change in your ability to taste or smell. 0 = No 1 = Yes	n.a
	Constipation	SCOPA.AUT.06 In the past month, did you have to strain hard to pass stools? 0 = never 1 = sometimes 2 = regularly 3 = often	SCOPA.AUT.06 In the past month, did you have to strain hard to pass stools? 0 = never 1 = sometimes 2 = regularly 3 = often
	Smoking	Smoking history: 0 = No 1 = Any <= 10 years 2 = Past 11-19 years 3 = Past >= 20 years 4 = Current 11-19 years 5 = Current >= 20 years	Smoking history: 0 = No 1 = Any <= 10 years 2 = Past 11-19 years 3 = Past >= 20 years 4 = Current 11-19 years 5 = Current >= 20 years
	Caffeine intake	Caffeinated beverage intake: 0 = No 1 = over 1 cups/day recent 2 = over 2 cups/day recent	Caffeinated beverage intake: 0 = No 1 = over 1 cups/day recent 2 = over 2 cups/day recent
D	Family history	Family history of PD: 1 = 1st degree relative 2 = 2nd degree relative 3 = 3rd degree relative	Family history of PD: 1 = 1st degree relative 2 = 2nd degree relative 3 = 3rd degree relative

I	Depression	<p>PDQ39.17 Due to having Parkinson’s disease, how often during the last month have you felt depressed? 0 = never 1 = Occasionally 2 = Sometimes 3 = Often 4 = Always (or cannot do at all)</p>	<p>MDS.UPDRS.1.03 DEPRESSED MOOD Over the past week have you felt low, sad, hopeless, or unable to enjoy things? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you carry out your usual activities or to be with people? 0: Normal: No depressed mood. 1: Slight: Episodes of depressed mood that are not sustained for more than one day at a time. No interference with patient’s ability to carry out normal activities and social interactions. 2: Mild: Depressed mood that is sustained over days, but without interference with normal activities and social interactions. 3: Moderate: Depressed mood that interferes with, but does not preclude the patient’s ability to carry out normal activities and social interactions. 4: Severe: Depressed mood precludes patient’s ability to carry out normal activities and social interactions.</p>
	Anxiety	<p>PDQ39.21 Due to having Parkinson’s disease, how often during the last month have you felt anxious? 0 = never 1 = Occasionally 2 = Sometimes 3 = Often 4 = Always (or cannot do at all)</p>	<p>MDS.UPDRS.1.04 ANXIOUS MOOD Over the past week have you felt nervous, worried, or tense? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you to follow your usual activities or to be with other people? 0: Normal: No anxious feelings. 1: Slight: Anxious feelings present but not sustained for more than one day at a time. No interference with patient’s ability to carry out normal activities and social interactions. 2: Mild: Anxious feelings are sustained over more than one day at a time, but without interference with patient’s ability to carry out normal activities and social interactions. 3: Moderate: Anxious feelings interfere with, but do not preclude, the patient’s ability to carry out normal activities and social interactions. 4: Severe: Anxious feelings preclude patient’s ability to carry out normal activities and social interactions.</p>
	RBD	<p>PD.NMS.25 Have you experienced any of the following in the last month? Talking or moving about in your sleep as if you are 'acting' out a dream. 0 = No 1 = Yes</p>	<p>RBD.SQ.6.1 and 6.2 I have or had the following phenomena during my dreams: 6.1. speaking, shouting, swearing, laughing loudly 6.2. sudden limb movements, “fights” 0 = No 1 = Yes</p>
G	Sex	<p>Biological sex: 1 = Female 2 = Male</p>	<p>Biological sex: 1 = Female 2 = Male</p>
T	Age	<p>Participant’s age at baseline visit.</p>	<p>Participant’s age at baseline visit.</p>

28 **Supplementary Table 4:**

29 **Candidate objective tests for Step 2 in Model 2.**

Factor	Variable	Objective tests used in DeNoPa	Objective tests used in PPMI
E	Hyposmia	Sniffin' Sticks	University of Pennsylvania Smell Identification Test (UPSIT)
D	DNA	n.a.	Genetic Risk Score (GRS)
I	Depression	Geriatric Depression Scale (GDS); Beck's Depression Inventory (BDI); Montgomery-Asberg Depression Scale (MADRS)	Geriatric Depression Scale (GDS)
	Anxiety	n.a.	State Trait Anxiety Inventory State (STAI-S)
	RBD	The REM Sleep Behavior Disorder Screening Questionnaire (RBD SQ)	The REM Sleep Behavior Disorder Screening Questionnaire (RBD SQ)
	CSF biomarkers	α -synuclein Tau	α -synuclein Tau

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