

Supplementary Material

Parkinson’s Disease Case Ascertainment in the Sister Study: A Cohort for Environmental Health Research

Supplementary Table 1. Examples of environmental and relevant data collection in the Sister Study that are of interest to Parkinson’s disease research

	Examples and Summary of data collection
Diet and Lifestyle	
Dietary habit	Block 98 Food Frequency Questionnaire, nutrient intakes, dietary patterns, and other dietary-related exposures such as cooking habits and consumption of organic foods
Lifestyle	Common lifestyle exposures such as smoking, alcohol drinking, exercise, anthropometrics, sleep habits, mostly assessed with detailed questions and updated in follow-ups
Personal care	Personal care products that women may have used (e.g., hair products, cosmetics, other grooming products) during ages 10-13 years and the past 12 months preceding questionnaire completion, and updated in follow-ups
Socioeconomic Characteristics	Background questions including country of birth, race, ethnicity, sexual orientation, marital status, education, income, parental figures during childhood and their education levels, general economic status and food security as a child, and questions about experiences with stress and coping in the past 30 days, partially updated in follow-ups
Medical history	General health, cancer, a long list of chronic diseases, family history of selected diseases (e.g., PD), updated in follow-ups
Medication use	Over-the-counter and prescribed medication use – inventory methods; special sessions about uses of painkillers and antibiotics, updated in follow-ups
Symptomatic screeners	Please see Supplementary Table 2 for examples of PD-relevant symptom collection
Environmental / Occupational	
Residential history	Primary residency at enrollment which was updated throughout follow-ups; other residential data, for example, lived the longest since the age of 20, and the residence where she lived the longest before age 14. Addresses have been geocoded and linked to exposure of interest (e.g., air pollution and census measures)

Residential Farm Exposures	Questions for participants who had lived on a farm during childhood or adulthood, including the history of farm residence, raising of animals, crops, and pesticides
Occupational job history	Questions about current employment status and history of all jobs, military service, and volunteer work that took at least 10 hours per week since the age of 18, updated in follow-ups
Occupation - Exposure History	Questions on work conditions, exposures, schedule, industry, usual activities, specific chemicals and other materials ever used in any of the jobs held, and exposure to computer screens and video displays, updated in follow-ups
Occupation Job Modules	Detailed questions are asked in separate modules for 19 occupations (e.g., cleaning and housekeeping, farming, dry cleaner, factory worker, and teacher), partially updated in follow-ups
Female exposures	
Reproductive factors	Reproductive history, menstrual cycles, planned or unplanned pregnancies, use of different birth control methods, updated in follow-ups
Hormones	Questions about the use of birth control methods that involve hormones, including hormonal birth control methods used for contraception, control of menstrual cycles, or other medical reasons, hormone replacement therapy, medical procedures that may stop menstrual periods, current menstrual status and date of last menstrual period, symptoms of menopause, and use of other hormones, updated in follow-ups
Biospecimen and house dust	Blood (n=50,433, plasma, serum, plasma, whole blood, blood clot, & lymphocytes), urine (n=50,705), toenails (n=49,835), and house dust (n=50,367)
Sense of Smell sub-study	A sub-study sample of 3,482 participants with their sense of smell tested using the Brief Smell Identification Test, all sub-study participants and PD patients also had genome-wide data using the Neuro-array platform

*These are incomplete summaries; for detailed data collection at enrollment and follow-up, please visit <https://sisterstudy.niehs.nih.gov/English/researchers.htm>)

Supplementary Table 2. Nonmotor symptoms of Parkinson’s disease and negative control symptoms assessed at the cohort's second and third detailed follow-up (DFU)

PD Nonmotor symptoms	How assessed	Analytical definition
Hyposmia	Do you suffer from a decrease in or loss of your sense of smell?	Yes/No
Dream-enacting behavior	Have you ever been told, or suspected yourself, that you seem to "act out your dreams" while asleep, for example, punching or flailing arms in the air, making running movements, shouting, or screaming?	Yes/No
Cognitive impairment	AD-8 cognition screener	Yes/No, AD-8 \geq 4 [1, 2]
Depression	DFU2: Medication use or CESD-10 screener DFU3: Medication use or PHQ-2 screener	Yes/No DFU2: CESD-10 \geq 10 or use of medication; DFU3: PHQ-2 \geq 3 or use of medication [3-5]
Insomnia	Do you have difficulty falling asleep or staying asleep on a regular basis? and How many nights in a typical month do you have trouble sleeping?	Yes/No, self-reported with frequency \geq 15 days per month
Constipation	Typically, how often do you have bowel movements? and How often do you use laxatives, not including fiber or fiber tabs?	Yes/No using laxatives $>$ 1-3 times/month OR DFU2: bowel movements $<$ 1 time/day; DFU3: bowel movements $<$ 5-6 times/week
Anxiety	DFU2/DFU3: Since [reference date], have you used any prescription medicines to treat or to prevent anxiety? and If yes, are you currently taking this medication? DFU3 only: GAD-2	Yes/No, DFU2: medication use; DFU3: GAD-2 \geq 3 or medication use [6]
Daytime sleepiness	In the past month, about how often did you feel excessively sleepy during the day?	Yes/No, self-report \geq 3 days/week
Pain rating	In the past 7 days, how would you rate your pain on average (on a scale 0-10)?	“none or mild” if 0-5; “moderate or severe” if 6-10
Fatigue	In the past 7 days, how would you rate your fatigue on average?	“none or mild” vs. “moderate, severe, or extremely severe”
Dry eyes	Since [reference date], have you experienced daily, persistent, troublesome dry eyes for more than 3 months, or a recurrent feeling of	Yes/No

	sand or gravel in your eyes, or use of tear substitutes more than 3 times a day?	
Dry mouth	Since [reference date], have you experienced daily feeling of dry mouth for more than 3 months, or frequent drinking of liquids to aid in swallowing dry foods, or recurrently or persistently swollen salivary glands?	Yes/No
Excessive sweating	Since [reference date], have you experienced excessive sweating other than due to menopause?	Yes/No
Unexplained/Unintentional weight loss	Since [reference date], have you experienced unexplained and unintentional weight loss of 10 or more pounds?	Yes/No
Dizziness*	Since [reference date], have you experienced feeling light-headed, dizzy, or weak when standing from sitting or lying down?	Yes/No
Urination during night*	Since [reference date], have you experienced getting up regularly at night to pass urine?	Yes/No
Unexplained pain*	Since [reference date], have you experienced unexplained pains (not due to known conditions such as arthritis)?	Yes/No
Daytime saliva dribbling*	Since [reference date], have you experienced dribbling of saliva during daytime?	Yes/No
Negative control symptoms – symptoms that are unlikely PD nonmotor symptoms		
Swelling in joints	Since [reference date], have you experienced swelling in your wrist, finger, elbow, or knee joints lasting six or more weeks?	Yes/No
Joint stiffness in morning	Since [reference date], have you experienced joint stiffness in the mornings, lasting at least one hour, and for more than six weeks (do not include stiffness related or due to an injury or surgery)?	Yes/No
Wheezing or whistling in chest	Since [reference date], have you experienced wheezing or whistling in your chest?	Yes/No
Shortness of breath during exercise	Since [reference date], have you experienced shortness of breath when hurrying on level ground, or when walking up a slight hill, or when climbing a flight of stairs at your usual pace?	Yes/No
Shortness of breath at rest	Since [reference date], have you experienced shortness of breath when at rest?	Yes/No
Shortness of breath when lying down	Since [reference date], have you experienced shortness of breath when lying down?	Yes/No

Shortness of breath when walking	Since [reference date], have you experienced shortness of breath when walking?	Yes/No
Swelling or edema in legs	Since [reference date], have you experienced swelling (or edema) in your legs?	Yes/No

Reference date is January 1, 2009 for DFU2 and January 1, 2012 for DFU3

* Question only asked at DFU 3.

Supplementary Table 3. Participant characteristics at Sister Study enrollment in relation to incident Parkinson’s disease (PD)

Characteristic	Final adjudication			Cohort-based adjudication		
	PD (n=194)	non-PD (n=50,513)	OR (95% CI)	PD (n=210)	non-PD (n=50,513)	OR (95% CI)
Age, N (%)						
<60	65 (33.5)	34,065 (67.4)	Reference	73 (34.8)	34,065 (67.4)	Reference
60-69	96 (49.5)	13,465 (26.7)	3.63 (2.64, 4.99)	100 (47.6)	13,465 (26.7)	3.38 (2.49, 4.59)
70-79	33 (17.0)	2,983 (5.9)	5.57 (3.64, 8.52)	37 (17.6)	2,983 (5.9)	5.61 (3.76, 8.39)
Race, N (%)						
Non-Hispanic White	178 (91.8)	42,256 (83.7)	Reference	191 (91.0)	42,256 (83.7)	Reference
Non-Hispanic Black	4 (2.1)	4,440 (8.8)	0.26 (0.10, 0.70)	4 (1.9)	4,440 (8.8)	0.23 (0.09, 0.63)
Others	12 (6.2)	3,817 (7.6)	0.85 (0.47, 1.53)	15 (7.1)	3,817 (7.6)	1.00 (0.59, 1.70)
Education, N (%)						
Below college	36 (18.6)	7,288 (14.4)	1.29 (0.88, 1.90)	35 (16.7)	7,288 (14.4)	1.10 (0.75, 1.61)
College	99 (51.0)	31,155 (61.7)	Reference	113 (53.8)	31,155 (61.7)	Reference
Graduate	59 (30.4)	12,070 (23.9)	1.51 (1.09, 2.09)	62 (29.5)	12,070 (23.9)	1.41 (1.03, 1.92)
Smoking status, N (%)						
Never	114 (58.8)	28,360 (56.1)	Reference	119 (56.7)	28,360 (56.1)	Reference
Former	68 (35.1)	18,003 (35.6)	0.80 (0.59, 1.08)	77 (36.7)	18,003 (35.6)	0.88 (0.66, 1.18)
Current	12 (6.2)	4,150 (8.2)	0.87 (0.48, 1.60)	14 (6.7)	4,150 (8.2)	1.01 (0.58, 1.79)
Daily caffeine intake, N (%)						
Quartile 1	52 (26.8)	12,325 (24.4)	Reference	57 (27.1)	12,325 (24.4)	Reference
Quartile 2	48 (24.7)	12,343 (24.4)	0.93 (0.62, 1.37)	54 (25.7)	12,343 (24.4)	0.94 (0.65, 1.37)
Quartile 3	41 (21.1)	13,501 (26.7)	0.74 (0.49, 1.12)	46 (21.9)	13,501 (26.7)	0.74 (0.50, 1.10)
Quartile 4	53 (27.3)	12,344 (24.4)	1.02 (0.69, 1.50)	53 (25.2)	12,344 (24.4)	0.90 (0.62, 1.33)

Adjusted for baseline age, race, education, smoking status, and daily caffeine intake.

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