

SUPPLEMENTAL INFORMATION

Supplemental Methods:

Air pollution exposure assessment

We were interested in long-term air pollution exposure, and thus, considered the main study exposure window as a 10-year exposure with a 5-year lag time (15 years before PD diagnosis for patients or interview for controls) to account for a prodromal PD period (Supplemental Fig. 1). The exposure windows covered a very similar length and temporal period on average for patients and controls in each wave. For PEG1, we offset the control interview year with the average PD duration at baseline, resulting in exposure periods that were comparable in length and temporal time. The mean index year for PD patients was 2001.9 (SD = 2.5 years) and 2004.4 (SD = 1.5 years) for controls. For PEG 2, we did not need any adjustment as the average index year was already the same for patients and controls. The mean index year was 2009.1 (SD = 3.1 years) for patients and 2009.2 (SD = 0.5 years) for controls. To assess exposure across the study window of interest, we excluded participants who had missing air pollutant data $\geq 40\%$ of the averaging period in the study window. The missing pollutant data was due to participants who did not provide their residential or workplace address. This mostly was an issue for workplace address, as patients had usually stopped working due to disease progression. For those with missing pollutant data for $< 40\%$ of the averaging period, we estimated the missing data by calculating the average concentration of previous and subsequent years. This approach allowed us to include the largest possible number of participants while utilizing available data rather than assuming zero exposure for those with no address information. The summary exposure measure was computed separately for residential and workplace location for each participant. This represents on average 9.8 years of air pollution exposure information at residence and 9.2 years at workplace for study participants.

Pesticide exposure assessment

We assessed exposure to specific pesticide active ingredients near agricultural pesticide application sites using recorded data and a geographic information system-based model (Cockburn et al., 2011). Since 1974, California law has required the recording of all commercial agricultural pesticide use. This information was stored in the PUR database of the CA-DPR, detailing application locations, poundage, crop type, acreage, and application method. This comprehensive database spans over 40 years of agricultural pesticide applications in the tri-county area (Kern,

Fresno, and Tulare) during 1974-2017. Merging this with land-use and crop cover maps, we identified pesticide applications at specific agricultural sites (California Department of Water Resources). Our participants provided lifetime residential and workplace addresses, geocoded through a multi-step process (McElroy et al., 2003). For each pesticide and participant, we calculated pounds of pesticide applied per acre within a 500m buffer around each address annually since 1974, weighing the total poundage by the proportion of acreage treated (lbs/acre) (Paul et al., 2023).

Supplemental Figures:

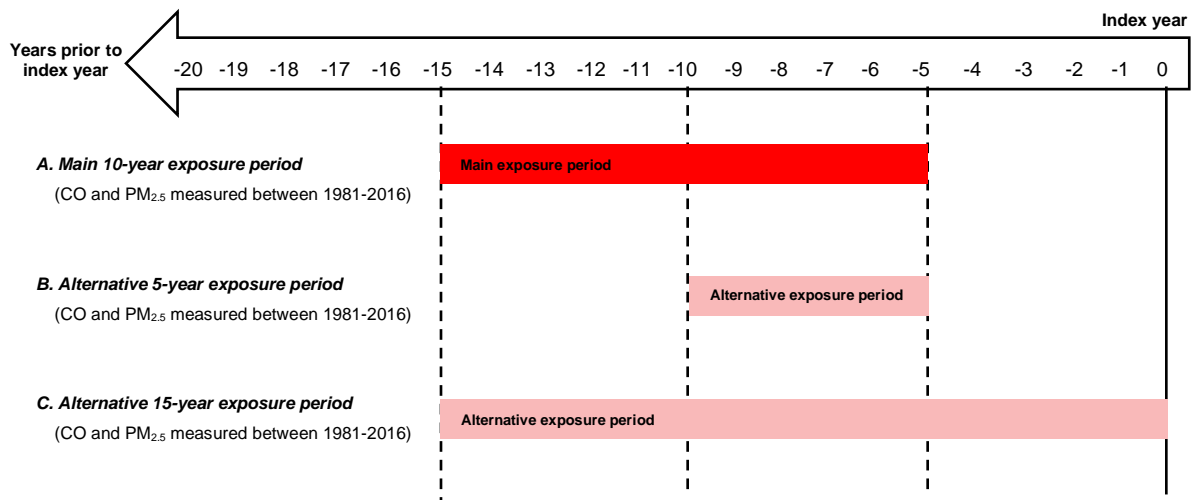


Fig. S1. Study design with main and alternative exposure periods and lag time.

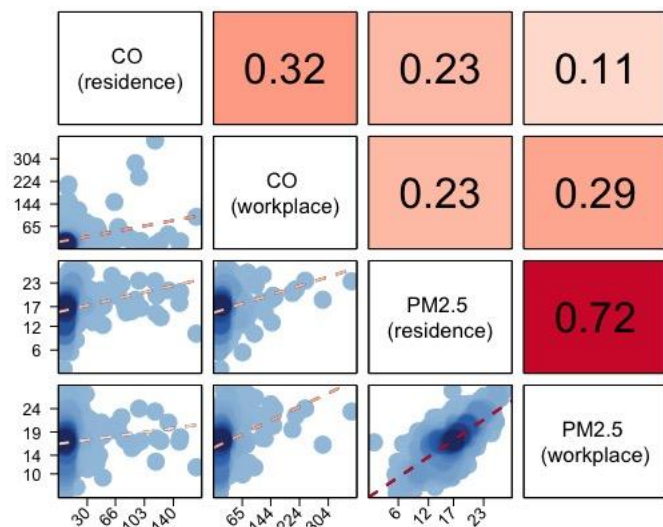
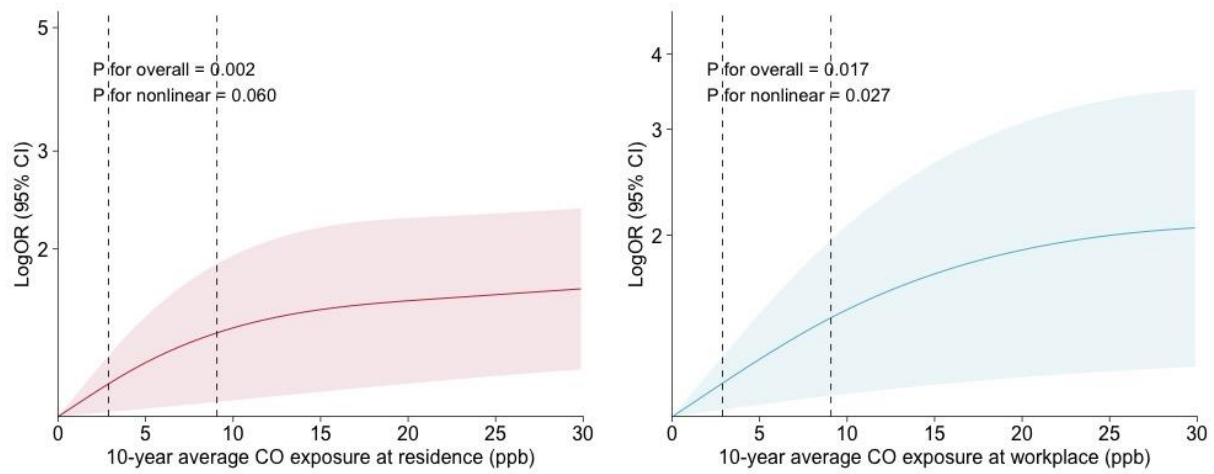


Fig. S2. Correlations between 10-year average CO (ppb) and PM_{2.5} (μg/m³) exposures with a 5-year lag time. Pearson correlations were tested only among the 576 participants who had measurements of CO and PM_{2.5} exposure levels estimated at both their homes and workplaces.

A



B

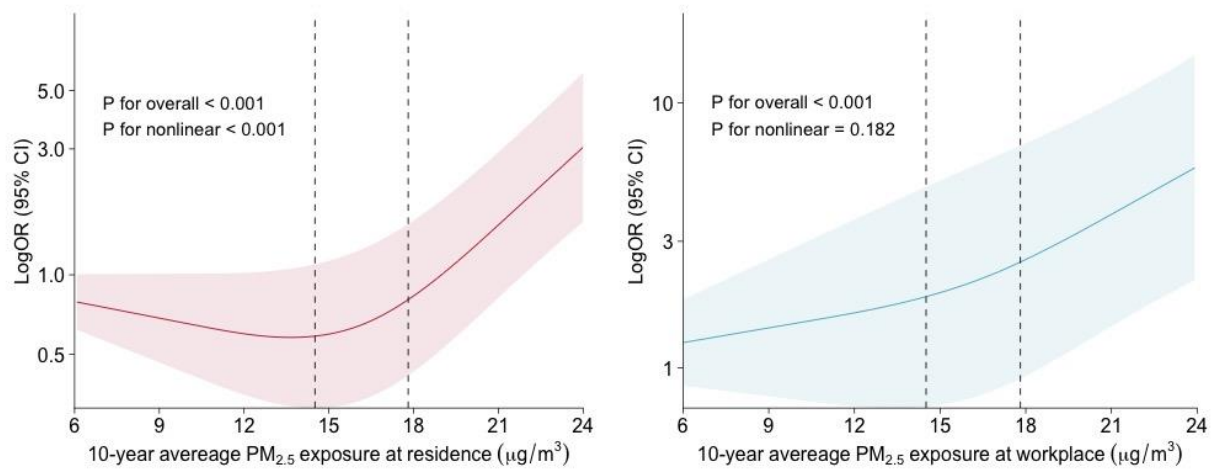


Fig. S3. Estimated effects of 10-year average A) CO and B) PM_{2.5} exposures with a 5-year lag time on PD using restricted cubic spline function models. We selected three knots at the 10th, 50th, and 90th percentiles of exposure. Dashed vertical lines represent tertile boundaries. Models were adjusted for age, sex, race, education, study wave, smoking status, and pesticide exposure.

Supplemental Tables:

Table S1. Descriptive statistics of 10-year average air pollution exposure with a 5-year lag time at residence and workplace.

Air pollutants	n	Mean (SD)	Percentile				IQR	
			Min	25th	50th	75th		
CO (ppb)								
Residence	1539	10.21 (20.13)	0.01	1.66	4.31	9.86	254.57	8.19
Workplace	645	17.40 (30.93)	0.01	3.44	8.44	18.87	368.45	15.43
PM_{2.5} (µg/m³)								
Residence	1671	15.96 (4.30)	1.15	13.29	16.27	18.62	29.39	5.33
Workplace	724	16.10 (4.43)	0.88	13.21	16.56	18.83	28.14	5.61

Table S2. Association between 5-year average CO exposure with a 5-year lag time and Parkinson's disease.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous CO (ppb) ^c	697/862	1.07 (1.02, 1.12)	1.07 (1.02, 1.13)	1.08 (1.03, 1.15)
T1 (0.01-1.96)	258/339	Reference	Reference	Reference
T2 (1.97-6.51)	237/304	1.02 (0.81, 1.30)	1.06 (0.83, 1.35)	1.19 (0.93, 1.53)
T3 (6.52-362.00)	202/219	1.21 (0.94, 1.56)	1.23 (0.94, 1.61)	1.40 (1.07, 1.85)
<i>p</i> -trend ^d		0.11	0.13	0.04
Workplace				
Continuous CO (ppb) ^c	322/306	1.01 (0.97, 1.06)	1.03 (0.99, 1.08)	1.03 (0.99, 1.09)
T1 (0.01-1.96)	67/65	Reference	Reference	Reference
T2 (1.97-6.51)	94/94	0.97 (0.62, 1.51)	1.13 (0.70, 1.81)	1.25 (0.76, 2.05)
T3 (6.52-362.00)	161/147	1.06 (0.71, 1.60)	1.47 (0.95, 2.30)	1.74 (1.09, 2.78)
<i>p</i> -trend ^d		0.62	0.07	0.02

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 7.74 ppb.

^dBased on linear model using the tertile midpoints.

Table S3. Association between 15-year average CO exposure without a 5-year lag time and Parkinson's disease.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous CO (ppb) ^c	693/864	1.06 (1.01, 1.12)	1.06 (1.01, 1.13)	1.08 (1.02, 1.14)
T1 (0.01-2.46)	251/339	Reference	Reference	Reference
T2 (2.47-7.50)	238/292	1.10 (0.87, 1.39)	1.16 (0.91, 1.49)	1.27 (0.99, 1.64)
T3 (7.51-327.00)	204/233	1.18 (0.92, 1.52)	1.22 (0.93, 1.59)	1.36 (1.03, 1.79)
<i>p</i> -trend ^d		0.27	0.30	0.14
Workplace				
Continuous CO (ppb) ^c	294/269	1.02 (0.96, 1.08)	1.04 (0.98, 1.12)	1.05 (0.99, 1.13)
T1 (0.01-2.46)	59/58	Reference	Reference	Reference
T2 (2.47-7.50)	85/91	0.92 (0.57, 1.47)	1.12 (0.68, 1.85)	1.19 (0.71, 2.01)
T3 (7.51-327.00)	150/120	1.23 (0.80, 1.90)	1.79 (1.11, 2.90)	2.01 (1.22, 3.33)
<i>p</i> -trend ^d		0.13	0.01	<0.01

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 8.73 ppb.

^dBased on linear model using the tertile midpoints.

Table S4. Association between 10-year average CO exposure with a 5-year lag time and Parkinson’s disease among participants with both residential and occupational addresses.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous CO (ppb) ^c	299/277	1.07 (0.98, 1.18)	1.08 (0.99, 1.20)	1.10 (1.00, 1.22)
T1 (0.01-2.87)	112/105	Reference	Reference	Reference
T2 (2.88-9.06)	109/108	0.95 (0.65, 1.38)	1.02 (0.69, 1.52)	1.18 (0.78, 1.77)
T3 (9.07-368.00)	78/64	1.14 (0.75, 1.75)	1.34 (0.84, 2.14)	1.55 (0.95, 2.53)
<i>p</i> -trend ^d		0.41	0.18	0.11
Workplace				
Continuous CO (ppb) ^c	299/277	1.03 (0.98, 1.09)	1.05 (0.99, 1.12)	1.06 (1.00, 1.13)
T1 (0.01-2.87)	59/61	Reference	Reference	Reference
T2 (2.88-9.06)	79/87	0.94 (0.59, 1.50)	1.08 (0.66, 1.76)	1.10 (0.66, 1.83)
T3 (9.07-368.00)	161/129	1.29 (0.84, 1.98)	1.72 (1.09, 2.72)	1.86 (1.16, 3.01)
<i>p</i> -trend ^d		0.08	0.01	<0.01

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 10.27 ppb.

^dBased on linear model using the tertile midpoints.

Table S5. Association between 5-year average PM_{2.5} exposure with a 5-year lag time and Parkinson's disease.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous PM _{2.5} (µg/m ³) ^c	764/919	1.25 (1.09, 1.43)	1.31 (1.13, 1.51)	1.41 (1.21, 1.65)
T1 (0.68-13.30)	249/318	Reference	Reference	Reference
T2 (13.31-17.10)	261/311	1.07 (0.85, 1.35)	1.10 (0.87, 1.40)	1.23 (0.96, 1.58)
T3 (17.11-28.20)	254/290	1.12 (0.88, 1.42)	1.18 (0.92, 1.51)	1.42 (1.09, 1.84)
<i>p</i> -trend ^d		0.35	0.19	0.01
Workplace				
Continuous PM _{2.5} (µg/m ³) ^c	353/342	1.23 (1.00, 1.51)	1.41 (1.13, 1.76)	1.53 (1.22, 1.94)
T1 (0.68-13.30)	107/119	Reference	Reference	Reference
T2 (13.31-17.10)	122/98	1.38 (0.95, 2.01)	1.55 (1.05, 2.30)	1.77 (1.18, 2.67)
T3 (17.11-28.20)	124/125	1.10 (0.77, 1.58)	1.30 (0.89, 1.91)	1.62 (1.08, 2.45)
<i>p</i> -trend ^d		0.59	0.18	0.02

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 5.75 µg/m³.

^dBased on linear model using the tertile midpoints.

Table S6. Association between 15-year average PM_{2.5} exposure without a 5-year lag time and Parkinson's disease.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous PM _{2.5} (µg/m ³) ^c	760/923	1.11 (0.97, 1.26)	1.14 (0.99, 1.32)	1.20 (1.03, 1.40)
T1 (1.08-13.90)	248/313	Reference	Reference	Reference
T2 (13.91-17.20)	258/311	1.05 (0.83, 1.32)	1.10 (0.86, 1.40)	1.21 (0.94, 1.56)
T3 (17.21-27.50)	254/299	1.07 (0.85, 1.36)	1.10 (0.84, 1.44)	1.27 (0.95, 1.69)
<i>p</i> -trend ^d		0.56	0.46	0.09
Workplace				
Continuous PM _{2.5} (µg/m ³) ^c	327/301	1.06 (0.87, 1.29)	1.28 (1.02, 1.61)	1.34 (1.06, 1.71)
T1 (1.08-13.90)	107/103	Reference	Reference	Reference
T2 (13.91-17.20)	110/91	1.16 (0.79, 1.72)	1.43 (0.95, 2.15)	1.62 (1.06, 2.49)
T3 (17.21-27.50)	110/107	0.99 (0.68, 1.45)	1.35 (0.87, 2.09)	1.58 (1.00, 2.50)
<i>p</i> -trend ^d		0.99	0.14	0.04

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 5.23 µg/m³.

^dBased on linear model using the tertile midpoints.

Table S7. Association between 10-year average PM_{2.5} exposure with a 5-year lag time and Parkinson’s disease among participants with both residential and occupational addresses.

Residence	Cases/controls	Odds ratio (95% CI)		
		Unadjusted	Model1 ^a	Model2 ^b
Continuous PM _{2.5} (µg/m ³) ^c	351/328	1.16 (0.96, 1.41)	1.36 (1.09, 1.71)	1.49 (1.18, 1.90)
T1 (0.88-14.50)	120/128	Reference	Reference	Reference
T2 (14.51-17.80)	116/101	1.23 (0.85, 1.77)	1.37 (0.94, 2.01)	1.51 (1.02, 2.26)
T3 (17.81-29.40)	115/99	1.24 (0.86, 1.79)	1.52 (1.00, 2.33)	1.95 (1.24, 3.08)
<i>p</i> -trend ^d		0.23	0.04	<0.01
Workplace				
Continuous PM _{2.5} (µg/m ³) ^c	351/328	1.24 (1.03, 1.50)	1.51 (1.22, 1.88)	1.59 (1.27, 2.01)
T1 (0.88-14.50)	104/118	Reference	Reference	Reference
T2 (14.51-17.80)	125/96	1.48 (1.02, 2.15)	1.85 (1.25, 2.76)	2.08 (1.38, 3.16)
T3 (17.81-29.40)	122/114	1.21 (0.84, 1.75)	1.55 (1.03, 2.36)	1.79 (1.16, 2.79)
<i>p</i> -trend ^d		0.28	0.02	0.01

^aAdjusted for age, race, sex, education, and study wave.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 5.46 µg/m³.

^dBased on linear model using the tertile midpoints.

Table S8. Two-pollutant model: association between 10-year average CO exposure with a 5-year lag time and Parkinson’s disease adjusted for 10-year average PM_{2.5} exposure with a 5-year lag time.

Residence	Cases/controls	Odds ratio (95% CI)		
		Adjusted for PM _{2.5}	Model1 ^a	Model2 ^b
Continuous CO (ppb) ^c	688/851	1.05 (1.00, 1.11)	1.06 (1.01, 1.13)	1.07 (1.01, 1.14)
T1 (0.01-2.87)	242/343	Reference	Reference	Reference
T2 (2.88-9.06)	242/292	1.08 (0.84, 1.39)	1.16 (0.89, 1.51)	1.25 (0.96, 1.63)
T3 (9.07-368.00)	204/216	1.16 (0.87, 1.55)	1.27 (0.94, 1.71)	1.38 (1.02, 1.87)
<i>p</i> -trend ^d		0.39	0.26	0.15
Workplace				
Continuous CO (ppb) ^c	336/309	1.02 (0.97, 1.08)	1.04 (0.99, 1.11)	1.05 (0.99, 1.12)
T1 (0.01-2.87)	70/73	Reference	Reference	Reference
T2 (2.88-9.06)	97/97	1.01 (0.63, 1.60)	1.12 (0.68, 1.83)	1.10 (0.66, 1.84)
T3 (9.07-368.00)	169/139	1.25 (0.79, 1.97)	1.60 (0.99, 2.61)	1.66 (1.01, 2.74)
<i>p</i> -trend ^d		0.20	0.03	0.02

^aAdjusted for age, race, sex, education, study wave, and PM_{2.5} exposure.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 10.27 ppb.

^dBased on linear model through the tertile midpoints.

Table S9. Two-pollutant model: association between 10-year average PM_{2.5} exposure with a 5-year lag time and Parkinson's disease adjusted for 10-year average CO exposure with a 5-year lag time.

Residence	Cases/controls	Odds ratio (95% CI)		
		Adjusted for CO	Model1 ^a	Model2 ^b
Continuous PM _{2.5} (µg/m ³) ^c	688/851	1.48 (1.26, 1.74)	1.53 (1.28, 1.84)	1.62 (1.34, 1.97)
T1 (0.88-14.50)	189/271	Reference	Reference	Reference
T2 (14.51-17.80)	229/306	1.04 (0.80, 1.35)	1.04 (0.79, 1.36)	1.15 (0.87, 1.53)
T3 (17.81-29.40)	270/274	1.31 (0.98, 1.75)	1.26 (0.92, 1.74)	1.45 (1.04, 2.03)
<i>p</i> -trend ^d		0.07	0.16	0.03
Workplace				
Continuous PM _{2.5} (µg/m ³) ^c	336/309	1.19 (0.93, 1.52)	1.38 (1.04, 1.84)	1.49 (1.11, 2.02)
T1 (0.88-14.50)	84/88	Reference	Reference	Reference
T2 (14.51-17.80)	126/103	1.22 (0.80, 1.87)	1.34 (0.86, 2.10)	1.57 (0.99, 2.52)
T3 (17.81-29.40)	126/118	1.01 (0.65, 1.59)	1.13 (0.68, 1.85)	1.34 (0.79, 2.28)
<i>p</i> -trend ^d		0.96	0.68	0.31

^aAdjusted for age, race, sex, education, study wave, and CO exposure.

^bAdjusted as in model 1 plus smoking status and pesticide exposure.

^cChange per interquartile range (IQR) of 5.46 µg/m³.

^dBased on linear model through the tertile midpoints.

Supplemental References

California Department of Water Resources, Land Use Surveys.

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