

Supplementary Material

Independent and Joint Associations of Tea Consumption and Smoking with Parkinson's Disease Risk in Chinese Adults

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Supplementary Material 2. Questions about tea consumption and smoking in the CKB study.

Information on tea consumption was assessed by the following questions: (1) During the past 12 months, how often did you drink any tea (never or rarely, only occasionally, only at certain seasons, every month but less than weekly, usually at least once a week)? For those who answered "usually at least once a week", we further asked: (2) During the past 12 months, on how many days did you drink tea in a typical week (1-2 days/week, 3-5 days/week, daily or almost every day)? (3) At about what age did you start drinking tea almost weekly? (4) Which kind of tea do you drink mostly (green /jasmine tea, oolong tea, black tea, other tea), and how many cups do you usually drink on days when you drink tea (with 300 ml as a standard cup size)? (5) How often do you change tea leaves during a day? (6) How much tea leaves do you usually add each time (with a picture showing the amount of tea leaves in grams)? For those who answered other than "usually at least once a week" to question (1), we then asked: (7) In the past, did you ever have a period of at least 1 year during which you usually drank tea at least once a week?

Information on smoking was assessed by the following questions: (1) How often do you smoke tobacco now (do not smoke now, only occasionally, on most days, daily or almost every day)? (2) How much tobacco do you usually smoke? (filter cigarettes [number/day], non-filter cigarettes [number/day], hand-rolled cigarettes [liang/month], pipe or water pipe [liang/month], cigars [number/day]). For those who answered "on most days" or "daily or almost every day" to question (1), we then asked: (3) At about what age did you first start smoking on most days? For those who answered "do not smoke now" or "only occasionally" to question (1), we then asked: (4) In the past, how frequently did you smoke (did not smoke, smoked only occasionally, smoked on most days, smoked daily or almost every day) and how many years ago did you last stop smoking regularly?

Supplementary Table 1. Association between tea consumption and risk of PD according to sex.

| | Men (n=210,202) | | | Women (n=302,521) | | | <i>p</i> _{interaction} |
|--|-----------------|-------------------|------------------|-------------------|-------------------|------------------|---------------------------------|
| | Cases | Cases/PYs (/1000) | HRs (95%CI) | Cases | Cases/PYs (/1000) | HRs (95%CI) | |
| Tea consumption frequency and leaf grams | | | | | | | 0.773 |
| Never in life | 104 | 0.25 | 1.00 | 222 | 0.15 | 1.00 | |
| Less than daily | 180 | 0.20 | 0.89 (0.69,1.15) | 169 | 0.13 | 0.95 (0.76,1.19) | |
| Daily (all) | 156 | 0.17 | 0.67 (0.50,0.89) | 91 | 0.17 | 0.69 (0.50,0.95) | |
| Daily consumption (g/day) | | | | | | | |
| ≤3.0 | 79 | 0.18 | 0.63 (0.45,0.88) | 72 | 0.2 | 0.74 (0.53,1.05) | |
| >3.0 | 77 | 0.16 | 0.70 (0.51,0.97) | 19 | 0.12 | 0.55 (0.33,0.91) | |
| Duration of consumption (y) | | | | | | | 0.618 |
| Never in life | 104 | 0.25 | 1.00 | 222 | 0.15 | 1.00 | |
| Daily consumption (y) | | | | | | | |
| <25 | 53 | 0.11 | 0.62 (0.42,0.90) | 25 | 0.09 | 0.77 (0.48,1.22) | |
| ≥25 | 103 | 0.24 | 0.68 (0.48,0.97) | 66 | 0.26 | 0.58 (0.34,1.00) | |
| Types of tea consumed | | | | | | | 0.252 |
| Never in life | 104 | 0.25 | 1.00 | 222 | 0.15 | 1.00 | |
| Daily consumption | | | | | | | |
| Green tea | 127 | 0.17 | 0.66 (0.47,0.92) | 88 | 0.18 | 0.77 (0.49,1.18) | |
| Others | 29 | 0.18 | 0.61 (0.37,1.01) | 3 | 0.07 | 0.36 (0.11,1.15) | |

CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease; PYs, person years.

Multivariable analyses were adjusted for the same variables as model3 in Fig. 1 and were stratified jointly by regions and age at baseline in 5-year intervals.

Supplementary Table 2. Sensitivity analyses of the association between tea consumption and risk of PD.

| | Never in life | Less than daily | Daily (all) | Daily consumption (grams/day) | |
|---|---------------|------------------|------------------|-------------------------------|------------------|
| | | | | ≤3.0 | >3.0 |
| Excluding cases identified during the first 2 years of follow-up (n=512,669) | | | | | |
| Cases | 298 | 330 | 240 | 146 | 94 |
| Cases/PYs (/1000) | 0.16 | 0.15 | 0.17 | 0.18 | 0.15 |
| HRs (95%CIs) | 1.00 | 0.93 (0.79,1.11) | 0.71 (0.57,0.88) | 0.71 (0.55,0.90) | 0.72 (0.55,0.94) |
| Excluding cases identified during the first 5 years of follow-up (n=512,494) | | | | | |
| Cases | 243 | 263 | 187 | 112 | 75 |
| Cases/PYs (/1000) | 0.13 | 0.12 | 0.13 | 0.14 | 0.12 |
| HRs (95%CIs) | 1.00 | 0.92 (0.76,1.12) | 0.72 (0.56,0.91) | 0.71 (0.54,0.93) | 0.73 (0.54,0.98) |
| Excluding participants with prevalent cancer, stroke, or coronary heart diseases at baseline (n=487,209) | | | | | |
| Cases | 276 | 308 | 221 | 137 | 84 |
| Cases/PYs (/1000) | 0.15 | 0.15 | 0.16 | 0.18 | 0.14 |
| HRs (95%CIs) | 1.00 | 0.92 (0.77,1.10) | 0.68 (0.54,0.85) | 0.68 (0.53,0.88) | 0.67 (0.51,0.89) |
| Excluding participants with a medical history of head injury at baseline (n=507,070) | | | | | |
| Cases | 324 | 341 | 246 | 151 | 95 |
| Cases/PYs (/1000) | 0.17 | 0.16 | 0.17 | 0.19 | 0.15 |
| HRs (95%CIs) | 1.00 | 0.91 (0.77,1.07) | 0.69 (0.56,0.85) | 0.69 (0.55,0.88) | 0.68 (0.52,0.88) |
| Further adjusting for intake of meat, fresh fruits, and vegetables (n=512,723) | | | | | |
| Cases | 326 | 349 | 247 | 151 | 96 |
| Cases/PYs (/1000) | 0.17 | 0.16 | 0.17 | 0.19 | 0.15 |
| HRs (95%CIs) | 1.00 | 0.92 (0.78,1.09) | 0.69 (0.56,0.84) | 0.69 (0.54,0.87) | 0.68 (0.53,0.88) |
| Further adjusting for the duration of storing pesticide at home (n=512,723) | | | | | |
| Cases | 326 | 349 | 247 | 151 | 96 |
| Cases/PYs (/1000) | 0.17 | 0.16 | 0.17 | 0.19 | 0.15 |
| HRs (95%CIs) | 1.00 | 0.92 (0.78,1.09) | 0.68 (0.55,0.84) | 0.68 (0.54,0.87) | 0.68 (0.52,0.88) |

CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease; PYs, person years.

Multivariable analyses were adjusted for the same covariates as model3 in Fig. 1, as appropriate.

Supplementary Table 3. Subgroup analysis of associations between tea consumption and risk of PD according to potential baseline risk factors (n=512,723).

| | Never in life | | Less than daily | | Daily | | <i>p</i> _{interaction} |
|--------------------------------|---------------|------|-----------------|------------------|-------|------------------|---------------------------------|
| | Cases | HRs | Cases | HRs (95% CIs) | Cases | HRs (95% CIs) | |
| Age at baseline (y) | | | | | | | 0.208 |
| <50 | 29 | 1.00 | 42 | 0.86 (0.51,1.45) | 33 | 0.90 (0.47,1.73) | |
| 50-59 | 84 | 1.00 | 111 | 0.99 (0.72,1.36) | 57 | 0.55 (0.36,0.83) | |
| ≥60 | 213 | 1.00 | 196 | 0.91 (0.73,1.12) | 157 | 0.72 (0.55,0.93) | |
| Region | | | | | | | 0.851 |
| Urban | 173 | 1.00 | 173 | 0.92 (0.74,1.16) | 85 | 0.64 (0.47,0.86) | |
| Rural | 153 | 1.00 | 176 | 0.93 (0.72,1.20) | 162 | 0.73 (0.54,0.99) | |
| Education | | | | | | | 0.803 |
| Middle school or higher | 109 | 1.00 | 149 | 0.91 (0.70,1.18) | 94 | 0.73 (0.53,1.00) | |
| Primary school or lower | 217 | 1.00 | 200 | 0.93 (0.75,1.16) | 153 | 0.66 (0.50,0.87) | |
| Alcohol consumption | | | | | | | 0.442 |
| Daily | 14 | 1.00 | 41 | 1.08 (0.58,2.04) | 38 | 0.65 (0.33,1.26) | |
| Less than daily | 312 | 1.00 | 308 | 0.90 (0.76,1.08) | 209 | 0.69 (0.56,0.87) | |
| Dairy products consumption | | | | | | | 0.123 |
| ≥4 days/week | 70 | 1.00 | 63 | 0.72 (0.50,1.04) | 33 | 0.42 (0.26,0.66) | |
| <4 days/week | 256 | 1.00 | 286 | 1.00 (0.83,1.21) | 214 | 0.78 (0.62,0.99) | |
| Physical activity ^a | | | | | | | 0.018 |
| higher level | 103 | 1.00 | 85 | 0.67 (0.49,0.92) | 68 | 0.76 (0.51,1.12) | |
| lower level | 223 | 1.00 | 264 | 1.04 (0.85,1.27) | 179 | 0.67 (0.52,0.86) | |
| BMI (kg/m ²) | | | | | | | 0.929 |
| ≥24.0 | 164 | 1.00 | 172 | 0.86 (0.68,1.09) | 109 | 0.60 (0.44,0.80) | |
| <24.0 | 162 | 1.00 | 177 | 0.99 (0.78,1.25) | 138 | 0.78 (0.58,1.06) | |
| Prevalent hypertension | | | | | | | 0.855 |
| Yes | 164 | 1.00 | 156 | 0.87 (0.68,1.12) | 125 | 0.64 (0.48,0.87) | |
| No | 162 | 1.00 | 193 | 0.96 (0.76,1.21) | 122 | 0.71 (0.53,0.95) | |

| | Never in life | | Less than daily | | Daily | | <i>p</i> _{interaction} |
|--------------------|---------------|------|-----------------|------------------|-------|------------------|---------------------------------|
| | Cases | HRs | Cases | HRs (95% CIs) | Cases | HRs (95% CIs) | |
| Prevalent diabetes | | | | | | | 0.421 |
| Yes | 37 | 1.00 | 27 | 0.73 (0.42,1.26) | 21 | 0.62 (0.32,1.20) | |
| No | 289 | 1.00 | 322 | 0.95 (0.79,1.13) | 226 | 0.69 (0.56,0.87) | |

BMI: body mass index; CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease.

Multivariable analyses were adjusted for the same covariates as model3 in Fig. 1, as appropriate.

^a METs were divided into two groups according to sex-specific median of total physical activity level.

Supplementary Table 4. Association between smoking and risk of PD according to sex.

| | Men (n= 210,202) | | | Women (n= 302,521) | | | <i>p</i> _{interaction} |
|--|------------------|-------------------|------------------|--------------------|-------------------|------------------|---------------------------------|
| | Cases | Cases/PYs (/1000) | HRs (95%CI) | Cases | Cases/PYs (/1000) | HRs (95%CI) | |
| Smoking status | | | | | | | 0.342 |
| Never or occasional | 161 | 0.28 | 1.00 | 464 | 0.14 | 1.00 | |
| Former | 104 | 0.36 | 0.99 (0.77,1.29) | 5 | 0.19 | 0.57 (0.23,1.40) | |
| Current (all) | 175 | 0.13 | 0.68 (0.54,0.86) | 13 | 0.17 | 0.68 (0.38,1.21) | |
| Current smoker (cig or equivalent/day) | | | | | | | |
| <20 | 92 | 0.15 | 0.76 (0.58,0.99) | 11 | 0.18 | 0.67 (0.36,1.25) | |
| ≥20 | 83 | 0.11 | 0.60 (0.45,0.80) | 2 | 0.16 | 0.71 (0.17,2.91) | |
| Duration of smoking | | | | | | | 0.916 |
| Never | 161 | 0.28 | 1.00 | 464 | 0.14 | 1.00 | |
| Current smoking (y) | | | | | | | |
| <30 | 52 | 0.07 | 0.83 (0.58,1.18) | 4 | 0.11 | 0.65 (0.24,1.77) | |
| ≥30 | 123 | 0.21 | 0.65 (0.50,0.84) | 9 | 0.23 | 0.68 (0.34,1.36) | |
| Years since stopped smoking | | | | | | | 0.366 |
| Never or occasionally | 161 | 0.28 | 1.00 | 464 | 0.14 | 1.00 | |
| Stopped smoking (y) | | | | | | | |
| ≥6 | 79 | 0.46 | 1.17 (0.88,1.56) | 4 | 0.24 | 0.67 (0.25,1.86) | |
| <6 | 25 | 0.22 | 0.67 (0.43,1.03) | 1 | 0.10 | 0.34 (0.05,2.41) | |

CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease; PYs, person years.

Multivariable analyses were adjusted for the same variables as model3 in Figure2 and were stratified jointly by regions and age at baseline in 5-year intervals.

Supplementary Table 5. Sensitivity analyses of the association between smoking and risk of PD.

| | Never or occasional | Former | Current (all) | Current smoking (cig or equivalent/day) | |
|---|---------------------|------------------|------------------|---|------------------|
| | | | | <20 | ≥20 |
| Excluding cases identified during the first 2 years of follow-up (n=512,669) | | | | | |
| Cases | 588 | 103 | 177 | 94 | 83 |
| Cases/PYs (/1000) | 0.16 | 0.33 | 0.12 | 0.14 | 0.11 |
| HRs (95%CIs) | 1.00 | 0.94 (0.74,1.21) | 0.64 (0.52,0.80) | 0.69 (0.53,0.88) | 0.59 (0.45,0.78) |
| Excluding cases identified during the first 5 years of follow-up (n=512,494) | | | | | |
| Cases | 478 | 81 | 134 | 73 | 61 |
| Cases/PYs (/1000) | 0.13 | 0.33 | 0.12 | 0.14 | 0.11 |
| HRs (95%CIs) | 1.00 | 0.88 (0.67,1.17) | 0.59 (0.46,0.75) | 0.64 (0.48,0.85) | 0.53 (0.39,0.73) |
| Excluding participants with prevalent cancer, stroke, or coronary heart diseases at baseline (n=487,209) | | | | | |
| Cases | 551 | 93 | 161 | 83 | 78 |
| Cases/PYs (/1000) | 0.15 | 0.33 | 0.12 | 0.13 | 0.10 |
| HRs (95%CIs) | 1.00 | 0.98 (0.75,1.27) | 0.61 (0.48,0.77) | 0.65 (0.49,0.85) | 0.57 (0.42,0.76) |
| Excluding participants with a medical history of head injury at baseline (n=507,070) | | | | | |
| Cases | 619 | 106 | 186 | 102 | 84 |
| Cases/PYs (/1000) | 0.16 | 0.34 | 0.13 | 0.15 | 0.11 |
| HRs (95%CIs) | 1.00 | 0.94 (0.74,1.20) | 0.66 (0.53,0.82) | 0.72 (0.57,0.93) | 0.58 (0.44,0.76) |
| Further adjusting for intake of meat, fresh fruits, and vegetables (n=512,723) | | | | | |
| Cases | 625 | 109 | 188 | 103 | 85 |
| Cases/PYs (/1000) | 0.16 | 0.35 | 0.13 | 0.15 | 0.11 |
| HRs (95%CIs) | 1.00 | 0.96 (0.75,1.22) | 0.66 (0.53,0.82) | 0.73 (0.57,0.93) | 0.58 (0.44,0.77) |
| Further adjusting for the duration of storing pesticide at home (n=512,723) | | | | | |
| Cases | 625 | 109 | 188 | 103 | 85 |
| Cases/PYs (/1000) | 0.16 | 0.35 | 0.13 | 0.15 | 0.11 |
| HRs (95%CIs) | 1.00 | 0.96 (0.75,1.22) | 0.66 (0.53,0.82) | 0.73 (0.57,0.93) | 0.58 (0.44,0.77) |

CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease; PYs, person years.

Multivariable analyses were adjusted for the same covariates as model3 in Fig. 2, as appropriate.

Supplementary Table 6. Subgroup analysis of associations between smoking and risk of PD according to potential baseline risk factors (n=512,723).

| | Never | | Former | | Current | | <i>p</i> _{interaction} |
|--------------------------------|-------|------|--------|------------------|---------|------------------|---------------------------------|
| | Cases | HRs | Cases | HRs (95% CIs) | Cases | HRs (95% CIs) | |
| Age at baseline (y) | | | | | | | 0.848 |
| <50 | 72 | 1.00 | 6 | 1.24 (0.48,3.22) | 26 | 0.67 (0.35,1.29) | |
| 50-59 | 183 | 1.00 | 17 | 0.72 (0.40,1.28) | 52 | 0.58 (0.38,0.89) | |
| ≥60 | 370 | 1.00 | 86 | 1.00 (0.76,1.32) | 110 | 0.69 (0.53,0.90) | |
| Region | | | | | | | 0.130 |
| Urban | 297 | 1.00 | 56 | 0.90 (0.65,1.25) | 78 | 0.80 (0.59,1.09) | |
| Rural | 328 | 1.00 | 53 | 1.03 (0.72,1.46) | 110 | 0.57 (0.43,0.77) | |
| Education | | | | | | | 0.289 |
| Middle school or higher | 219 | 1.00 | 48 | 0.96 (0.67,1.36) | 85 | 0.82 (0.60,1.11) | |
| Primary school or lower | 406 | 1.00 | 61 | 0.93 (0.67,1.29) | 103 | 0.55 (0.41,0.74) | |
| Alcohol consumption | | | | | | | 0.324 |
| Daily | 18 | 1.00 | 21 | 1.41 (0.71,2.81) | 54 | 1.24 (0.67,2.28) | |
| Less than daily | 607 | 1.00 | 88 | 0.94 (0.73,1.22) | 134 | 0.59 (0.47,0.74) | |
| Dairy products consumption | | | | | | | 0.140 |
| ≥4 days/week | 107 | 1.00 | 34 | 1.50 (0.95,2.38) | 25 | 0.91 (0.55,1.53) | |
| <4 days/week | 518 | 1.00 | 75 | 0.82 (0.62,1.09) | 163 | 0.61 (0.48,0.77) | |
| Physical activity ^a | | | | | | | 0.210 |
| higher level | 174 | 1.00 | 28 | 1.14 (0.70,1.87) | 54 | 0.57 (0.37,0.87) | |
| lower level | 451 | 1.00 | 81 | 0.91 (0.69,1.19) | 134 | 0.70 (0.55,0.90) | |
| BMI (kg/m ²) | | | | | | | 0.216 |
| ≥24.0 | 309 | 1.00 | 58 | 0.93 (0.67,1.30) | 78 | 0.74 (0.54,1.01) | |
| <24.0 | 316 | 1.00 | 51 | 0.98 (0.70,1.39) | 110 | 0.62 (0.46,0.83) | |
| Prevalent hypertension | | | | | | | 0.079 |
| Yes | 303 | 1.00 | 53 | 0.85 (0.60,1.20) | 89 | 0.71 (0.52,0.96) | |
| No | 322 | 1.00 | 56 | 1.10 (0.78,1.53) | 99 | 0.63 (0.47,0.84) | |

| | Never | | Former | | Current | | <i>p</i> _{interaction} |
|--------------------|-------|------|--------|------------------|---------|------------------|---------------------------------|
| | Cases | HRs | Cases | HRs (95% CIs) | Cases | HRs (95% CIs) | |
| Prevalent diabetes | | | | | | | 0.640 |
| Yes | 62 | 1.00 | 10 | 0.70 (0.32,1.51) | 13 | 0.84 (0.41,1.73) | |
| No | 563 | 1.00 | 99 | 1.00 (0.78,1.29) | 175 | 0.66 (0.52,0.82) | |

BMI: body mass index; CI, confidence interval; HR, hazard ratio; PD, Parkinson's disease.

Multivariable analyses were adjusted for the same covariates as model3 in Figure2, as appropriate.

^a METs were divided into two groups according to sex-specific median of total physical activity level.