Journal of Neural Transmission
https://doi.org/10.1007/s00702-025-02976-2

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

# Association between alcohol consumption and mortality in Parkinson's disease

You Hyun Park[1,5] · Yong Wook Kim[2,4] · Dae Ryong Kang[3,5] · Seo Yeon Yoon[2,4]

Received: 9 April 2025 / Accepted: 23 June 2025


## Abstract

Previous studies on the association between alcohol consumption and risk of Parkinson's disease (PD) have produced controversial results. However, the relationship between alcohol consumption and mortality in PD has scarcely been investigated. Among the nationwide population data from Korea National Health Insurance Service, newly diagnosed PD (ICD-10 code: G20 and a rare intractable disease registration code: V124), between 2009 and 2017, were selected. Alcohol consumption habit was obtained from a self-reported questionnaire on the National Health Screening Program. 32,419 individuals with PD were followed-up longitudinally until December 31, 2017, and all-cause mortality was evaluated. During the follow-up period (mean 4.37 ± 2.67 years), 9,049 deaths occurred. When nondrinkers are used as a reference group, there were significant associations between alcohol consumption and all-cause mortality in mild (hazard ratio [HR] 0.78, 95% confidence interval [CI] 0.71–0.84) and moderate drinkers (HR 0.69, 95% CI 0.58–0.82), but not in heavy drinkers (HR 0.84, 95% CI 0.69–1.02). In the sensitivity analysis using never drinkers as the reference group, the results also showed an overall 20% reduced mortality risk among drinkers with PD. Regarding changes in alcohol consumption behavior before and after diagnosis, the mortality rate was higher in former drinkers (HR 1.20, 95% CI 1.02–1.41) and lower in constant drinkers (HR 0.74, 95% CI 0.65–0.83) than in never drinkers. Alcohol consumption appears to be associated with reduced all-cause mortality in PD, suggesting potential neuroprotective effects on disease progression. Although drinking does not appear to be detrimental to all-cause mortality in individuals with PD, alcohol consumption in PD requires attention considering individual motor and non-motor symptoms. Future studies in other ethnic groups are warranted to validate the association between alcohol consumption and disease progression, including mortality, in PD.

**Keywords** Parkinson disease · Alcohol drinking · Alcohol abstinence · Mortality · Cohort studies

## Introduction

Parkinson's disease (PD) is the second most common neurodegenerative condition after Alzheimer's disease. Its etiology is multifactorial, involving both genetic and environmental contributions. Previous studies have uncovered connections between lifestyle factors and the risk of PD. For example, physical activity (PA), smoking, and caffeine are thought to reduce the risk of PD (Hernán et al. 2002; Fang et al. 2018; Mappin-Kasirer et al. 2020), whereas dietary habits such as dairy intake have been shown to increase the risk (Jiang et al. 2014; Hughes et al. 2017). A relationship between alcohol consumption and PD risk has also been noted in case-control and cohort studies, but the results have been inconsistent (Bettiol et al. 2015; Jiménez-Jiménez et al. 2019; Kim I. Y. et al. 2020a; Peters et al. 2020).

✉ Seo Yeon Yoon
syyoon23@yuhs.ac

1 Department of Biostatistics, Graduate School of Yonsei University, Seoul, Republic of Korea

2 Department and Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

3 Department of Precision Medicine & Biostatistics, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea

4 Institute for Innovation in Digital Healthcare, Yonsei University, Seoul, Korea, Republic Of

5 National Health Big Data Clinical Research Institute, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic Of

Published online: 07 July 2025

Despite knowledge about an association between alcohol consumption and PD risk, studies examining the association between alcohol use and mortality in this group have been scarce (Paul et al. 2019). A recent cohort study of patients with PD reported that never-drinkers have increased mortality relative to ever-drinkers; however, in the study, alcohol consumption before the PD diagnosis was used to predict mortality after the diagnosis (Paul et al. 2019). Furthermore, as this study investigated multiple lifestyle factors vis-à-vis disease progression including mortality, detailed information about alcohol consumption was limited (Scherr et al. 1992).

PD is a progressive neurodegenerative disease characterized by a gradual loss of dopaminergic cells in the substantia nigra pars compacta. As neuroprotective factors for PD development can also modify disease progression including mortality, we examined the association between alcohol consumption and mortality in individuals with PD in order to clarify their association and suggest a guide for alcohol consumption in PD. In this study, we used prospectively collected nationwide cohort data to overcome the limitations of previous research, including recall bias and exclusion of potentially-confounding variables, such as smoking (Palacios et al. 2012; Bettiol et al. 2015; Jiménez-Jiménez et al. 2019). Specifically, we investigated the association between post-diagnosis alcohol consumption and all-cause mortality in individuals with PD. We also evaluated the relationship between changes in alcohol consumption behavior before and after the PD diagnosis and subsequent mortality.

## Methods

### Standard protocol approvals, registrations, and patient consents

The data can be used after approval of the Institutional Review Board and the Korea NHIS Big Data Operations Department (https://nhiss.nhis.or.kr/bd/ay/bdaya 001 iv.do). No separate ethics approval was required.

### Data source

We used the national claims database of the National Health Insurance Service (NHIS) of Korea. The database contains the medical records of the entire Korean population covered by the obligatory NHIS and Medical Aid programs. Sociodemographic information and healthcare utilization information for inpatient and outpatient visits, including diagnoses, procedures, surgery, and prescription records, are available in the database. Diagnoses are coded according to International Classification of Disease-10th Revision-Clinical Modification (ICD-10-CM) nomenclature. The NHIS provides not only claims data but also health screening examination data. The NHIS provides a free biannual national health screening program (NHSP) to all beneficiaries aged≥40 years, and the NHSP database includes patient history, physical examinations, anthropometric measurements, and questionnaire data.

### Study population

In 2006, the Korean government implemented a registration program for rare intractable diseases, which provides disease-specific codes. The rare intractable disease code for PD is V124. In this study, we screened cases of newly-diagnosed PD patients (ICD-10 code G20; rare intractable disease registration code V124) between January 2008 and December 2017, excluding those diagnosed with secondary parkinsonism or atypical parkinsonism (ICD-10 codes G21-G23). We also excluded individuals diagnosed with PD before 2009, to include only new PD patients diagnosed after 2009 (washout period: 2008). Thereafter, we identified PD patients who had participated in the NHSP at least once within 2 years of their initial diagnosis. Individuals with missing data were excluded. Finally, we longitudinally followed these 32,419 PD patients to investigate the association between alcohol use and death. The patient enrollment flowchart is presented in Supplementary File 2.

### Alcohol consumption

As part of the NHSP, individuals who currently drink alcohol completed self-report questionnaires about their average alcohol consumption per day and week. Questions included: 'How many days a week do you drink on average?' and 'How much do you usually drink a day (cups)?' Although beverages may have different alcohol percentages, previous studies have shown that the alcohol content per cup is similar in Korea regardless of beverage type (Kim Y. G. et al. 2020b; Yoo et al. 2021). Therefore, each self-reported cup was converted to 8 g of alcohol. Based on the total alcohol intake per week from NHSP questionnaire within two years form PD diagnosis (baseline), participants were classified into four primary groups: heavy drinkers (more than 210 g of alcohol per week), moderate drinkers (105–209 g of alcohol per week), mild drinkers (less than 104 g of alcohol per week), and nondrinkers (individuals who were not currently drinking at baseline, including never- and former drinkers).

Changes in alcohol consumption behavior were assessed by identifying patterns of alcohol use within the two years before and after the PD diagnosis. Participants were categorized into three groups based on their drinking behavior over this period: constant drinkers (individuals who continued to

drink alcohol both before and after their PD diagnosis), former drinkers (individuals who consumed alcohol before the PD diagnosis but stopped drinking afterward), and never-drinkers (individuals who have never consumed alcohol at any time).

### Other variables

The endpoint of this study was all-cause mortality in patients with PD until December 31, 2017. All-cause mortality was assessed using death records from the Korean NHIS database, which provides comprehensive data on patient outcomes, including mortality, for all registered individuals in Korea.

Demographic variables, such as age and sex, were based on data entered at the time of diagnosis. The financial income deciles of participants were categorized into two groups based on the NHI premium: low-income level (the lower 25% group) versus not low-income. The Charlson Comorbidity Index (CCI) and other comorbidities were identified based on the corresponding disease diagnostic codes. Comorbidities of participants in this study included hypertension (I10-I13, I15), dyslipidemia (E780-E785), pneumonia (J10-J18), osteoporosis (M80-M82), and depression (F23, F33). The levodopa equivalent daily dose (LEDD) was used to index disease severity. Anthropometric factors, including height, weight, and blood pressure, were noted. Body mass index (BMI) was calculated as weight divided by height (kg/m2). Plasma glucose, lipids, and hemoglobin levels were determined through venous sampling after fasting for > 8 h.

Information about lifestyle factors, including smoking and PA, were gleaned from self-report questionnaires. Smoking status was categorized based on the Centers for Disease Control and Prevention into the following three groups: current smoker (had smoked in their lifetime and currently smoked), ex-smoker (had smoked in their lifetime but did not currently smoke), and never-smoker. PA was classified into two groups by converting the intensity of PA and the number of weekly exercises per intensity level into a standard metabolic equivalent (MET): (1) light-intensity activities (< 600 MET × min/week) and (2) moderate/vigorous-intensity activities (≥ 600 MET × min/week) (Craig et al. 2003; Ainsworth et al. 2011; Lear et al. 2017).

### Statistical analysis

The characteristics of participants according to alcohol consumption status were compared using analyses of variance (ANOVA) for continuous variables and Chi-square tests for categorical variables. Results are presented as means ± standard deviations for continuous variables and as frequencies and percentages for categorical variables. Survival analysis over time was performed through a log-rank test using Kaplan-Meier curves. Cox proportional hazards regression analyses were performed to estimate hazard ratios (HRs) and their 95% confidence intervals (CIs) for the association between alcohol consumption and all-cause mortality, with adjustment for covariates. We used three progressive models: Model 1 was unadjusted; Model 2 was adjusted for age, sex, income level, and residential area; and Model 3 was further adjusted for CCI, comorbidities, lifestyle factors (smoking status and PA), anthropometric data, and LEDD. To minimize abstainer bias in examining the association between alcohol consumption and mortality in PD, we performed a sensitivity analysis using never drinkers as the reference group. Statistical analyses were performed using SAS version 9.2 (SAS Inc., Cary, NC, USA). Statistical significance was set at $P < 0.05$.

## Results

### Baseline characteristics of the study population

The baseline characteristics of the participants are shown in Table 1. Among individuals with PD, 27,401 (84.52%), 3,957 (12.21%), 649 (2.00%), and 412 (1.27%) were classified as non, mild, moderate, and heavy drinkers, respectively. Drinkers were younger and more likely to be male than non-drinkers. The mean age of heavy drinkers was 65.71 years, approximately five years lesser than that of nondrinkers. Nondrinkers had much higher CCI scores and were more likely to have comorbidities than drinkers. Nondrinkers were less likely to smoke and perform regular physical activities than drinkers. The BMI and waist circumference of drinkers were higher than those of nondrinkers. The mean values of blood pressure, triglycerides, and fasting glucose in moderate and heavy drinkers were higher than those in nondrinkers. The mean LEDD in heavy drinkers was also higher than that in nondrinkers.

### Risk of all-cause mortality in PD by alcohol consumption

Within the total participants with PD, 9,049 individuals (27.91%) died during the follow-up period (mean 4.37 ± 2.67 years). Table 2 shows the HRs for all-cause mortality according to alcohol consumption status, using nondrinkers as the reference. Mortality rate was highest in nondrinkers (74.57/1000 person-years), followed by heavy drinkers (58.42/1000 person-years), mild drinkers (54.99/1000 person-years), and then moderate drinkers (43.91/1000 person-years). In univariate analyses, the HRs

**Table 1** Demographic and medical characteristics of patients with Parkinson's disease

| Variables | Nondrinkers ($n$=27,401) | Mild drinkers ($n$=3,957) | Moderate drinkers ($n$=649) | Heavy drinkers ($n$=412) | $P$ value |
|---|---|---|---|---|---|
| Age (years) | 70.83±9.13 | 67.81±10.37 | 64.51±10.69 | 65.71±10.29 | <0.0001 |
| Male (%) | 10,524 (38.41%) | 2,729 (68.97%) | 599 (92.30%) | 391 (94.90%) | <0.0001 |
| Low income level | 5,119 (18.68%) | 738 (18.65%) | 113 (17.41%) | 85 (20.63%) | 0.6320 |
| Residential area (urban) | 10,728 (39.15%) | 1,787 (45.16%) | 299 (46.07%) | 161 (39.08%) | <0.0001 |
| Insurance type | | | | | 0.3787 |
| National health insurance | 26,349 (96.16%) | 3,825 (96.66%) | 628 (96.76%) | 398 (96.60%) | |
| Medical aid | 1,052 (3.84%) | 132 (3.34%) | 21 (3.24%) | 14 (3.40%) | |
| Charlson Comorbidity Index | 3.95±2.57 | 3.48±2.61 | 3.09±2.34 | 3.20±2.45 | <0.0001 |
| *Hypertension | 17,905 (65.34%) | 2,397 (60.58%) | 378 (58.24%) | 255 (61.89%) | <0.0001 |
| *Dyslipidemia | 12,915 (47.13%) | 1,877 (47.43%) | 265 (40.83%) | 160 (38.83%) | <0.0001 |
| *Pneumonia | 15,333 (55.96%) | 1,932 (48.82%) | 277 (42.68%) | 176 (42.72%) | <0.0001 |
| *Osteoporosis | 10,183 (37.16%) | 840 (21.23%) | 56 (8.63%) | 46 (11.17%) | <0.0001 |
| *Depression | 8,169 (29.81%) | 951 (24.03%) | 120 (18.49%) | 62 (15.05%) | <0.0001 |
| Smokers | | | | | <0.0001 |
| Never smoker | 22,495 (82.11%) | 1,936 (48.93%) | 250 (38.52%) | 148 (36.01%) | |
| Ex-smoker | 3,696 (13.49%) | 1,358 (34.32%) | 253 (38.98%) | 150 (36.50%) | |
| Current smoker | 1,205 (4.40%) | 663 (16.76%) | 146 (22.50%) | 113 (27.49%) | |
| Physically active subjects | 9,923 (36.21%) | 1,685 (42.58%) | 380 (58.55%) | 219 (53.16%) | <0.0001 |
| Body mass index (kg/m$^2$) | 23.75±3.38 | 24.04±3.08 | 24.10±3.02 | 24.32±3.17 | <0.0001 |
| Waist circumference (cm) | 82.82±14.44 | 84.15±8.85 | 85.31±8.40 | 86.66±8.42 | <0.0001 |
| Systolic blood pressure (mmHg) | 126.62±16.06 | 126.06±15.15 | 126.86±15.23 | 129.58±14.86 | 0.0003 |
| Diastolic blood pressure (mmHg) | 76.17±10.06 | 76.23±9.66 | 77.50±10.17 | 78.20±10.17 | <0.0001 |
| Laboratory findings | | | | | |
| Total cholesterol (mg/dL) | 183.34±40.34 | 182.78±38.89 | 181.25±38.75 | 184.61±38.32 | 0.4411 |
| Triglyceride (mg/dL) | 127.06±73.08 | 122.85±87.90 | 133.48±102.61 | 150.29±106.13 | <0.0001 |
| Hemoglobin (g/dL) | 13.12±1.57 | 13.89±1.49 | 14.36±1.44 | 14.27±1.55 | <0.0001 |
| Fasting glucose (mg/dL) | 106.04±29.56 | 105.61±27.69 | 107.65±29.41 | 109.86±28.60 | 0.0208 |
| Levodopa equivalent daily dose | 401.35±466.85 | 378.34±252.70 | 376.47±234.77 | 403.10±254.31 | 0.0153 |

Values are presented as mean±SD or number (%). *Other comorbidities not included in the Charlson Comorbidity Index

CCI=Charlson comorbidity index

**Table 2** Cox proportional hazard regression analysis of all-cause mortality in Parkinson's disease according to alcohol consumption

| Alcohol consumption | PD ($n$) | Mortality ($n$) | Person-years | Mortality rate | Model 1[a] | $P$ value | Model 2[b] | $P$ value | Model 3[c] | $P$ value |
|---|---|---|---|---|---|---|---|---|---|---|
| Nondrinkers | 27,401 | 8,062 | 108112.41 | 74.57 | 1.00 | | 1.00 | | 1.00 | |
| Mild drinkers | 3,957 | 740 | 13456.53 | 54.99 | 0.72 (0.66–0.77) | <0.0001 | 0.71 (0.65–0.76) | <0.0001 | 0.78 (0.71–0.84) | <0.0001 |
| Moderate drinkers | 649 | 134 | 3051.84 | 43.91 | 0.57 (0.48–0.68) | <0.0001 | 0.59 (0.50–0.71) | <0.0001 | 0.69 (0.58–0.82) | <0.0001 |
| Heavy drinkers | 412 | 113 | 1934.39 | 58.42 | 0.76 (0.63–0.92) | 0.0041 | 0.72 (0.60–0.87) | 0.0007 | 0.84 (0.69–1.02) | 0.0800 |

The mortality rate is the incidence of mortality per 1000 person-years

[a]Model 1: unadjusted

[b]Model 2: adjusted for age, sex, income level, and residential area

[c]Model 3: adjusted for age, sex, income level, residential area, Charlson Comorbidity Index, comorbidities, lifestyle factors (smoking, physical activity), blood pressure, anthropometric data, and levodopa equivalent daily dose

of the mild, moderate, and heavy drinkers were 0.72 (95% CI 0.66–0.77), 0.57 (95% CI 0.48–0.68), and 0.76 (95% CI 0.63–0.92), respectively. This trend persisted even after adjustment for age, sex, income level, and residential area (Model 2). After further adjustment for CCI, comorbidities, lifestyle factors, anthropometric data, and LEDD (Model 3), the HR of the heavy drinkers (0.84) was not statistically significant (95% CI 0.69–1.02). Survival rates were estimated using Model 3 in the multivariable-adjusted survival curves (Supplementary File 2).

| | | PD (n) | Mortality (n) | Person-years | Mortality rate | Adjusted HR (95% CI) | *P* for trend |
|---|---|---|---|---|---|---|---|
| **Male** | Nondrinkers | 10,524 | 3,895 | 37777.94 | 103.10 | 1.00 | p<.0001 |
| | Mild drinkers | 2,729 | 615 | 10194.52 | 60.33 | 0.74 (0.68-0.82) | |
| | Moderate drinkers | 599 | 133 | 2811.23 | 47.31 | 0.70 (0.59-0.84) | |
| | Heavy drinkers | 391 | 110 | 1857.07 | 59.23 | 0.82 (0.68-1.00) | |
| **Female** | Nondrinkers | 16,877 | 4,167 | 70334.47 | 59.25 | 1.00 | p=.4872 |
| | Mild drinkers | 1,228 | 125 | 3262.01 | 38.32 | 0.98 (0.81-1.20) | |
| | Moderate drinkers | 50 | 1 | 240.61 | 4.16 | 0.20 (0.14-1.03) | |
| | Heavy drinkers | 21 | 3 | 77.33 | 38.80 | 2.25 (0.73-5.12) | |

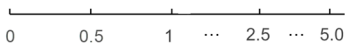
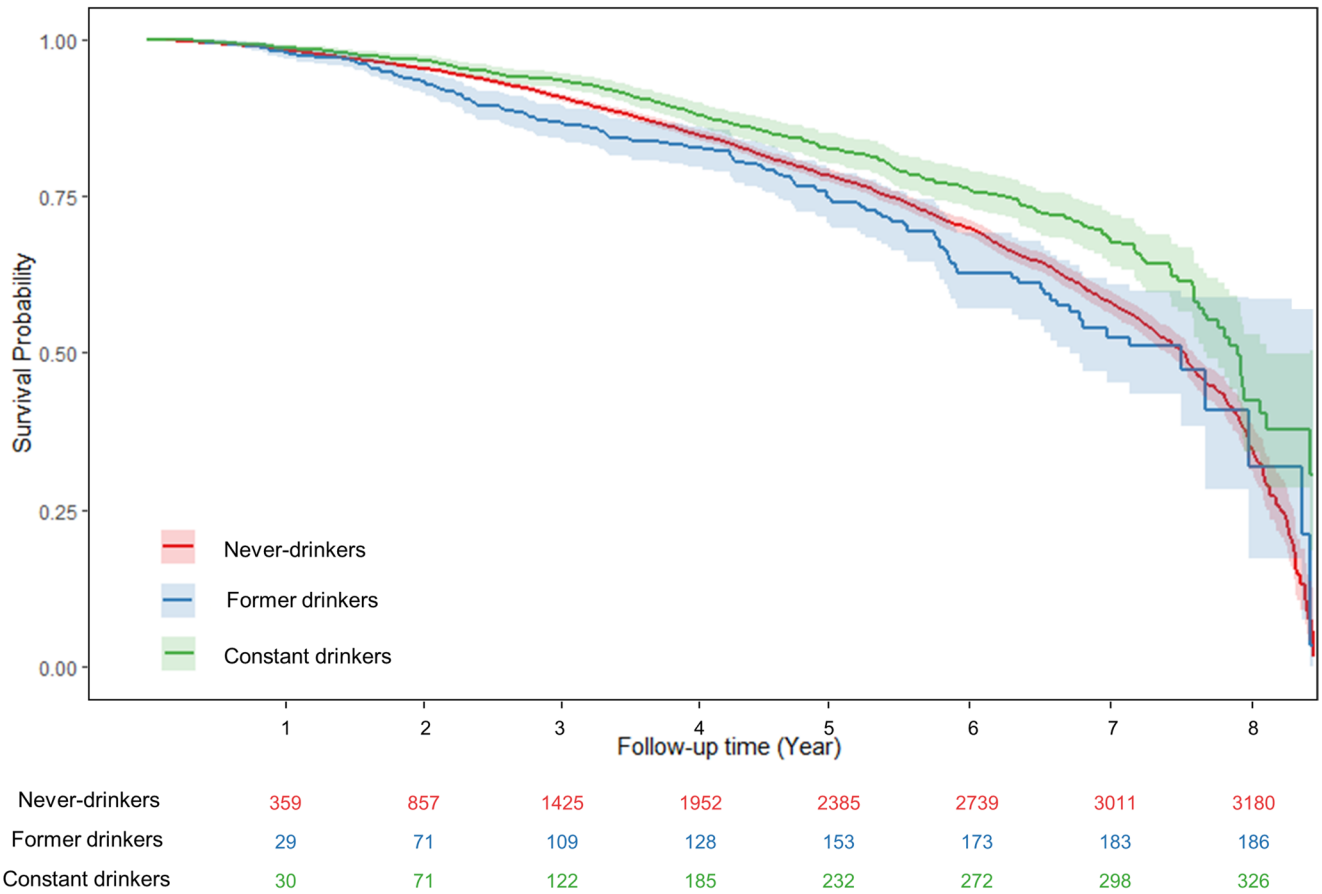



**Fig. 1** Adjusted hazard ratios for all-cause mortality in patients with Parkinson's disease stratified by sex and according to level of alcohol consumption




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Never-drinkers | 359 | 857 | 1425 | 1952 | 2385 | 2739 | 3011 | 3180 |
| Former drinkers | 29 | 71 | 109 | 128 | 153 | 173 | 183 | 186 |
| Constant drinkers | 30 | 71 | 122 | 185 | 232 | 272 | 298 | 326 |

**Fig. 2** Multivariable-adjusted survival curves in individuals with Parkinson's disease according to alcohol consumption behavior change before and after the diagnosis. Shading represents 95% confidence intervals

In a subgroup analysis by sex, there was a significant association between alcohol consumption and mortality in males, except among heavy drinkers ($P < 0.001$, Fig. 1). However, there was no significant association between alcohol consumption and mortality in females ($P = 0.4872$).

In the sensitivity analysis using never drinkers as the reference group, alcohol consumption was still significantly associated with a reduced mortality rate in PD (mild drinkers, HR 0.85, 95% CI 0.79–0.90; moderate drinkers, HR 0.75, 95% CI 0.66-086; heave drinkers, HR 0.79, 95% CI 0.67–0.94) (Table 3 and Fig. 2).

## Risk of all-cause mortality of PD by alcohol consumption behavior change

We investigated the risk of all-cause mortality according to changes in alcohol consumption behavior before and after the diagnosis of PD. The analysis was conducted on 17,485

**Table 3** Sensitivity analysis of all-cause mortality in Parkinson's disease according to alcohol consumption using never drinkers as the reference group

| Alcohol consumption | PD (*n*) | Mortality (*n*) | Person-years | Mortality rate | Model 1[a] | *P* value | Model 2[b] | *P* value | Model 3[c] | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|
| Never drinkers | 14,169 | 3,305 | 48343.01 | 68.37 | 1.00 | | 1.00 | | 1.00 | |
| Mild drinkers | 3,957 | 740 | 13456.53 | 54.99 | 0.81 (0.76–0.86) | < 0.0001 | 0.60 (0.56–0.64) | < 0.0001 | 0.85 (0.79–0.90) | < 0.0001 |
| Moderate drinkers | 649 | 134 | 3051.84 | 43.91 | 0.70 (0.61–0.79) | < 0.0001 | 0.47 (0.41–0.54) | < 0.0001 | 0.75 (0.66–0.86) | < 0.0001 |
| Heavy drinkers | 412 | 113 | 1934.39 | 58.42 | 0.71 (0.60–0.84) | 0.0041 | 0.46 (0.39–0.55) | < 0.0001 | 0.79 (0.67–0.94) | 0.0092 |

The mortality rate is the incidence of mortality per 1000 person-years

[a]Model 1: unadjusted

[b]Model 2: adjusted for age, sex, income level, and residential area

[c]Model 3: adjusted for age, sex, income level, residential area, Charlson Comorbidity Index, comorbidities, lifestyle factors (smoking, physical activity), blood pressure, anthropometric data, and levodopa equivalent daily dose

individuals with intact NHSP records within the two years before and after diagnosis. When never-drinkers were used as a reference group, former drinkers were found to have increased risk of mortality (HR 1.20, 95% CI 1.02–1.41), whereas constant drinkers had decreased risk (HR 0.74, 95% CI 0.65–0.83) (Supplementary File 1 and 2).

## Discussion

In this nationwide cohort study of 32,419 individuals with PD, we investigated the association between alcohol consumption and rates of all-cause mortality. We found that mild and moderate drinkers had approximately 20 to 30% reduced mortality compared to nondrinkers, while there was no significant association between heavy drinking and mortality in PD. In the subgroup analysis by sex, the association between alcohol consumption and all-cause mortality was significant only in males. In the sensitivity analysis considering abstainer bias, alcohol consumption remained significantly associated with reduced mortality in PD. With regard to changes in alcohol use before and after the PD diagnosis, relative to never drinkers, the mortality rate was higher in former drinkers and lower in constant drinkers. Based on our results, alcohol consumption seems to be associated with reduced mortality in PD, suggesting possible neuroprotective effects on disease progression.

There have been previous studies on the association between lifestyle factors and the incidence and progression of PD. PA has been shown to be associated with reduced incidence and mortality of PD such that a neuroprotective effect of exercise has been suggested (Fang et al. 2018; Yoon et al. 2021). Many studies have also identified smoking as a neuroprotective factor against PD development (Hernán et al. 2002; Mappin-Kasirer et al. 2020), even though smoking has shown a non-significant association with PD mortality in a relatively small number of previous studies (Chen et al. 2006; Driver et al. 2008). The association between alcohol consumption and PD development has been more controversial. Previous case-control studies have shown that the proportion of never drinkers is higher among individuals with PD than healthy controls (Jiménez-Jiménez et al. 1992, 2019; Ragonese et al. 2003). The effects of alcohol on dopaminergic systems, as well as genetic factors such as alcohol-dehydrogenase 1B or 1 C, have been suggested as mechanisms for the neuroprotective effects of alcohol on PD (Buervenich et al. 2005; Kilcoyne et al. 2014; Ma and Zhu 2014). However, the association between alcohol use and PD risk was not significant in some prospective cohort studies (Palacios et al. 2012; Kim I. Y. et al. 2020a; Peters et al. 2020). Discrepancies in study design can be attributed to a recall bias in retrospective designs and insufficient control of potentially-confounding variables. Yet, at the same time, studies on the association between alcohol consumption and mortality in individuals with PD have been scarce (Paul et al. 2019). Therefore, in this study, we examined the association between alcohol consumption habits and all-cause mortality while addressing the drawbacks of previous studies.

Alcohol consumption, especially heavy drinking, has been associated with numerous health problems such as traffic accidents, injuries, and various diseases, including liver cirrhosis and cancer (Rehm et al. 2010). On the other hand, the association between alcohol consumption and mortality has been presented as J- or U-shape in general population in many previous studies (Grønbaek et al. 1998; Stockwell et al. 2016b), and the authors suggested that light to moderate drinking was associated with reduced mortality, especially cardiovascular-related deaths (Scherr et al. 1992; Grønbaek et al. 1998). Suggested mechanisms for the protective effects of alcohol on the cardiovascular system include reduced platelet aggregation and increased high-density lipoprotein concentrations (Veenstra et al. 1990;

Suh et al. 1992). Recently, however, methodological limitations, such as a abstainer bias, have been raised regarding previous results, several studies have adopted more rigorous approaches to control for potential biases in the association between alcohol consumption and mortality (Makelä et al. 2005; Liang and Chikritzhs 2013). Subsequently, recent meta-analyses, after accounting for these biases, reported non-significant association between alcohol consumption and all-cause mortality in general population (Stockwell et al. 2016a; Zhao et al. 2023).

In our results, light to moderate drinking was associated with 20–30% reduced mortality in individuals with PD, whereas heavy drinking was not significantly associated with mortality. To address abstainer bias, we additionally performed a sensitivity analysis using never drinkers as the reference group, excluding former drinkers form the nondrinkers category. The results of sensitivity analysis also revealed an approximately 20% reduced mortality risk among drinkers compared to never drinkers with PD. The HRs of sensitivity analysis slightly increased compared to those in the main analysis, suggesting the presence of some abstainer bias when using nondrinkers as the reference group. Nevertheless, our findings overall indicate that alcohol consumption is associated with reduced all-cause mortality in PD, suggesting potential neuroprotective effects of alcohol on disease progression, including mortality.

As for alcohol consumption behavior change before and after the PD diagnosis, former drinkers showed 20% increased mortality and constant drinkers presented 26% reduced mortality compared to never drinkers in our study. These results are in line with previous findings in the general population of 20 to 29% increased mortality in former drinkers (Grønbaek et al. 1998; Stockwell et al. 2016b). In our study, nondrinkers were older and had more comorbidities than drinkers, raising the possibility that patients in relatively poor health tend to abstain from drinking after the PD diagnosis but show increased mortality nonetheless. In subgroup analyses by sex, the association between alcohol consumption and mortality was significant only in males. However, caution should be exercised when interpreting this outcome. Not only was the proportion of drinkers 26% in males and 7% in females, there was an extremely small number of moderate- to heavy-drinking females in PD, making it unlikely to find significant effects in females.

The current study has several limitations. First, types of alcoholic beverages were not considered in the analysis. Second, the number of heavy drinkers was relatively small, especially in females, potentially making the sample underpowered to find certain effects. Third, alcohol consumption at the time of the PD diagnosis was used for analysis, and it is possible that participants' habits changed afterward. Fourth, alcohol consumption was assessed through self-reported questionnaires, which may have introduced misclassification (Rehm Jurgen et al. 2008). Occasional drinkers who reduced their intake due to comorbidities might have identified themselves as nondrinkers, potentially inflating the mortality risk in the reference group (Fillmore et al. 2007). Fifth, our data were based on an East Asian population; therefore, caution is needed when generalizing our results to other geographic or ethnic groups. Finally, as this was a population-based cohort study, we cannot pinpoint the exact mechanisms underlying the association between alcohol consumption and mortality in PD. Future studies are needed to elucidate the pathogenesis of the association between alcohol use and mortality in PD.

In this nationwide cohort study of 32,419 participants with new-onset PD, the association between alcohol consumption and all-cause mortality was investigated. Our results suggested that alcohol consumption was associated with reduced mortality in PD even after accounting for abstainer bias. With regard to alcohol consumption behavior change before and after the PD diagnosis, the mortality rate was higher in former drinkers and lower in constant drinkers than in never-drinkers. Based on our results, it appears that alcohol has a neuroprotective effect in PD and is associated with slow disease progression, including mortality. However, alcohol consumption in PD requires continued attention considering the potential effects of alcohol on motor and non-motor symptoms of patients. Further studies with diverse ethnic groups are needed to confirm these findings so that we may understand the generalized association between alcohol consumption and PD progression.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s00702-025-02976-2.

**Acknowledgements** This study was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2024-00337352).

**Author contributions** Conceptualization: YHP and SYY. Funding acquisition: SYY. Methodology: YHP and DRK. Supervision: YWK and SYY. Visualization: YHP and SYY. Writing—original draft: YHP and SYY. Writing—review & editing: YWK and SYY. Approval of final manuscript: all authors.

**Funding** This study was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2024-00337352).

**Data availability** The source NHIS data do not belong to the researchers and we are not allowed to transfer data file to a third party under Korean law. The data can be used after approval of the Institutional Review Board and the Korea NHIS Big Data Operations Department ( https://nhiss.nhis.or.kr/bd/ay/bdaya 001 iv.do).

## Declarations

**Ethical approval** The data can be used after approval of the Institutional Review Board and the Korea NHIS Big Data Operations Department (https://nhiss.nhis.or.kr/bd/ay/bdaya 001 iv.do). No separate ethics approval was required.

**Consent to participate/ publication** Not applicable.

**Competing interests** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.



## References

Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr., Tudor-Locke C, Greer JL, Vezina J, Whitt-Glover MC, Leon AS (2011) 2011 compendium of physical activities: a second update of codes and MET values. Med Sci Sports Exerc 43(8):1575–1581. https://doi.org/10.1249/MSS.0b013e31821ece12

Bettiol SS, Rose TC, Hughes CJ, Smith LA (2015) Alcohol consumption and parkinson's disease risk: A review of recent findings. J Parkinsons Dis 5(3):425–442. https://doi.org/10.3233/jpd-150533

Buervenich S, Carmine A, Galter D et al (2005) A rare truncating mutation in ADH1C (G78Stop) shows significant association with Parkinson disease in a large international sample. Arch Neurol 62(1):74–78. https://doi.org/10.1001/archneur.62.1.74

Chen H, Zhang SM, Schwarzschild MA, Hernán MA, Ascherio A (2006) Survival of parkinson's disease patients in a large prospective cohort of male health professionals. Mov Disord 21(7):1002–1007. https://doi.org/10.1002/mds.20881

Craig CL, Marshall AL, Sjöström M et al (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35(8):1381–1395. https://doi.org/10.1249/01.Mss.0000078924.61453.Fb

Driver JA, Kurth T, Buring JE, Gaziano JM, Logroscino G (2008) Parkinson disease and risk of mortality: a prospective comorbidity-matched cohort study. Neurology 70(16 Pt 2):1423–1430. https://doi.org/10.1212/01.wnl.0000310414.85144.ee

Fang X, Han D, Cheng Q, Zhang P, Zhao C, Min J, Wang F (2018) Association of levels of physical activity with risk of Parkinson disease: A systematic review and Meta-analysis. JAMA Netw Open 1(5):e182421. https://doi.org/10.1001/jamanetworkopen.2018.2421

Fillmore KM, Stockwell T, Chikritzhs T, Bostrom A, Kerr W (2007) Moderate alcohol use and reduced mortality risk: systematic error in prospective studies and new hypotheses. Ann Epidemiol 17(5):S16–S23

Grønbaek M, Deis A, Becker U, Hein HO, Schnohr P, Jensen G, Borch-Johnsen K, Sørensen TI (1998) Alcohol and mortality: is there a U-shaped relation in elderly people? Age Ageing 27(6):739–744. https://doi.org/10.1093/ageing/27.6.739

Hernán MA, Takkouche B, Caamaño-Isorna F, Gestal-Otero JJ (2002) A meta-analysis of coffee drinking, cigarette smoking, and the risk of parkinson's disease. Ann Neurol 52(3):276–284. https://doi.org/10.1002/ana.10277

Hughes KC, Gao X, Kim IY, Wang M, Weisskopf MG, Schwarzschild MA, Ascherio A (2017) Intake of dairy foods and risk of Parkinson disease. Neurology 89(1):46–52. https://doi.org/10.1212/wnl.0000000000004057

Jiang W, Ju C, Jiang H, Zhang D (2014) Dairy foods intake and risk of parkinson's disease: a dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol 29(9):613–619. https://doi.org/10.1007/s10654-014-9921-4

Jiménez-Jiménez FJ, Mateo D, Giménez-Roldan S (1992) Premorbid smoking, alcohol consumption, and coffee drinking habits in parkinson's disease: a case-control study. Mov Disord 7(4):339–344. https://doi.org/10.1002/mds.870070407

Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG (2019) Alcohol consumption and risk for parkinson's disease: a systematic review and meta-analysis. J Neurol 266(8):1821–1834. https://doi.org/10.1007/s00415-018-9032-3

Kilcoyne B, Shmulewitz D, Meyers JL et al (2014) Alcohol consumption mediates the relationship between ADH1B and DSM-IV alcohol use disorder and criteria. J Stud Alcohol Drugs 75(4):635–642. https://doi.org/10.15288/jsad.2014.75.635

Kim IY, Yang TO, Heath AK et al (2020a) Alcohol intake and parkinson's disease risk in the million women study. Mov Disord 35(3):443–449. https://doi.org/10.1002/mds.27933

Kim YG, Han KD, Choi JI, Boo KY, Kim DY, Lee KN, Shim J, Kim JS, Kim YH (2020b) Frequent drinking is a more important risk factor for new-onset atrial fibrillation than binge drinking: a nationwide population-based study. Europace 22(2):216–224. https://doi.org/10.1093/europace/euz256

Lear SA, Hu W, Rangarajan S et al (2017) The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. Lancet 390(10113):2643–2654. https://doi.org/10.1016/s0140-6736(17)31634-3

Liang W, Chikritzhs T (2013) The association between alcohol exposure and self-reported health status: the effect of separating former and current drinkers. PLoS ONE 8(2):e55881. https://doi.org/10.1371/journal.pone.0055881

Ma H, Zhu G (2014) The dopamine system and alcohol dependence. Shanghai Arch Psychiatry 26(2):61–68. https://doi.org/10.3969/j.issn.1002-0829.2014.02.002

Makelä P, Paljärvi T, Poikolainen K (2005) Heavy and nonheavy drinking occasions, all-cause and cardiovascular mortality and hospitalizations: a follow-up study in a population with a low consumption level. J Stud Alcohol 66(6):722–728. https://doi.org/10.15288/jsa.2005.66.722

Mappin-Kasirer B, Pan H, Lewington S, Kizza J, Gray R, Clarke R, Peto R (2020) Tobacco smoking and the risk of Parkinson disease: A 65-year follow-up of 30,000 male British Doctors. Neurology 94(20):e2132–e2138. https://doi.org/10.1212/wnl.0000000000009437

Palacios N, Gao X, O'Reilly E, Schwarzschild M, McCullough ML, Mayo T, Gapstur SM, Ascherio AA (2012) Alcohol and risk of parkinson's disease in a large, prospective cohort of men and women. Mov Disord 27(8):980–987. https://doi.org/10.1002/mds.25050

Paul KC, Chuang YH, Shih IF, Keener A, Bordelon Y, Bronstein JM, Ritz B (2019) The association between lifestyle factors and parkinson's disease progression and mortality. Mov Disord 34(1):58–66. https://doi.org/10.1002/mds.27577

Peters S, Gallo V, Vineis P et al (2020) Alcohol consumption and risk of parkinson's disease: data from a large prospective European cohort. Mov Disord 35(7):1258–1263. https://doi.org/10.1002/mds.28039

Ragonese P, Salemi G, Morgante L, Aridon P, Epifanio A, Buffa D, Scoppa F, Savettieri G (2003) A case-control study on cigarette, alcohol, and coffee consumption preceding parkinson's disease. Neuroepidemiology 22(5):297–304. https://doi.org/10.1159/000071193

Rehm J, Irving H, Ye Y, Kerr WC, Bond J, Greenfield TK (2008) Are lifetime abstainers the best control group in alcohol epidemiology? On the stability and validity of reported lifetime abstention. Am J Epidemiol 168(8):866–871

Rehm J, Baliunas D, Borges GL et al (2010) The relation between different dimensions of alcohol consumption and burden of disease: an overview. Addiction 105(5):817–843. https://doi.org/10.1111/j.1360-0443.2010.02899.x

Scherr PA, LaCroix AZ, Wallace RB, Berkman L, Curb JD, Cornoni-Huntley J, Evans DA, Hennekens CH (1992) Light to moderate alcohol consumption and mortality in the elderly. J Am Geriatr Soc 40(7):651–657. https://doi.org/10.1111/j.1532-5415.1992.tb01954.x

Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T (2016a) Do moderate drinkers have reduced mortality risk?? A systematic review and Meta-Analysis of alcohol consumption and All-Cause mortality. J Stud Alcohol Drugs 77(2):185–198. https://doi.org/10.15288/jsad.2016.77.185

Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T (2016b) Do moderate drinkers have reduced mortality risk? A systematic review and meta-analysis of alcohol consumption and all-cause mortality. J Stud Alcohol Drugs 77(2):185–198. https://doi.org/10.15288/jsad.2016.77.185

Suh I, Shaten BJ, Cutler JA, Kuller LH (1992) Alcohol use and mortality from coronary heart disease: the role of high-density lipoprotein cholesterol. The multiple risk factor intervention trial research group. Ann Intern Med 116(11):881–887. https://doi.org/10.7326/0003-4819-116-11-881

Veenstra J, van de Pol H, Schaafsma G (1990) Moderate alcohol consumption and platelet aggregation in healthy middle-aged men. Alcohol 7(6):547–549. https://doi.org/10.1016/0741-8329(90)90046-f

Yoo JE, Shin DW, Han K, Kim D, Jeong SM, Koo HY, Yu SJ, Park J, Choi KS (2021) Association of the frequency and quantity of alcohol consumption with Gastrointestinal Cancer. JAMA Netw Open 4(8):e2120382. https://doi.org/10.1001/jamanetworkopen.2021.20382

Yoon SY, Suh JH, Yang SN, Han K, Kim YW (2021) Association of physical activity, including amount and maintenance, with All-Cause mortality in Parkinson disease. JAMA Neurol 78(12):1446–1453. https://doi.org/10.1001/jamaneurol.2021.3926

Zhao J, Stockwell T, Naimi T, Churchill S, Clay J, Sherk A (2023) Association between daily alcohol intake and risk of All-Cause mortality: A systematic review and Meta-analyses. JAMA Netw Open 6(3):e236185. https://doi.org/10.1001/jamanetworkopen.2023.6185